SKIN, LOCOMOTOR AND SOFT TISSUE PATHOLOGY

Extended abstarct
UDC: 616.591:616.379-008.64:616.071

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Skin disorders in diabetic patients and pathohistological diagnostics

ABSTRACT

From the ethiopathogenetical point of view associations between certain dermatoses and diabetes haven't yet been explained. Therefore diagnostics of these skin diseases is complicated, and pathohistological analysis might be necessary. 160 diabetic patients (95 with insulin-independent diabetes mellitus (IIDM) and 65 with insulin-dependent diabetes (IDDM)) and skin lesions have been examined according to the standard dermatovenerological and pathohistological procedure. The average number of skin diseases per patient was 1,34 in IIDM group and 1,53 in IDDM (t=1,71, p=0,08). From the total number of 160 (100%) patients, pathohistological examination was necessary in 9 (5.6%): 2 patients with Scleroedema (2.1%) in IIDM group, 4 with Necrobiosis lipoidica (4.2%) in IIDM group and 1 (1.5%) in IDDM group, and 2 with granuloma annulare (2.1%) in IDDM group. Accurate observation of skin diseases in diabetic patients also comprises pathohistological analysis.

KEYWORDS: Skin Diseases, Scleredema Adultorum; Necrobiosis Lipoidica; Granuloma Annulare, Diabetes Mellitus; Cytodiagnosis

INTRODUCTION

Diabetes mellitus is a type of the disease which affects all organ systems and tissues of the human body, therefore skin disorders are frequent, occurring early in the course of the disease and having serious prognosis. Association of dermatological diseases in diabetic patients with endocrine disorder has not been explained yet, as well as the pathogenesis of skin lesions. Therefore, diagnostics of these patients might be complicated and skin biopsy necessary.

MATERIALS AND METHODS

In this prospective study 160 adult diabetic patients were included, with the age range between 18-65 years, and they were divided in 2 groups; the first group consisted of 95 patients with insulin-independent diabetes mellitus (IIDM), and the second group of 65 insulin-dependent diabetes (IDDM) patients. Patients were examined according to the standard dermatovenerological and pathohistological procedure.

RESULTS

From the total of 160 patients (100%) in 9 (5.6%) skin biopsy was a necessary part of the diagnostic process.

DISCUSSION

Table 1: Average number of skin diseases per patient in IIDM and IDDM group

	number	X	SD	min	max	range
IIDM	95	1.34	0.59	1	3	2
IDDM	65	1.53	0.81	1	3	3

Scleroedema occurred in 2 (2.1%) of IIDM patients, what was lower than the usual number found in the literature (3%) (1). One of our patients with scleroedema had Dupytren contracture, which is also associated with diabetes. In the other patient, diabetic dermopathy occurred in the meantime. In both patients scleroedema lesions didnít disappear during 9 years of the follow up period, due to obesity and bad metabolic regulation of diabetes, as it was described in the literature (1). In the pathohistological analysis of skin, degenerative changes of collagen and blood vessels, consistent with scleroedema, were found (2,3). The majority of authors consider scleroedema as part of diabetic alteration of the connective tissue (2,4-7), and less numerous are those who believe in coincidental association of scleroedema and diabetes mellitus (8). From the ethiopathogenetical point of view, the most probable explanation is altered collagen and glucoasaminoglycan metabolism due to an decreased insulin action (4). The amount of collagen and ground substance is increased. Other authors support the theory about decreased catabolism of constitutive parts of basal membrane and mesenchyme as a whole (9). Findings in our 2 patients go in favour of synchronous appearance of lesions in microcirculation and connective tissue, or even causal interrelationship between them. A persistence of scleroedema skin lesions up to 20 years has been mentioned in literature reports (10). Diagnosis of necrobiosis lipoidica was confirmed in 4 IIDM patients (4.2%), and in 1 (1.5%) in IDDM group. Considering the total of 160 patients, the number of 5 cases of necrobiosis lipoidica (3.12%) is similar to the reports in literature. Dimitrescu has shown 3% incidence of necrobiosis lipoidica in diabetics (11), Devečerski 0.3-3% (12), Pye 3%(13), what is greater than 2.1% in report of Leković et al. (14). None of these reports have given precise characteristics of diabetic patients groups. All of our necrobiosis lipoidica cases had cutaneous lesions on legs, predominantly on shins, with a typical clinical picture and pathohistological finding (3,15). We havenot found any of atypical forms of necrobiosis lipoidica (15-17). According to the recent literature data necrobiosis lipoidica may be considered as a cutaneous marker of diabetes mellitus (1,15). Only about 10- 20% of all necrobiosis lipoidica patients have no connection with diabetes, in all the others diabetes, or glucose intolerance, or positive familial history of diabetes can be found. The main question still remains concerning the initial moment in the appearance of necrobiosis lipoidica (1,15). Whether it is collagen degeneration followed by vascular changes and inflammatory reaction, or inflammation promoted necrobiosis reaction, or vascular changes appearing as a primary factor. Several authors reported that necrobiosis lipoidica starts as a neutrophilic vasculitis, based on immunological reaction to an unknown stimulus, which may provoke changes that lead to necrobiosis lipoidica. The release of mediators (cytokines) from inflammatory cells or tissues cause decrease of collagen synthesis in affected fibroblasts (1). Deposits of C3 complement component, fibrinogen and immunoglobulins (IgM, IgA) around dermal blood vessels, IgM and C3 on dermoepidermal junction, and fibrinogen in zones of necrosis, all speak in favour of the hypothesis of a patho-

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

genetic role of immune vasculitis (1,15). However, all of the recent findings are not enough to support this theory. The role of skin trauma has been mentioned in pathogenesis of necrobiosis lipoidica (1). In 2 of our necrobiosis lipoidica patients (1.25% of the whole group) findings of capillary resistance, capillaroscopy and digital photopletysmography were normal, which is in accordance with the reports in literature that about 1/3 necrobiosis lipoidica need not have vascular changes (15). Only 2 of our patients (2,1%) in IIDM group had granuloma annulare. Leković et al. reported even lower number of granuloma annulare (0,7%) than in our research. Pathohistology of our granuloma annulare cases was typical and consistent with the literature data (3,5,7,18), even though for the accurate diagnosis immunohistological examination are sometimes necessary (19). Thiers (18) connects granuloma annulare and diabetes via necrobiosis lipoidica, due to similar histology and vascular changes similar to these in diabetic microangiopathy. Diabetic patients have an increased vascular permeability (18). Also, in this research we found a decreased capillary resistance and an altered finding of capillaroscopy in both of our granuloma annulare patients. Still, the number of our patients is too low for any valid conclusion. Recent literature states that the mayor alterations in granuloma annulare are situated in dermal elastic tissue (20).

CONCLUSION

The examination of skin lesions can not be omitted in valid observation of diabetic patients, due to numerous cutaneous manifestations, with pathohisthological examination as an inevitable step in the diagnostic process.

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Archive of Oncology 2001;9(Suppl 1):131-3.

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The finding of demodex in skin biopsy samples

ABSTRACT

Demodex is an arthropode which parasites the human and animal skin. Its classification has been based on the most common host. The presence of Demodex most often induces no pathologic changes to the skin, but it may be ssociated with acnes, rosacea, granulomatous and eosinophil dermatitis and folliculitis. The material of the investigation included 213 biopsy samples of the skin lesions.Of them, 100 samples were taken and analysed at the Medical Center of Banja Luka and 113 ones at the Medical Centre of Zrenjanin. Demodex spp. is registered in 47 (22.06%) of 213 analysed skin biopsies. A significant difference is recorded in infestation by the parasite between the region of Banja Luka (17%) and the region of Zrenjanin (26.54% of the cases). The 48-57 and 68-77 years old age groups are found to be most frequently affected in the region of Banja Luka or Zrenjanin respectively. The parasite is not registered in the 8-17 years old age group. The male population is more frequently affected in the region of Banja Luka, while in the region of Zrenjanin such gender differences are not registered. In the region of Banja Luka Demodex is most often found in the hairy head area (45.45%) or the face area in the affected population of the region of Zrenjanin (42.59%). The presence of Demodex is more frequently registered in the biopsy material from the region of Zrenjanin.

KEY WORDS: Skin Diseases; Biopsy; Mite Infestations

INTRODUCTION

Demodex is a parasite of the species of Arthropoda, the class of Arachnida, the order of Acarus and the superfamily of Demodicoidea (1). One of the possible classifications of the genus of Demodex is based on the most common host - the animal: D. equi, D. bovis, D. ovis, D. canis, D. cuniculi, D. musculi, D. caprae, D. phylloides. Two unique types have recently been described to the detail - D. folliculorum parasiting the hair fillicle, and D. brevis, inhabiting deeply into the sebaceous glands (2,3). The diagnostic procedure to establish the presence of Demodex includes a microscopic examination of the content ejected from a hair follicle, a skin biopsy sample analysis and a cellophane tape method (Radulovic et al). A mature Demodex spp. is a worm-like arthropoda whose body consists of a shorter cephalothorax and a longer abdomen. The following parts can be differentiated on the cephalothorax: a roundish head (gnatosoma) with a mouth-like aparatus andpodosoma (propodosoma and metapodosoma), bearing four pairs of stunted legs with claws. The abdomen (opistosoma) is grooved by transversal striae. A male organism is 0.3mm long, while the length of a female one is 0.39mm. The genesis of the parasite from the ovum to the adult takes 14.5 days, including several genetic stages: a larve - protonymph - nymph (1,2,4). The biopsy skin sections often contain transversal and oblique sections of the parasite which inhabits a hair follicle and sebaceous gland. D. folliculorum can be differentiated from D. brevis only in rare longitudinal parasite sections. In one pilosebaceal complex even several parasites can be identified, some of which inhabit a hair follicle and the others a sebaceous gland. Demodex folliculorum can be easily identified by the cellophane tape-skin-print-method. (Radulovic et al) and microscopy of the native samples. The pathogenic relevance of the parasite's presence is unclear. In the majority of cases, the presence of Demodex in the skin does not induce any pathological changes. Acnes and rosacea can be complicated by parasitic acariasis (5). The presence of Demodex can be associated with granulomatous dermatitis and folliculitis (6). The objective of the paper is to present: the frequency of the biopsy material infestation by Demodex spp.; the differences in infestation of the two geographical regions (the region of Banja Luka and Zrenjanin; the frequency of Demodex spp.finding related to the age, sex and localization in a certain skin area.

MATERIALS AND METHODS

The material of the investigation included 213 biopsy or excision samples of pathologic skin lesions. Of them, 100 samples were taken and analysed at the Medical Centre of Banja Luka and 113 ones at the Medical Centre of Zrenjanin. The pathologic analysis included an examination of each single skin biopsy sample in 2-10 tissue sections sized 1,5cm2 which were often processed into semiserial sections stained by a routine HA method. Besides identifying the primary pathologic lesion, each histologic section was thoroughly examined for the presence of Demodex spp. The examined material was classified into two series - Series I including the samples processed at the Medical Centre of Banja luka and Series II including the sample processed at the Medical Centres of Zrenjanin. Each series was separately subclassified into 8 age-groups in the range of 8-87 years of age, defining the distribution of Demodex spp. infestation related to the age, sex and localization in certain skin regions. The needed parameters were estimated applying the descriptive analysis methods and the test of two sets proportion equality, z-test.

RESULTS

Of 213 examined skin biopsies, Demodex spp.was registered in 47 ones (22.06%), 17 /100 (17%) in the series from Banja Luka and 30/113 (26.54%) in the series from Zrenjanim. By the z-test it has been revealed there is a statistically significant difference in infestation of the two geographical regions $P(z21.733) = 0.9582$.

The 48-57 and 68-77 years old age groups were most often affected by the presence of Demodex in the series from Banja Luka and Zrenjanin respectively. However, its presence wasn't registered in the 8-17 years old age group in either if the series (Table 1,2).

The sex-related distribution of Demodex spp in the region of Banja Luka is reviewed in Table 3. It reveals a statistically significant difference in infestation between the males and females in this series $P(z22.189)=0.1230$, unlike the series from Zrenjanin, which does not exhibit such sex differences in infestation, $P(z20,357)=0.6368$, as it is shown in Table 4.

A sex-related statistically significan difference in Demodex spp. infestations between the two regions is registered only for females $P(z22.385)=0.9913$. Demodex is more often found in the female of the series from Zrenjanin.

In the series from Banja Luka Demodex was most frequently found in the hairy skin regions and then in the face regions, front chest, the back area, while in 30 biopsy samples. taken from the remaining skin area Demodex wasn't registered (Table 5). In the series from Zrenjanin the most common localizations of Demodex infestation were the face region, hairy head areas,

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The manuscript was received: 19. 03. 2000.

Accepted for publication: 17. 04. 2000.

front chest and the back region, while in 18 biopsy samples of the remaining skin Demodex spp. wasn't registered (Table 6).

Demodex spp. is most commonly registered in the hairy head area or in the face region. The parasite infestation of these skin regions (hairy head area + face) differs in the two regions). Of the total of 46 biopsy samples taken from these skin regions in the series from Banja Luka, Demodex spp. was registered in 15 (31.25%) biopsies, while in the series from Zrenjan 28/68 biopsies of the same skin regions were infested by Demodex spp (41.17%). Evidently, there is a statistically significant difference in Demodex spp. infestation of the two skin areas between the analysed geographical regions. P(z20.9715)=0.8340.

Table 1. Age-related Demodex spp. infestation in the series from Banja Luka

Age	Total biopsy count	D+	D-
8-17	2	0	2 (100.00%)
18-27	10	1 (10.00%)	9 (90.00%)
28-37	11	0	11 (100.00%)
38-47	17	1 (5.88%)	16 (94.12%)
48-57	11	4 (36.36%)	7 (63.64%)
58-67	28	8 (28.57%)	20 (71.43%)
68-77	18	3 (16.66%)	15 (83.34%)
78-87	3	0	3 (100.00%)
Total	100	17 (17.00%)	83 (83.00%)

Table 2. Age-related Demodex spp. infestation in the series from Zrenjanin

Age	Total biopsy count	D+	D-
8-17	7	0	7 (100.00%)
18-27	16	3 (18.75%)	13 (81.25%)
28-37	13	3 (23.07%)	10 (76.93%)
38-47	19	6 (31.57%)	13 (68.43%)
48-57	12	2 (16.66%)	10 (83.34%)
58-67	21	5 (23.80%)	16 (76.20%)
68-77	22	10 (45.45%)	12 (54.55%)
78-87	3	1 (33.33%)	2 (66.67%)
Total	113	30 (26.54%)	83 (73.46%)

Table 3. Sex-related Demodex spp. infestation in the series from Banja Luka

	Males	Females
D+	13 (25%)	5 (9.61%)
D-	36 (75%)	47 (90.39%)
Total	48	52

Table 4. Sex-related Demodex spp. infestation in the series from Zrenjanin

	Males	Females
D+	13 (25%)	17 (27.86%)
D-	39 (75%)	44 (72.14%)
Total	52	61

DISCUSSION AND CONCLUSION

There were 213 biopsy samples submitted to the analysis. Demodex spp. was registered in 47 (22.06%) ones. Among 100 samples from the region of Banja Luka, Demodex was found in 17 (17%)specimens, while in the series of 113 biopsies from the region of Zrenjanin it was registered in 30 (26.54%) samples, revealing a statistically significant difference in Demodex spp. infestation between the two geographical regions. Similar discrepancies in Demodex spp. infestation have also been reported in the literature. Some authors have reported Demodex spp. infestation in 29% of the analysed biopsy samples (7). The Yugoslav authors have reported Demodex spp. infestation in 44.2% of the skin biopsy material (8). In the series from Banja Luka the parasite is most often found to affect the 48-57 years old age group - 4

Table 5. Skin lokalizations of Demodex spp. infestation in the series from Banja Luka

Skin localization	Face	Hairy head area	Front chest	Back	Others
D+	10 (28.57%)	5 (45.45%)	1 (10%)	1 (7.14%)	0
D-	25 (71.43%)	6 (54.55%)	9 (90%)	13 (92.86%)	30 (100%)
Total	35	11	10	14	30

Table 6. Skin lokalizations of Demodex spp. infestation in the series from Zrenjanin

Skin localization	Face	Hairy head area	Front chest	Back	Others
D+	23 (42.59%)	5 (35.71%)	1 (8.33%)	1 (6.66%)	0
D-	31 (57.41%)	9 (64.29%)	11 (91.67%)	14 (93.34%)	18
Total	54	14	12	15	18

(36.36%) cases, while in the series from Zrenjanin it is most frequently found in the 68-77 years old age group - 10 (45.45%) cases. The 8-17 years old age group hasn't been affected in either of the two regions, correlating quite well to the literature reports (2). Our study has disclosed a statistically significant difference in Demodex spp. infestation between the sexes in the region of Banja luka, which is however absent in the region of Zrenjanin. In the series from Banja Luka Demodex spp. is most commonly registered in the heary head area - 5 (45.45%) biopsies, but in the face region in the series from Zrenjanin - 23 (42.59%) biopsy samples. Some others have reported there exists a correlation between the parasite infestation and the number of sebaceal glands, but not the number of hairy follicles (7).

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Extended abstract
UDC: 53.085.35:576.31:343.615

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Morphological characteristic of acute lesions of the meniscus

ABSTRACT

Meniscal lesions occur as a consequence of an intensive trauma which elicits a tear of the collagen fibers vertical to the force of pressure, or by the effect of normally intensive forces on an already degeneratively changed meniscus. Acute lesions are tears which occur within two months from the injury. The fragments of acutely injured menisci obtained by artroscopic meniscectomy from 12 persons with the average age of 22,4 years were analyzed. The anamnestic data and discrete pathologic changes in injured menisci, mostly in the form of a hyaline degeneration and fibrilations, confirm the traumatic etiology of the tear in young persons. The proliferation of the connective tissue was noticed only in the vascularized meniscal regions described in literature as possible sources of regeneration. The presence of a proliferated hypercellular tissue and individual signs of its metaplasia into the meniscal fibrocartilage show how old meniscal injury was. Besides the repairing-regenerative meniscal capacity, for the successful restoration of its function, it is necessary to reestablish the physiological biomechanical relations in the knee meniscus. In young persons, the lesions develop due to a very intensive trauma which causes a tear of the collagen fibres vertical to the pressure force. Only when the lessions are localized in the vasularized knee meniscal regions, the reparation by the connective tissue is expectable, which,in the case of the proper reestablishment of the biochemical relations in the knee meniscus, will transform into the firocartilage as an expression of the meniscal regeneration.

KEYWORDS: Menisci, tibial; Knee Injuries + pathology

INTRODUCTION

Knee menisci are crescent-shaped articular bodies situated between the articular surface of the femur and tibia. Thanks to thier fibrocartilaginous structure, they exert two actions: they respond like a cartilage to the forces of pressure, and like a ligament to the forces of traction (1). Meniscal lesions are caused by an intensive trauma which elicits a tear of the collagen fibers vertical to the effect of the force, or by the effect of the normally intensive force on an already degeneatively changed meniscus. It is considered that degenerative changes of the meniscus are likely to occur after 40 years of age (2). The aim of the work was to determine, based on the histologic structure of the fibrocartilage around and in the immediate vicinity of lesions up to two months old, the etiology of acutely induced tears in young persons and presence and dynamics of reactive changes depending on the part of the meniscus injured.

MATERIALS AND METHODS

The histologic analysis comprised the fragments of acutely injured menisci obtained by artroscopic meniscetomy within two months from injury from 12 persons, 10 males and 2 females, whose average was 22,4 years. In all cases, the medial meniscus was damaged, the lesions of the meniscal body prevailing over the lesions of the horns (8:4); in ten patients, the combination of a meniscal lesion with a lesion of the anterior crossed ligament was found. The fragments of the injured menisci were prepared after the standard histologic technique to obtain paraffin sections 5-7u thick; they were stained acording to the staining techniques for the cartilaginous tissue (3), such as: hematoxylin-eosin for the topographic examinations, Mann-Dominici method for the metachromatic reaction characteristic of sulphate glycosaminoglycans of the cartilaginous intercellular substance, and Mallory method for detection of the presence and direction of stretching of collagen fibers. The frozen sections were cryostat sectioned, and lipids were detected with Sudan III.

RESULTS

Light microscopy of the injured menisci revealed various morphologic pictures in dependence on the location of the lesions (tears), i.e. the presence of vasularisation. The lesions found in the avascular areas of the meniscal body (the inner two thirds of the meniscal body) were characterized by an irregular distribution and nonuniform reduction of the number of chondrocytes, hyperchromatic and picnotic nuclei; the structure of the facicles of collagen fibers was mostly normal, mildly wavy, with some tiny oblique fibers. There were no significant hyaline and mucous degenerative changes. The fragments separated by the tear could not join in the two-month period from injury to operation. Metachromasia, which under normal circumstances clearly demarcates the chondrocyte lacunae in the form of a chondromatic field, was present in the generally equal degree as in the preserved fibrous cartilage of the meniscus. In the lesions found in the vascularized meniscal regions (capsular side of the body and meniscal horns), there was proliferation of hypercellular connective tissue, which partly or totally bridges the gap between the fragments, caused by the tear, thus making the spatial and functional contact. In some cases , there was a gradual transformation of the proliferated connective into the fibrocartilaginous tissue. The newly formed fibrocartilaginous tissue was built of two cell populations: spindle chondrocytes, whose lacunae were less noticeable in standard histologic sections, and roundish chondroblasts situated in clearly demarcated chondroplasts. Unlike the normal fibrocartilage, which is made of parallelly fasciate collagen fibres with a mildly wavy course and inserted strips of oval chondrocytes with clearly defined chondroplasts, the newly formed firocartilage did not exibit the usual meniscal structure. In the surroundings of the tears localized in the outer capsular third and the midlle third of the body, there were fibrilations, fissure-like tears bordering on the homogenized and hyaline-changed fascicles of the collagen fibres. The lesions of the meniscal chorns were characterized by less intensive alterations in comparison with the lesions of the meniscal body and by a more successful reparation process followed by the proliferation of the connective tissue and blood vessels and the consequent chondrification as a manifestation of regeneration. Lipid degeneration was not proved in the analysed mateial.

DISCUSSION

Since the lesions of the meniscus were mostly localized in its vascularized and well-inervated parts, pain and bleeding in the knee joint initiated surgery within 2 months from the injury. The anamnestic data and discrete pathologic changes in the injured menisci, mostly in the form of hyaline degeneration and fibrilation, confirm the traumatic etiology of the tears in

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

Extended abstract
UDC: 53.085.35:576.31:343.615
Archive of Oncology 2001;9(Suppl 1):134-5.

young people1 (1,2,4). The connective tissue proliferation was noticed only in the vascularized areas of the meniscus, which are described as a possible sources of regeneration (4). The finding of an exclusively hypercellular tissue indicated that the lesion took place less than 3 weeks before (4,5); the metaplasia of the newly formed connective tissue into the meniscal fibrocartilage necessarily takes an additonal time, which all emphasizes the acuteness of the tear and anamnestically obtained fact that the lesion was not older than two months at the moment of meniscectomy. Besides the repairing-regenerative potential of the meniscus, for the successful reestablishment of the function, it is necessary to reestablish physiological biomechanical relations in the knee joint primarily by the removal of the free fragments of the cartilage by bringing together the preserved parts of the meniscus and curing the crossed ligament lesions (4,6).

CONCLUSION

In young people, the lesions are elicited by a very intensive trauma which causes tear of the collagen fibres vertical to the force (1,2). Only when the lesions are located in the vascularized meniscal areas, the repearation by the connective tissue can take place (4), which, in the case of the proper reestablishment of the biomechanical relations in the knee joint, will undergo metaplasia into the fibrocartilage as an expression of the meniscus regeneration (4,6). A certain degree of degenerative changes in the form of hyaline degeneration can be seen even in younger persons, but should not be considered as the cause of the meniscal lesion.

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The stimulation of cartilage repair

ABSTRACT

The articular cartilage is a highly differentiated avascular tissue whit low regeneration potential. Degeneration of the cartilage is widespread, and the treatment is not very successful and easy. The aim of this investigation was to analyse the possibilities of surgical stimulation of the patellar cartilage repair. The investigation was carried out on dogs as experimental animals; on one half of the same patella, spongialisation with forage was done, whereas the other half of the patella was used for comparison. Sixteen animals were sacrificed in two terms. The first group was sacrificed 6 weeks after the operation, and the second one 6 months later, when the late reparatory process took place. Both macroscopic and hystologic analysies were performed. In early phase, surgical defects were partly covered with connective tissue, while in the later phases, the defects were completely filled with an irregular chondral tissue. In most cases, the reparation tissue was an avascular hondroid tissue with oval cells and bright citoplasm. The intercellular space was filled with amorphous substance and fine connective fibers. The experimental results show that the surgical stimulation of the patellar cartilage repair is possible, and that the result of stimulation is a tissue that in functional and morphologic features resembles the chondral tissue.

KEYWORDS: Cartilage, Articular; Regeneration

INTRODUCTION

The frequency of degenerative changes in the knee is high, with an incidence rising with age. Their treatment is very difficult, and there is a widespred opinion that #only few orthopeadic surgeons are satisffied with it#. This is so because the cartilage is a highly differentiated tissue, without blood vessels, which makes it incapable of repair. Many authors think that the cartilage, due to its specific characteristics, regenerates only by a reparation process in which a fibrous tissue of an unknown origin is formed. For most of them, it originates from the subchondral bone marrow. However, this repairing tissue differs from the normal articular cartilage in that it has no characteristic stratification, and abundant collagen fibers do not exhibit the typical distribution in three levels with a significantly decreased number of the cells. The aim of the study was to determine the morphologic properties of

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

the reparation tissue formed after the application of spongialisation with forage in different phases of the reparation process.

MATERIALS AND METHODS

The stimulation of the reparation was done in three phases. In the first one, the experimental surgical resurfancing was done, in the second one, the animals were sacrificed, and in the third one, the histologic analysis was carried out. The iatrogenic cartilange lesion preceded spongalisation with forage, which was performed on one half of the patella, and the second one was used for comparing the results of resurfacing. It was done on 16 patellas; after the patellar decortication, half of the animals were subjected to a transcartilaginous forage, whereas the other one to an extracartilaginous forage. The experimental animals were sacrificed after 6 weeks (early phase) and 6 months (late phase). The fixation was in 10% formalin, and decalciffication in vinegar acid. The preparations were stained after Mallory with aniline blue, i.e. light green combined with orange and phospho-molybdic acid and toluidine blue.

RESULTS

The defect of the medial patellar surfaces in the early reparation phase was wholly covered with a repairing tissue. A smaller part of the defect was filled with a tissue covering the bottom of the defect, which was of yellowish colour and uneven surface. There was a firm and close contact with the bone base. The other, larger portion of the surface was covered by a newly formed even tissue of white-bluish colour, with smooth surface in places and resembling, by all its characteristics, the normal articular cartilage. In the late phase, the reparation covered the whole surface of the defect; it consisted mostly of white-bluish tissue with firm and elastic consistence and en even surface like in the normal cartilage. In case of extracartilaginous forage, the tissue is similar to the normaal cartilage, but to a much lower degree than in transcartilaginous forage. By the maturation of the newly formed tissue, in the late reparation phases it assumed all the properties of the chondroid tissue, with large, oval chondrocytes having light cytcplasm, disbuted most frequently in pairs situated in their lacunae. The intercelluar space was filled with an amorphous substance containing fine connective fibers. They all stretched in one and the same direction, vertical to the reparation surface. The cellular elements in the upper zones of the reparation were distributed one beneath the other, forming cyllindrical isogonic accumulations similar to the radial zone in the normal articular cartilage. There was a noticeable lack of blood vessels, as a necessary prerequisite for the cartilage formation. The largest part of the reparation was a hypocellular chondroid tissue.

DISSCUSION

In analysing the regenerative capacity of the articular cartilage, one should bear in mind that the hyaline cartilage is an avascular, highly differentiated tissue which, therefore, cannot be restored. Theoretically, a tissue which would replace a degeneratively changed articular cartilage could originate from the very cartilage, bone base or from synovia. Today, it has been generally aecepted that during the restoration of the articular cartilage, the fibrous, fibrocartilngious, and cartilaginous tissue could be formed, i.e. a tissue very similar to the cartilage, which was also registered in this experiment. However, this cartilaginous tissue is not absolutely identical to the articular cartilage because it usually has an irregular surface, it is thinner, and with somewhat different distribution of collagen fibers, and different relations of cells with the intercellular space; it usually does not reach the level of the articular cartilage of the opposite patellar facets. The occurrence of such a reparation, with a different quality, is due to the perforations of the patellar cortex, where an abundant fountain-like reparation tissue was registered as if springing from the bone tissue. Ths process of reparation, after the application of this operative procedure, is initiated from the spongy bone by the proliferetion of the cells of the endosteum and the stroma of the medullary canals, which, in time, differentiate into chondroblasts and chondrocytes. The chondrocytes originate from the pluripotent cells of the endosteum of the medullary canals, which are transformed into chondroblasts instead of osteoblasts. The reparing tissue, according to its morphologic characteristics, corresponds to the hyaline cartilage, but since the intercellular substance does not contain chondroitin sulphate, it is more correct to talk about a chondroid tissue. The reparation differs from the articular cartilage by its composition and distribution of the fibrous structures. In same preparations, there was a tendency of adopting the typical distribution of fibers, so that they stretched parallel in some superficial zones, whereas in the deeper leyers they were vertical, collagen fibers unnoticeble, thus imitating the normal articular cartilage. The absence of blood vessels in them points to a conclusion that in the differentiation of the young connective tissue of the early phase of reparation into the chondroid tissue of the late phase, the avascularisation of this tissue plays the key role.

CONCLUSION

It is possible to stimulate surgically, by spongialisation with forage, the proliferative processes of the articular cartilage repair from the bone tissue, i.e. from the cells of endossteum or stromal myelocytes. During the early reparation phase, the presence of immature tissue was registered, whereas the presence of the fibrocatilaginous or chondroid tissue was detected in the late phase.

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Extended abstract
UDC: 616-006.591:616.018.1

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Tumor margin and mast cell presence in fibrohistiocytic tumor

ABSTRACT

Mast cells represent a heterogenous population of the multifunctional effector cells of the immune system. It has been observed that the presence of a higher number of mast cells in the malignant tumors goes together with a lower grades of malignancy and better prognosis. We have assumed that the tumor margin type, being the specific indicator of the tumor-host interaction, could be brought into connection with the presence of intra- and peritumor mast cells. We analysed presence of the intra- and peritumor mast cells and types of tumor margins in 121 fibrohistiocytomas diagnosed in ten year period. The mast cells were counted on the speciment stained with Giemsa on ten accidentaly selected visual fields, magnified by 400x, while tumor margins were clasified into infiltrative, compressive and mixed. Statistically significantly higher number of benignant fibrous histiocytomas posessed infiltrative margins in relation to the malignant ones, where the compressive margin was the dominant one ($p<0.05$). A group of tumors with a mixed margin was composed of G3 malignant tumor. In the group of all fibrohistiocytomas, in a subepidermal part, around the tumors with infiltrative and compressive margin, there were significantly less mast cells than around the mixed margina ($p<0.05$). In a whole group of malignant fibrous histiocytomas the number of intratumor mast cells next to the compressive margin was significantly higher, comparing to the group composed of the mixed marginas ($p<0.05$). When the storiform and pleomorphic subtype, which was mostly represented (31), was separated, except this finding ($p<0.05$), it was found out that the number of peritumor mast cells around the infiltrative margin was significantly lower than the number of peritumor mast cells around the mixed margin ($p<0.05$). The most active role of the peritumor mast cells can be located around the mixed margin of G3 malignant tumor group. The behaviour of the intratumor mast cells in a malignant group differs from that of the peritumor mast cells.

KEYWORDS: Histiocytoma, Fibrous; Mast cells

INTRODUCTION

Mast cells represent a heterogenous population of the multifunctional effector cells of the immune system. As far back as the 60's, in a great number of experimental works, the attention was drawn to the cytotoxical effect of mast cells to the tumour cells, as well as to the stimulation of their proliferation(1,2). The occasional histological studies of mostly limited specimen showed that the mast cells presence in a tumor stands in a positive correlation with lower malignancy grades and a better outcome (3,4). The pathogenesis of a possible prognostic significance of the mast cells presence in and around tumors is complex and unclear one. A great number of studies have been trying to bring into connection the role of mast cells in the angiogenesis, remodeling tumor stroma and modulation immune and inflammatory answer with a tumor pathobiology and peritumor associated stroma (5,6,7). We have assumed that the type of the tumor margin, being the specific indicator of tumor-host intereaction, could be brought into connection with a mast cells presence in and around the tumor stroma. The aim of this study was to establish the correlation between the tumor margine type and the frequency of mast cells presence in and around the fibrohistiocytic tumors of different biological potentials.

MATERIALS AND METHODS

Totally 121 fibrohistiocytic tumors, diagnosed in the Institute of Radiology and Oncology os Serbia from 1985-1996, were analysed. The tumor group consisted of 68 benignant fibrous histiocytomas (BFH), 39 malignant fibrous histiocytomas (MFH) and 14 dermatofibrosarcoma protuberans (DFSP). The malignancy grade was established, in accordance with the FNNCL group criteria, as G1, G2 and G3. The tumor margins where classified as the infiltrative (I), compressive (K) and mixed (K+I). In the selected tumor margine specimen, stained according to Giemsa method, the mast cells where counted on 10' accidentaly selected visual fields, magnified by 400x, immediately next to the tumor margin, in fact, in and around the tumor (subepidermally and in a depth). The data collected were statistically calculated by the means of Student T and X^2 test.

RESULTS

In the analysed tumor specimen, statistically significantly higher number of BFH possessed (I) margin, in relation to the MFH group, where (K) margin was the most frequent one ($p<0.05$). In MFH group with the (K) margin, the majority of tumors have a G3 malignancy, while more G2 tumors (in relation to G3 ones) posses the (I) margin, and all the tumors with a (K+I) margin are G3. There is only one BFH with the (K+I) margin. The number of the peritumor mast cells in a subepidermal location of all the fibrohistiocytic tumors, together with (I) and (K) margin, is statistically significantly lower than around the same group of tumors with (K+I) margin ($p`0.05$). In MFH group statistically significantly higher number of mast cells was found in a stroma of (K) margin tumors, in relation to the number of tumor mast cells of the same group with (K+I) margins ($p<0.05$). When the storiform and pleomorphic subtype of MFH group (31 tumors) was selected, the results were as follows: The number of intratumor mast cells next to the (K) margin remained statistically significantly higher than the number of intratumor mast cells next to (K+I) margin ($p<0.05$), the number of peritumor mast cells around the (I) margin was statistically significantly lower than the number of peritumor mast cells around the (K+I) margin ($p<0.05$) and the number of the mast cells in MFH stroma with (K+I) margin was neglectally low.

DISSCUSION

The analysis of tumor margins in the examined group of fibrohistiocytic tumors showed that the (K) margin was the most frequent one in the malignant group (about 50%) and (I) margin in the benignant group (about 70%), and also in an intermediated malignancy group (about 57%). The tumor percentage with (I) margin lowers from the benignant, over the intermediated, to the malignant group, while the percentage of (K) and (K+I) margin tumors increases in a reverse order. In MFH group the (K) margin tumor percentage increases with the malignancy grade increasing. The whole MFH group with (K+I) margin is composed of the G3 malignancy tumors. The highest num-

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

ber of mast cells around the (K+I) margin, of all the fibrohistiocytic tumors, as well as of MFH group, shows that the most active participation of peritumor mast cells was observed around the (K+I) margin of the G3 malignant tumor group. Significant number of mast cells, associated with its degranulation, have been demonstrated histologically around the perifery of an invasive rat mammary adenocarcinoma (8). Degradation of the stromall connective tissue is a common feature of the invasive neoplasia and host-tumor cell intereactions are probably important for these. A mast cell has the potential to induce collagenolytic activity from both host fibroblasts and tumor cells and are important for growth and invasive properties demonstrated by an experimentall model of cancer(9,10). Statistically significantly higher number of the intratumor mast cells in MFH group, having (K) margin, in relation to the MFH group with (K+I) margin, which had an exceptionally small number of intratumor mast cells, points out to a possible different influence of the intratumor mast cells when forming the tumor margin in relation to the peritumor mast cells.

CONCLUSION

The most active role of the peritumor mast cells can be located around the mixed margin of G3 malignant tumor group. The behaviour of the intratumor mast cells in a malignant group differs from that of the peritumor mast cells.

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Vimentin as an internal control for optimising antigen retrieval procedures in immunohistochemistry

ABSTRACT

Vimentin (54kD) is an intermediate filament that is uniformly distributed in every tissue sample (in vessels and stromal cells). Epitopes of vimentin are very susceptible to formaldehyde fixation and thus we use vimentin as an internal control of the quality of antigen preservation, the uniformity of tissue fixation with formaldehyde and as a control for optimising antigen retrieval procedures. We performed a series of experiments in which tissues were subjected to fixation for various periods of time (6-96h). These samples are then used for detection of vimentin, and some of them are used for comparation of the quallity of immunostaining to vimentin and EMA, cytokeratin, c erb B2-oncoprotein, estrogen and progesterone receptors. DAKO monoclonal mouse anti human Vimentin antibody M 0725 (clone V9) is used as a primary antibody, and DAKO LSAB+(K 690) as a system for visualization. For the comparative immunostainings we used EMA (DAKO M 0613), estrogen receptor (DAKO M7047), cytokeratin (DAKO M0821), c-erb- B_2 oncoprotein (DAKO A0485) and progestrerone receptor (DAKO M 3569) as a primary antibodies. Antigen retrieval procedures are performed in 0.05M citrat buffer pH 6.0, 0.05M Tris-HCl buffer pH 7.6 and 1%$ZnCl_2$ in microwave owen. Tissues fixed in formaldehyde for prolonged periods (72h and more) showed a marked decrease or complete loss of vimentin immunoreactivity. For these samples we performed antigen retreval procedures with different target retrieval solutions and different heating periods. We obtained best results with 5 minutes of heating in 0.05M citrat buffer pH 6.0. We also found that some diagnostically important antigens (EMA, cytokeratin, c erbB_2-oncoprotein, estrogen and progesterone receptors) show a sensitivity to fixation comparable to that shown by vimentin epitopes. Antigen retrieval procedures must be performed if the tissues are fixed in formaldehyde for 72h and more. It is possible to recover epitopes of vimentin that were captured in the formalin induced cross-linkings. Immunostaining to vimentin is a good model system for optimising antigen retrieval procedures.

KEY WORDS: Immunohistochemistry; Antigens + analysis; Epitopes; Vimentin; Tissue Fixation

INTRODUCTION

Immunohistochemistry is an important tool in both the diagnostics and the research. The factors that have a major impact on the results of immunos-

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

taining are:(1) tissue fixation, (2) demasking of antigens, (3) sensitivity of the system for visualisation, (4) quality of the primary antibodies. In practice, formaldehyde is the most often used fixative, since it is inexpensive, easy to prepare, and provides excellent preservation of morphological details. Unfortunately, formaldehyde fixation is at the same time a major cause for the limits of immunohistochemistry in paraffin sections. The most important molecular change is the formation of the cross-links between the proteins involving hydroxymethylene bridges. These bonds are responsible for the masking of epitopes hampering or abolishing antibody binding. Hydroxymethylene groups may form coordinate bonds with calcium ions or facilitate cross-links between calcium ions and oxygen atoms of both the side chains of glutamate or aspartate residues as well as the main polypeptide chain carboxyl groups. Formaldehyde-effected bonds obviously lead to changes of the three-dimensional structure of proteins. The resulting steric alteration causes the masking of epitopes and makes them inaccessible for the antibodies. Fixation in formaldehyde is a rather slow process and needs at least 24h to be accomplished (Fox et al. 1985). Thus shorter fixation time will interrupt the fixation process which will continue during tissue dehydratation by ethanol. This results in a variable and irreproducible mixture of changes induced in the antigen by formaldehyde (cross linking) and ethanol (coagulation). On the other hand, prolonged fixation times may cause the formation of excessive cross-links.Heat induced antigen retrieval procedures reverse some of these alterations by breaking down cross-linkings, restoring the conformation of the epitope and removing calcium ions by precipitation or chelatisation with citrate (Morgan et al 1994.). Epitopes of vimentin are partially sensitive to formaldehyde. Because vimentin is distributed in every tissue sample (in vessels and stromal cells), it is ideal to serve as an internal control of the quality of the tissue fixation, antigen presevation and as a control for antigen retrieval procedures.

MATERIALS AND METHODS

We use a fresh postmortem tissue samples as a material for our experiments, and fixed them in a 4% buffered neutral formalin for 6-96h. Fixed tissues were dehydrated in ethanol, cleared in xylene, and embedded in paraffin blocks. Five μ sections were cut and mounted on poly-L-lysine coated slides. The sections are then used for detection of vimentin. For the samples that showed decreased imunoreactivity of vimentin we performed antigen retrieval procedure in a microwave oven, for 1-20 minutes at the highest power setting (720W). We used 0.05M citrat buffer pH 6.0, 0.5M Tris-HCl buffer pH 7,6 and 1% $ZnCl_2$ as target retrieval solutions. DAKO monoclonal mouse anti human vimentin antibody M0725 (clone V9) is used as a primary antibody and DAKO LSAB+ as a visualization system. For the comparative immunostainings we used EMA (DAKO 0613), estrogen receptor (DAKO M7047), cytokeratin (DAKO M0821), c $erbB_2$-oncoprotein (DAKO A0485) and progesterone receptor (DAKO M3569) as primary antibodies.

RESULTS

The tissue samples that were fixed for 72h and more showed a marked decrease or a complete loss of vimentin immunoreactivity. For this samples we performed antigen retrieval procedures at 720W in a microwawe oven for 1,2,5,10 and 20 minutes. We also tested three different target retrieval solutions: 0.05M citrat buffer pH 6.0, 0.5M Tris-HCl buffer pH 7.6 and 1% $ZnCl_2$. Best results were obtained with 5 minutes of heating in 0.05M citrat buffer pH 6.0. Prolonged heating periods increased background stainigs. We have also found that epitopes of EMA, cytokeratin, c erb B_2-oncoprotein, estrogen and progesteron receptors show a sensitivity to fixation comparable to that of vimentin epitopes, so it can be said that vimentin could be used as an internal control in selection of fields for the interpretation of immunohistochemical stainings.

DISCUSSION

It is possible to recover epitopes of vimentin that were captured in the formalin induced cross-linkings.Heat and acid retreval solution induced acid hydrolysis, which denatures and breaks the tissue proteins at or near the links made by the formalin between adjacent amino acids. Standardization of antigen retrieval procedures is very important, since the heterogenous distribution of immunoreactivity as a result of poor fixation, may be misinterpreted as a heterogeneity of antigen expression. This problem is very frequent in our consultation case materials. In these cases the selection of the field for interpretation is faciliated by identification of the areas that exhibit the strongest vimentin reactivity. Microwave antigen retrieval methods are simple to perform and they could be used to reduce the incidence of false negative immunostaining results. It can be said that immunostaining to vimentin can be used for optimising antigen retrieval procedures.

CONCLUSION

Antigen retrieval procedures must be performed if the tissues are fixed in formaldehyde for 72h and more. It is possible to recover epitopes of vimentin that were captured in the formalin induced cross-linkings. Immunostaining to vimentin is a good model system for optimising antigen retrieval procedures.

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Archive of Oncology 2001;9(Suppl 1):139-40.

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Pathohistologic characteristics of chronic acquired hyperkeratotic palmoplantar dermatoses - differential-diagnostic problems

ABSTRACT

Acquired chronic palmoplantar hyperkeratotic dermatoses are not rare in every day dermatological practice. Etiologically these diseases are different. The most common among them are psoriasis vulgaris (PV), contact allergic dermatitis (CAD), contact non-allergic (irritant) dermatitis (CID), and mycotic palmoplantar infections (M). For establishing the diagnosis in such cases, correct anamnesis, clinical examination of palmoplantar skin and skin of the other body regions are important, but pathohistological, allergological and micotoical examination are of greater importance. The aim of our study was to examine pathohistologic characteristics of the most common chronic acquired palmoplantar hyperkeratotic dermatoses and to notice eventual individual characteristics. Palmoplantar skin lesions in 48 patients (24 males and 24 females, 12-78 years old), 12 with proved PV, CAD, CID and M, were examined pathohistologically. In all cases dominant feature was hyperkeratosis, with parakeratosis always in PV, often CAD and CID, and rare in M. Stratum granulosum was moderate or thinned. Spongiosis, vesicles and their sequels in epidermis were seen in CAD, CID and PV, rare in M. All examined dermatoses are characterised by more or less marked inflammatory dermal infiltrate, which is specially abundant in PV and CAD. Pathohistological feature in chronic acquired hyperkeratotic palmoplantar dermatoses, even though sometimes may be very similar, considered together with the other data, especially in clinical alergological and mycological examinations, may be significant factors for establishing definite diagnosis.

KEYWORDS: Keratoderma, Palmoplantar; Psoriasis; Dermatitis, Allergic Contact; Mycoses

INTRODUCTION

Acquired chronic palmoplantar hyperkeratotic dermatoses are not rare in every day dermatological practice. Etiologically these diseases are different. The most common among them are psoriasis vulgaris (PV), contact allergic dermatitis (CAD), contact non-allergic (irritant) dermatitis (CID), and mycotic palmoplantar infections (M) (1-5).

For establishing diagnosis in such cases, correct anamnesis, clinical examination of palmoplantar skin and skin of the other body regions are important, but pathohistological, allergological and micotoical examination are of greater importance (4-6). The aim of our study was to examine pathohistologic characteristics of most common chronic acquired palmoplantar hyperkeratotic dermatoses and to notice eventual individual characteristics.

MATERIALS AND METHODS

Palmoplantar skin lesions in 48 patients (24 males and 24 females, 12 - 78 years old), 12 with proved PV, CAD, CID and M, were examined pathohistologically, after biopsy, routine processing, fixation in 10% formaldehyde and staining by hematoxylin-eosine method (7).

RESULTS

Each of examined dermatoses are characterised by more or less expressed inflammatory infiltrate in dermis, especially papillary. This infiltrate is the most marked in PV and CAD, less marked in CID, and poor in M. Possible differentiating characteristic of this infiltrate in CAD toward other dermatoses is oftener presence of greater number of degranulated eosinophile leucocytes. Elongation of dermal papillae was seen in PV, rarely in CAD. Oedema of papillary, and occasionally reticular, dermis was often noticed in CAD, rarely and with less intensity in CID. Oedema of papillary dermis was also seen in 5 cases of M, and was missing in PV. Hyperkeratosis was marked in all cases, with unequal acceptance for staining in corneal layer. In PV in all cases parakeratosis was noticed, also in 4 cases of CAD and CID each, while in M there was almost exclusively orthokeratosis. Acanthoses were moderately expressed in CAD and CID, sporadically or diffuse in PV, and minimal in M. Stratum granulosum was in all cases moderate of tinned. Even though examination was performed in chronic cases of dermatoses, spongiosis, vesicles and vesicles sequels relatively often were seen in epidermis of CAD and CID. Spongiosis was also seen in PV, and vesicle sequels were oftener present than Munroo microabsceseses. Vesicles were very rare in M. In all 4 groups of dermatoses, in some cases, stratum lucidum was noticed.

DISCUSSION

Pathohistological feature in most common acquired chronic palmoplantar hyperkeratotic dermatoses may be very similar (8,9,10). Even though, some diagnostically useful histological characteristic of individual dermatoses sometimes may be noticed. Pathohistological feature must be considered together with the other examinations - clinical, alergological and mycological. The most significant changes in all examined dermatoses were in epidermis. Unequal acceptance for staining in corneal layer suggests that all epidermal proliferative units (11-13) are not in equal state of proliferative activity i.e. not in the same state of keratin maturation. Hyperkeratosis is common characteristic of all four examined diseases. Parakeratosis is permanent characteristic in PV and often in CAD and CID. The finding of relatively large number of vesicle formations and their sequels in chronic states of examined diseases, especially CAD and CID is unexpected, but partially may be explained by permanent contact with allergen or irritants which are primary etiological factors in these states. In pathological conditions with accelerate keratinisation straum granulosum is thin or missing, and marked or thickened in conditions with slowed process of keratinization (9,14). More or less marked reduction of stratum granulosum was seen in all four examined proliferative conditions.

CONCLUSION

Pathohistological feature in chronic acquired hyperkeratotic palmoplantar dermatoses, even though sometimes may be very similar, considered together with the other data, expecially in clinical examinations, alergological tests

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The manuscript was received: 17. 03. 2000.

Accepted for publication: 14. 04. 2000.

and mycological examinations, may be significant factors for establishing definite diagnosis and determination on correct treatment.

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Calcaneal bone cyst

ABSTRACT

The calcaneal bone cyst is a rare lesion with a typical location. Pathogenesis of the calcaneal cyst is unknown. We analyzed the bioptic material of the Institute of Pathology, Medical school in Belgrade in the period 1964 - 1997, including the cases with a histopathological diagnosis of the solitary bone cyst and 15 calcaneal bone cysts. We made a pathohistological differetiation between these lesions. At the Bone Biopsy Register of the Institute of Pathology, Medical school in Belgrade 15 calcaneal bone cysts have been registered, wich accounts for 3.66% of solitary bone cysts of all localizations. The clinical and radiological diagnosis was the bone cyst. The main clinical symptom was pain and it was present in 11 cases (73.3%). The youngest patient was 11 years old, the oldest was 46 years; the average age of patients was 19,7 years. The lesion was twice as frequent in males as in females (men 66.76%, women 33.33%). Clinical and radiological features are very unspecific because the lesion does not disturb the mechanical stability of the foot. Differential diagnosis between the calcaneal bone cyst and the solitary bone cyst is important because prognosis and therapy are different.

KEY WORDS: Calcaneus; Bone Cysts; Cytodiagnosis

INTRODUCTION

The calcaneal bone cyst is an infrequent lesion with a characteristic location in the trochlear processus - Revelli's triangle of calcaneus. It is due to a special lamellar arrangement of the spongiosa caused by the muscle and ligamentous lines of force. The lesion must be distinguished from the solitary bone cyst because the calcaneal bone cyst is a specific pathologic entity. Clinical features are very unspecific. Most cases are painless and discovered as incidental findings after an ankle and foot injury. Patients are young adults in the second and third decade of life. This lesion does not disturb the mechanical stability of the foot and it can't cause a pathologic fracture. Radiological characteristics of this lesion are the same as in the solitary bone cyst. It is oval or quadrangular and is often surrounded by a border of sclerosis.

MATERIALS AND METHODS

We analyzed the bioptic material of the Institute of Pathology, Medical school in Belgrade in the period from 1964 till 1997., only cases with histopathological diagnosis of the solitary bone cyst. We separated the solitary cysts of the calcaneus and researched them histopathologically.

RESULTS

At the Bone Biopsy Register of the Institute of Pathology, Medical school in Belgrade 15 calcaneal bone cysts have been registered, wich accounts for 3.66% of solitary bone cysts of all localizations. The clinical and radiological diagnosis was the bone cyst. The main clinical symptom was pain and it was present in 11 cases (73.3%). The youngest patient was 11 years old, the oldest was 46 years; the average age of patients was 19,7 years. The lesion was twice as frequent in males as in females (men 66.76%, women 33.33%).

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The manuscript was received: 17. 03. 2000.

Accepted for publication: 14. 04. 2000.

Pathogenesis of the calcaneal cyst is unknown; some authors considered that it is organization of bleeding, another suggested that the calcaneal cysts develops from a congenital tissue remnant in the region of the primary ossification center of the calcaneus. These two theories (congenital defect and bleeding) do not exclude each other. Pathohistological diagnosis of the solitary bone cyst was conceived on constant and variable histology characteristics. The thin fibrotic membrane with flattened synovial-like epithelium was the constant characteristic. Besides fibroblasts, collagen fiber, rare osteoclasts and giant cells, the membrane of cyst could contain fields of hemorrhage (with or without hemosiderin and cholesterol crystals), lymphocytes, small focus of osteoid or cement like substances- the variable characteristic. We analyzed pathohistological characteristics of the calcaneal cysts and have found it histologically different from the solitary bone cyst. The cyst membrane is not typical, it is usually thin or quite absent (two cases). The zone of fresh and old bleeding is more marked (nine cases), usually with cholesterol crystals (seven cases), sometimes with surrounding giant cell reaction (three cases). Fibrous zones are also more extensive (seven cases). The calcaneal bone cyst is usually composed mostly of fatty bone marrow, with tiny foci or rough calcification, which is the reason why some authors suggest it is actually a calcaneus lipoma. The cement-like substance noted in seven cases is a useful diagnostic index, particullrly in cases when the cyst membrane is not differentiated well.

DISCUSSION

Due to specific and constant X-ray features, histological properties which are different from the typical histopathological presentation of the solitary bone cyst, the calcaneal bone cyst has been recognized as a specific entity. It is also important that the lesion does not affect the mechanical stability of the bone and, thus, does not lead to a pathological fracture. We don't have a patient with pathologic fractures in our series of 15 calcaneal cysts. Therefore, it is believed that if the change is asymptomatic and if other more aggressive changes have been ruled out (aneurysmal bone cyst, tumors), a surgery is not necessitated. Thus, the diagnosis of the calcaneal bone cyst may exclude the need for an operation. The surgical therapy could be escaped because some authors believed that the calcaneal cyst could be spontaneously complemented. We have noticed large fibrotic bands in the bioptic material from some calcaneal cysts. This zone of proliferated fibrotic tissue could be a sign of spontaneous complementation of the cyst space.

CONCLUSION

The calcaneal bone cyst is an infrequent lesion with a characteristic location in Revelli's triangle of calcaneus. Radiological characteristics of this lesion are the same as in the solitary bone cyst, but histopathologically we could make a differential diagnosis of these two cysts. The lesion must be distinguished from the solitary bone cyst because the calcaneal bone cyst is a specific pathologic entity and the therapy is different. Sometimes the therapy is not necessery because the calcaneal cyst could be spontaneously complemented.

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Livedoid vasculitis idiopathica

ABSTRACT

Livedoid vasculitis, also known as segmental hyalinizing vasculitis or livedo reticularis with summer ulceration, is a chronic disease with lesions affecting the feet and lower legs. Early lesions show purpuric macules and papules, but characteristic features are recurrent, bizarrely shaped, painful ulcers that heal to leave hyperpigmentation and atrophie blanche. The aetiology of the disorder is unknown. Young women with characteristic clinicopathological picture of idiopathic form of livedoid vasculitis. Examination revealed oedema of both lower extremities. All lesions were more prominent on the right calf. There was an erythematous plaque irregular in shape, measuring 8x10 cm, covered with numerous crusts and scales. Within the plaque there were ulcers round to oval or irregular, measuring lxl cm. Similar lesions erythematous and purpuric papules and plaques, ulcers and atrophic scars were scattered on both ankles and dorsa of the feet. Atrophic scars were surrounded with hyperpigmentation and telangiectasia. Lesions were painful both spontaneously and on palpation. In addition , livedo reticularis was presented on all four limbs. Results of performed laboratory xaminations were within normal limits or negative. Biopsy of the skin showed fibrin deposition within both the wall and lumen of the affected dilated vessels in deep dermis and in the adipose subcutaneous tissue. Patients with livedoid vasculitis should be examined extensively in order to rule out primary immunologic and vaso-occlusive disorders that may result in a similar clinical appearance, and to avoid aggressive therapeutic approaches that may result from incorrect diagnosis.

KEYWORDS: Vasculopathy; Skin Diseases, Vascular; Leg Ulcer

INTRODUCTION

Livedoid vasculitis also known as segmental hyalinizing vasculitis, livedo vasculitis, livedo reticularis with summer ulcerations, atrophie blanche, or PURPLE (Painful Purpuric Ulcers with Reticular Pattern Of Lower Extremities) is a chronic disorder clinically manifested by recurrent painful ulcerations, localised chiefly but not exclusively on the lower leg or foot. It is characterised by the presence of ivory-white lesions surrounded by hyperpigmentation and telangiectasia, with or without preceding purpuric macules infiltrated papules or plaques, haemorrhagic blisters and painful ulcers (1,2). Pathogenesis is largely unknown. Shornick and al. in 1983 recommended criteria for differentiation between two varieties of atrophie blanche: idiopathic (with distinct clinical and pathological picture that affects mostly young women, and has no underlying cause), and secondary to other disease (arteriosclerosis, connec-

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 11. 04. 2000.

tive tissue disease, diabetes mellitus, dysglobulinaemia, arterial hypertension, stasis dermatitis)(3).

CASE REPORT

A 38-year-old woman had painful ulcers on both lower extremities and had a mottled discoloration in livedo pattern on her upper and lower extremities for 18 years. She sometimes felt heaviness in legs and oedema. Although some ulcers have healed after several months, leaving white atrophic scars, new lesions subsequently developed. Since 1982 she has exacerbations during the summer and remissions during the winter. A variety of topical agents and oral medications had been tried without a significant effect. She didn't have other illnesses, has one child, and she smokes cigarettes.

RESULTS

The examination revealed oedema of both lower extremities. All lesions were more prominent on the right calf. On the extensor side of the right calf there was an erythematous plaque irregular in shape 8x10 cm in diameter, covered with numerous crusts and scales.Within the plaque there were ulcers round to oval or irregular, measuring lxl cm. Similar lesions erythematous and purpuric papules and plaques, ulcers and atrophic scars were scattered on both ankles and dorsa of the feet. Atrophic scars were surrounded with hyperpigmentation and telangiectasia. Lesions were painful both spontaneously and on palpation. In addition , livedo reticularis was presented on all four limbs. The results of laboratory evaluations including sedimentation rate, complete blood cell count, platelet count, prothrombin time, partial thromboplastin time, blood chemistry, HBsAg, anti-HCV, TPHA, VDRL, rheumatoid factor, ASTO factor, antinuclear antibody, C3,C4, CIC, cryoglobulins, urinalysis were within normal limits or negative. Fibrinogen was elevated during disease activity.Other investigations like PPD3, venous plethysmography, digital photoplethysmography, oscilography of lower extremities, X ray of the lungs and heart, US of upper abdomen and search for focal infection were within normal limits or negative. Capillaroscopy of the nailfold revealed very slow blood circulation. A biopsy of skin from a purpuric plaque was performed and showed a mixed perivascular inflammatory infiltrate of medium degree around the dilated vessels in the middermis. In some of them the fibrin thrombi were formed and the necrosis of the wall was noted, but without nuclear dust or fibrinoid necrosis. In the infiltrate the mononuclear cells dominated. The deposition of hemosiderin pigment in the skin was noted and was interpreted as the end result of a disruption of the dermal capillary bed and the extravasation and destruction of erythrocytes normally found in a large number of clinical entities, among them the livedo reticularis as well. The rest of the skin was within the normal morphological appearance. The diagnosis of primary vasculopathy (vasospastic disorder) with secondary trombosis was made. She was treated with compression therapy only. From the beginning of the therapy, 2 years ago, she is in remission.

DISCUSSION

Livedoid vasculitis is a clinical manifestation of the skin ishaemia, due to local occlusion of vessels of the mid-dermal and deep-dermal location. The precise mechanism is poorly understood. Frequent association with other elements of venous insufficiency and with capillaritis suggests that increased intracapillary pressure plays a part in the aetiology (1). Some investigators found decreased fibrinolytic activity in patients with livedoid vasculitis suggesting coagulopathy. A defective release of tissue plasminogen activator has also been demonstrated. It may represent a localised immune complex disease, with infectious agents, autoantigens, and tumour antigens being potential antigenic sources. Others feel that livedoid vasculitis like livedo reticularis is the clinicopathological expression of a primary vasospasm (2). There is also a possibility that increased homocysteine levels alone or in combination with other trombophilic defects may be associated with an increased risk of cutaneous or other organ small-vessel thrombosis (5). In differential diagnosis we should consider gravitational or arteriosclerotic ulcer and their scar, when the condition is located around the ankle. Also one shoud rule out leucocytoclastic vasculitis. If the lesions are on the body they may be confused with discoid lupus erythematosus or malignant atrophic papulosis-Degos' disease. Although this disorder has previously been considered a localised form of cutaneous vasculitis, biopsy reveals the absence of significant granulocytic perivascular infiltrate or leukocytoclasia, nuclear fragmentation and fibrinoid necrosis which argues against vasculitis, being more in keeping with a trombo-occlusive process and differentiates this disorder from immune complex-mediated necrotizing vasculitis. Thus the term vasculopathy describes this disorder more appropriately than the term vasculitis (4). Current therapeutic approach is the use of drugs that stimulate endogenous fibrinolytic activity, that inhibit trombus formation, or that cause vasodilatation (2,6). Attempts with compressive therapy are rare and some consider it seldom successful (1). Our patient has very well responded to the compression therapy, with no more attacks of new ulcer formation and with considerable alleviation of pain.

CONCLUSION

Patients with livedoid vasculitis should be examined extensively in order to rule out primary immunologic and vaso-occlusive disorders that may result in a similar clinical appearance. A correct diagnosis is essential in order to avoid aggressive therapeutic approaches that may result from incorrect diagnosis.

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Archive of Oncology 2001;9(Suppl 1):143.

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Condylomata acuminata - surgical therapeutic opinion

ABSTRACT

Condyloma acuminatum is a common skin benign tumor on external genitalia and perianal region of female and male patients. The lesions are usually few in number and fairly small, but they may aggregate to form large cauliflower-like masses. The authors report the case of a male patient 41 years of age with a massive condyloma acuminatum on genital and perianal region. On clinical examination the painful, bleeding, malodorous large tumor-like lesion on his penis, testises and perianal region was detected. The illness began 7 years ago with a few fairly small, smooth warts. A surgical specimen was sent for pathologic analysis and was diagnosed as a benign condyloma acuminatum. After the operation tissue defect healed in six weeks. From the surgical point of view, benign tumors of the skin may produce a destruction of the body surface and are removed for two reasons. They may be responsible for a cosmetic deformity and as a preventive measure in the development of a skin cancer. Clinically, the distinction between benign (condylomata acuminata) and malignant (Buschke-Loewenstein tumor) lesions is usually dufficult, especially if the first are macerate, secondarily inflamed with ulceration, infection and malodor.

KEYWORDS: Condyloma Acuminata; Carcinoma, Verrucous; Surgery

INTRODUCTION

Condyloma acuminatum is a common skin benign tumor on external genitalia and perianal region in female and male patients. The lesions are usually few in number and fairly small, but thay may aggregate to form large cauliflower-like masses (1). This lesions represent a clinical diagnostic problem in regard to differentiation from Buschke-Loewenstein tumor, which is a malignant tumor (2). Many scientific articles show that condyloma acuminatum and Buschke-Loewenstein tumor contain the type 6 and 11 Human Papilloma Virus (1-4). Condylomas have a certain malignant potential activated in a time (3).

CASE REPORT

A male patient, 41 age old, was admitted to the Department of plastic and reconstructive surgery, Institute of Surgery, Clinical Center-Novi Sad, complaining on pain, bleeding, malodor in a large tumor-like lesion on his penis, testises and perianal region. The illness began 7 years ago with a few, fairly small, smooth warts. At that time the patient was without physical discomfort. The patient was quite healthy before. He did not smoke and moderately consumed alcohol drinks. His occupation was a commertial worker. All members of his family were healthy. After a few months the lesion became a wide and firm. Then, warts began to aggregate to form large cauliflower-like masses. Aboute five months before his arrivel to the Department, his tumor was et times macerated and inflamated, with bleeding and malodor, the patient reported a loss of weight. Before adminission, he had no physical examination. After a complete clinical investigation, a total surgical electroexcision was performed. The wound was left without reconstruction of the postoperative tissue defect. Histopathological examination confirmed condyloma acuminatum without malignant alteration. Postoperative treatment required an intensive wound care every day. The patient was in our Departement for three weeks. The wound was reepithelizated the six weeks after a surgical excision. Half a year after surgery the patient is disease free, without any local recurence and physical discomfort.

CONCLUSION

The clinical diagnosis and surgical treatment for the majority of condyloma acuminata is clear (1). For large and massive lesions it is preferable to refer a patient to the clinical treatment for an individual surgical procedure, which depends on the site and size of tumors, the fitness and morbidity of the patient and an expected functional and cosmetic result (3). The histopathologic analysis is obligatory for all patients with condylomas becose the clinical diagnostic problem in regard to its differentiation from a malignant alteration still persists (2,3).

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The manuscript was received: 10. 03. 2000.

Accepted for publication: 11. 04. 2000.

Case report
UDC: 616.24:616.514:616-091.8

Archive of Oncology 2001;9(Suppl 1):144-5.

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Cutaneous leukocytoclastic vasculitis associated with anticardiolipin antibodies and hypocomplementemia in a patient suffering from chronic idiopathic urticaria, livedo reticularis and Raynaud's phenomenon

ABSTRACT

Leukocytoclastic vasculitis is synonymous with necrotizing vasculitis. Cutaneous leukocytoclastic vasculitis (CLV) is restricted to vasculitis in the skin, without involvement of vessels in other organ. Recurrent episodes of chronic idiopathic urticaria are an uncommon clinical manifestation of CLV. Known as urticarial vasculitis (UV), it represents the prototype of an immune complex-mediated damage to the small vessels. A-38-year-old woman with a history of recurrent episodes of chronic idiopathic urticaria and angioedema during the past 15 years. The last attack associated with malaise, fever and arthralgias started two weeks after the upper respiratory tract infection. She has been suffering from Raynaud's phenomenon (RP) and livedo reticularis (LR) since early childhood. On examination there were lesions of LR on the thighs. The placques typical for UV were seen on forearms, trunk and lower legs. Laboratory investigation revealed: increase in ESR; slight decrease in RBC and Hb; decreased IgG; persistant decrease in C3 and C4 level; elevated C1q bind. CIC; moderate increase in anticardiolipin antibodies class IgM (ACA-IgM). On capilaroscopy of the finger nailfolds, capillary loops were hardly visible because of the impaired supply, the other loops showed very narrowed lumen, filliform in appearance. The diagnosis of acute CLV was confirmed by light microscopy of the skin taken from a urticarial lesion. Our patient lacked the typical criteria for primary antiphospholipid syndrome (APS) and did not satisfy those for systemic lupus erythematosus (SLE). In spite of these, an increased ACA level and hypocomplementemia in the presence of LR and RP make this case of CLV very peculiar.

KEYWORDS: Vasculitis, Hypersensitivity; Antibodies, Anticardiolipin; Urticaria; Skin Diseases, Vascular; Raynaud's Disease

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The manuscript was received: 10. 03. 2000.

Accepted for publication: 11. 04. 2000.

INTRODUCTION

Recurrent episodes of chronic urticaria (CU) and angioedema (AE) are uncommon clinical manifestations of cutaneous leucocytoclastic vasculitis (CLV). Known under the term of urticarial vasculitis (UV), it represents the edematous form of necrotizing vasculitis (NV) (1). Other skin manifestations include foci of purpura in the wheals, livedo reticularis (LR), nodules and bullae. Raynaud's phenomenon may also be seen. Apart from idiopathic form, UV may precede, associate or express a systemic disease (i.e. connective tissue disease, malignancies) (2). CLV represents the immune complex-mediated damage to the small blood vessels, most often the postcapillary venules. A persistent CLV affecting superficial capillares and venules, exacerbates the local stasis and changes in the vessel morphology, so that LR may be the end result. LR is mottled bluish discoloration of the skin in the netlike pattern due to low flow rates in the superficial venous plexus. It may be classified as idiopathic, and secundary LR. Thus, in an acquired multisystem disorder of hypercoagulation, known as antiphospholipid syndrome (APS), LR may occur in more than one half of the patients as the first clinical sign (3). The mainstay of the diagnosis of APS is the clinical event of thrombosis or miscarriage, in the presence of anticardiolipin antibodies (ACA) and/or lupus anticoagulant (LA) (4,5). In patients with SLE, elevated level of ACA and LR seem to predict the worse prognosis. It remains unclear wheather ACA are epiphenomena or whether they are directly involved in pathogenesis and prognosis of CLV (6)?

MATERIALS AND METHODS

A 38-year-old married woman, psychologist, with a history of recurrent episodes of chronic idiopathic urticaria during the past 15 years. Each attack was associated with malaise, fever, high temperature (up to 37.4°C) and arthralgias. The last attack has started 3 months ago, two weeks after an episode of the upper respiratory tract infection treated with cephalosporines and aspirin. It was characterized by lesions not only pruritic but also painfull, that lasted for longer than 24 hours, leaving residual hyperpigmentations. She has been suffering from Raynaud's phenomenon and livedo reticularis since early childhood. There was no past history of thrombosis, thrombocytopenia or spontaneous abortion. Family history revealed that her father also had Raynaud's phenomenon and livedo reticularis, and died from a heart attack when he was 80-yeras old. On examination, there were lesions of livedo reticularis predominantly on the thighs. Erythematous, indurated well defined circumscribed areas of edema in a plaque manner typical for urticarial vasculitis were seen on forearms, trunk and lower legs.

RESULTS

Laboratory findings: ESR: 23/55, RBC: 3.7 x 10^9/l, WBC: 9.2 x 10^9/l, PLT: 189 x 109/l, Hb: 112 g/l, urinalysis: Hb: +, 5 RBC in sediment, fibrinogen 2.0 g/l, sugar: 4.1 mmol/l, triglycerids: 2.5 mmol/l (ref. <2.3), cholesterol: 6.2 mmol/l (ref. <6.5), HDL: 0.80 (ref. >1.5), LDL: 4.3 (ref. <3.5), LDL/HDL: 5.3 (ref. <3), PTT: 13.8 sec. (ref: 11.0-20.0), APTT: 29.2 sec (ref. 27.0-35.0), liver and kidney functional tests: within normal limits, IgG: 5.89 g/l (ref. 8-18), IgA: 1.25 g/l (ref. 0.9-4.5), IgM: 2.9 g/l, (ref. 0.6-2.8), cryoglobulines: negative, C3: 1.08 g/l; 1.0 g/l (ref. 1.2-2.3), C4: 0.36 g/l, 0.14 g/l (ref. 0.2-0.4), C1q bind: 3.4 (ref. <1.5 mcg), latex RF: +; Ig RF: 29.6 IU/ml (ref. <60), VDRL: negative, TPHA: negative, ACA IgG: < 10 U/ml (ref. <14.1), ACA IgM: 42.4 U/ml (ref. <4.6), after eight weeks - ACA IgG: < 10 U/ml, ACA IgM: 43 U/ml, anti ds DNA: 12 IU/ml (ref <50). Chest X ray: normal.

Ophtalmologic examination including fundus: normal. Biopsy specimen from urticarial lesion (light microscopy): showed superficial and deep dermal perivascular infiltrate rich in neutrophils, lymphocytes and histiocytes, partially invading lower epidermis; fibrinoid degeneration of blood vessel wall with predominantly neutrophylic infiltration into the vessel wall associated with nuclear dust; abundant nuclear debris in the intersctices of the dermal collagen. The diagnosis of acute leukocytoclastic vasculitis was made. DIF: deposition of immunoglobulins and complement were not seen neither in the affected vessels nor along the basement membrane zone. Capillaroscopy of the finger-nailfolds: capillary loops hardly visible because of the impaired supply, some of them with lumen narrowed, filiform. Laboratory investigation did not confirm the presence the current or previous infection.

DISCUSSION

Apart from the endothelial/leukocyte interaction mediated mostly by activated neutrophils, it has been proposed that other factors such as the susceptibility of the blood vessels in the area, should be considered in the pathogenesis of CLV (1). Thus, it is assumed that in many cases CLV develop without clinical and biological signs of systemic involvement. In a limited number of cases, CLV is associated with signs of internal injury due to the vasculitic process. In another group of the patients CLV is the expression of a systemic disease (i.e., connective tissue disease, malignancies). One of the main problems is to establish if CLV is a disorder limited to the skin, and/or if it is the clinical spy of a current or future systemic disease (2). It is well known that patients with UV have minimal signs or symptoms of a systemic disease. Most common are AE, arthralgias and signs such as pulmonary disorders and glomerulonephritis. The C1q binding by an IgG protein may play a role in decreasing complement. Patients with hypocomplementemia are most likely to have a systemic involvement. The C1q precipitin reaction typifies hypocomplementemic urticatrial vasculitis (HUV) (1). The development of SLE has been documented in a patient with HUV (7). On the other side, it is still uncertain whether antibodies against the antigens derived from the apoptotic cell death mediated by the Fas/bcl 12 system, such as ACA, ANCA (antineutrophilic citoplasmic antibodies) and AECA (antiendothelial cell antibodies) represent epiphenomena, or are directly involved in the pathogenesis of CLV and UV (2,6). If they are directly involved, should the prognostic criteria of CLV include other soluble factors (2)? With regard to the previously mentioned susceptibility factors, it is for debate whether cutaneous microcirculation substantially differs from other districts in its biological response to neutrophils? The microvasculature has characteristic physiological features that distinguishes it from the rest of the circulatory bed (eg, low flow and low preassure states, ionic microdomains, adhesive subendothelial matrix). The microvascular endothelium expresses a spectrum of constitutive and inducible molecules, and shows responsivness to various proinflammatory stimuli, playing a central role in the normal physiology of the skin and diseased states, including CLV, but the major immunologic differences between the microvasculature of different organs, including the skin, have not been documented (8).

CONCLUSION

Our patient lacked the typical criteria for the diagnosis of primary APS and did not satistfy the criteria of SLE. In spite of these, the elevated level of ACA with hypocomplementemia in the presence of LR and RP, make this case of CLV very peculiar.

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Archive of Oncology 2001;9(Suppl 1):146-7.

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Dermatomyositis - a case report

ABSTRACT

Dermatomyositis (DM) is a systemic disorder of autoimmune nature, characterised by idiopathic inflammatory myopathia and with characteristic cutaneous manifestations. Clinically, there are two forms of DM: a childhood form (usually prior to the age of 10), frequently complicated by the development of calcinosis, and an adult form (between 40 and 60 years of age) which is in 20-30% linked to cancer. We are presenting a patient fulfilling all the criteria, for establishing the diagnosis of DM (characteristic skin changes, symmetric proximal muscle weakness, serum elevations of muscle enzymes, the classic electromyographic and muscle biopsy findings of inflammatory myopathy). Because of the muscle weakness, electromyographic evaluation was performed. There were diffuse myogenic lesions without denervation lesion being registered and with preserved motoric conduction speed. This finding matches completely the picture of dermato/polymyositis in a chronic stage. On the basis of the pathohistological analysis of skin and muscle specimens the diagnosis of dermatomyositis was confirmed. Subacute evolution and lack of malignancy point to a fairly good prognosis. Further observation and periodical check-ups are necessary for the sake of a prompt detection of malignant process.

KEYWORDS: Dermatomyositis; Polymyositis; Diagnosis; Histochemistry; Prognosis

INTRODUCTION

Dermatomyositis (DM) is a systemic disorder of autoimune nature, characterised by idiopathic inflammatory myopathia and with characteristic cutaneous manifestations. Clinically, there are two forms of DM: a childhood form (usually prior to the age of 10), frequently complicated by the development of calcinosis, and adult form (between 40 and 60 years of age) which is in 20-30% linked to cancer. Skin changes include heliotrope rash, erythema on the photo exposed skin areas (periorbital, neck, upper parts of the trunk), violaceous flat papules over metacarpophalangeal and interphalangeal joints (Gottron's papules), periungual erythema and telangiectasia, and a scaly alopecia (1,2). In DM, apart from the skin, muscles are most commonly affected. In more severe cases pharyngeal and respiratory muscles and myocardium can be affected too.

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The manuscript was received: 10. 03. 2000.

Accepted for publication: 11. 04. 2000.

CASE REPORT

A 56-year old patient, was admitted to hospital because of erythema on the scalp, the face (especially periorbitally and on the eyelids), on the neck and the chest, on the back of the hands and periungvaly. Also there were erytheosquamous plaques on the elbows and knees. On the back of the hands, over metacarpophalangeal joints, there were flat violaceous papules. Eyelids oedema was present. From the history we found that skin changes developed over the period of 6 months accompanied by progressive weakness of the limb muscles and intermittent itch. Two months prior to the onset of the disease, the patient had an operation of the perforated duodenal ulcer. There were no illnesses in the family of any hereditary importance.

RESULTS

On admission to hospital, a physical examination showed no abnormalities. Laboratory analyses that reveal alterations were: Leukocytes count 12.52x109 (Ne: 82.9%, Ly: 5.7%, Mo: 10.1%, Eo: 0.2%, Ba: 0.2%); LDH 456 IU/l, and after 2 weeks this result was normal like other so called muscle enzymes (CPK, SGOT). Levels of fibrinogen, ASTO, creatinine, creatinine clearance, urea, total proteins, serum electrolytes, SGPT and gGT were normal. ANA were negative. HLA type: A2, -/B35, -Cw4. Because of muscle weakness, electromyographic evaluation was performed. There were diffuse myogenic lesions without a denervation lesion being registered and with preserved motoric conduction speed. This finding matches completely the picture of dermato/polymyositis in chronic stage. On the basis of the pathohistological analysis of the skin and muscle specimens the diagnosis of dermatomyositis was confirmed. Epidermis was of uneven thickness and basal layer of cells was degeneratively changed. Papillary dermis was oedematous and inflammatory infiltration of lymphocytes and plasma cells was moderate. Infiltration was also present between muscle fibbers and around interstitial blood vessels. Muscle cells of striated muscle were partly of less apparent striation, with moderate hyperplasia of the nucleus. Considering the age of the patient and possibility of coexistence of DM with malignancy, a detailed examination of the patient was performed. All findings indicating the malignancy were normal. After establishing the diagnosis of DM methylprednisolon was given in the dose of 80 mg daily, which was gradually reduced. We gave the lowest possible therapeutically dose because of the duodenal ulcer and the response to this dose was good.

DISCUSSION

In the described patient , the diagnosis of DM was established, according to the criteria of Bohan and Peter. Besides characteristic skin changes for the final diagnosis of DM, 3 more signs must be present. Those criteria include symmetric proximal muscle weakness, serum elevations of muscle enzymes (CPK, LDH, SGOT), the classic electromyographic and muscle biopsy findings of an inflammatory myopathy. The prognosis is good, except in patients with a malignancy and pulmonary involvement (3). Most of the carcinomas develop within 2 years after establishing the diagnosis (1,4). Significant predictive factors for the development of cancer in DM are necrotic skin ulcerations and pruritus (5). About 70% of patients survive a 5 year period (6,7). Bad prognostic signs, considering survival rate are: advanced age, the presence of malignancy and elevated sedimentation rate (8). About half of the patients enter remission and can discontinue therapy after 5 years (4).

CONCLUSION

Considering the presence of cutaneous signs and fulfilment of all criteria, the definite diagnosis of DM was established. Subacute evolution and lack of

malignancy point to a fairly good prognosis. Further observation and periodical check-ups are necessary for the sake of prompt detection of a malignant process.

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Case report
UDC: 616.521:616-098.1:904
Archive of Oncology 2001;9(Suppl 1):147-8.

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Large plaque parapsoriasis in 17 year old male patient

ABSTRACT

The parapsoriasis group of diseases includes large plaque parapsoriasis, small plaque parapsoriasis and pityriasis lichenoides. We have described a 17- year old male patient who has developed large plaque parapsoriasis (all plaques were over 5 cm in diameter). Numerous round and oval, well-defined, pink and violaceus scaling plaques were localised on the buttock area and thighs. Skin biopsy demonstrated mildly hyperkeratotic and markedly parakeratotic epidermis with elongated rete ridges. There was a lymphocytic and histiocytic infiltrate with sparse granulocytes in upper dermis, invading the lower parts of epidermis. Dilated blood vessels were surrounded with mild, already mentioned, infiltrate. There were no changers of skin adnexal structures. These findings confirmed the clinical diagnosis of parapsoriasis. Such patients should be carefully examined, every 3 to 6 months, in order to record possible transformation to cutaneous lymphoma.

KEYWORDS: Parapsoriasis; Mucosis Fungoides + pathology

INTRODUCTION

Parapsoriasis is a group of disorders which is characterised by a persistent, scaling, inflammatory eruption. Two clinico-pathological features divide the parapsoriasis group apart from other purely inflammatory dermatoses: the relation to malignant lymphoproliferative lesions and the coexistence and/or overlapping of entities in this group. The current, generally accepted classification includes three entities: large plaque parapsoriasis (LPP), small plaque parapsoriasis (SPP) and pityriasis lichenoides. Each of these entities has unique skin lesions and several morphologic variants (1).

PATIENTS AND METHODS

A 17- year old male patient, during the period of a year, developed numerous round and oval, well defined, patches and very thin plaques which were localised on the trunk, buttock area and thighs. These patches were pink in colour but some of them showed violaceous hue. All were greater than 5 cm, up to 10 cm in diameter and covered with small and scanty scales. Itching was present from the very beginning of the disease. This clinical picture pointed to LPP that was conformed by a pathohistological examination. The

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

patient was treated with Psoralen and ultraviolet A (PUVA) therapy.

RESULTS

Skin biopsy demonstrated mildly hyperkeratotic and markedly parakeratotic epidermis with elongated rete ridges. There was a lymphocytic and histiocytic infiltrate with sparse granulocytes in the upper dermis, invading the lower parts of the epidermis. Dilated blood vessels were surrounded with a mild, already described, infiltrate. There were no changers of skin adnexal structures. These findings confirmed the clinical diagnosis of parapsoriasis. There were no pathological changes in performed laboratory tests (sedimentation rate, red and white blood cells count, platelets count, differential white blood cell count, urine analysis, urea, serum levels of creatinine and bilirubin, liver transaminases, blood glucose concentration) as well as in chest x - ray.

DISCUSSION

LPP and SPP are in general, diseases of middle-aged and older people, with the peak incidence in the fifth decade. LPP is distinguished from SPP by the lager size (more than 5 cm in diameter), asymmetrical distribution and irregular shape of its lesions that are less discrete and often poikilodrematous. Both LPP and SPP may persist for years to decades. A common feature of the parapsoriasis group of diseases is that all of them appear to be a cutaneous T cell lymphoproliferative disorder (1).

About 10 to 30 percent of cases of LPP progress to mycosis fungoides (MF) (2). In contrast to the malignant potential of LPP, SPP is a clinically benign disorder, and rarely if ever progresses to MF. Differentiation of LPP from early MF is based on histopathologic criteria (Table 1) developed at Stanford University (1).

Patients with LPP should be carefully examined every 3 to 6 months for the evidence of progression. Repeated multiple biopsies of suspected lesions should be performed (1).

The diagnosis of early cutaneous T-cell lymphoma is a difficult point in dermatology. Recently, Southern blot analysis and polymerase chain reaction has been used to detect monoclonal population of T-lymphocytes in initial lesions, in which clinical and histological findings are unspecific (3).

Table 1. Histopathologic criteria for MF

Histopathologic criteria for MF
Multiple Pautrier microaggregates
Diffuse infiltration of many individual atypical lymphocytes* into epidermis+
A few small intraepidermal clusters of a few atypical lymphocytes
A few individual intraepidermal atypical lymphocytes
Dense upper dermal band like interface infiltrate that includes atypical lymphocytes
Mild to moderate polymophous upper dermal infiltrate that includes atypical lymphocytes and has a focal interface pattern
Extension of the infiltrate into the deep dermis
Categories diagnostic of MF: 1; 2; 3+4+5; 3+4+6+7
Categories consistent with MF: 3+5; 3+6; 4+5; 4+6+7
Categories suggestive of MF: 3; 4; 5; 6

*Lymphocytes with scant cytoplasm and hyperchromatic, convulted (cerebriform) nuclei. Cell size may vary

+ Epidermal involvement is characteristically net associated with prominent intercellular oedema (spongiosis)

CONCLUSION

Patients with large plaque parapsoriasis need permanent monitoring because of a possible progression to MF. The diagnosis of an early stages of this disease is a difficult challenge for both the dermatologist and dermatopathologist.

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Archive of Oncology 2001;9(Suppl 1):149-150.

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Cutaneous meningioma of the scalp in an infant

ABSTRACT

Ectopic cutaneous meningiomas (CM) comprise a diverse group of lesions with different pathogenesis and clinical features. We report an 8-month-old female infant with an asymptomatic subcutaneous nodule on the forehead, slowly growing since birth, and also having incomplete syndactyly middle-ring finger of the left hand and complete syndactyly three toes on the feet. No bony defect under the nodule and any CNS lesions were noted. After the complete excision of the subcutaneous firm, gray nodule, 0.8 cm in diameter, histopathological and immunohistochemical characteristics indicate meningothelial CM. This congenital lesion fits into type I CM by Lopez et. al. classification. CM should be considered as differential diagnosis of hard, cutaneous or subcutaneous lesions arising on the scalp, face, or paravertebral region. Clear relations and histological distinctions between CMs rudimentary meningoceles, and hamartomas with an ectopic meningothelial component, have not yet been established, and have no practical implications.

KEY WORDS: Meningioma; Skin Neoplasms; Infant; Syndactyly

INTRODUCTION

Ectopic meningiomas are very rare tumors that occur most commonly in the cutis or subcutis of the scalp, face and paravertebral region. The term cutaneous meningioma (CM) comprises a diverse group of lesions with differing pathogenesis and clinical features. They are classified into three groups by Lopez et al. (1). Type I - primary CM occurs in children and young adults and it is usually present since birth. It has been thought to arise from ectopic arachnoid cell rests as a result of developmental defect in the closure of the neural tube. They share many features in common with meningoceles. In most cases the connection with the CNS is likely to have involuted. Type II - occurs around sensory organs of the head and along the course of cranial and spinal nerves. It represents a cutaneous extension from an ectopic soft tissue meningioma, probably arising from arachnoid cell rests displaced along nerve sheaths. Type III - represents an extensions into the skin from CNS meningioma infiltrating across bone or a bone defect. Type I CM is regarded as a congenital, nonneoplastic lesion, whereas the others are acquired, neoplastic proliferations in adults. Clinical appearance of CMs resembles a variety of common skin lesions, but the histopathologic appearance is usually characteristic (1-4).

CASE REPORT

An 8-month-old female infant presented with a slowly growing, 1 x 0.8 cm, subcutaneous nodule in her scalp, 1 cm posterior to the right frontal hairline. It was presented since birth with overlying discrete hair tufts. It was associated with incomplete syndactyly middle-ring fingers of the left hand and complete syndactyly three toes of the feet. She had a mildly enlarged head suspected for hydrocephalus. Neurological examinations and ECHO of the CNS were normal. No bony defects or connection of the cutaneous lesion with intracranial structures were found. The preoperative diagnosis was dermoid cyst. After a complete excision, subcutaneous firm, gray nodule, 0.8 cm in diameter, with a fibrous cut surface, was presented. Microscopically, nests of meningothelial cells intermingle with the fibrocollagenous tissue, forming whorls, small strands, lacy arrays and linear streaks. The meningothelial short spindled and oval cells have bland, oval or rounded nuclei, and homogeneous eosinophilic cytoplasm with indistinct border. There are rare syncytial and multinucleated foci, and also characteristic psammoma bodies, and rare small, rounded, collagenous bodies. Nuclear pleomorphism is absent, and mitotic activity is very low. Immunohistochemical staining reveals tumor cells to be strongly positive for vimentin and epithelial membrane antigen (EMA) and negative for S-100 and cytokeratins. The diagnosis of cutaneous meningothelial meningioma was established. Six months after the excision the child is without local recurrence a any other related lesions.

DISCUSSION AND CONCLUSION

The skin lesion in our patient histologically and clinically fits into the cutaneous meningothelial meningioma of type I. This one is among the youngest children diagnosed with these lesions. In the largest reported series by Lopez et al. (1), among 16 patients discovered with type I CM , only one was an infant. The lesion may be mistaken clinically for cutaneous lesions including cysts, skin tag, naevi, vascular lesions, and fibroma. It might be associated with circumscribed alopecia, congenital melanocytic naevus (5), adenomatous hyperplasia of the eccrin glands (6), and as in our case, with congenital localized hypertrichosis (hair tufts) (7). Association with von Recklinghausen's disease (8) and ovarian fibroma (9) were also reported. Our case represents the first reported association of CM with malformations of fingers and toes. A local excisions is adequate treatment for these lesions and complications may result from associated bony or craniospinal defects. The differentiation from the type II and type III CM have an essential importance and appropriate imaging studies must exclude an intracranial component of the disease. Some histopathological diagnostic dilemmas due to resemblance to metastatic carcinoma, vascular tumors and giant cell fibroblastoma can easily be resolved by immunohistochemical studies. Clear relations and histological distinctions between CMs rudimentary meningoceles, and hamartomas with an ectopic meningothelial component, have not yet been established, and have no practical implications (1,10,11).

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The manuscript was received: 14. 03. 2000.

Accepted for publication: 17. 04. 2000.

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Metastasis of malignant skin melanoma in heart and pericardium

ABSTRACT

Primary tumors of the heart in humans are rare in comparison to other organ tumors. Benign heart tumors are more frequent than malignant tumors. Malignant tumors of the heart and pericardium are most frequently metastasis of other organ tumors. Female patient admitted to the hospital due to the fatigue, weakness, dyspnea and tachicardia with operated melanoma of the right lower leg (1995). Clinical examination, laboratory analysis, ECG, echocardiography and explorative laparatomy with tumor biopsy were performed. Echocardiographic examination revealed large circular pericardial effusion and oval tumor formation, size 85x35 mm attached to the parietal pericardium. Biopsy of tumor from the right auricula and biopsy of pericardium were done. Due to the tumor dissemination, it was not possible to perform total tumor resection. Histo-pathological finding showed that tumor tissue consist of atypical melanocytes with low mitotic activity. Diffuse tumor infiltration with atypical melanocytes was found in the pericardial tissue. Although melanoma is malignant tumor with high malignancy potential, sporadic cases of succesfull surgical tumor resection from the heart cavities, with long survival time and good quality of life have been described. We can conclude that in some cases especially in younger patients, surgical resection of the tumor could be the therapy of choice for this patients.

KEYWORDS: Melanoma; Neoplasm Metastasis; Heart Neoplasms + secondary

INTRODUCTION

Primary tumors of the heart in humans are rare in comparison to other organ tumors. Benign heart tumors are more frequent than malignant tumors (1). Malignant tumors of the heart and pericardium are most frequently metastasis of other organ tumors (2,3). They are usually manifested with pericardial effusion (4) but echocardiographic examination often reveals morphological changes due to the solid tumor mass. The following tumors often give metastasis to the heart: leukaemia, malignant melanomas, lung and breast carcinoma, lymphomas, and other tumors (5). In males, melanomas, mesotheliomas and lung carcinoma and in females melanomas, lung and kidney carcinomas most often disseminate to the heart (6).

CASE REPORT

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The manuscript was received: 13. 03. 2000.

Accepted for publication: 17. 04. 2000.

Patient M.V. 63 years old female, admitted to the hospital due to the fatigue, weakness, dyspnea and tachicardia. This symptoms lasted several months before the admission. In 1995 patient operated melanoma of the right lower leg (nodular type, by Klark IV, tickness by Breslow 10 mm). On admission the patient was consciuos, non febrile with peripheral cyanosis and NYHA III group. The patient had regular cardiac rhytm, soft heart sounds with no murmurs. TA: 90/60 mmHg. She had good cardiac function. Laboratory findings showed increased sedimentation rate (84) and signs of hipochromic anemia, RBC: 3.34x106, Hb: 9.5 g/l. Heart and lung X-ray showed enlarged cardiac shadow. ECG: sinus rhytm, heart rate: 80/min, negative T wave in I, II, III, aVL, V4-V6. Echocardiographic examination revealed normal morphology and function of heart valves, normal diameters of cardiac chambers (left atrium 39 mm, left ventricle (LV) EDD 50 mm, ESD 26 mm) and good ejection fraction (EF). Transmitral flow showed disturbed LV relaxation. Large circular pericardial effusion was established. The measured distance between visceral and parietal pericardium was: 10 mm behind LV inferior wall, 30 mm behind LV lateral wall and 22 mm in front of the right ventricle. In parasternal transversal view, from the level of mitral valve to the level of papilary muscle, oval tumor formation, size 85x35 mm attached to the parietal pericardium was detected. In apical 4-ch view this formation (measured diameter was 40 mm) was seen in the projection of heart apex. Explorative laparatomy was performed and large quantity of dense, hemoragic pericardial effusion with thicked pericardium was found. Huge tumor formation was found in pericardium in front of all LV anterior wall, apex and LV lateral wall. Biopsy of tumor from the right auricular appendage and biopsy of pericardium were done. Due to the tumor dissemination, it was not possible to perform total tumor resection. Histo-pathological finding showed that tumor tissue consist of atypical melanocytes with low mitotic activity. Diffuse tumor infiltration with atypical melanocytes was found in the pericardial tissue. Tumor cells were not pigmented. Immunohistohemic reaction with antibodies against S-100 protein (specific marker of malignant melanoma) (7) was positive.

DISSCUSION

Malignant melanoma is one of the most malignant tumors in the human body. After the liver, heart is the most frequent place for the metastasis of this tumor. In clinical practice, secondary deposits of this tumor in the pericardium are rarely discovered during the life time. The progression of this ilness is sometime unpredictible. Cases of melanoma metastasis, 25 years after the resection of primary tumor (8) (with different tumor localisation) was described. Melanoma metastasis are often clinicaly expressed as pericardial effusion. Cases of acute cardiac tamponade (9), even sudden death in this patients have been described. In previous years diagnosis of the tumor and its metastasis was often done #post-mortem#. Introducing ultrasound as non-invasive diagnostic method enabled better evaluation of tumor metastasis in the heart and pericardium. Implementation of new ultrasound technics, especially transoesophageal ultrasound with better resolution, enabled ultrasound guided tumor biopsy (10,11). This method gives the oppportunity to establish the nature of the tumor mass and to find the appropriate therapy. Although melanoma is malignant tumor with high malignancy potential, sporadic cases of succesfull surgical tumor resection from the heart cavities, with long survival time and good quality of life have been described (12). We can conclude that in some cases especially in younger patients, surgical resection of the tumor could be the therapy of choice.

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Archive of Oncology 2001;9(Suppl 1):152.

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Markers for the acquired immunodeficiency syndrome (AIDS)

ABSTRACT

We present the results of autopsy on a 58 years old man with Kaposi sarcoma and pulmonal Pneumocystis carinii infection. These are the clinical and pathohistological markers for AIDS.

KEYWORDS: Acquired Immunodeficiency Syndrome; Sarcoma Kaposi; Pneumocystis Carinii

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a form of the severe cellular immunodeficency caused by an immunodefficiency virus (HIV) (1,2). This immunodefficiency state predisposes individuals to a broad range of opportunistic infections and neoplasms, especially Kaposi sarcoma and lymphoma (1,3). Transmission of HIV may occur through sexual contact, through the blood and via maternal-fetal routes (4-6). The virus selectively infects the CD4+ (T4) T-lymphocytes, resulting in quantitative and qualitative defects in these cells. CD4+ cells play a crucial role in the immune response and their impaired function results in a compromised function of a variety of other types, including B cells. The most common manifestations of AIDS are unexplained generalised lymphadenopathy and constitutional symptoms such as fever, weight loss and diarrhoea (4). The manifestations are also those of opportunistic infections and neoplasms, especially Kaposi sarcoma (1,2,7).

RESULTS

We report the case of a middle age (58) man who spent 40 years in the prison, where he died. The most important autopsy finding was Kaposi sarcoma and pulmonal Pneumocystis carinii infection. The affected fields of the lungs were airless, red and beefy. Histologicaly, the alveolar spaces were filled by an amphophyllic, foamy, amorphous material resembling proteinaceous edema fluid, composed of proliferating parasites and cell debris. There was also an accompanying mild interstitial inflammatory reaction, with widening of the septa, protein and fibrin exudation, pneumocyte proliferation, escape of the red cells formation from hyaline membranes. Kaposi cutaneous sarcoma manifested by the red-purple coalescent macules, papules, plaques and rare nodular tumors measuring 4cm in diameter. Nodular lesion consisted of plump, spindle-shaped stromal cells containing irregular, angulated, slit-like spaces filled with red cells and lined by recognizable endothelium, interwined with normal vascular channels.

DISCUSSION

Pneumocystis carinii is a ubiquitous organism that does not produce disease in normal individuals, but causes a severe pneumonia in most patients with AIDS (1,4). Pneumocystis carinii is a fungus, based on the properties of its cell wall, the paucity of its intracellular organelles, and philogenetic analysis of its small-subunit ribosomal RNA sequence (3). Inhaled Pneumocystis carinii is atracted to the type 1 alveolar epithelial cells and multiply within the alveolar space. This infection occurs when CD4+ helper T cells number falls below 200 per cmm (5). Kaposi sarcoma, as the initial manifestation of AIDS, is found in approximately 15% of the cases. It is recognized as an indolent cutaneous disease with predilection for elderly men. Kaposi sarcoma is a multisystem neoplasm in AIDS patients, usually presenting with red-to-purple skin lesions (2,7,8).

Extranodal non-Hodgkin's lymphoma of the B-cell or Burkitt type is the second most common neoplasm occuring in AIDS (4). The pathogenesis of Kaposi's sarcoma is unknown. Epidemiologic features suggest a viral etiology. HIV itself is a co-factor in patients with AIDS. The data suggest that growth factors released by T lymphocytes and HIV tat protein (released by retrovirus-infected CD4+ T lymphocytes) act together to induce the proliferation of Kaposi sarcoma spindle cells. Cytokines, produced by the activated lymphoid cells, permit continual self-renewal, activation and proliferation of non-neoplastic endothelial cells (7).

CONCLUSION

Opportunistic infection of Pneumocystis carinii type and Kaposi sarcoma are both clinical and pathological markers of the acquired immunodeficiency syndrome.

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The manuscript was received: 21. 03. 2000.

Accepted for publication: 14. 04. 2000.

Case report
UDC: 616.59-006:616-091.8

Archive of Oncology 2001;9(Suppl 1):153-4.

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Osteoid osteoma - local recurrence or rest tumor

ABSTRACT

Osteoid osteoma is a benign osteoblastic lesion of the bone. Osteoid osteoma is the lesion with a typical and recognizable radiography, gross and microscopic characteristics. A radical surgery is curable and only few cases of recurrence were reported. We examined two cases of the recurrence of osteoid osteoma after a radical en-block resection. One of them had two recurrences after the radical resection and the second one was the so called gigantic osteoid osteoma. The other patient had #double nidus#.

KEYWORDS: Osteoma, Osteoid; Neoplasm Recurrence, Local

INTRODUCTION

Osteoid osteoma is a benign osteoblastic lesion of the bone. This lesion was described in 1935. Jaffe defined osteoid osteoma as a specific clinicopathologic entity. It is a relatively common tumor of the bone, and comprises 2-3% of all primary bone tumors. The lesion occurres twice as often in males as in females. It is most frequent between 10 and 20 years, and very rare under 5 years and above the age of 40. The youngest patient reported was 8 months old; the oldest was 70 years old. The lesion is often solitary, and may be found in all bones. Most freqently involved bones are: femur (43%) and tibia (23%). Typical location is cortex of the long tubular bone. The ribs, the patella, the calvarium and the orbit are the rarest sites of involvement. The multiple osteoid osteoma is extremely rare. Clinical signs are progressive; the first sign is pain, and it is sharp, stronger at night and after alcohol consuming. In a significant number of patients (75%) nonsteroidal anti-inflammatory therapy results in the relief of pain (positive aspirin test). Some authors consider that it is a result of the positive effect of aspirin in prostaglandin's blockade (PGE2 and PGI1). Prostaglandins have hiperalgetic effect and their synthesis in osteoid osteoma is increased. Pain is usually associated with swelling, local palpatory sensibility and redness; because of that, the tumor clinically looks like inflammation.

Radiographically, the typical finding is a radiolucent central nidus that is seldom larger than 1.2 cm. This nidus is surrounded by a peripheral sclerotic ring-like reaction. In radioscintigraphy the nidus is marked as a "hot zone" because it binds the radiofarmac.

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The manuscript was received: 19. 03. 2000.

Accepted for publication: 17. 04. 2000.

Osteoid osteoma has a typical and recognizable macroscopical shape in the bone. The tumor is oval, circular or elliptic and resembls a nest (nidus). The elliptic form is specific only for children, under 2 years as a consequence of a rapid growth. The tumor is usually up to 2 cm in diameter, rarely bigger than 3 cm (gigantic osteoid osteoma). The tumor color varies; an „immature tumor" has numerous blood vessels, dark-red color and soft consistency, „mature tumor" rich with bone tissue, is white-yellow in color and firm in consistency. Histologically, the nidus is distinguished from the surrounding sclerotic bone. It is composed of mesenchimal tissue, blood vessels and nerve fibers. There are large bands of osteoid in irregular arrangement (woven bone). The tumor tissue is hypercellular, with many osteoblasts, osteoclasts and osteocytes. These cells take part in rapid bone metabolism inside the tumor. Irregular maturation is present in the woven bone and the central part is #the oldest# part of the tumor. Differential diagnosis includes: osteoblastoma, osteoclastoma, osteomyelitis, abscessus Brody, eosinophylic granuloma etc.

Osteoid osteoma can be surgically treated. Preoperative localization with rentgenography, scintigraphy, computerized tomography (CT) and sometimes immunofluorescency is necessary because a precise localization facilitates a surgical intervention. Surgical therapy includes a curettage and radical en-block resection. In recent years osteoid osteoma has been treated by percutaneous laser method, percutaneous biopsy with CT scanning and sclerosation with 96% alcohol. Generally osteoid osteoma doesn't have relapses. Radical surgery is curable and only few cases of recurrence were reported by Jaffe, Dunlop and Halzel.

CASE REPORTS

First case: A 9 year old boy with pain in the left femur's region, a positive aspirin test and typical rendgenography. The initial therapy was a curettage, and histopathologically osteoid osteoma was diagnosed. After a year the boy had identical clinical signs, and because of that an en-block resection was made. The histological diagnosis was the same-osteoid osteoma. The third surgical intervention (second resection) was made after 5 years. In en-block resection the tumor-osteoid osteoma was present (3,5x1,5cm). It was an unusually big nidus, and a gigantic osteoid osteoma or osteoblastoma was suspected.

Second case: An 8 year old boy with pains in the knee, appearing 6 months before. Radiography was made and the diagnosis was osteoid osteoma. A surgery-radical resection was performed and in the resected part of the bone osteoid osteoma was histologically confirmed. The tumor contained two niduses, one 1.5x1.5cm, and the second was smaller 0.3x0.3cm; it was a very rare form of #double nidus#. After 5 years the patient had night pains in the knee and an osteolytic lesion seen on rendgenography. En-block resection was made and pathological diagnosis was osteoid osteoma again.

DISCUSION

From 1979 to 1998. 153 osteoid osteoma cases were registered in the Register of the bone and joint tumors at the Institute of pathology, School of medicine, Belgrade. The tumor was 1,7 times more frequent in males (males 97, females 56). The lesion occured predominantly (50% or 76 cases) in the second decade of life. The youngest patient was 22 months old, the oldest was 54 years old. The most commonly involved bone was femur (64 cases, 41,8%), and the rare locations were: index (6), polex (4), os ilei (1), os pubis (1), clavicula (1). We reviewed 2 (two) cases of osteoid osteoma with recurrent tumors after en-block resection and histopathological identification. In the first case, a 9 year-old boy, curettage was made in 1992., and osteoid osteoma was identified histopathologically. One year after (1993.) the boy had the same symptoms and a radical surgery was made. In the block-resectied part of the bone, we found calcified nidus and a fresh lesion in the surrounding area. In 1998. an en-block tumor excision was repeated, and then the tumor, which has a shape of a band (3,5x1, 0cm), was histopathologically

described. It was a reason to think about differential-diagnosis between osteoblastoma and osteoid osteoma. The size of the first and the second tumor, surrounding sclerotic bone and typical clinical signs suggested osteoid osteoma. The second patient, an 8 year-old male, had two osteoid osteoma surgically removed in 1982. One was 1.5x1.5 cm, and the second was 0.3x0.3 cm. The smaller was situated beside the bigger, one separated with a fibrovascular zone. In 1987. the patient had recurrent specific clinical symptoms; because of that the second en-block resection was made. Histopathologically OO was confirmed.

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Epidermolysis bullosa hereditaria

ABSTRACT

Epidermolysis bullosa (EB) constitutes a heterogeneous group of inherited disorders that produces blister formations in response to a minimal skin trauma. Various types of diseases exist in respect to the mode of inheritance, severity and distribution of skin changes and at the histologic level of skin cleavage. The authors report a case of a 23-month-old boy with bullas occurring since birth on trauma prone regions. The biopsy of his skin was performed with light and electron microscopy, as well as of the prenatal skin of the 22-week-old fetus from the second pregnancy of the same parents. The light microscopy of a fresh bulla showed the subepidermal separation, with intact epidermis in the roof of the blister. In the base of the cleavage, no inflammatory cells were present. Electron microscopy showed that the separation occurred in the area beneath the lamina densa, and the roof was made of the epidermis with preserved lamina densa, lamina lucida and the basal cell plasma membrane with its hemidesmosomes. The diagnosis of dermolytic type of epidermolysis bullosa with a recessive mode of inheritance was made. In the second child, the light and electron microscopy of prenatal skin biopsy, showed no alterations in the skin morphology. For the exact diagnosis, the light and electron microscopy are obligatory and the use of immunofluorescence and monoclonal antibodies are desirable. In families at risk for the occurrence of genodermatosis, the prenatal biopsy of the fetal skin in gestation period 18 to 20 weeks is recommended.

KEYWORDS: Epidermolysis Bullosa + genetics + diagnosis; Mechanobullous disease

INTRODUCTION

Epidermolysis bullosa (EB) constitutes a heterogeneous group of inherited mechanobullous disorders caused by mutation in the gene for collagen VII, that produces blister formation in response to minimal skin trauma (1). It belongs to the group of genodermatosis, and should be differentiated from the epidermolysis bullosa acquisita, which is an autoimmune disorder. The estimated incidence of EB is one infant in 50.000 births, but very severe forms occur once per 500.000 individuals (2). The classification of the various

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The manuscript was received: 15. 03. 2000.

Accepted for publication: 10. 04. 2000.

types of EB is based on: the mode of inheritance- autosomal dominant, autosomal recessive; the level of separation within the skin: intraepidermal, junctional and dermolytic separation; special clinical features: disease severity, presence and absence of scaring; degree of generalization or localization of the process. No classification has been universally accepted at present. Usually EB is divided into four major groups with the subgroups: 1. Nonscaring EB with intraepidermal blisters and dominant inheritance, 2. Nonscaring EB with junctional separation, atrophy and recessive inheritance, 3. Scaring EB with dermolytic separation and recessive inheritance, 4. Scaring EB with dermolytic separation and dominant inheritance (3). Because of the great differences in prognosis the exact identification of the type of EB is very important.

CASE REPORT

The patient was a boy 23-months old with numerous bulla of the skin. Blisters began to appear almost at the time of birth, generalized, but more in easily injurable places (hands, elbows, feet, and knees). Bullas occurred spontaneously and could be provoked by a very weak mechanical trauma, leaving small scars. Nails were dystrophic. The parents were healthy, without any known family history of skin diseases. The pregnancy and delivery were without complications. In the genetic counseling the parents were advised that in the case of the next pregnancy, an early examination should be performed. In the second pregnancy, prenatal biopsy of the fetal skin was performed in the 22nd week and light and electron microscopically analyzed.

RESULTS

Light microscopy of a fresh bulla showed a subepidermal separation, with intact epidermis in the roof of the blister. In the lumen of the bulla the serous fluid was present. In the base of the cleavage, in the papillary dermis no inflammatory cells were found. The diagnosis of non-inflammatory subepidermal bullous disease was made. Electron microscopy showed that the separation occurred in the area beneath the lamina densa, and the roof was made of the epidermis with preserved lamina densa, lamina lucida and basal cell plasma membrane with its hemidesmosomes. In the dermis, at the blister base, the complete absence of anchoring fibrils was diagnosed. The diagnosis of dermolytic (dystrophic) type of epidermolysis bullosa with a recessive mode of inheritance was made. In the second child, the light and electron microscopy of prenatal skin biopsy showed no alterations in the skin morphology. The pregnancy was carried on and a healthy boy was born with only a small superficial scar in his left buttock region, at the previous biopsy site.

DISCUSSION

When analyzing the skin biopsy which contains a subepidermal blister with little or no inflammatory infiltrate, a limited number of disease fall into a differential diagnosis, but still the whole group of non-inflammatory subepidermal bullous diseases must be taken into consideration. For example: bullous pemphigoid, porphyria cutanea tarda, pseudoporphyria, bullous amyloidosis, traumatic blisters ect (4). Although their differentiation does not pose a great problem the determination of the level of separation within the skin is one of the most important tasks. The major subdivisions of EB comprises a group of genetic diseases producing separation in the epidermis (EB simplex group), a group producing separation at the level of the plasma membrane of basal keratinocytes, hemidesmosomes, and lamina lucida (junctional EB group) and a group producing separation at the level below the lamina densa in the subbasal reticular zone (dermolytic or dystrophic group) (5). Anchoring fibrils are adhesive suprastructures that ensure the connection of the epidermal basement membrane with the dermal extracellular matrix. The fibrils represent polymers of collagen VII, the major structural fibril component. Aberration in the network structures (hemidesmosomes, anchoring filaments and anchoring fibrils which form an interconnecting network extending from the intracellular milieu of basal keratinocytes across the dermal-epidermal basement membrane to the underlying dermis) can result in the fragility of the skin. This defective collagen synthesis has been demonstrated in all forms of EB and this line of investigation is very active (1).

CONCLUSION

Although the EB and the rest of the hereditary bullous dermatoses are rare disorders it is necessary to perform the biopsy to make an exact diagnosis, and besides the light and electron microscopy as obligatory methods, the use of immunofluorescence and monoclonal antibodies are desirable. Also in families at risk for the occurrence of genodermatosis the prenatal biopsy of the fetal skin in gestation period 18 to 20 weeks is recommended. Nowadays the DNA from the fetal tissue obtained by chorionic villus biopsy is analyzed.

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Can malignant melanoma be classified into apudomas?

KEYWORDS: Melanoma; Apudoma

Pears (1966) has introduced the acronymous term APUD (Amine Precursor Uptake and Decarboxylation) for the group of cells having as common the histogenetic, cytochemical, immunocytochemical and ultrastructurals characteristics. Later on, in 1979, into the APUD family he introduced also the melanocytes/melanoblasts, and coined the term APUDOMAS for these cells tumours. In view of the belief mentioned earlier, as well as the traditional opinions of other authors about the histogenesis of pigment tumours, the objective of this work were the following issues: cytochemical characteristics of malignant melanomas (MM), enzymohistochemical characteristics of MM - investigation of the cholinesterase activity, immunohistochemical method for detection of a marker (chromogranine) specific for apudomas. Material obtained after the surgery of 20 MM was used. It was fixated in the 10% formaldexyde and in the Bouin's solution. Pseudocholinesterase activity was investigated on the cryostatic sections 10 m thick. The following methods were apllied: cytochemical methods, Grimelius' argyrophyllic reaction (3), Masson's argentafine reaction, Formaldehyde-induced fluorescence, II - enzymohistochemical method for pseudocholinesterase activity investigation (4), PAP method. Studied MM are argyrophyllic (positive) with pronounced argyrophyllic polymorphism. All argyroffilic tumours are simultaneously argentaffilic (positive). Investigating the activity of pseudocholinesterase we observed the enzymatic polymorphism in the MM parenchyma. MMs have all the characteristics included into the APUD concept and their inclusion into the APUD cell group of tumours is justified. Apudomas are the constant object of investigation. Molecular biology has discovered a peptide receptor on apudomas, especially somatostatin receptors (5). Thanks to this fact, a somatostatin analogue called octreotide is successfully used as the hormonal therapy of apudomas. (6) With the fact in mind that MMs are classified into the apudoma-group and that such hormonal therapy has shown results, we argue that new molecular findings will in a future find its adequate therapeutic use.

Archive of Oncology 2001;9(Suppl 1):156.

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Correlation between localization and histopathological characteristics of skin tumors

KEYWORDS: Skin Neoplasms; Neoplasms by site; Neoplasms by Histologic Type; Histopathology

Establishing possible associations between most frequent localization and histopathological characteristics of skin tumors and tumor-like lesions. Histopathological characteristics of 3785 skin tumors and tumor-like lesions were analyzed in relation to their localization. Statistical significance was measured with ANOVA and x2 test. Four most common localizations of excised lesions were the back (9.2%), forehead (4.6%), neck (4%) and hands (3.2%). Benign lesions were statistically more frequent in all aforementioned places, except on forehead, where malignant tumors prevail (67%; $p<0,00001$). Comparing with values found in analyzed population as a whole (adnexal tumors being most numerous-33.5%, followed by epidermal-28.2%, pigmented-20.7% and dermal-mesenchymal-17.5%), pigmented lesions were present significantly more often on the back (44.4%), adnexal on forehead (54.6%), and epidermal on hands (56.7%), while distribution on neck region most closely recapitulated general trend. Basal cell carcinoma (28%), intradermal nevocellular nevi (14.6%), seborrheic keratosis (10.5%) and squamous cell carcinoma (7.9%) were predominant individual histopathological diagnosis, with variations depending on part of the body surface: intradermal nevocellular nevi prevail on the back (27%), basal cell carcinoma were above the average number on forehead (47.7%) and squamous cell carcinoma on hands (25.6%). Statistically significant associations between certain localization and histopathological type and biological behavior of skin tumors exist in analyzed material, possibly due to an action of environmental causative factors as well as predisposition of some areas for development of particular type of skin tumor.

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Biological properties of tumors induced by BHK-21 cell line in hamsters

KEYWORDS: Neoplasms; Vaccines; Carcinogenicity Tests; Cells, Cultured Cell Line, Transformed; Hamsters

One of unexpected complications in animal vaccination is tumor development, like a vaccine-site sarcoma in cats, as described recently. The possibility of human vaccine contamination with oncogenic retroviruses, especially when using a primate tissue as a source of a cell culture substrate, was documented before. The baby hamster kidney (BHK-21/C 13) cell culture, tumorigenic for hamsters, has been widely employed for the production of biologicals for animals. Recently, this cell line has been legalized for human vaccine production by the WHO. One of the tests in current use for examination of the cell culture substrate safety is tumorigenicity in laboratory animals. We examined the biological properties of tumours caused by BHK cells in hamsters. Young adult Syrian golden hamsters of both sexes were subcutaneously, intraperitoneally, intramuscularly and subdurally inoculated with 106 BHK-21/C 13 cells. Giant solitary tumor nodules developed in the place of inoculation 7-14 days later causing death to the animals up to 30 days. The tumor nodules grew expansively and rapidly, and were characterised by central necrotic areas. Cell morphology was fusiform in shape and fasciculated distribution, like in „in vitro“ BHK culture. The inflamatory process did not develop around the tumorous tissue, and the metastases have not been noticed so far. In vivo, only in hamsters, as the biological source of these cells, the inoculation of the culture tissue induces tumors. In contrast to our model, really tumorigenic cell lines produced tumors in animals only after irradiation, antylymphocyte serum treatment or in nude mice without competent cellular immunity. The healthy hamsters rarely develop tumours after the inoculation with mouse neuroblastoma cells (Na 2) or Hep-2 cell lines in similarly experiments. We may conclude that the cells of BHK cell line, as transformed hamster cells, continue to grow as an in vivo culture after inoculation; they neither elicit an immunologic reaction nor do they produce metastases. Because there are not characteristics of malignant tumours and we support the use of BHK cell line for the production of human vaccines, especially rabies vaccine.

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Sex related differences in topographic distribution of skin lesions

KEYWORDS: Skin Neoplasms; Sex Factors; Neoplasms by Site

Analysis of correlation between patients' sex and topographic distribution of different skin lesions. 3785 skin tumors and tumor-like lesions were grouped according to their origin as adnexal (A), dermal (D), epidermal (E) and pigmented (P), and their topographic distribution was analyzed in relation to patients sex. Statistical significance was estimated using (2 test and Fisher's exact test. A/D ratio was 6.0 (1027/171) on head, 0.9 (179/201) on neck and trunk and 0.2 (62/291) on extremities; $p<0.00001$. E/P ratio was 3.0 (113/38) on hands, 2.0 (662/339) on head, 1.5 (142/54) on extremities and 0.5 (152/313) on trunk; $p<0.00001$. On particular localization, variations were extreme: for A/D from 0.09 (1/11) in breast region to 31.00 (31/1) on nose; for E/P from 0.08 (1/13) in sternal region to 43.00 (86/2) on lower lip. Regarding patients' sex, A/D ratio varied from 0.08 (1/12) in gluteal region to 16.00 (16/1) on nose, in female patients, and from 0.06 (2/31) in femoral to 22.00 (22/1) in nasal region, in males. For E/P ratio, variations ranged from 0.06 (1/16) in lumbar region to 9.00 (18/2) on lower lip, in females, and from 0.17 (1/6) on chin to 37.00 (37/1) on hands, in males. On certain parts of the body significant differences in A/D and E/P ratio were found in male and female patients: for A/D on hands 0.1 in females and 0.4 ($p<0.01$) in males, and for E/P ratio on head (1.2 in females versus 4.3 in males; $p<0.00001$), trunk (0.4 vs. 0.7; $p<0.01$) and hands (1.9 vs 6.3; $p<0.01$) Despite pronounced variations, A/D ratio decreases from head to trunk and extremities, whereas E/P ratio increases (although less consistently) in reverse direction, with statistically significant connection to patients sex, particularly on specific localization.

Archive of Oncology 2001;9(Suppl 1):158.

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Age related differences in tumors and tumor-like lesions of the skin

KEYWORDS: Skin Neoplasms; Age Factors; Histopathology

Analysis of age differences in male and female patients with skin tumors and tumor-like lesions. 3785 skin tumors and tumor-like lesions were classified according to their origin and histopathological diagnosis, and correlated with patients' age. Statistical measurements were performed with t-test. Average age of male patients was 53,2 years and 49,9 years of females ($p<0.00001$). Regarding biological behavior of skin lesions, significant differences in age distribution were noticed among benign lesions as a whole (male 43,2 years, female 41,5 years; $p<0.05$), benign pigmented (30,9 vs. 34,7 years; $p<0.01$) and malignant epidermal lesions (63,6 vs. 69,8 years; $p<0.0001$). Considering exact histopathological diagnosis, age differences were found among squmous cell carcinomas (63,7 vs. 69,7 years; $p<0.001$), compound nevi (21,6 vs. 29,2 years; $p<0.05$) and molluscum contagiosum (19,5 vs. 47,3 years; $p<0.05$). Comparing average age of male and female patients with skin tumors on various localizations, statistically important differences were observed in temporal region (62,5 vs. 52,1 years; $p<0.01$), on ears (64,9 vs. 44,2; $p<0.01$), on the neck (51,1 vs. 45,2 years; $p<0.05$) and in axillary region (51,9 vs. 38,5; $p<0.05$). In general, male patients were of older age as a group and among those with benign lesions, whereas females were older in cases that belong to benign pigmented (especially compound nevi) and malignant epidermal (particularly squamous cell carcinoma) lesions. Interestingly, male patients with molluscum contagiosum were much younger than females with the same diagnosis. Statistically significant differences in age distribution related to histopathological type of skin tumors and tumor-like lesions exist among male and female patients, some of them being caused, probably, by environmental and social factors.