CENTRAL NERVOUS SYSTEM PATHOLOGY

Extended abstract
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Myoclonic epilepsies and Lafora body disease: biopsy diagnosis

ABSTRACT

Myoclonic epilepsies represent a large group of heterogenous diseases. The most important disorder in this group is Lafora body disease (LBD). It is characterized by accumulation of intracytoplasmic inclusions named Lafora bodies (LB) in the CNS and some other organs. Biopsy findings of 12 cases LBD are presented. In 2 cases of brain cortical biopsy numerous Lafora bodies were found. In other cases diagnosis was made by muscle (3), peripheral nerve (3) and axillar skin (4) biopsy. All patients suffered from myoclonic epilepsy and other neurological disorders. In addition to routine techniques, special histological and histochemical methods were applied on frozen, paraffin and semithin epon sections. In all cases PAS, PAS diastase, alcian blue, methyl violet, toluidine blue and acid cresyl were performed. In muscle, nerve and skin biopsy specimen Lafora bodies were found in sufficient number. Cortical cerebral biopsy show numerous LBs, laying in the neuronal and glial cytoplsm and their processes or free in the tissue. In the cases of axillary skin biopsies there were abundance of LBs in the epithelial and myoepithelial cells of ducts of sweat appocrine and eccrine glands. In small intradermal nerve branches single LBs were found, too. Definitive diagnosis of LBD and exact differentiation from the other causes of myoclotic epilepsies depends on biopsy. Axillary skin biopsy is more reliable to make a definitive diagnosis of LBD. The abscence of LBs in biopsy specimen does not rule out the diagnosis of LBD.

KEYWORDS: Epilepsy, Myoclonic + diagnosis; Biopsy; Inclusion Bodies

INTRODUCTION

Myoclonic seizures are sudden, brief involuntary muscle contractions, which may affect an individual muscle, a small group of muscle fibers or many different muscles. Myoclonic contractions are commonly found in almost all types of epilepsy as well as in wide variety of diseases of the CNS, including spinal cord (6). In one group of these diseases myoclonic seizures are a clinical sign, which is not dominant amongst many other signs and symptoms. To this group belong many inborn and acquired conditions for example subacute sclerosing panencephalitis, Creutzfeldt-Jacob's disease, some cases of leucodystrophies, lipidoses and many other disorders. The other group consists of those patients in whom myoclonic seizures predominate in clinical picture. This group, termed the progressive myoclonus epilepsies (PME), represents a large group of heterogeneous diseases characterized by severe myoclonus, seizures, and progressive neurological deterioration. The most important and most common in this group are Lafora body disease and Lundborg-Unverricht disease (4,6). Although these two entities, as well as many other conditions within this group are clinically, pathologically and genetically distinguished, exact diagnosis were common dependent on biopsy, because pathological basis of myoclonus is etiologically diverse and pathologically variable (2,5). The prognosis of the wide spectrum of these disorders is various and biopsy diagnosis is very important, particularly in order to separate Lafora body disease (LBD) from other disorders. LBD is an abnormality of carbohydrate metabolism. The underlying enzyme defect is yet unknown. The first clinical sign occur between 10 and 18 years with generalized convulsions, myoclonic jerks and intellectual deterioration and dementia. Death usually occurs 10 to 15 years after onset. The disease is an autosomal recessive disorder. Abnormal carbohydrate metabolism causes accumulation of glucose polymers (polyglucosan) in the CNS and some other organs. The hallmark of LBD is the characteristic intracytoplasmic inclusion named Lafora body (LB) in the neuronal and glial cells of the CNS and in various other cells of the body: peripheral nerves, skeletal and cardiac muscle, liver and in sweat ducts epithelial cells in the skin. The wide variation in the degree of involvement of skeletal muscle and peripheral nerve do not make them a prime choice for biopsy. Liver biopsy and especially skin biopsy appear to be the more reliable to make a definitive diagnosis (1,3-6).

MATERIALS AND METHODS

In this study we present 12 patients with progressive myoclonic seizures and dementia, which were found to have Lafora bodies: 2 brains, 3 skeletal muscles, 3 peripheral nerves and 4 axillar skin biopsies, from totally 19 patients who were biopsied looking for Lafora bodies. In addition to routine techniques, special histological and histochemical methods depending of the tissue were applied on frozen, paraffin and semithin epon sections. In all cases PAS, PAS diastase, alcian blue, methyl violet, toluidine blue and acid cresyl were performed.

RESULTS

In both cases of the cortical cerebral biopsy there were numerous LBs of varying size, homogenous and concentric, laying in the neuronal and glial cytoplasm and their processes or free in the tissue. There was moderate diffuse neuronal loss and gliosis. In the rare single cells there may be several small LBs. In one case of muscle biopsy only 3 LBs were found in the muscle fibres and 1 in a small perimisial nerve branch. In the second case, they were present in about 2% of muscle fibres on a cross section. The third case showed more numerous LBs, but they were very unevenly distributed with tendency to concentrate in the small groups of muscle fibres. All three peripheral nerves (n. suralis) biopsies showed intraxonal LBs in a less number of the paraffin and epon longitudinal and cross sections. In one case in about 30 sections only 3 LB were found. In other 2 cases they were more common and present 1 to 3 per nerve fascicle cross-section on approximately every fourth paraffin section.

Three cases of the axillary skin biopsies showed abundance of LBs in the epithelial and myoepithelial cells of ducts of sweat appocrine and eccrine glands. In one of these cases they were located nearly exclusively in the myoepithelial cells. In the forth case LBs were very rare and single. In many sections no one LB was seen, although numerous glands were present. Single LB was seen in the small intradermal nerve branches in all four cases.

DISCUSSION

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Definitive diagnosis of LBD and exact differentiation from the other causes of myoclonus and epilepsy depends on biopsy, because some patients of this great group of heterogenous diseases have a similar clinical course but LBs are found only in LBD (4,6). Nevertheless, it must be emphasized that Lafora body is not specific for LBD. The generic name for LBs is "polyglucosan bodies" (PB), because they are unusual glucose polymeres. Different names have been given to polyglucosan bodies according to their location. If present in neurons they are called Lafora bodies, in astrocytes - coropora amylacea and if present only in outer part of pallidum - Bieschowsky bodies (3). In the CNS and commonly in the other tissues LBs are obligate in Lafora body disease, adult polyglucosan body disease and Andersen's disease. As sporadic they can be found in a broad range of degenerative neurological disorders. In the central and peripheral nervous system their presence may be related to normal older age (1,3,6). The wide variation in the degree of involvement of skeletal muscle and peripheral nerve do not make them a prime choice for biopsy. Axillary skin biopsy, as our cases show, is more reliable to make a definitive diagnosis of LBD. It must be emphasized that absence of LBs in a biopsy specimen does not rule this diagnosis out (2,5,6).

CONCLUSION

Definitive diagnosis of LBD and exact differentiation from the other causes of myoclotic epilepsies depends on biopsy. Axillary skin biopsy is more reliable to make a definitive diagnosis of LBD. The abscence of LBs in biopsy specimen does not rule out the diagnosis of LBD.

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Tumors of the choroid plexus

ABSTRACT

Tumors involving the choroid plexus can be primary and metastatic. The primary tumors - papilloma, meningioma, carcinoma of the choroid plexus and one metastatic adenocarcinoma, have been presented. The analyses have been done of the autopsy material of 300 choroid plexus from the patients who died between 0 and 94 years of age. The taken samples were coloured with many histochemical method. Our investigation showed that primary and metastatic tumors of the choroid plexus are rare among intracranial tumors and they are almost always localized in the cerebral ventricles. The papilloma is, on macroscopic and microscopic observation, very similar to the normal appearance of the choroid plexus. It is invariably associated with hydrocephalus interior. Heavy calcifications were present in papillomas and meningio-mas and were detected in roentgenograms. Thereby the diagnosis may bee established in living patients and their removal can result in curement. The primary papillary carcinoma with invasion of the adjacent cerebral tissue was also registered. During autopsy any primary malignant tumor was indistinguishable in any organs. Interesting was the case of metastatic bronchial adenocarcinoma in the choroid plexus and many other organs, excluding the brain.

KEYWORDS: Choroid Plexus Neoplasms

INTRODUCTION

Papilloma, primary carcinoma and metastatic tumors in the choroid plexus are rare. Intraventricular meningiomas of the choroid plexus are also very rare unlike the meningiomas situated on the cerebral convexity and other sites, which are most common. Papilloma of the choroid plexus is more frequently found with the children, but has been esta-blished in any age. The difference between sexes is not significant. It is more frequently localized in the IV-cerebral ventricle, but it has also been described in all ventricles. It can vary in size and be of soft consistency, cauliflower-like, of small or big grain surface, pink. In case of the rapid growth it fills the whole area of the corresponding ventricle, penetrating from one ventricle to the other through the existing openings. Histo-logically it is composed of many finger like papillae, which on their surface contain cuboidal or columnar cells. Sometimes, the cells have lashes. The stroma is composed of the vascular connec-tive tissue, sometimes edematous and myxomatous with cysts, psammoma bodies, calcification and the bone tissue. Blood vessels of the stroma vary in number and size. Most meningiomas are located in the lateral ventricles, arising in the glomus of the choroid plexus. Meningioma of the choroid plexus appear earlier in life, but may occur in elderly ages as well. The female preponderance is maintained. In gross appearance meningiomas are encapsu-

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lated, nodular, spherical or ovoid mass, firm, pink or red-brown with granular cut surface. Most meningiomas weigh between 50 and 200 g, but they may achieve as 400 g. One of the reported tumors weighed only 5 g. This small asymptomatic meningioma was detected at autopsy. Heavy calcifications may be present in some meningiomas and may be detected in roentgenograms of the scull. Microscopic study reveals main types of meningioma: epitheliomatous, fibroblastic or fibrous, angioblastic, sarcomatous and mixed. Most meningiomas are of the mixed type. Primary carcinoma of the choroid plexus may be papillary carcinoma and papillary adenocarcinoma. The survival is only a few months after the onset of the symptoms. Solitary metastases in the choroid plexus without cerebral ones are extremely rare. A metastatic carcinoma in the choroid plexus arising within the bronchus, breast, stomach and bowel was described. Metastatic carcinoma must be differentiated from the primary carcinoma.

AUTOPSIED PATIENTS AND METHODS

The analyses have been done on the bases of macroscopic and microscopic observations of the autopsy material from 300 choroid plexus, patients who died between 0 and 94 years of age. The taken samples were coloured with histo-chemical methods with choroid hematoxylin and eosin, Alcian and Turnbull‘ blue, Von Kossa reticulin and Van Gieson.

RESULTS

Papilloma of the choroid plexus

It was a male, 2-year old child. The clinical diagnosis was: Cystis cerebellomedullaris permagna. Hydrocephalus interior. Cra-niotomia posterior et evacuatio cytis. The macroscopic observation during autopsy showed a papillomatous cauliflower-like tumor localized in glomus of the choroid plexus, walnut size, leaning on and being connected with the atrophic parts of the choroid plexus. Papilloma almost completely occupied the lateral ventricle of the left cerebral hemisphere, it was of a soft consistency, pink and reddish. It pushed corpus callosum leftwise, making the third ventricle more narrow, while the right ventricle vas very much widened-hydrocephalus interior. The right hemisphere of the cerebellum was mainly destructed as a consequence of the surgical intervention. Histologically the papilloma was composed of numerous closely spaced laterally and longitudinally cut finger-like papillae, covered by simple columnar cells, placed on the basal membrane under which the vascular connective and edematous stroma was present. The capillary blood vessels of the stroma were enlarged and excessively filled with blood.

Meningioma of the choroid plexus

It was an incidental post mortem findings in a woman 78-years old. The clinical diagnosis was: Status asthmaticus. The macroscopic observation revealed a hardly visible, well encapsulated, firm, small knot, like a pin-head, greyish pink in colour, which was localised in the cystic glomus of the choroid plexus, by the left lateral ventricle. Histological appearance was that of a mixed type of meningioma with fasciculated fibrous structure and fibroblastic cells. Whorls or nests of plump meningocytes, numerous psammoma bodies and small calcifications was also present.

Primary carcinoma of the choroid plexus

It was a male at the age of 20. The clinical diagnosis was: Tumor cerebri. Macroscopic diagnosis after autopsy was: Tumor cereb-ri. Pinealoma? Carcinoma of the choroid plexus? Ependymoma? Infiltratio neoplastica ventriculi III et lateralis. The macroscopic observation during autopsy showed a papillomatous cauliflower-like tumor, soft, greyish-white in colour, indistinctly limited, shadowy in structure, partially necrotic, sized 3x2 cm. The tumor was localized in the third and lateral cerebral ventricles. Invasion of the adjacent cerebral tissue was present. A primary malignant tumor was indistinguishable in any organ. Histologically, the papillary carcinoma was composed of numerous finger-like papillae, with a partial loss of papillary structure, with great nuclear pleomor-phism, abnormal mitoses, cytoplasmatic vacuolation and necrosis. The fibrous connective stroma was slightly present unlike the abundant vascular one.

Metastatic tumor in the choroid plexus

It was a male, 48-years old. The clinical diagnosis was: Renes polycystosi. Neoplasma. Metastases generalisate. The macroscopic observation showed a metastatic tumor in the choroid plexus of the left ventricle. Metastatic knot was ovoid, well limited, firm, white in colour sized 1x1 cm, on cut face shadowy in structure. Almost the same metastases were found in the liver, heart, kidneys, adrenals, spine, ribs, lymph nodes, except the cerebral. Primary tumor was bronchial adenocarcinoma - moderately and poorly differentiated localized in one of peripherally branch of the left main bronchus.

DISCUSSION

Tumors of the choroid plexus are almost always are in the ventricle. Papilloma is invariably associated with hydrocephalus interior. Histologically, papiloma must be diferentiaded from intraventricu-lar papillary ependymoma, Epithelial cells in papilloma are on the basal membrane, above the vascular connective stroma. In papillary ependymoma papillae are formed by plump of many neoplastic ependymal cells, having fibrillary process radiating around the vascular wall, known as a perivascular pseudorosettes. Fibrillary neuroglial tissue serve as a stroma of papillary ependymoma. In our case of mixed meningioma many psamomma bodies are present. Psamomma bodies with calcifications may be detected in rentgenograms of the skull. Criteria for differential diagnosis of a primary carcinoma of the choroid plexus and papilloma are: loss of characteristic papillare structure, numerous mitoses with cellular pleomorphism, necrosis, invasion of the adjacent cerebral tissue. Sometimes invasion of the serroun-ding structures is a more reliable indication of malignant potential than cytological considerations. A stroma of the vascular connective ti-ssue is important for excluding an ependymal nature of the lesion.

Metastases of bronchial carcinoma in the choroid plexus are extremely rare. Less common sites of metastases of the bronchial carcinoma are the myocardium, pancreas, ovaries, intestined, testis, nails, nose and foot-sale. In our case it is interesting that a common cerebral metastases was excluded.

CONCLUSION

The papilloma is, on macroscopic and mic-roscopic observation, very similar to the normal appearance of the cho-roid plexus. It is invariably associated with hydrocephalus inte-rior. Heavy calcifications were present in papillomas and meningio-mas and were detected in roentgenograms. Thereby the diagnosis may bee established in living patients and their removal can result in curement. The primary papillary carcinoma with invasion of the adjacent cerebral tissue was also registered. During autopsy any primary malignant tumor was indistinguishable in any organs. Interesting was the case of metastatic bronchial adenocarcinoma in the choroid plexus and many other organs, excluding the brain.

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Xanthogranulomas of the lateral ventricles choroid plexus

ABSTRACT

We present an autopsy case of a bilateral xanthogranuloma of the lateral ventricles choroid plexus which was asymptotic and CT invisible, accidentally discovered on autopsy. A male patient, 48 years old, with diabetes mellitus type II, adipose liver and destructive cardiac muscle lipomatosis, died in the endotoxic schock due to a purulent, abscedent bronchopneumonia and purulent, haemorrhagic meningitis.

KEYWORDS: Choroid Plexus + pathology; Granuloma + pathology; Diabetes Mellitus, Non-Insulin-dependent; Xanthomatosis

INTRODUCTION

Xanthogranulomas of the choroid plexsus (XGCP) of the cerebral ventricular system are rare entities. They are symptomatic or asymptomatic, and may occure in the third ventricle causing hydrocephalus with massive hypothalamic dysfunction, a sudden deterioration and death. Some authors report focal areas of abnormal T2 signal in tegmentum and middle cerebellar peduncules (MR appearance), suggesting posterior fossa lesions. They, most likely, correspond to cholesterol granulomas of extracranial provenance. The male preponderance in XGCP has become statistically significant. XGCP and XCP - xanthomas of the choroid plexsus are closely related to each other, but represent two different, independent lesions. XCP are closely related to tendon xanthomas of the skin. XGCP, in the other hand, to cholesterol granulomas of external provenance. Radical extirpation should be the treatment of choice in the third ventricle.

CASE REPORT

A male patient 48 years old, a bus driver, asked for a doctor for sudden neck pain and loss of conciousness. He had a ten-year history of diabetes, so he was admitted to the Clinic of Endocrinology. No signs of neurologic disturbance were present, but EEG of the cerebral activity was nonmodulated, unsynchronised and disorganised. It was in a and b spectrum, without u - slow activity. CT revaled only dilatated lateral ventricles and an old vascular insult site. The patient then suddenly developed bronchopneumonia and meningeal signs appeared. So, he was transported to the Clinic for Infectious Disease for further treatment. But, he didn‘t respond to any antibiotic therapy and within three days he died. On autopsy, in lateral ventricles, bilateraly, we found accidentaly, tumors of a hazel size, rolled into the choroid plexsus, firm and with white calcifications on the surface and inside. The ventricles were dilated, but not obstructed. Microscopically, the tumor contained a lot of crys-

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taline, needle shaped structures, or clefts in paraffin, foamy cells, lymphocites and macrophages with haemosiderin. A huge number of spheric calcifications were also present. Microscopic examination of other organs revealed fatty liver, amyloidosis of pancreatic insulas, severe lipomatosis of the cardiac muscle, purulent, abscendent bronchopneumonia and accute purulent, haemorrhagic meningitis. We have concluded that the patient died of an endotoxic schock, finally developing pulmonary oedema.

DISCUSSION

The metabolic disorder of a diabetic type induces a lipid disturbence and, most probably, hyperlipidemia (no clinical evidence), causing these rare tumors, but without signs of obstructive hydrocephalus. Because of the rare occurrence and uncertain behaviour, it remains unclear whether these solitary CNS lesions induce the rising of the intracranial pressure what may account for a depression of the respiratory center in the medulla oblongata and an infection of the lungs, which then propagates to the brain.

CONCLUSION

Xanthogranuloma is a rare benign cerebral tumor, not classified by WHO. It may be symptomatic or asymptomatic, depending on its localisation. The analysis of rather poor literature data, has revealed hyperlipidemia in those patients. The Juvenile Xanthogranuloma makes an exeption. It is believed to be in some connection with a histiocytic proliferative disorder, or systemic non-Langerhans cell histiocytosis. Some authors suggest the term XGCP should be replaced by the term CHOLESTEROL GRANULOMA.

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Meningioma infiltrating the parietal bone and subcutaneous tissue of the skull

ABSTRACT

In this study, the authors describe a case of fibroblastic meningiom, primarily localised in the parietal part of dura mater, which infiltrates and destroys the bone, subcutaneous tissue partly ulcerating them. This alteration is understood as skin basalioma, and it has been surgically treated three years after the first sign of a change of the skin alteration. The surgical treatment included radical excision of the altered skin, bone and dura mater. The one year post-operative periods was regular, and no local recidive occurred up to date.

KEYWORDS: Meningioma; Neoplasm Invasiveness; Skull Neoplasms + secondary

INTRODUCTION

Meningiomas are tumours of the Central Nervous System that develop relatively often. They originate from the specialised meningoendotelial cells of arachnoidea, therefore, they are localised outside of the brain. 20% of all primary cranial cavity tumours belong to meningioma (1). Their most common sites in frontal part of cranium are hemisphaere convexity, falx, small wing of the sphenoid bone and sulcus olfactorius. Brain chambers, cerebellopontine angle, foramen magnum and area of medulla spinalis are clinically important locations for meningioma, although they develop very rarely there. They are usually solitary, but multiple tumours may also develop, however, they are mostly connected to von Recklinghausen's neurofibromatosis, type 2 (2). Small meningeal nodule may develop in skin or subcutaneous tissue of the skull, paravertebral region, mostly in childhood, without noticing the intra-cranial meningioma (3). Regarding their characteristics, they are benign, slow-growing, localised tumours, non-infiltrating but compressing the brain. Infiltration of mesenchymal tissue is rare without malignant characteristics from cytological point of view. Invasion of cranial bone marrow very often stimulates osteoblastic proliferation as well as their hyperostosis. Infiltration may spread into pericranium and m. temporalis. Lower frontal meningioma often infiltrate into orbit, n. opticus and external eye muscles (4,5). According to histology, classification of tumours originating from meningoendotelial cells is the following: meningioma meningoendothelial, fibrous (fibroblastic)

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meningioma, transitional (mixed) meningioma, psammomatus meningioma, angiomatous meningioma, microcystic meningioma, secretory meningioma, clear cell meningioma, choroid meningioma, lymphoplasmocyte-rich meningioma, metaplastic meningioma, atypical meningioma, papillary meningioma, anaplastic (malignant) meningioma (6). Anaplastic malignant meningioma show very clear malignant cytological picture, high mitotic index, brain tissue infiltration, and abundant necroses (4-6).

CASE REPORT

Š.M. female, 60, from Novi Grad (Blatno), a housewife. At the age of 23, fell from the horse-drawn carriage when her head and left ear were injured. The operation on her left ear was performed at Bihać hospital where she was treated then. As a consequence, she has had poor hearing to that ear ever since. No child or hereditary diseases. The illness has started 3 years ago, when a small red excrescence was noticed on a skin of the skull, which hurted and bleeded while combing. Since January 1998, she has noticed faster growth of the excrescence, and in April 1998 visited doctor for the first time in her town, followed by referring her to a Plastic Surgery Clinic. During the check up, an ulcerous tumour was noticed in the right parietal part, 8x8 cm with elevated borders and white hairy strata. The patient is neurologically average. The working diagnosis: Tumor cutis regio parietalis lateris dextri (Basalioma susp. ?). The patient is hospitalised at the Department of Plastic and Reconstructive Surgery, where she was prepared for the operation. The operation included radical excision of the skin in the tumour area up to healthy skin, then the tumour of the part of the bone was removed up to healthy bone, as well as the tumour alteration in dura mater. Brain mass seems unchanged. Dura mater was reconstructed from the surrounding periosteum, skin defect was mended by local skin part, and secondary region was covered by the free skin transplant from the upper leg following Thiersch's method. Pathohistological finding: Material was submitted in three separate bottles (I, II, III), fixed in 10% formalin. Material in a Bottle I contains a ring form skin sample, 8x8x1 cm. The skin ring is covered with hair. A skin defect, 4 cm in a diameter, is in a central part of a sample. Along the cut, there is grey-white tissue, of a solid consistence, localised close to the skin defect, where the distance is at least 1 cm of the resection border. Histologically, the tissue examined in 4 histologic cuts, consists of the skin, subcutaneous fat tissue, and tumour tissue - partly necrotic, made of spindle formed cell bundles with uniform, oval nuclei without atipia and mitotic activity. Tumour surrounding area is infiltrated with neutrophil cells and macrophags. Stroma of the tumour consists of collagen, reticuline fibres and blood vessels .

Dg: MENINGIOMA FIBROBLASTICUM NECROTICUM ET ULCERATUM CUTIS

Material in a Bottle II consists of several bone fragments, up to 3 cm. Histologically decalcificated tissue is made of usual bone elements, partly covered with tumour tissue creating finger-like convexities in a bone tissue. Tumour consists of the same morphologic elements as in Paragraph I.

Dg: MENINGIOMA FIBROBLASTICUM INFILTRANS OSSIS CUM OSTEOLYSIS.

Material in the Bottle III is a plate form cut of dura mater, 3x3 cm, greyish colour, partly grey-white colour, of a solid consistence.

Histologically, the tissue consists of dura mater elements, mostly with tumour tissue of the same histological characteristics as in a Paragraph I. In the tumour itself, there are single psammoma bodies .

Dg: MENINGIOMA FIBROBLASTICUM DURAE

Post-operation period, one years was regular, the patient has been monitored in the out-patient department (primary health care institution), lesion site has appropriately been healed, no post-operation sequelas nor recidives have been noticed, no signs of neurological insufficiencies.

DISCUSSION

Meningioma are intra-cranial tumours, which frequently develop. They develop more often in female population (3:2). Trauma of head is considered an important ethiological factor for meningioma development. If there are no cytological atypia and mitosis of the meningioma infiltrating into dura mater, osteodestruction to skull bones, and invasion to subcutaneous tissue of the skull; then this meningeom is not considered malignant (4-6). Rarely meningioma have biologically malignant characteristics (1.76%), and 43% of them have extracranial metastases (7). There are cases described in the literature such as ectopic meningioma in cavum nasi, sinus maxillaris, orbit, ear, lungs (4,8). Yugoslav authors describe a meningeal tumour with miliary lung metastases (9). Most meningioma are treated surgicaly, and x-ray treatment is not of a significant importance in their treatment.

CONCLUSION

Meningiomas are tumors of the central nervous system that develop relatively often. 20% of all primary cranial cavity tumors belong to maningiomas. They are benign, slow-growing, localised tumors. Rarely, meningioma infiltrate into skull.

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Case report
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Histological and immunohistochemical analysis of the ganglioglioma of the vellum medullare superior

ABSTRACT

Ganglioglioma is a slow growing tumor, often benign, composed of both ganglion and neoplastic glial cells (astrocytes). A 15-years old boy with a six years history of headache, disturbed gait, visual problems and memory deficit, was for the fist time admitted to hospital. He died one day later with symptoms of increased intracranial pressure. The autopsy was done and the brain was prepared for neuropathological investigation. The speciments for microscopical analysis were stained with H&E, Gomori reticulin, Cresyl violet, Klüver-Barrera, PAS and immunostained with GFAP, Synaptophysin and Ki-67. Macroscopically, there was tumor (1,5 cm in diameter) of the vellum medullare superior. It infiltrated quadrigeminal lamina, tegmentum mesencephali and pontis and partially occupied Sylvius aqueduct and forth ventricle with a consequent anterior symmetrical hydrocephalus. Microscopically, the tumor diagnosed as ganglioglioma (WHO grade II) was composed of neoplastic ganglion and glial (astrocytic) cells. Ganglion cells, were, dysmorphic, mostly large, often bi- or multinucleated. synaptophysin-possitive with visible Nissle substance. Astrocytic component was fibrillary and strongly GFAP-possitive. Nuclear labeling for Ki-67 was observed in the astrocytic component with a relatively low (less than 1,5%) labeling indices. Our case represents the slow growing ganglioglioma of vellum medullare superior (brain stem) with a relatively long duration (6 years) prior to death. According to the literature data, for tumors involving this region the mean duration of symptoms before diagnosis is usually shorter (1,5 years). The infiltrative character of tumor was not correlated with aggressive behavior.

KEYWORDS: Ganglioma; Brain Neoplasms; Brain Stem; Immunohistochemistry

INTRODUCTION

Ganglioglioma is a neuroectodermal tumor composed of both ganglion and neoplastic glial cells (astrocytes). It shares common characteristics with gangliocytoma the neoplasm consisted of mature ganglion cells alone. Ganglioglioma occurs most frequently in children and young adults with a little predominance in male. In general, it is a slow growing tumor. The duration of symptoms before diagnosis may be from 1 month to 50 years. The most common location is temporal lobe with epilepsy as a presenting clinical symptom. In fact, ganglioglioma represent the most common neoplasm in the patient with medically intractable temporal lobe epilepsy. Besides the temporal lobes it may occur throughout the CNS, while the uncommon sites include cerebellum, pineal gland and spinal cord (1). Here, we present the histological and immunohistochemical analysis of the ganglioglioma of the vellum medullare superior.

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CASE REPORT

A 15-years old boy, according to the heteroanamnestic data, had a history of headache, disturbed gait, slowly progressive visual problems and memory deficit, six years prior to death. A day before fatal outcome he was for the first time admitted to the hospital. The patient died with symptoms of increased intracranial pressure (severe headache, vomitting), malaise and immobility. The autopsy was done and the brain was performed for the neuropathological investigation after the formalin fixation. The speciments for microscopical analysis were stained with H&E, Gomori reticulin, Cresyl violet, Klüver-Barrera, PAS and immunostained with GFAP, Synaptophysin and Ki-67.

RESULTS

Grossly, in the region of vellum medullare superior there was an ovale tumor, 1,5 cm in diameter. It infiltrated the superior and lateral parts of the pontine tegmentum and partially occupied the lumen of the forth ventricle. Surrounding cerebellar tissue was compressed, but not infiltrated. Rostrally, the tumor infiltrated quadrigeminal lamina and tegmentum mesencephali. Mesencephalon was deformed and larger. Sylvius aqueduct was partially filled and obstructed by tumor tissue with a consequent anterior symmetrical hydrocephalus.

Microscpical findings: The tumor was composed of admixed neoplastic ganglion and glial (astrocytic) cells. Ganglion cells, often concentrated in small clusters, were dysmorphic, mostly large, often bi- or multinucleated with visible Nissle substance and occasionaly visible neuritic processes. The astrocytic component was fibrillary. In the stroma there was network of reticulin fibres and perivascular lymphocytic infiltration. The immunostains demonstrate the expression of synaptophysin in ganglion cells while the astrocytic component was strongly GFAP-possitive. Nuclear labeling for Ki-67 was observed in the astrocytic component with a relatively low (less than 1,5%) labeling indices. The diagnosis of ganglioglioma (WHO grade II) was made.

DISCUSSION AND CONCLUSION

In our case, the benign ganglioglioma of the vellum medullare superior (WHO grade II) with low (less than 1,5%) K-67 labeling indices show the tendency to infiltrate the surrounding structures of the brain stem. However, this infiltrative tumor characteristic was not correlated with its aggressive behaviour. It is well known that ganglioglioma may extend locally into adjacent leptomeninges or the glial component may give rise to an infiltrative appearance at the border between tumor and brain parenchyma. According to the clinical follow-up, the ganglioglioma behave in a benign fasion and lend itselves to surgical resection (2). Malignant ganglioglioma however have been documented. Malignant change most often involve the glial component, which eventually assumes the features of glioblastoma (2).

Histological WHO grade of ganglioglioma depend on the astrocytic component of ganglioglioma. It may be pilocytic (WHO grade I), fibrillar (WHO grade II) or anaplastic (WHO grade III). Ki-67 labeling indices, involving only the glial component, are usually relatively low (1-2%) even in the cases of anaplastic ganglioglioma (3,4). Increased frequency of Ki-67 labelling may indicate aggressive tumor behavior and tendency to recurrence (5). However,

the correlation of anaplasia with outcome is inconsistent and this fact can help in elucidation that ganglioglioma may have clinical stability with survival for many years. Our case represents the slow growing ganglioglioma of vellum medullare superior (brain stem) with a relatively long duration (6 years) prior to death. According to the literature data, for tumors involving this region the mean duration of symptoms before diagnosis is usually shorter (1,5 years) (1).

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Pontine capillary telangiectases: report of two cases

ABSTRACT

Capillary telangiectases are composed of multiple dilated capillaries with intervening brain parenchyma. This vascular malformation is very rare and it is found most frequently in the pons. We report our two cases with that location. Two brains were fixed in 10% buffered formaldehyde. The specimens for microscopical investigation were embedded in paraffin and stained with the following methods: H&E, Gomory's reticulin, Masson's trichrome, Van Gieson elastica, Masson Fontana, Von Kossa, and Perl's reaction for iron. Immunocytochemical staining for GFAP using LSAB+Kit and DAB was also performed. Grossly, dark brown discoloration measured about 1,5 cm in diameter was found in the left pontine basilary region of the first case, and at the level of right superior olivary nucleus in the second case. Microscopically, in both cases the lesion was composed of numerous, dilated, blood-filled spaces, which were surrounded by thin layer of reticulin. Their walls were devoid of both smooth muscle cells and elastic fibers, but many of them contained fine linear calcification. The vessels were separated by intervening neural tissue, which showed moderate amount of fibrillary gliosis and slight axonal degeneration. The neurons did not appear abnormal , but some of them contained Von Kossa positive fine granular pigment in their cytoplasm. In one of our cases there was signs of recent hemorrhage. Some previous studies indicate that sometimes there is calcium in the wall of capillary teleangiectatic blood vessels but they did not mention the presence of calcium pigment in the neuronal cytoplasm as we found in our cases.

KEYWORDS: Telangiectasis; Pons; Neurons; Calcium; Glial Fibrillary Acidic Protein

INTRODUCTION

Vascular malformations of the central nervous system are congenital anomalies of blood vessels that are result of disordered mesodermal differentiation between the 3rd and 8th weeks of gestation. Virchow has given first classification of these angiomatous anomalies in the middle of the 19th century (1). The more recent classification proposed by McCormick in 1966 describe five anomalies, namely the telangiectasia, the varix, the cavernous angioma, the venous angioma and the arteriovenous malformation. The clinical presentation of these different CNS vascular malformations can overlap and they represent the combination of location, morphology and etiology. V. R. Challa et al. in 1995 (3) gives the last modified classification according to

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all these factors. The overall incidence of these malformations in autopsy material ranges from 0.1% to 4% in different series (4). Telangiectasis literally means a single dilated vessel. In practice, a single lesion composed of multiple dilated capillaries with intervening brain parenchyma has been called capillary telangiectasis. They can occur singly or multiply or in association with other malformations. Capillary telangiectasis is predominantly encountered in adults from the fourth to the eight decades. There are no differences between sexes. Capillary telangiectasis are usually small (less than 2 cm) and asymptomatic.They are most frequently found in the basal region of the pons, but they can also occur in the other parts of the brain, the cerebellum and the spinal cord. Spontaneous hemorrhage is an extremely rare complication of capillary telangiectasis.

MATERIALS AND METHODS

Brain from two cases (72 years old male with clinical diagnosis of right-sided hemiparesis and cerebrovascular insult and 70 years old female with clinical diagnosis of paranoid psychosis and coma) were fixed in 10% buffered formaldehyde. Multiple sections of the brainstem and the specimens of other representative parts of the brain were embedded in paraffin and stained with the following methods: H&E, Gomory's reticulin, Masson's trichrome, Van Gieson elastica, Masson Fontana, Von Kossa, and Perl's reaction for iron. Immunocytochemical staining for GFAP using LSAB+Kit and DAB was also performed.

RESULTS

Grossly, the most important lesion was found in the pons of both cases as dark brown discoloration resembling hemorrhage, measuring about 1,5 cm in diameter. In the first case it was located in the basal region of the upper pons, predominantly in the left lower quadrant and in the second case it was in the basal pons at the level of right superior olivary nucleus. Microscopically, in both cases the lesions were composed of numerous, thin-walled, endothelial-lined, blood-filled spaces of slightly varying diameter, surrounded by thin layer of reticulin. Silver impregnation and trichrome stainings reveals the capillary nature of these vessels devoid of both smooth muscle cells and elastic fibers, but many of them contained fine mostly linear deposition of calcium. The vessels were separated by intervening pontine parenchyma in which neurons did not appear abnormal, but some of them contained Von Kossa positive (Masson Fontana and Perl's negative) fine granular pigment in their cytoplasm. Also, in both cases there were signs of slight axonal degeneration, and immunocytochemical staining on GFAP revealed moderate proliferation of fibrillary astrocytes and their processes between capillary telangiectasis as well as in the surrounding region. In the first case there was signs of recent hemorrhage.

DISCUSSION

Clinical presentation of capillary telangiectases is very variable (5). From the literature data (4,5) it is known that capillary telangiectases may cause neurologic symptoms by hemorrhage into malformation or less commonly because of their size. Our cases were clinically with right-sided hemiparesis and psychosis respectively. Capillary teleangiectases with signs of recent hemorrhage, was responsible for neurological signs in our first case. A point distinguishing capillary telangiectases from cavernous hemangiomas is the presence of brain parenchyma between dilated blood vessels and absence of gliosis, hemosiderin pigment, siderophages and hyaline thickening of vessel walls with calcifications. Previous studies(4,5) indicate the possibility for calcification of vessel walls in capillary teleangiectases. We found it in both of our cases, and beside that, fine granular Von Kossa positive (Masson Fontana and Perl's negative) calcium pigment was present in the cytoplasm of otherwise normal-appearing neurons inside the lesions. We did not find literature data about this feature. In the one case of pontine teleangiectases Teilmann described melanotic pigment in many of nerve cells in the nuclei pontis. The exact nature of the capillary teleangiectases is uncertain. Challa et al. studied small capillary teleangiectasis in laboratory with serial celloidin sections stained for alkaline phosphatase (AP) enzyme to confirm their origin. They showed no AP activity in the endothelium of these vessels, suggesting that they are functionally venules, which are normally negative for AP.

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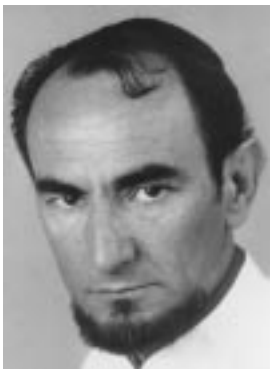
Patohistological and immunohistochemical diagnostic of the spongiform encephalopathy

KEYWORDS: Creutzfeld-Jakob Syndrome; Scrapie; PrPSc Proteins; Encephalopathy, Bovine Spongiform; Histocytochemistry

Spongiform encephalopaties are transmissible degenerative diseases of the nervous system associated with long incubation period, slow and progressive course of the disease, characteristic spongiform changes of the nervous system and absence of immunological respons . Examples of these diseases include Creutzfeld-Jakob disease (CJD) and kuru in humans, scrapie in sheep and goats as well as bovine spongiform encephalopathy (BSE) in cattle. The pathological features of these diseases are vacuolation, astrocytosis, neuronal loss and, in a subset of cases, amyloid plaque formation. The vacuolar changes are manifested as either vacuolation of neuronal pericarya or grey matter neuropil. Other forms of neuronal degeneration included chromatolysis, neuronophagia and hyperchromatic shrunken neuron are considered to be less significant. Neuronal loss could be shown, but only by the application of morphometric methods. The lesions always appeared to be bilaterally symmetrical. The vacuolar tended to be accompanied by glial reaction. In vacuolated areas, there is a clear increase in both the size and number of glial nuclei. On morphological grounds, such nuclei seemed to belong predominantly to reactive astrocytes, undergoing hypertrophy and hyperplasia. The accumulation within the CNS of pathological isoform of the protein, PrP, is now a well accepted fundamental neuropathological feature of the scrapie- like disease. The detailed topographical and cellular localisation of PrP accumulation and its relatinoship to morphological changes could be shown in immunohistochemical preparations. The alterations are most common in the gray matter of the brain stem and often a diagnosis of scrapie and BSE can be made by examining section of the medulla alone.

IN MEMORIAM



Academician Professor Dr Vojislav Vuzevski, first honorary international member of the Yugoslav Association of Pathologists

(1932-1999)

Vojislav Vuzevski was born on December 11th 1932 in Kladovo, Macedonia. His father Dušan, was a professor in a high school and his mother Viktorija a teacher. He finished the high school in Skoplje in 1951. He graduated from the Medical Faculty, Skoplje in 1960, and was elected Assistant professor of Pathology in 1963. He passed a pathology specialist's exam in 1967. From 1963 to 1967 together with Professor dr Dragoslav Miletić he conducted practical teaching classes at a newly opened School of Medicine, Institute of Pathology, Niš. During 1966 and 1967 as the holder of Fulbright foundation scholarship he was on expert and scientific advanced course at the Medical Faculty Pitsburg and Veteran Administration Hospital, Pitsburg, USA. There, he did the research in a new field of medicine at that time the implementation of electron microscopy in clinical and experimental pathology.

From 1969 he was employed at the Institute for Clinical Pathology, Erazmus University in Rotterdam (Netherlands) as Senior research fellow and from 1985 as Associate professor. In 1976 he was confered a doctor's degree on medical sciences at the Erazmus University with the thesis " Ultrastructural Basis of Acute Renal Allograft Rejection". From 1988, at Erazmus University he was the head of the Department for diagnostic electron microscopy. He had an adaptation crises in Netherlands with great nostalgy for Macedonia and Serbia.

On June 26th 1997 he was elected a member of the Macedonian Academy of Sciences and Arts and on October 23rd 1997 a foreign member of the Serbian Academy of Sciences and Arts-SASA (the proposal came from academicians V. Kanjuh, Z. Petrović and corresponding member V. Bošnjaković). He was a member of the International Academy of Pathology-British Division; Society for Cutaneous Ultrastructure Research; Royal Microscopic Society of Great Britain and Nederlandse Vereniging voor Electronen Microscopy.

Scientific activities of Academician Vuzevski included wide implementation of electron microscopy in the clinical and experimental medicine, especially in research of histogenetic origin of tumors and their biological characteristics. He studied ultrastructural differentiation of tumor cells, composition of cytoskeleton and extracellular matrix, cell's adhesion molecules and their role in invasive and metastatic tumor characteristics. He was the first in the world to give the following contributions to the medical science:

-a full description of ultrustructural morphology of peripheral nerve tumors and dermatofibrosarcoma protuberans,

-the review of parallel electron-microscopic characteristics of myxoid soft tissue tumors with the description of new cell types in intramuscular myxomas;

-the review of evolution of morphological changes in transplanted kidney during acute rejection by electron microscopy.

He published 270 scientific works (35 in Yugoslavia) with 29 cited 600 times, according to Science Citation Index. His works were also quoted in 20 medical textbooks and scientific monographies.

He is the author of the following books published in Yugoslavia: "The basis of experimental and clinical transplantation" publ. Naučna Knjiga, Belgrade, 1989 and Lačković V, Bumbaširević V. and Vuzevski V: Histological atlas, publ. "Vladimir", Belgrade, 1995. He is the author of the following books published abroad: "Ultrastructural basis of acute renal allograft rejection" Acad. Thesis Erazmus Univ. of Rotterdam, 1976, Publ. Meinema-Delft 1976 and "Diagnostic histopatologic kult", Textbook edit. Fak. Kedokteran Univ. Indonesia Jakarta, 1988. He is the co-author in 4 books and has 8 chapters in other authors' books.

He was connected with Serbia and Yugoslavia by a longstanding co-operation. He was the member of the Working group for cardiovascular pathology of the Yugoslav Association of Cardiology. In SASA, he gave two lectures ("Modern approaches to etiopathogenesis of atherosclerosis" and "Electron microscopy of lung tumors") and an introductory lecture "Electron microscopy in clinical medicine - expensive toy or valuable method". Also, he participated in two scientific projects:

with Academician V. Kanjuh and corresponding member of SASA M. Ostojiž "Histopathological and electron-microscopic characteristics of coronary artery lesions" (he was the member of Academician V. Kanjuh's scientific team for the investigation of pathologic morphology and morphologic-clinical correlation of cardiovascular diseases) and with Academician V. Pantić "Ultrastructural changes of hypothalamus cells under the influence of gonadal steroids".

At the Military Medical Academy, Medical Faculty in Belgrade (elected "Professor by invitation") and the Serbian Society of Physicians he gave lectures by invitation from the field of tumor electron microscopy, especially tumors in AIDS syndrome. Several associates from Belgrade and Novi Sad Medical Faculty had research visits to his Department for electron microscopy at the Erazmus University, Rotterdam. His electron microscope was always the best at the time and isolated from all sounds and shocks in the world of "endlessly small" where he spent his fruitfull scientific investigations.

Despite sanctions against FRY, he co-operated with and visited Serbia and SASA. At the 6th Congress of renovated Yugoslav Associations of Pathologists, 1994. in Zlatibor, he was elected the first honorary international member of the Association. He participated at the 7th Congress in Podgorica and Budva in 1996 and 8th Congress in Sremska Kamenica 1988. (with excellent "slide seminars"). He is the co-author in two chapters in the medical textbook by S. Nedeljković, V. Kanjuh, M. Vukotić "Kardiologija", Beograd, 1994. The last work in Serbia was "Kaposi sarcoma and AIDS" (V. Vuzevski, V. Kanjuh and E. Stolz) printed in Glas Odelj. Med. Nauka SASA, 1998.

During NATO bombing of Yugoslavia, unexpectedly and almost impercetibly, he faced a hopeless health problem (carcinoma of coecum with liver metastasis). Despite that, he was interested in the consequences of bombing (bombing of the Institute of Pathology, Medical Faculty Niš, non-functioning electron microscope due to haevy detonations etc.) but never mentioned his health status. According to the words of his wife Radmila (a Serb, graduated at the Philologic Faculty, group for English language and literature, Belgrade) and daughter Ana (a lawyer, finished the Law school in Leiden) "he knew that we had rough time and didn't want us to worry about his problem".

He died on Ocotober 7th, 1999 in Rotterdam, where he was burried. The writer of this text organized and spoke at the following commemorations: Chair of Pathology, School of Medicine (in English), Belgrade on October 11th 1999; VII meeting of the Department of Medical Sciencies SASA on October 27th 1999 and Meeting of the Section for Pathology, Serbian Society of Physicians on Novembar 3rd 1999 in Belgrade. He also wrote a necrologue for 1999 SASA Annual book, Belgrade, SASA, 2000.

Academician Vojislav Vuzevski was a pathologist-scientist with international reputation, one of the leading Netherland's and European pathologist and a great friend of Serbian people, a highly appreciated professor and associate of Serbian pathologists, Yugoslav Association of Pathologists and SASA.

Academician Vladimir KANJUH