CARDIOVASCULAR SYSTEM PATHOLOGY

Extended abstract
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The expression of PECAM-1 on vascular and endocardial endothelial cells from surgically excised mitral valves

ABSTRACT

PECAM-1 has the distinctive feature of being expressed on several of the major cell types associated with the vascular compartment. This makes it iniquely positioned to mediate multiple and important cell-cell interactions involving platelets, leukocytes and endothelial cells, and may represent a potential target for new therapeutic agents. Morphological and immunohistochemical studies were performed on 20 human mitral valves, taken from 12 males and 8 females, mean age was 59 years. Adhesive molecule the PECAM-1 was detected with PAP method on endocardial and vascular endothelial cells of mitral valves. We observed that only a group of endocardial endothelial cells expressed the tested adhesive molecule. an intensive expression on PECAM-1 was visible in the mitral valve with numerous ssmall blood vessels. Smooth muscle cells located nearbz the nexlz created blood vessels, also shown intensively positive reaction on PECAM-1. Immunoreactivity of PECAM-1 is distinctly intensive of endothelial cells of small blood vessels of the valves stroma. Endothelial cells of the stroma of newly created blood vessels shown a weak of immunoreactivity against PECAM-1 in comparison to small diametar blood vessels. Intensive imunoreactivity against PECAM-1 shown endothelial cells of stromal vessels surrounded with infiltration of mononuclear cells. The most intensive reactivity of PECAM-1 shows endothelial cells of small blood vessels of valves, stroma and endothelial cells of the stromal vessels surrounded by mononuclear cells.

KEYWORDS: Heart Valve Diseases; Antigens, CD31; Immunohistochemistry; Endothelium, Vascular

INTRODUCTION

Many changes in the classification of cardiovascular disease during the twenteith century reflect a changing etiology of diseases, clinical comprehension and technological advances. In particular, the etiology of valvular disease has changed dramatically in the last five decades (3). The significant reduction of acute rheumatic fever and its sequelae, and the recognition of nonrheumatic causes of valvular disease are responsible for the metamorphosis in the etiology of valvular disorders (6). PECAM-1 has the distinctive feature of being expressed on several of the major cell types associated with the vascular compartment (1). This makes in uniquely positioned to mediate multiple and important cell-cell interactions involving platelets, leukocytes and endothelial cells (4,5). Thus, PECAM-1 may represent a potential target for new therapeutic agents directed at a variety of pathological states. The wide distribution of PECAM-1 among vascular associated cells suggested that it may have a number of important physiological functions. The ability of anti-PECAM-1 antibodies to block normal endothelial cell-cell contacts ind influence cell migration point to a role in angiogenensis and wound healing (1). PECAM-1 may also contribute to early cardiovascular development (2).

MATERIALS AND METHODS

This examination was performed on 20 surgical excised mitral valves, taken from 12 males and 8 females the mean age was 59 years. Mitral valves selected for histological and imunohistochemical examination were fixed in 10% neutral formalin for 18 hours and absolute methanol for 24 h and embedded in paraffin. Paraffin sections were stained by haematoxilin-eosin (HE), Periodic-acid Shiff (PAS), alcian blau (AB), Masson, Weigert-van-Gieson, Paff-Halmi and peroxidase-antiperoxidase (PAP) methods.

Immunohistochemistry. To demonstrate PECAM-1 on the mitral valves by peroxidase-antiperoxidase (PAP) method, primary mice-anti-human PECAM-1 monoclonal antibody (1:20, Bender MedSystem, Austria), secondary rabbit-anti mice Ig (1:100 Dianova), and PAP mice complex (1:500 Dako) were used. Incubations were performed at room temperature for 30 min each. Between each incubation slep slides were washed with Trisbeffered saline (TBS, 0,1M Tris-HCl with 0,9% NaCl, pH 7,6). Endogenous peroxidase was blocked by incubation with 0,3% hydrogen peroxide in methanol at room temperature for 30 min. Visualization of PAP reaction was achieved with diaminobensidine (DAB/O, 1M imidazole-HCl, pH 7,1) for 10 minutes. The samples were then counterstained with hematoxzlin and coversliped. Negative controls for mAbs were incubated will normal rabbit serum.

RESULTS

After performed patohistological analyses, we have selected samples of the mitral valve with representative changes (calcification, myxomatous degeneration, neovascularization, valvulitis) for immunohistochemical research. Adhesive molecule PECAM-1 was detected with PAP method in endocardial and vascular endothelial cells of mitral valves. We observed that only a group of endocardial endothelial cells expressed the tested adhesive molecule. An intensive expression on PECAM-1 was visible in the mitral valve with numerous small blood vessels. Smooth muscle cells located near by the newly created blood vessels, cells the which have also shown an intensive positive reaction on PECAM-1. Immunoreactivity of PECAM-1 is distinctly intensive of endothelial cells of the small blood vessels of the valves stroma. Endothelial cells of stroma with the newly created blood vessels have shown weakly immunoreactivity against PECAM-1, in comparison with blood vessels small in diameter. Intensive imunoreactivity against PECAM-1 has shown endothelial cells of the stromal vessels surrounded with infiltration of mononuclear cells.

DISCUSION

Among vascular cell adhesion molecules, PECAM-1 has the distinctive feature of being expressed on several of the major cell types associated with the vascular compartment (1). This makes it uniquely positioned to mediate multiple and important cell-cell interactions involving platelets, leukocytes and endothelial cells (4,5). Thus, PECAM-1 may represent a potential target for new therapeutic agents directed at a variety of pathological states. Recent works have revealed that it is capabile of complex have ligand interactions, although the specific ligands involved are still unknown. The wide distribution of PECAM-1 among vascular associated cells suggested that it may have a

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number of important physiological functions. The ability of anti- PECAM-1 antibodies to block normal endothelial cell-cell contacts and influence cell migration point to a role in angiogenesis and wound healing (1). PECAM-1 may also contribute to early cardiovascular development (2). Immunohistochemical examination of PECAM-1 expression, has shown presence on endocardial and vascular endothelium in different degree, from a very discrete to a very intensive. Endothelium of blood vessels with small diameter has stronger immunoreactivity on PECAM-1, in comparison with endothelial cells of large blood vessels. PECAM-1 is constitutively expressed and concentrated in the lateral borders between endothelial cells and expressed on the surfaces of neutrophils, monocytes, and some T cell subsets, as well as on platelets. Numerous complications in cardiovascular surgery appear because of endothelial cells and neutrophils activity. Once adherent to the endothelium, neutrophils release cytotoxic proteases and oxygen-derived free radicals, which are responsible for much of the end-organ damage seen after cardiovascular operations. Recently the cellular and molecular mechanisms of endothelial cell activation have become increasingly understood (5). Therapies will be developed allowing the selective or collective inhibition of vascular endothelial activation during the perioperative period.

CONCLUSION

The most intensive reactivity of PECAM-1 shows endothelial cells of small blood vessels of valves, stroma and endothelial cells of the stromal vessels surrounded by mononuclear cells.

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Myocardial bridges over the left anterior descending coronary artery - autopsy study

ABSTRACT

The left anterior descending coronary artery's (LAD) transient sinking into the myocardium and reappearing on the heart surface has been described by Tandler (1913) and Crainiciany (1922). However, we still do not know whether the myocardial bridges (MBs) over the coronary blood vessels are abnormalities or varieties. The aim of this study was to determine the incidence of MBs over the LAD in our population and to evaluate the possible impact of myocardial bridging phenomenon on coronary circulation. Study was performed on 575 consecutive autopsies of people deceased from natural causes, performed in the Institute for Forensic Medicine at Belgrade University Medical School 1994 'till 1998. Cases with proved MBs, ranged from 20-75 years and were of both sexes. Blocks of the overbridged vessel with adjacent myocardium were taken and underwent routine processing for light microscopy (H.E., van Gieson). In 62.95% of the cases death was caused by heart problems. The incidence of MBs in our population was 4.69%. Myocardial bridges were present with a statistically greater significance (88.89%) in people deceased from a heart-cause problem, and more frequent in men (77.78%). In the greater majority of cases (88.89%), the overbridged vessel suffered from atherosclerotic changes majorily (70.37%) advanced or complicated, and neighbouring myocardium showed degenerative changes (fibrosis by itself or accompanied with lipomatosis). The most frequent cause of death in those cases was myocardial infarction of the LAD-supplying areas. Our findings cannot support the concept of so called myocardial bridges protective role from atherosclerosis on the overbridged vessel. Even more, they undoubtedly suggest that MBs compromise the coronary circulation of the corresponding area.

KEYWORDS: Coronary Vessel Anomalies; Coronary Vessels + anatomy and histology; Autopsy

INTRODUCTION

The left anterior descending coronary artery's (r. interventricularis anterior) transient sinking into the myocardium and reappearing on the heart surface has been described by Tandler (1913) and Crainiciany (1922). Later

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studies showed that left anterior descending coronary artery (LAD) is the most frequently overbridged blood vessel. On the other hand, we still do not know whether the myocardial bridges (MB) over the coronary blood vessels are abnormalities or varieties. Thus, although Geiringer's (1951) report of myocardial bridges' protective role in atherosclerosis of the overbridged vessel-segment has had many supporters (Lee et al, 1972; Morales et al, 1980; Angelini et al, 1983; Channer et al, 1989; Ge et al, 1995; Ishii and Asuya, 1996; Tauth and Sullebarger, 1997) there are different opinions on the issue too (Edwards et al, 1956; Polacek, 1961; Colleran et al, 1996; Ishikawa et al, 1997). The aim of this study was to determine the incidence of MB over the LAD in our population, and to evaluate the possible impact of myocardial bridging phenomenon on coronary circulation.

MATERIALS AND METHODS

Our study was performed on 575 consecutive autopsies of people deceased from natural causes, performed in the Institute for Forensic Medicine at Belgrade University Medical School from 1994 'till 1998. Cases with proved MBs, ranged from 20-75 years and were of both sexes (6 female and 21 male). The mean age of male was 60,3 ±18, 8 and for female 48,1 ± 21,0 but the difference was statistically insignificant. For the microscopic examination, samples of the overbridged vessel with adjacent myocardium were taken, i.e. cut transversally in 5mm wide blocks. The blocks underwent routine processing for light microscopy and were stained with haematoxylin and eosin, and van Gieson as well.

RESULTS

Autopsy confirmed that the death was natural in all of the examined cases. In 362 out of 575 cases (62.95%), death was caused by heart problems. The incidence of heart-caused deaths in the group of natural ones varied from 56.77% to 71.68% in regard to the year examined. However, the difference was statistically insignificant. The most frequent cause of death was myocardial infarction (301 out of 362 cases of heart-caused deaths) localized in the walls of left ventricle and interventricular septum. Significantly less frequent causes of death were heart tamponade (17 out of 362), acute myocarditis (13 out of 362), and diffuse cardiosclerosis (12 out of 362). In 27 (4.69%) out of 575 naturally caused deaths, the presence of MB over the left anterior descending branch of the left coronary artery was found. Twenty-one out of 27 cases (77.78%) were male and 6 out of 27 (22.22%) were female. The difference appears to be statistically significant. A singular MB overbridged all of our LAD-cases. Their size greatly varied: the length between 3,0mm and 50,0mm (average 17,31mm ± 14,12mm), and width between 2mm and 7mm (average 3,85mm ± 1,46mm). Twenty-one of the aforementioned cases (77.78%) belonged to the group of heart-caused deaths. In 24 out of 27 MB-cases, the wall of the overbridged vessel showed atherosclerotic changes: (A) In 5 cases the overbridged LAD showed atheromatous plaques of eccentric position, but of smaller dimensions. Media presented a slight growth of connective tissue's fibers, but with no hyalinization. In these cases, myocardium expressed only signs of parenhimatous degeneration. (B) In 10 of the cases, the overbridged vessel showed fair atheromatous changes (in sites of atheromatous plaques, endothelium was missing, basal membrane was thickened and media presented with layer-separation and connective tissue growth). Myocardium showed signs of myofibrosis and lipomatosis (presence of fat within muscle cells leads to myocardial layer-separation and muscle fiber deterioration); (C) In the remaining 9 of the cases, atheromatous changes were dominant, presenting focal calcifications, ulceration and hemorrhage within the plaque. In that part of the blood vessel, the media was completely destroyed. These changes correspond to the stage of complicated atheromatous lesions. Small vessels of a certain number of cases from this group which had no history of hypertension, showed signs of hyperplastic arteriolopathy - eccentric laminar thickening of the wall and proportional narrowing of its lumen. In all of these cases, myocardium showed signs of cardiofibrosis.

DISCUSSION

The present autopsy study revealed the incidence of myocardial bridges in our population (4.69%) to be much lower than in some other reports (22% by Geiringer, 58% by Lee, 86% by Polacek). However, this type of a study has been done for the first time in our population. On the other hand, in our series myocardial bridges were present with a statistically greater significance (24/27, i.e. in 88.89% of the cases) in people deceased from a heart-cause problem. They were three times more frequent in men than women. The similar findings have been reported, first, by Polacek (1961), and lately by Baldassare et al. (1996), and Cheng (1997) too. In the greater majority of our cases (24/27, i.e. in 88.89%), the overbridged vessel suffered from atherosclerotic changes, which were majorily (19/27, i.e. in 70.37% of the cases) advanced or complicated. In all of those cases with atherosclerotic changes on overbridged left anterior descending coronary artery, the neighboring myocardium showed degenerative changes (fibrosis by itself or accompanied with lipomatosis). The most frequent cause of death in the cases with myocardial bridges was myocardial infarction of the LAD-supplying areas.

CONCLUSION

Our findings cannot support the concept of so called myocardial bridges protective role from atherosclerosis on the overbridged vessel. Even more, our results undoubtedly suggest that myocardial bridges compromise the coronary circulation of the corresponding area.

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Sudden death - a six-year autopsy study

ABSTRACT

Mors subita denotes an abrupt, sudden death; by the WHO definition, it means any death which is "unexpected, natural (nonviolent), occurring within 24 hours from the onset of acute symptoms". From 1993 to 1998, the autopsy was performed on 210 patients who died of sudden death. The causes of death were divided into cardiac and noncardiac. Cardiac causes were subdivided into coronary and noncoronary, and noncardiac ones into vascular and nonvascular causes. The analyzed group comprised 144 (68.57%) male and 66 (31.43%) female patients, with the average age x=65.07 years. Sudden cardiac death was established in 172 (81.90%) patients, and noncardiac in 38 (18.09%). Among cardiac causes of death, coronary ones (146 patients-84.88%) significantly dominated over noncoronary ones (26 patients-15.12%). All coronary causes of death were directly related to a significant narrowing of the lumen (>75%) of at least one of the three major epicardial coronary arteries elicted by an atherosclerotic change. Noncoronary causes of a cardiac death were hypertensive heart diseases in 18 cases, changes in the myocardium caused by valvular disease in 5 cases, and specific myocardial disease in 3 cases. The most frequent cause of vascular noncoronary sudden death is a rupture of a dissected aortic aneurysm (16 cases-51.43%). Noncardiac nonvascular causes of death were bleeding from a gastric ulcer in 2 patients and a shock caused by an acute haemorrhagic pancreatitis in 1 patient. Men more often succumb to sudden death than women, most endangered being males above 60 years of age. Cardiac causes of sudden death dominate, the most frequent are atherosclerotic and coronary cardiac disease. Among noncardiac death causes, the vascular ones prevail over nonvascular ones and are caused mostly by hypertension.

KEYWORDS: Death, Sudden; Death, Sudden, Cardiac; Autopsy

INTRODUCTION

The term mors subita has been used for the last 450 years to denote a sudden or abrupt death (1). It is interesting that up to nowadays there has been no precise definition of sudden death, i.e. how sudden it really is; therefore, it has been defined as the death occurring instantaneously, or within one, two, six or 12 or 24 hours after the onset of the symptoms. According to the WHO definition, sudden death is any death which is #unexpected, natural (nonviolent), occurring 24 hours from the onset of acute symptoms# (2). On the other hand, the impossibility to anticipate the occurrence of sudden death explains the wide and continuous interest in this problem.

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MATERIALS AND METHODS

The autopsy material from 210 victims of nonviolent and nontraumatic death within 12 hours after the onset of acute symptoms was used in the study. All autopsies were performed in the Department of Pathology and Immunology of the Institute of Lung Diseases in Sremska Kamenica in the period 1993-1998. All cases were sent from the Clinic of Cardiology in Sremska Kamenica. The causes of death were divided into cardiac and noncardiac. The cardiac causes were subdivided into coronary (atherosclerotic and nonatherosclerotic) and noncoronary (primary and secondary diseases of the cardiac muscle). Noncardiac causes were divided into vascular and nonvascular. The obtained data were statistically analyzed.

RESULTS

In the period 1993-1998, in the Clinic of cardiology in Sremska Kamenica, 1920 patients died; 935 of them were subjected to autopsy, of whom 210 patients had the clinical picture of sudden death. The group comprised 144 (68.57%) males and 66 (31.43%) females ($x2=85.50$; $p=3.84$). The average age of the males was $x=63.68\pm10.97$ (range 26-87 years), and of the females $x=68.09\pm9.17$ (range 35-92 years). The causes of sudden death in 172 (81.90%) cases were cardiac, and in 38 (18.09%) noncardiac, which means that they significantly differ ($x2=85.50$; $p=3.84$). Among cardiac causes, the coronary ones significantly prevailed (88.88%) over noncoronary ones (15.12%) ($x2=34.59$; $p=3.84$). All coronary causes of death were directly connected with a significant narrowing of the lumen (>75%) of at least one of the three major epicardial coronary arteries because of an atherosclerotic change. As regards the morphological causes of death in patients with coronary disease, the majority of them died due to an acute cardiac insufficiency (126-86.30%), which was manifested by a lung edema in 66 (52.38%) cases, by myocardial infarction in 45 (35.71%) cases, and by thrombosis of the coronary arteries in 15 (11.90%) cases. In 20 (13.70%) patients with significant atherosclerotic stenosis of the coronary arteries, no morphological substrate of death was found. Their death was considered as cardiac insufficiency most probably caused by an atherosclerotic heart disease. Noncoronary causes of death mutually differed statistically (($x2=15.31$; $p=5.99$). In 18 (69.23%) cases, they were ascribed to hypertensive heart disease, in 5 (19.23%) cases, to changes of myocardium elicited by valvular disease (in all of them, it was a calcifying aortic valve stenosis), and in 3 (11.54%) cases, to an idiopathic or specific myocardial disease (hypertrophic cardiomyopathy, myocarditis and amyloidosis). The morphological cause of death in 19 (73.08%) cases was a lung edema, and in 7 (26.92%) cases, it was cardiac insufficiency.

In the group of noncardiac causes of sudden death, statistically dominant ($x2=26.95$; $p=3.84$) were vascular (35-92.10%) over nonvascular (3-7.89%) causes. This group comprised 35 cases, of whom 25 (71.43%) were males and 10 (28.57%) females. The average age of the patients was $x=63.23\pm12.02$ years. In 15 (42.86%) cases, the basic disease was atherosclerosis, in 14 (42.86%) cases it was hypertensive heart disease, in 4 (11.43%) cases death was caused by phlebothrombosis of the deep veins of the legs, and in 2 (5.72%) cases it was the Marfan's syndrome. The rupture of the dissected aortic aneurysm was the most frequent morphological cause of death. In 8 cases, aneurysm was caused by atherosclerosis, in 8 cases it developed in the scope of systemic hypertension, and in 2 cases within the Marfan's syndrome. Massive thromboembolism of the lungs was found in 8 (22.86) patients. In all cases, the source of emboli was phlebothrombosis of the deep veins of the legs. In one half of the cases, it developed during a decompensated atherosclerotic heart disease, and in the other, it developed in extremely obese persons. In 9 (25.71%) autopsies, a cerebrovascular insult was found (4 cases of encephalomalatia and 5 cases of bleeding). The main cause of death was atherosclerosis in 3 cases and hypertension in 6 cases.

A group of noncardiac nonvascular causes comprised 3 cases (2 males and 1 female). The morphological cause of death was a gastric ulcer bleeding in 2 cases, and a shock due to an acute haemorrhagic pancreatitis in 1 patient.

There were no sex differences as to the causes of sudden death.

DISCUSSION

Sudden death most frequently happens outside the hospital, often at home, in the office, during sports activities, etc. It is often unwitnessed, and the victims are usually people who have always been of good health" and asymptomatic. This is why it is necessary to identify on time persons with high risk of sudden death. This way of demise occurs in all age groups, although there are two peaks of incidence in relation to life age. The first peak is noticeable in the period between birth and the sixth month of neonatal life, when sudden death is mostly caused by congenital cardiovascular diseases. The second peak occurs between 45 and 75 years of age and is most frequently caused by ischaemic heart disease (3). In an autopsy study dealing with the problem of sudden death in China, it was shown that males had five times the rate of women (4). We established this ratio as two to one, whereas Pu1kariž et al. (5) showed the ratio to be 1.5 to 1. In the same study, it was reported that the largest number of sudden death happened in the age of 60-69 years, which agrees with our study pointing to the average age of 65 years. According to the literature data, cardiac causes of sudden death dominate. In 80% of the cases, they are ascribed to atherosclerotic and coronary heart disease (2,6-8), which is corroborated by our results as well. Cardiac cause of death was found in 82% of autopsy cases, and coronary diseases in 70% of the cases. Morphologically viewed, the death of patients with coronary disease is in 85% of the cases ascribed to acute cardiac insufficiency.

Noncoronary causes of cardiac death may be various and are connected with changes in the heart (e.g. hypertrophy, interstitial fibrosis, etc.) occurring in different cardiomyopathies and specific diseases of the cardiac muscle (most frequently hypertrophied cardiomyopathy, myocarditis, amyloidosis), valvular diseases (calcifying aortic valve stenosis, prolapse of the mitral valve) etc. (2). Such changes in the heart were established in 15% of the patients from the group of cardiac death causes. Among the diseases causing sudden death, hypertensive heart disease dominated (69%). Less frequent was myocardial disease elicited by calcifying aortic stenosis (19%) and finally, cardiomyopathies and specific myocardial diseases (12%). The mechanism of death in all cases is considered as the consequence of ventricular arrhythmia. Morphologically viewed, the most frequent cause of death was a lung edema (73%), whereas cardiac insufficiency elicited by the above mentioned diseases caused death in 23% of the patients.

Noncardiac causes of sudden death are found in 18% of autopsy cases, with the prevalence of vascular ones (95%). Morphologically, the most frequent cause of death was a rupture of a dissected aortic aneurysm (51%). Its highest incidence was in persons around 60 years of age, and two to three times higher in men than in women. As generally accepted, in two thirds of the cases, it is caused by hypertension, and in the rest of the cases by atherosclerosis, syphilis, inflammation etc. (9). In our material, aortic aneurysms are elicited by a weakening of the blood vessel wall due to atherosclerosis in 44% of the patients, due to hypertension in 44% and due to Marfan(s syndrome in 11% of the cases. The second cause by frequency was a massive lung thromboembolism (23%). In 50% of the cases, it developed within a decompensated coronary heart disease, and in 50% due to phlebothrombosis in very obese patients. A cerebrovascular insult was found in 26% of the cases from this group. In 67% of the patients, it was caused by a hypertensive complication, and in 33% by atherosclerosis. There were three cases of sudden death induced by noncardiac and nonvascular diseases. Morphologically, the demise of these patients was considered as the outcome of shock, which in two of them developed after massive bleeding and in one due to a haemorrhagic necrotic pancreas.

CONCLUSION

The results of the study point out that men are more often the victims of sudden death than women, those above 60 years of age belonging to the highest risk group. Cardiac causes of death dominate, with the prevalence of atherosclerosis and coronary heart disease. In the group of noncardiac causes of death, the vascular dominate over nonvascular ones and are mostly caused by hypertension. The findings obtained testify to the acuteness of the problem of cardiovascular diseases and to the need of further investigation of pathogenic mechanisms and causes of sudden death in order to promptly stop the increase of its incidence.

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Morphological variations in isolated pulmonary atresia with intact ventricular septum. An autopsy study of 13 cases

ABSTRACT

Isolated pulmonary atresia (PA) with an intact ventricular septum shows significant variability which influences the prognosis of the ilness. Analysis of patho-morphological variations of PA with an intact ventricular septum and its significance for the survival time and the cause of death. 13 autopsied cases of PA with an intact ventricular septum. Autopsy technic suitable for congenital heart disease (CHD) and histo-pathologic analysis. The morphological data about the site of PA, type of afferent pulmonary arteries, right ventricle, tricuspid valve and orifice, atrial septum, age at death and causes of death were obtained. From morphological characteristics, wide persistent patent ductus arteriosus (PDA), systemic-pulmonary communications and the size of defect on atrial septum influenced significantly the survival time. Causes of death were directly linked to this CHD in 9 cases.

KEYWORDS: Pulmonary Atresia; Heart Defects, Congenital; Heart Ventricle; Myocardium; Hypoplastic Left Heart Syndrome

INTRODUCTION

Isolated pulmonary atresia (PA) is CHD present in two major forms: (A) PA with an intact ventricular septum and (B) PA with VSD. They are considered to be two separate entitates, both clinically and patho-morphologically. However, a significant variability exists within both entitates which influences the prognosis of the disease. In the fetal period, a critical stenosis of pulmonary artery could progress to PA. It can be established by fetal echocardiography and it is a indication for abortion. The aim of the study was to establish patho-morphological characteristics in 13 cases of PA with an intact ventricular septum with an emphasis on their relevance on the survival time and causes of death.

AUTOPSIED PATIENTS AND METHODS

At the Institute of Pathology, from 1926 to 1999, 1321 cases of CHD were diagnosed on autopsies, including 13 cases of PA with an intact septum (0.98% cases of all CHD). All cases were done by autopsy tehniques specialised for CHD and a histo-pathological analysis of the heart and lungs were performed.

RESULTS

Patho-morphological characteristics

In 9 cases the site of PA was at the level of the pulmonary artery orifice with a non- perforated membrane. In 3 cases the right ventricle infundibulum was atretic and in one case infundibulum was atretic with agenesis of the pulmonary trunk.

Examination of the trunk and branches of the pulmonary artery revealed hypoplasia in 12 cases. Hypoplasia was not significant due to the PDA which functioned for the pulmonary circulation from aorta. In only one case we found agenesis of pulmonary trunk and its branches and afferent pulmonary circulation through systemic-pulmonary arteries.

The right ventricle was a slit-like blind hole in 4 cases, hypoplastic in 5 cases, normal in 2 cases and enlarged in 2 cases. Hypoplastic right ventricle had a small cavity but also wall hypertrophy and often secondary endocardial fibroelastosis. Persistent myocardial sinusoids were numerous and clearly visible in 2 cases. In one of these 2 cases wide coronary-cameral fistulas existed and they drained the blood from the small right ventricle to coronary arteries. The tricuspide valve (TV) was hypoplastic in small hypoplastic right ventricles and atretic when the right ventricle was a blind hole. In 2 cases TV was normal and competent and in 2 cases with enlarged right ventricle TV showed Ebstein's anomaly. Communication on atrial level existed in all cases: foramen ovale apertum (7 cases), ASD (5 cases), and common atrium (1 case).

Survival time and causes of death

Eight cases died in the perinatal period and two cases till the end of the first month. Only 3 cases lived longer: 2, 8 and 17 months. The causes of death were: cardiac and cardiac-pulmonary failure in 9 cases, perinatal asfixia in 3 cases and sepsis in one case (due to the associated extracardiac anomalies).

DISCUSSION

A typical case of PA with an intact ventricular septum is characterised by atresia of the pulmonary orifice, hypoplasia of the pulmonary trunk and its branches, afferent pulmonary circulation through the persistent patent ductus arteriosus, small hypoplastic right ventricle and tricuspid valve and at atrial level: PFO or ASD. In 1/5 cases hypoplastic right ventricle does not have all normal parts: inflow tract (inlet), trabecular part and outflow tract (infundibulum). In the examined material only one case significantly differed from usual findings. In this case we found agenesis of the pulmonary trunk and its branches and afferent circulation functioned through systemic-pulmonary arteries. This type of PA is rare in the literature (1). According to the development of the right ventricle, the cases are classified to type I with a small and type II with a normal or enlarged right ventricle (2). Type I was more common than type II (ratio 9:4). The hypoplastic right ventricle had a small cavity, but the hypertrophied wall often had secondary endocardial fibroelastosis. There were apparent persistent myocardial sinusoids in 2 cases. In one of them we found wide cameral-coronary fistulas which drained the blood from the small right ventricle to both coronary arteries. This finding has both clinical and surgical importance (3,4). Besides hypoplasia, tricuspid valve in 2 cases showed Ebstein's anomaly. It was described that TV could show other changes like different types of dysplasia or complete agenesis (Kanjuh's anomaly) (5-8).

CONCLUSION

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Afferent and intrapulmonary circulation in cases of isolated pulmonary atresia. An autopsy and patho-histological study of 40 cases

ABSTRACT

In isolated pulmonary atresia (PA), on the level of its ostium, blood could not pass from the right ventricle to the pulmonary artery and life is possible only in cases where an alternative path for the oxygenation of blood exists. 40 patients with PA were autopsied with a technic suitable for congenital heart disease (CHD). A macroscopic and histo-pathologic analysis of afferent and intrapulmonary circulation were done. Afferent pulmonary circulation functioned through patent ductus arteriosus (PDA) in 25 cases and through systemic-pulmonary arteries in 14 cases. In the second group a longer survival was observed. In one case the left lung received blood through PDA and the right lung through systemic-pulmonary arteries. In several cases afferent pulmonary circulation was compromised by PDA closure, stenosis of systemic-pulmonary arteries and thrombosis of the hypoplastic pulmonary vascular bed. The function of afferent pulmonary circulation in cases of PA is crucial for the survival and possibilities for surgical intervention in these patients.

KEYWORDS: Pulmonary Atresia; Heart Defects, Congenital; Pulmonary Artery; Bronchial Arteries; Ductus Arteriosus, Patient

INTRODUCTION

Isolated PA is a CHD where the normal path of the venous blood from the right ventricle to the lungs is interrupted. In fact, non-perforated fibrous membrane exists on the site of pulmonary artery ostium. The pulmonary trunk is extremelly hypoplastic or atretic or it doesn't exist at all. Life is possible only when there exists an alternative path for the blood (for oxygenation) from the right ventricle to pulmonary capillaries (1,2). Since this CHD is "functionally modulated" in utero, the following alternative compensatory possibilities for

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Our data show that PA with an intact ventricular septum is a severe CHD with bad prognosis and unadequate therapy at present time (all cases were treated with medicaments without surgical intervention). Wide persistent patent ductus arteriosus is of crucial importance for this CHD since afferent circulation is functioning only through it (ductus-dependent anomaly). A wide communication on the atrial level is also important. The longest survival time was registered in cases with wide communications (wide PDA and systemic-pulmonary arteries and ASD). Cases with a normal or enlarged right ventricle did not have long survival time.

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afferent pulmonary circulation have been described: A. postanatal persistent PDA (3,4) or B. early embrional (prebronchial) systemic arteries for lungs; C. the existence of anomalous systemic-pulmonary arteries (5,6); D. functional adaptation (dilatation) of bronchial arteries (7) or E. normal systemic-pulmonary or F. systemic-bronchial collateral arteries. In these cases the described arteries overtake the role not only of „vasa privata“, but of „vasa publica pulmonum“ as well. In rare cases two CHD could be associated with PA and enable the flow of blood to lungs: G. aortic-pulmonary window (8) and I. by-pass of PA site with sinusoids communication between the right ventricular cavity and the pulmonary trunk in cases with an intact ventricular septum and competent tricuspid valve (a small and hypertrophic right ventricle empties only through myocardial sinusoids in coronary circulation (9)). The lungs could be supplied with blood via two paths: through PDA or through systemic-pulmonary arteries in uni- or multifocal way. The latter alternative paths of pulmonary circulation in PA are often functionally compromised. PDA sometimes closes postnataly despite the fact that PA is life-dependent on PDA. In fact, the histologic structure of PDA prepares it for the postnatal closure. Systemic arteries for lungs often show stenotic lesions. Intrapulmonary circulation is usually hypoplastic and often furtherly compromised with thrombosis (8).

AUTOPSIED PATIENTS AND METHODS

We autopsied 40 patients with PA (13 cases with intact ventricular septum and 27 cases with VSD) applying a technic suitable for a congenital heart disease (CHD). Macroscopic and histo-pathologic analysis of afferent and intrapulmonary circulation were done.

RESULTS

From 40 cases with PA, afferent pulmonary circulation functioned through PDA in 25 cases (including 4 cases in closure). In 14 cases it functioned through 2,3 or 4 systemic-pulmonary arteries (including one case a with stenotic artery for the left lung). In one case the left lung received blood through PDA and the right lung through systemic-pulmonary arteries. The normal left aortic arch was found in 30 cases and the right aortic arch in 10 cases. From 10 cases with the right aortic arch, 4 cases were with right PDA and 6 cases with systemic-pulmonary arteries. Diversely staged hypoplasia of the pulmonary trunk was found in 38 cases but always with existed lumen and communication with both branches of pulmonary artery. In one case, agenesis of the pulmonary trunk and branches was established and in another case agenesis of the right branch of the pulmonary artery was found. Due to the primary hypoplasia and low blood pressure in the pulmonary trunk, the elastic structure of the pulmonary trunk media was histologically "adult" in type on birth. Intrapulmonary circulation showed diversely staged hypoplasia of the pulmonary arterial branches (especially in cases with systemic-pulmonary afferent circulation). The number of elastic laminas in the arterial wall was decreased. The laminas were thinned and severely fragmented in comparison with the normal ones for the same age group. Besides hypoplastic branches of the pulmonary artery, compensatory hypertrophic branches of systemic-pulmonary arteries were also found (in cases with systemic-pulmonary afferent circulation). In 16 cases intravascular thrombosis was also found: in 13 cases of PA with intact septum and in 3 cases of PA with VSD.

DISCUSSION

The cases with afferent pulmonary circulation through systemic-pulmonary arteries had a longer survival time in comparison with the cases where pulmonary circulation functioned through PDA. However, the right ventricle diameter and condition of ventricular septum are relevant for the survival time. Namely, in cases with a small right ventricle and intact ventricular septum the survival time was shorter. Alternative compensatory paths of pulmonary circulation were often compromised with thrombosis, PDA closure (prostaglandin EI could maintain PDA open) and numerous thrombosis in hypoplastic pulmonary vascular bed. In one case the systemic-pulmonary artery for the right lung compressed esophagus' posterior wall and caused cyanosis during baby feeding and finally death due to aspiration bronchopneumonia (9).

CONCLUSION

The function of afferent pulmonary circulation in cases of PA is crucial for the survival and possibilities for surgical intervention in these patients.

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Isolated pulmonary atresia with ventricular septal defect. An autopsy study of 27 cases

ABSTRACT

The important features of isolated pulmonary atresia (PA) are: ventricular septal defect (VSD) or intact ventricular septum and different types of afferent pulmonary circulation. Analysis of pathomorphological substrate of PA with VSD and types of afferent pulmonary circulation and its relevance for the survival time and cause of death. 27 autopsied casees of PA with VSD. Autopsy technic suitable for congenital heart disease (CHD) and histo-pathologic analysis. The morphological data about site of PA, type of afferent pulmonary arteries, right ventricle and VSD, tricuspid valve and orifice, atrial septum, aortic arch, extracardiac anomalies, age at death, causes of death, correlation between clinical and autopsy diagnoses and performed surgical procedure were described. The longer survival time was registered in cases with sistemic-pulmonary arteries, enlarged right ventricle and large VSD with anatomically normal tricuspid valve.

KEYWORDS: Pulmonary Atresia; Heart Defects, Congenital; Pulmonary Artery; Heart Septal Defects, Ventricular

INTRODUCTION

Isolated pulmonary atresia (PA) is a CHD characterised with an interruption of thevenous blood flow from the right ventricle to the lung. A condition for postnatal life is the existence of an alternative afferent pulmonary circulation (1,2). However, the ventricular septum condition is important and this CHB is classified to PA with an intact septum and PA with VSD (3). Today, prenatal diagnosis of pulmonary atresia by fetal echocardiography is possible. In 1995 Dinarevic et al (4), reported improved surgical results. Namely, over the period 1973-1983 a corrective surgery was attempted in 9.6% of patients, with the mortality of 42%, but during 1983- 1993 surgery was performed in 39.1% of patients, with the mortality of 26%. Digilio et al (5), 1996 established that tetralogy of Fallot can be associated with many genetic conditions, but most patients are nonsyndromic. In contrast, patients with pulmonary atresia with VSD have a high incidence of genetic syndromes (especially CATCH 22 syndrome). Momma et al (6), 1996. showed that additional anomalies of the aortic arch, ductus arteriosus and pulmonary arteries are more common in patients with tetralogy of Fallot and pulmonary atresia with 22ql 1 deletion. Hofbeck et al (7), 199S. reported that of 21 patients with PA, VSD and major aortopulmonary collateral arteries, 10 patients (48%) were shown to have microdeletion in 22ql 1. This developmental disturbance seems to impair the connection of the peripheral pulmonary artery segments to the central pulmonary arteries.

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AUTOPSIED PATIENTS AND METHODS

At the Institute of Pathology, from 1926 to 1999 in 51791 autopsies, 1321 cases of CHD were diagnosed, including 40 cases of PA (3.02% of all CHD). In 13 (0.98 Zo) cases PA was with an intact septum and in 27 (2.04%) cases with VSD. Twelve patients were male and 15 were female. When we analyzed gender differences by the type of afferent pulmonary circulation, we had 4 males and 9 females with PDA and 4 females and 9 males with systemic-pulmonary arteries. One female had both PDA and systemic-pulmonary arteries. We applied specific autopsy tehniques for CHD and histo-pathological analysis of heart and lungs.

RESULTS

In all cases the site of PA was at the level of the pulmonary artery orifice with non- perforated membrane. In 2 cases, the right ventricle infundibulum was simultaneously narrowed. Examination of the trunk and the branches of pulmonary artery revealed hypoplasia diverse in intensity, but the lumen was always present. In 26 cases the pulmonary trunk communicated with both branches of the pulmonary artery and in one case agenesis of the right pulmonary artery was revealed. In 13 cases afferent pulmonary circulation functioned through PDA (including 4 PDA in closure) and in 13 cases through systemic-pulmonary arteries (including one case with the stenotic artery for the left lung). In one case the left lung received blood from PDA and the right lung from systemic-pulmonary arteries. The right ventricle was enlarged in 24 cases, mildly hypoplastic in 2 cases and small with wall hypertrophy in one case. In 26 cases, VSD was membranous-muscular type (large in 23 cases; large but partially covered with tricuspid valve which opened and closed VSD during heart cycle in one case; small in 2 cases) and in one case it was a part of the atrio-ventricular canal (8). The tricuspide valve was competent in 12 cases and insufficient in 12 cases. In 2 cases the orifice of the tricuspide valve was stenotic (in one case with accessory tissue of the tricuspide valve) and in one case the atrio-ventricular canal was found. The atrial septum was closed in 3 cases. Patent foramen ovale (PFO) was found in 16 cases, transformed PFO in ASD in one case, ASD secundum type in 5 cases, ostium primum defect in one case and lack of atrial septum in one case. The right aortic arch accompanied PA in 10 cases (including 2 cases with additional aberant left subclavia artery). Extracardiac anomalies were revealed in 7/27 cases. One case of with following anomalies was reported: situs inversus, lien accessorius, polysplenia, omphalocoela with inguinal hernia, duodenal atresia, polycystic kidneys with oneside megaureter and horseshoe kidney. The age of life at the time of death was between one day and 22 years. If we analyze the age of life at the time of death by the type of afferent pulmonary circulation we can see that in PDA survival was within the first 3 months of life (6 cases in the first week, 3 cases at the end of the first month and 4 cases till the end of 3' month). The cases with systemic-pulmonary arteries had longer survival time, between 22 days and 22 years (one case-2 days, 3 cases till the end of the first month, four cases till the end of first 3 months and one case with 11 months, one year, 2.5 years, 18 years and 22 years (8)). In only one case with both PDA and systemic-pulmonary circulation death the occured in 7' month. The causes of death were: heart failure in 10 cases (with two operated cases), bronchopneumonia in 6 cases, perinatal asfixia in 4 cases, PDA in closure in 4 cases, peritonitis in 2 cases and urosepsis in one case (due to the co-existed extracardiac anomalies). A precise clinical diagnosis was established in 3 cases (two of them were operated). A partially correct clinical diagnosis was obtained in 21 cases and inadequate diagnosis in 3 cases. In 2 cases Blalock-Taussig anastomosis was done (both died immediately

after the operation)

DISCUSSION

The analysis of the cases of PA with a long survival time showed that afferent pulmonary circulation functioned through numerous and wide systemic-pulmonary arteries. The right ventricle was always enlarged. VSD was large. The tricuspid valve was competent or insufficient. The longest survival time had a girl, 22 years of age with the PA associated with the common atrioventricular canal (8).

CONCLUSION

The longer survival time was registered in cases with sistemic-pulmonary arteries, enlarged right ventricle and large VSD with anatomically normal tricuspid valve.

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Immunohistochemical findings in acute atherosis associated with idiopatic intrauterine growth retarded infants and preeclampsia

ABSTRACT

Lesions of acute atherosis in placentas from pregnancies complicated by idiopathic intrauterine growth retardet (IIUGR) infants and preeclampsia were studied by an immunoperoxidase staining. Maternal vessels in the placental basal plate and underlying amniochorial membranes were histologically and immunohistochemically examinated in 50 cases. Twenty of them were from pregnancies complicated by IIUGR, twenty from pregnancies complicated by preeclampsia and ten from normal pregnancies, served as controls. Tissue blocks were routinely processed and slides were stained with H.E., PAS and Weighert for fibrin. Immunoperoxidase staining for IgM and IgG was performed in sections from basal and parietal deciduas. Acute atherosis was seen only in vessels that had not undergone physiologic vascular changes. These changes were found in the vessels of the decidua parietalis and decidua basalis. According to clinical data, acute atherosis was present in pregnancies complicated by IIUGR and preeclampsia, but not in normal uncomplicated pregnancies. Massive intramural granular deposits of IgM and slight deposits of IgG were found in all vessels with acute atherosis. No intramural deposition of immunoglobulins was observed in vessels with physiological changes. The presence of granular deposits of immunoglobulins within the vessel walls with acute atherosis may be related to an immunological disorder, probably mediated by immune complexes.

KEYWORDS: Fetal Growth Retardation; Pre-Eclampsia; Immunohistochemistry; Immunoglobulins; Placenta + blood supply

INTRODUCTION

During a normal pregnancy, an increased blood supply to the feto-placental unit is provided by physiologic vascular changes of the spiral arterial wall. These physiologic vascular changes are absent in complicated pregnancies and an arteriopathy, acute atherosis may also be seen. While the

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occurance of acute atherosis in preeclampsia is universally accepted, disagreement still exists regarding its coexistance with other complications of pregnancies, ex. idiopatic intrauterine growth retardiation. Histological and immunohistochemical examination of the spiral arteries in the placenta from pregnancies complicated by IIUGR and preeclampsia were the aim of this study.

MATERIALS AND METHODS

Placentas from 40 singleton full-term (37-42 weeks of gestation) intrauterine growth retardet infants showing acute atherosis were studied. Twenty of them were from pregnancies complicated by preeclampsia, 20 were from pregnancies complicated by IIUGR. Fetal growth retardiation was defined as a birth weight below the 10 percentile of the normal range form their gestational age. We used 10 placentas showing normal physiological changes in spiral arteries of the placental bed as controls. All of them were obtained from normotensive uncomplicated pregnancies with singletone full-term infants within the normal range for their gestational age. After macroscopical examination the placentas were cut into slides and standardized blocks were taken using the technique described by M. Vogel.Six blocks of placental parenchyma were taken, four from the central, and two from the marginal areas. In addition six blocks of the basal area corresponding to the entrance of spiral arteries were taken from the central portion of the placentas. A roll of membranes was prepared using the technique described by Benirschke. All the histological sections were staind with haematoxylin-eosin, PAS and Weighert for fibrin. Immunoperoxidase staining for localization of IgM and IgG was performed in several 5nm sections from basal and parietal deciduas. We used AVIDIN BIOTIN IMMUNOPEROXIDASE COMPLEX technique described by Hsu and all. - Strepta ABS complex/HRP duet, mouse/rabbit (Dakopatts). The intensity of the antigenical expression was semiquantitativly determined as:negative-0;mild to moderate-1; massive-3.

RESULTS

Acute atherosis was found only in vessels that had not undergone physiologic vascular changes.The earliest histologically convincing lesion acceptable as acute atherosis was fibrinoid necrosis with a perivascular mononuclear cell infiltrate, while lipophages within the vessel wall were a late phenomen. From 20 placentas with acute atherosis corresponding to intrauterine growth retarded infants from pregnancies compllicated by preeclampsia, 6 presented this lesion in parietal decidua and 11 in basal decidua. Eight of them showed the absence of a physiological change and the spiral arteries were normal in structure. From 20 placentas with acute atherosis corecponding to IIUGR infants, 4 pesented this lesion in parietal decidua and 16 in basal decidua. Four of them showed the absence of physiological changes. No lesions of acute atherosis or absence of physiological changes in basal decidua were found in placentas from normal pregnanicies. In all 40 cases with acute atherosis, massive granular intramural deposits of IgM and slight deposits of IgG were found. Immunoperoxidase staining revealed no intramural deposition of immunoglobulins within the physiological changes in the arteries of basal decidua in IIUGR groups or in controls. Also in the arteries uneffected by the physiological changes no intramural deposition of immunoglobulins was observed.

DISCUSSION

Lesions of acute atherosis have been found to be associated with intrauterine growth retardation with or without pregnancy induced hypertension. We have found massive deposits of IgM and slight deposits of IgG in vessels with acute atherosis from placenta of IURG infants, idiopathically or associated with preeclampsia. The fact that no immunoglobulin depositions were found within the physiologic changes in the spiral arteries of the placental bed and no deposits were seen in spiral arteries unaffected by the physiological changes, suggests that only acute atherosis may be related to an immunological disorder. The histological and immunohistochemical findings of the spiral arteries in the basal decidua are the same as in placentas from IIUGR and preeclampsia, so we could assume that IIUGR is a certain form of toxemia.

CONCLUSION

The presence of granular deposits of immunoglobulins within the vessel walls with acute atherosis may be related to an immunological disorder, probably mediated by immune complexes.

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