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Histoclinic of the abdominal aortic aneurysms

The research and observations made up to the present moment revealed that, from mechanics viewpoint, the formation and development of aneurysm is the result of the loss of material durability being the effect of long-term wear of the elements forming the wall of aorta. The most crucial is the process of intensified degradation of elastin, which is the basic structural albumin responsible for the elastic durability and the balance of forces acting on aorta wall. For many years atherosclerosis was considered to be the main cause of the aortic aneurysm. It resulted, among others, from the fact of the increase in the frequency of occurrence of both diseases with age and was interpreted as a natural process of aging. However, multicentre research on a wide scale changed the present viewpoint on the pathomechanism of the disease. It is presently considered that genetic, immunological, inflammatory, enzymatic and other factors contribute to aneurysm formation (14).

Normal aorta diameter in the section below draining off the renal arteries from the age of 65 to 74 is 2.01 ± 0.51 cm. The dynamics of the growth of aneurysm varies; it is most frequently slow, about 0.4 mm per year. In respect of the frequency of occurrence and complications, the most dangerous of which is the rupture, aneurysms are very serious clinical problem. Aneurysm rupture is the cause of 0.5 to 0.8 deaths in the whole population. The direct cause inducing the rupture is not known. Aneurysms are met 3 to 8 times more frequently in men than in women, with a general tendency to the increase in occurrence with age (6).

Elastin and collagen, main structural albumins of blood vessels, determine the mechanical properties of aorta. They occur mainly in the middle and external layers. Elastin is built in such a way that under the influence of the acting forces its fibres can even double their size and quickly return to their initial state. The synthesis of this albumin takes place in the smooth muscles only in the early childhood. The semi-duration period is about 70 years. Collagen is not a homogenous albumin. It occurs in aorta in 7 from among 15 known variations, most frequently type I and III. Its fibres are not prone to stretching, however, they are characterised by great mechanical durability. It is being synthesized throughout the whole life. Comparing the structure and conditions of both albumins it can be said that elastin is mainly responsible for the balance of the pressure forces acting on aorta wall, while collagen is a non-stretchable safety support (15).

It was proved that the inflammatory process takes an important part in the formation of aneurysm. In some patients the aneurysm wall is thickened with macrophage infiltrations and other inflammatory cells. These cells produce proteases which degrade albumins of the extracellular space. Macrophages

release plasminogen activators and also synthesize cytokines, which control the activity of the smooth muscles. In this way the process of the degradation of the aorta is accelerated. It was observed that the inflammatory aneurysms enlarge and induce the rupture faster (10).

For some years the relation between the chronic infection *Chlamydia pneumoniae* and the development of aneurysm has been searched for. Experiments were carried on, in which *Chlamydia phagocytosis* caused by macrophages was observed. In the early stage of the infection when bacteria multiplication in the host cells is little, the formation of phagolysosomes was not observed. Thus, *Chlamydiae* are not killed. Then, macrophages act as germ reservoir and contribute to the spread of infection. Soluble antigen is released to the environment and combines with specific antibodies and T lymphocytes. It is assumed, that *Chlamydia* slip away from the effector mechanisms of these lymphocytes which enables them to infect the neighbouring cells. The above immunological phenomena may cause an inflammatory reaction. Chronic infection may stimulate the immune response directed against the cell membrane of the host (8).

During the aneurysm formation, the angiogenesis process was observed. Capillaries appear in the middle layer, especially in the region of inflammatory infiltrations. This phenomenon is accompanied by the intense fibrinolytic activity. The described neovascularisation is the histopathological index of the aneurysm formation (5).

Genetic susceptibilities in the aneurysm formation are perceived since familial occurrence of this disease was stated. Other factors are being looked for the confirmation of this thesis, among others, less frequent aneurysm occurrence in people with Rh (-) factor or polymorphism of genes responsible for collagen transformation. The correlation of aneurysm occurrence was stated in patients with chronic respiratory failure mainly caused by pulmonary emphysema in the course of a-1 antitrypsin deficiency, which is the main elastase inhibitor. It is suggested that it is responsible for the occurrence of emphysema caused by the destruction of elastin in the lungs. It was stated that the phenotype with defective a-1 antitrypsin appears more often in patients with aortic aneurysm. The correlation is being looked for between the diseases with autoimmunity e.g. Hashimoto's goitre or rheumatoid arthritis and the aortic aneurysm. It is suggested that there is a correlation between specific antigens from the HLA group and the susceptibility to vascular pathologies (3,4).

MATERIAL AND METHODS

Material for the research consisted of sections of the anterior wall of abdominal aorta collected during planned operation of the aortic aneurysm, from patients treated at the Department of Vascular Surgery, Medical University of Lublin. The specimens were collected from January to June 2000. The scientific protocol was elaborated for each patient and it regarded sex, age, aneurysm diameter, family history, cigarette smoking, co-existing diseases: arterial hypertension, coronary heart disease, lower limbs ischaemia, patients with diabetes were excluded. Each patient had the ultrasonography of the abdominal cavity made, aortography, ECG, thorax X-ray, blood grouping and biochemical investigation. In the research, the samples were collected from 21 patients, including 2 women aged from 50-80, on average 69 years old. The aneurysm diameter ranged from 4.6 to 7cm, on average 5.5cm.

Aorta sections were fixed in the 10% buffered formalin and embedded in paraffin. Paraffin preparations were stained using the method of H+E, by Van Gieson, with resorcifuchsin and the alcian blue. In one case reticular fibre impregnation with silver according to Gomori was performed and also staining with the Brachet method.

RESULTS

While analyzing the scientific protocol it was stated that all patients had previously diagnosed arterial hypertension with the following values: systolic above 160 mm Hg and diastolic above 95 mm Hg, and were systematically pharmacologically treated. 8 patients were treated because of the coronary heart disease, including 4 patients who had undergone myocardial infarction. In this group 6 patients revealed the symptoms of the chronic lower limb ischaemia together with the occlusions of popliteal and femoral arteries. 2 patients had symptoms of the chronic respiratory failure and in these patients pulmonary emphysema was found in chest radiograms. All patients denied family history in the direction of aneurysms. Only 3 persons, including women, did not smoke cigarettes. None of the patients in the investigated group was observed to have clear hypercholesterolaemia or dislipidaemia. It should be noted, however, that all patients had the total cholesterol values in the range from 4.91-5.69 mmol/l (190-220 mg%). In 6 patients polyaneurytic syndrome was stated. In the course of operation, because of essential dilation of the iliac arteries, aorto-bifemoral forked prosthesis was implanted. In the ultrasonographic examination in these patients, the dilation of femoral and popliteal arteries was observed. Two deaths were noted on the second and fourth day after the operation because of the acute respiratory failure.

The histopathological evaluation of all investigated cases entitles to diagnose each time true aneurysm. In all the patients, within the aneurysmal dilation, it was noted that there was a thrombus of various size. In none of the cases it was possible to identify endothelium cells. In all the examined preparations atherosclerotic changes of the arterial wall, within aneurysm, were noted. It was usually fibrosis or calcification of the middle layer and in 1 case evident cholesterol concrements were noted (Fig.1). The permanent feature was haemorrhagic impregnation of the muscular layer, with the various degree of intensification in separate preparations. In 3 cases numerous inflammatory infiltrations were noted and they consisted of mononuclear cells in the muscular layer and adjacent fatty tissue. Accumulations of the inflammatory cells were usually revealed around the nutrient vessels and nerve fibres. In 2 cases these changes were accompanied by the narrowing of the nutrient vessels lumen and inflammatory infiltrations in their walls. In the preparations of one patient a profuse infiltration consisting of lymphocytes and plasma cells was noted and also the features of marked inflammation of the nutrient vessels (Fig. 2). In this case it was thought that we could have faced the tertiary syphilis. The performed serological reactions both VDRL and FTA proved to be negative. In each case evident reduction of the elastic fibres and disintegration of the collagen fibres within the aneurysm were observed (Fig. 3). Evident fibrosis was noticed in the middle coat and adventitia, which was accompanied by the decrease in the quantity and chaotic arrangement of collagen fibres. In 4 cases (in 3 cases with numerous inflammatory cells in the wall of aneurysm and in 1 with considerably profound atherosclerotic changes but without substantial inflammatory infiltration) neovascularisation features with profound intensification were observed (Fig. 4).

DISCUSSION

Aneurysm is defined as local aorta dilation by at least 50% in comparison to its normal size. The weakening of the aorta walls can be generalised in character. These changes may regard popliteal, iliac and femoral arteries, less frequently cervical and visceral arteries. The abdominal aortic aneurysm, including common iliac arteries, is the most frequently isolated aneurysmal change. On the other hand, the aneurysms of femoral and popliteal arteries, thoracic aorta or visceral arteries are very often the elements of the so-called multianeurysmal syndromes. Aneurysm occurs most frequently in the

abdominal section of aorta, below the ostium of renal arteries. There are some reasons for such location of the change. The wall of the abdominal artery in comparison to other sections is thinner and less elastic. The quantity of elastic laminas rapidly decreases after passing of the thoracic aorta into the abdominal one. The abdominal aorta, contrary to other large arteries, possesses meagre rete of its own nutrient vessels. Deterioration of the nutrition of the aortic wall takes place also because of thrombus formation inside the aneurysm — in this way decreases the possibility of the diffusion of the nutrients and oxygen through the external layer. In our material neovascularisation was observed in 4 cases and 3 of the cases were accompanied by markedly intensified inflammatory reaction consisting of lymphocytes, macrophages and plasmatic cells. The co-existence of the vascularisation and the inflammatory reaction was repeatedly described and the presence of macrophages in the inflammatory infiltration may be significant in the angiogenesis process (12).

The factor initiating aneurysm formation is the decrease of elastin contents. It was experimentally proved. The proteolytic enzymes from metalloproteinase group are responsible for the degradation of the structural albumins. Their activity in the aneurysm is markedly higher than in normal aorta, especially 9 metalloproteinases — the so–called MMp-9. It was also observed that in patients with aneurysm, proteolytic and antiproteolytic balance was revealed since the decrease in the contents of some metalloproteinases tissue inhibits, the so-called TIMPs, especially the TIMP-1 (2). The aorta extracellular structures are supplemented by the proteoglycans and glycosamonoglycans. Their reduced contents were observed also in aneurysm. As some trace elements are co-factors of the mentioned enzymes, therefore the deficiency of some and the excess of others may be significant in aneurysm development. It was observed that copper deficiency might cause the reduction of Lysol oxidase activity. It is the enzyme responsible for the synthesis of elastin cross-bond (7). In our material little amount of elastic fibres was observed and also the disorganisation of the smooth muscles fibres of the middle coat with the middle coat fibrosis and the adventitia fibrosis. These changes were also described by other authors (14,15).

Statistically a very crucial fact is, that it was found twice as frequently in patients with a long-term arterial hypertension. It is crucial, especially with regard to the increased risk of the aneurysm rupture in these patients (1). In our material all the patients had arterial hypertension diagnosed.

Inflammation of the middle coat and adventitia is a frequently described change in aneurysms. In the inflammatory infiltration there are T, B lymphocytes, macrophages and sporadically neutrophilic granulocytes. These types of changes were seen in our 3 cases and in 2 cases there occurred inflammation of the nutrient vessels without the co-existing thrombosis. In none of the cases the presence of granulomas or the formation of the lymphatic follicles was observed. Moreover, we did not prove the aneurysm wall necrosis with the co-existing inflammation and thrombosis of vasa vasorum; therefore none of our aneurysms can be called inflammatory. Results of the research of Satta and associates (12) reveal close relation of the chronic inflammation within the aneurysm with the neovascularisation and Tenascin expression — the oligomeric glycoprotein of the extracellular matrix. Tenascin localised in the endothelium and the wall of the newly created vessels in correlation with mononuclear cells of the inflammatory infiltration, causes monocytes adherence to the epithelium thus impairing their migration through the vessels wall (9,11).

Aneurysm, similarly to many other diseases, does not possess homogenous etiology. The multiplicity of theories as well as the described disease pathomechanism allows approaching the essence of the problem. The histopathological examinations are indispensable in recognizing and understanding the pathomechanism of the abdominal aortic aneurysm.

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EXPLANATION TO FIGURES

Fig. 1. Fibrosis, calcification and crystal of cholesterol in the aneurysm wall. H+E. Magn. 180x.

Fig. 2. Inflammatory infiltration and nutrient vessels in the aneurysm wall consisting of lymphocytes and plasmocytes. H+E. Magn. 360x.

Fig. 3. Reduction of the elastic fibres and disintegration of collagen fibres in the aneurysm wall. H+E. Magn. 420x.

Fig. 4. Neovascularisation in the aneurysm wall. H+E. Magn. 180x.

SUMMARY

The aim of this study was to analyze the scientific protocol of 21 patients operated due to abdominal aortic aneurysm. Arterial hypertension was the common feature for the whole group. Typical microscopic changes for true aortic aneurysm in all histopathological findings were approved. A different in size thrombus was always present inside the aortic sac. In every case atherosclerotic lesions were recognized in the aneurysm wall. In some samples the multiple inflammatory infiltration consisting of mononuclear cells were observed. Simultaneously an intensive angiogenesis process was seen.

Histoklinika tętniaków aorty brzusznej

Celem pracy była analiza protokołu naukowo-badawczego dla grupy 21 chorych operowanych z powodu tętniaka aorty brzusznej. Jedynie nadciśnienie tętnicze było wspólną cechą dla ocenianych chorych. We wszystkich preparatach histopatologicznych potwierdzono rozpoznanie tętniaka prawdziwego aorty brzusznej, z typowymi zmianami w obrazie mikroskopowym. W obrębie poszerzenia tętniakowatego zawsze stwierdzano różnej wielkości skrzeplinę. W każdym przypadku rozpoznano zmiany miażdżycowe w ścianie tętniaka. W niektórych preparatach stwierdzono liczne nacieki zapalne, złożone z komórek jednojądrowych, oraz intensywnie nasiloną angiogenezę.

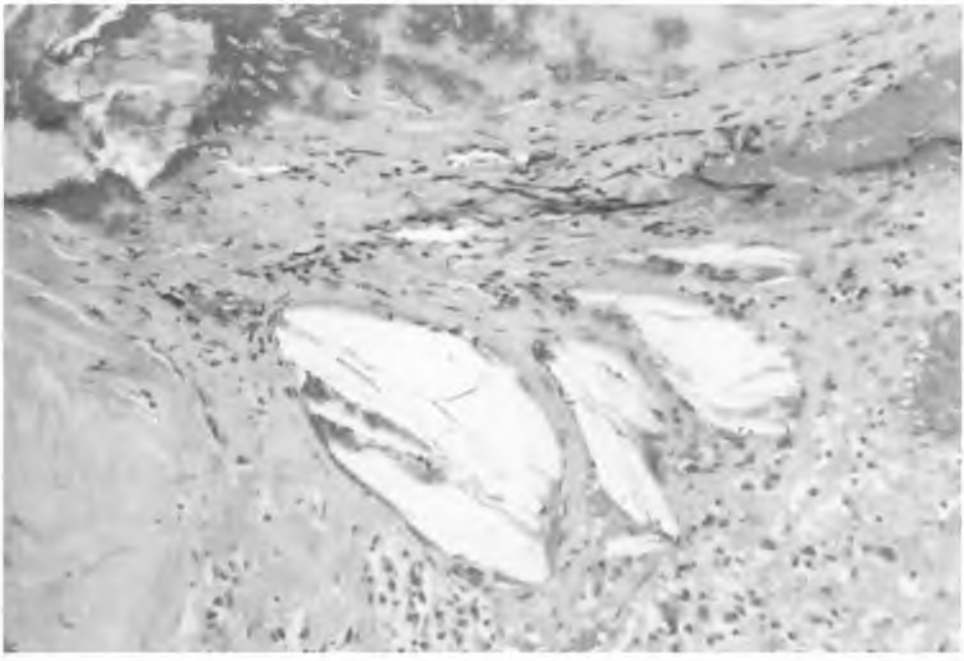

Fig. 1

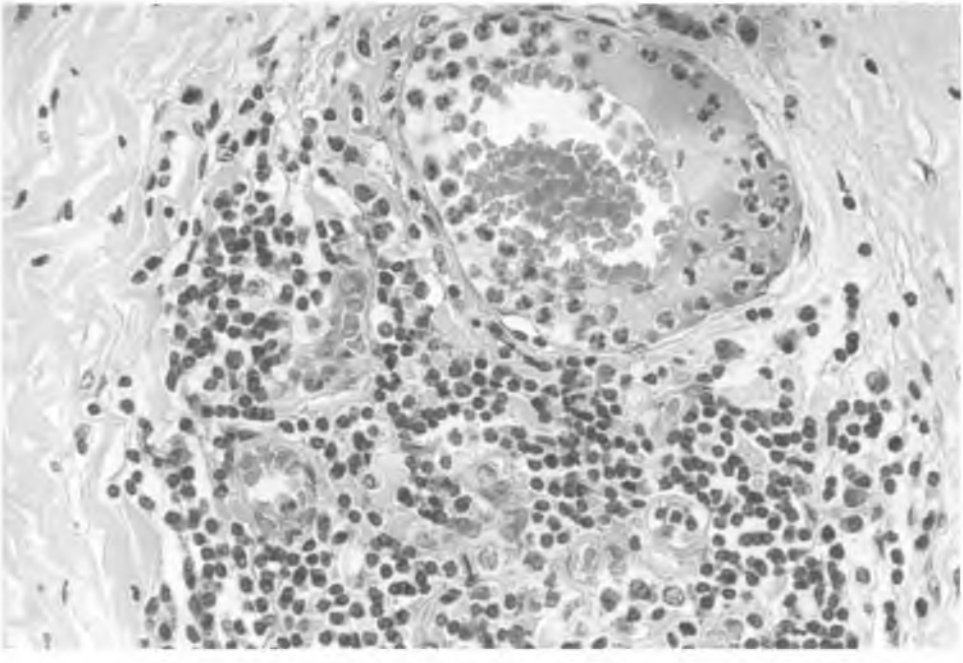

Fig. 2

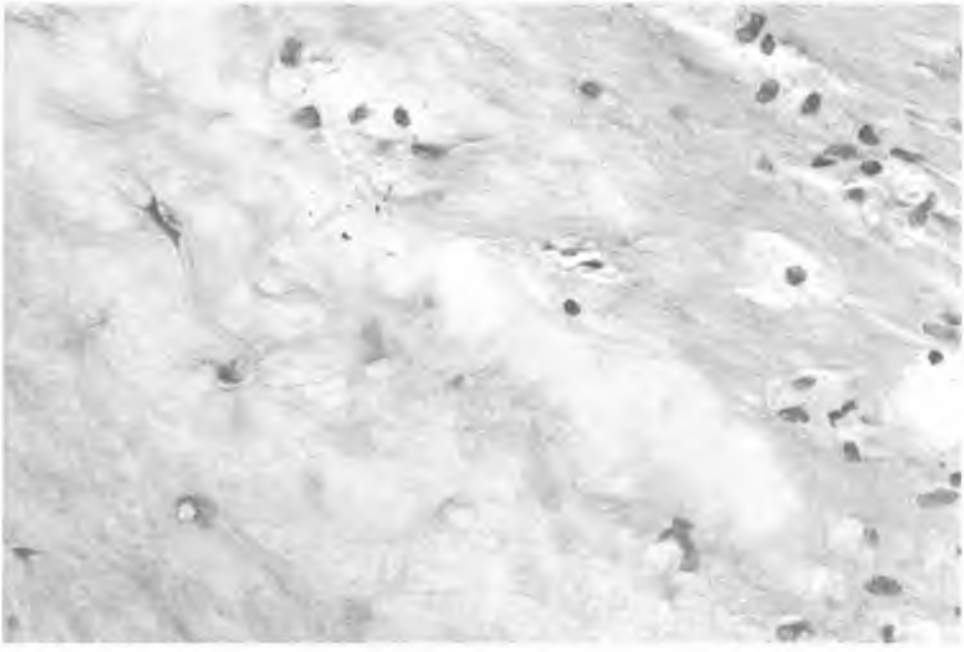

Fig. 3

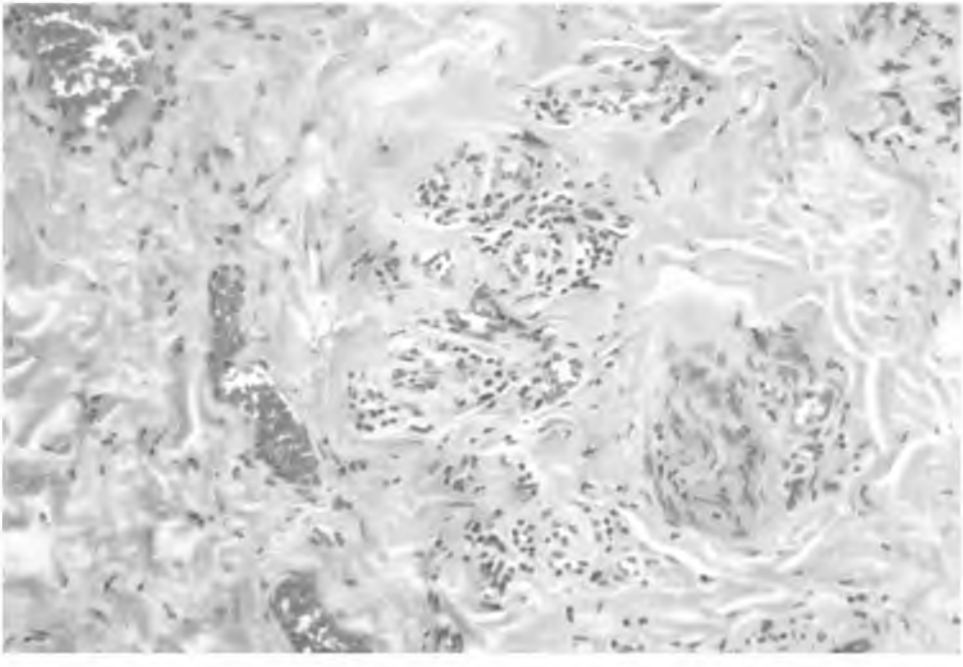

Fig. 4