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Medianecrosis of the Aorta (MNA) – Gsell-Erdheim Syndrome: Main Histopathological Features

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Twenty four cases of Gsell-Erdheim syndrome observed in 1999–2001 have been examined. There were 20 men (83.4%) and 4 women (16.6%). The age ranged from 22 to 69 years but 6 men (25%) died at age under 50. The following variants of aortic lesions were revealed in autopsy material: intimal tear with the following dissection which extends along the aorta to variable distances – in most cases into iliac arteries. The morphologic changes, associated with were: anuclear zones, elastolysis, thinning, dyschromia and fragmentation of elastic fibers, focal hyperelastosis. Such changes were revealed in all parts of the aortic wall, independently of the site of rupture.

Introduction

Diseases, which lead to development of dissecting aneurysms of the aorta (DAA), are well known and their main morphologic features are already described. This statement refers to atherosclerosis, syphilis, nonspecific aorto-arteritis. But today a great part of progressively increasing amount of DAA is associated with medianecrosis of the aorta – Gsell-Erdheim syndrome. Aspects of morphogenesis and etiology of medianecrosis of the aorta are actually in our days [1, 4–7]. We think, it may be explained by insufficient studying on morphological features of DAA and especially of non-atherosclerotic aneurysms of the aorta – Gsell-Erdheim syndrome.

The aim of the study was to examine main microscopic changes of the aortic wall in Gsell-Erdheim syndrome.

Material and Methods

Twenty four cases of Gsell-Erdheim syndrome observed in Lviv Institute of Clinical Pathology during 1999–2001 were analyzed (47.05% of all DAA seen in this period). There were 20 men (83.4%) and 4 women (16.6%). The age ranged from 22 to 69 years but 6 men (25%) died at age under 50. An aortic wall was studied at four standard levels – ascending part, aortic arch, thoracic part and abdominal part. In every case histopathological examination of the aortic wall was done, using routine HE staining, resorcin-fuxin (Hart), picrofuxin (Weigert), Masson's trichrome, and alcian blue.

Results

Analysis of the internal layer in 11 cases (45.8%) showed intimal hyperplasia with focal-diffuse thickening (1/3 of the aortic wall) due to accumulation of extracellular matrix elements, foam cells, deposition of glycosaminoglycans (GAG). Plaques were seen only in 1/3 of the cases and were located mainly in the abdominal aorta and in the area of bifurcation. The predominant type of the plaques was fibrofatty, rarely atheromatosis was revealed. Focal depositions of GAG were seen in the areas of plaques.

GAG depositions occurred in all cases. They were presented by the layers of basophilic alcian blue-positive substance between the smooth muscle cells (SMC) and fibrillar components. Elastic fibers (EF) and collagen fibers (CF) orientation was preserved.

Even in routine HE staining foci of homogenous basophilic substances, parallel to EF and dissecting them were revealed. Single and more commonly multiple cystic cavities, which fuse and form large areas filled with GAG, were revealed. In special staining such areas showed focal elastolysis. The changes were mostly seen in subintimal layer, but in 1/3 of the cases diffuse lesions, which involved the whole media were revealed.

Cystic cavities (CC) – small round cavities with well defined alcian blue-positive margin [3, 7, 8] were revealed in GAG depositions in all cases. Their size was the same as the cellular size. In some cases they were single, but more

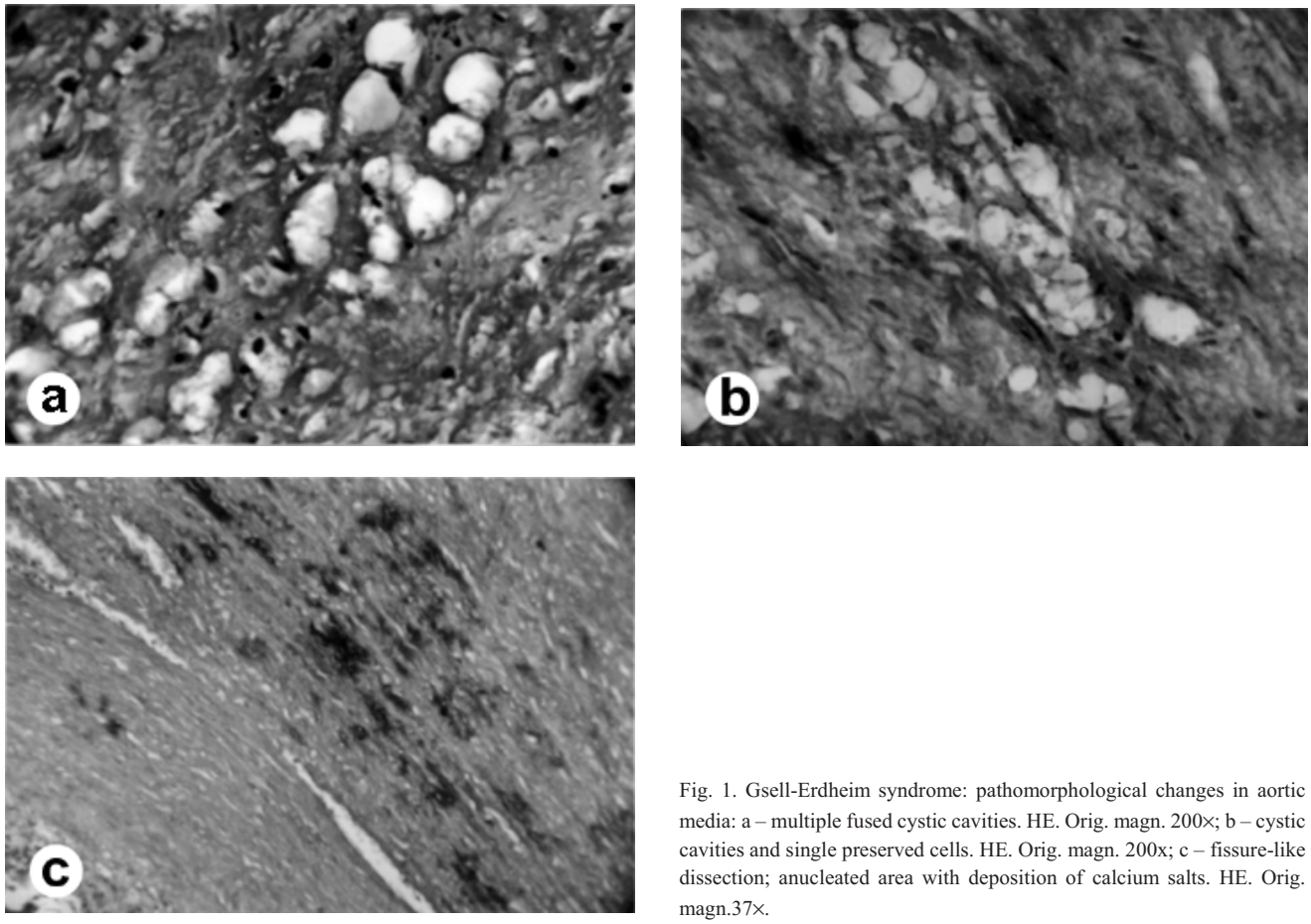

Fig. 1. Gsell-Erdheim syndrome: pathomorphological changes in aortic media: a – multiple fused cystic cavities. HE. Orig. magn. 200×; b – cystic cavities and single preserved cells. HE. Orig. magn. 200x; c – fissure-like dissection; anucleated area with deposition of calcium salts. HE. Orig. magn.37×.

frequently (18 cases) in one field of view (40×5) 25–30 cavities may be counted (Fig. 1a). In most cases they were not connected with one another, but rather often several fused cavities may be seen (Fig. 1b). In 1/3 of the cases CC were empty, in other cases they were filled with accumulations of alcian blue-positive substances, which are defined as mucopolysaccharides. CC wall in some areas was destroyed. CC probably are the cells with severe alterative-degenerative changes. Since the predominant cell type of aortic media is SMC and CC is a common finding in all parts of the media, we may suggest that alteration refers to SMC.

In all cases anuclear areas were revealed. Some of them were ribbon-like (18); the others had irregular shape and were associated with abnormalities of fiber orientation (6). Such areas were located mainly in the middle or lower 1/3 of the media. While the width of the anuclear ribbon-like areas was similar in different parts of the aorta, their length was variable. The greatest length was in the zone of rupture. According to the size, focal and diffuse changes were described. Fibrillar components in such areas were preserved (in Hart staining such areas were invisible). Accumulations of mucoid substances, rarely deposits of calcium salts and hemorrhages were also revealed (Fig. 1c). In most cases these areas were located near the zone of dissection, but interconnections were not always evident.

Changes in the media, which were described above, in all cases were associated with the foci of medianecrosis – areas with disorientation and disaggregation of the main structural components. They were revealed in the different parts of the media, their size was 1/3–1/2 of the medial thickness and they had irregular margins. Lysis of EF and multiple CC were seen in such zones.

Degenerative changes of EF were revealed in all cases. They include different grades of reversible and irreversible changes of the single fibers. The common type of reversible changes was swelling of EF, when the fibers become thick, pale – hypochromic, especially in the central part. Irregular focal swellings with formation of ribbon-like structures were found in 10 cases. Commonly such changes were associated with the loosening – loss of defined margins. The changes were revealed mainly in medial layer. EF in intima and adventitia were normal. Such changes were seen in single fibers and in large areas – 1/3–1/2 of the media. There was combination of hypochromic and hyperchromic fibers, and the changes were associated with other types of EF lesions (swelling, defibrillation).

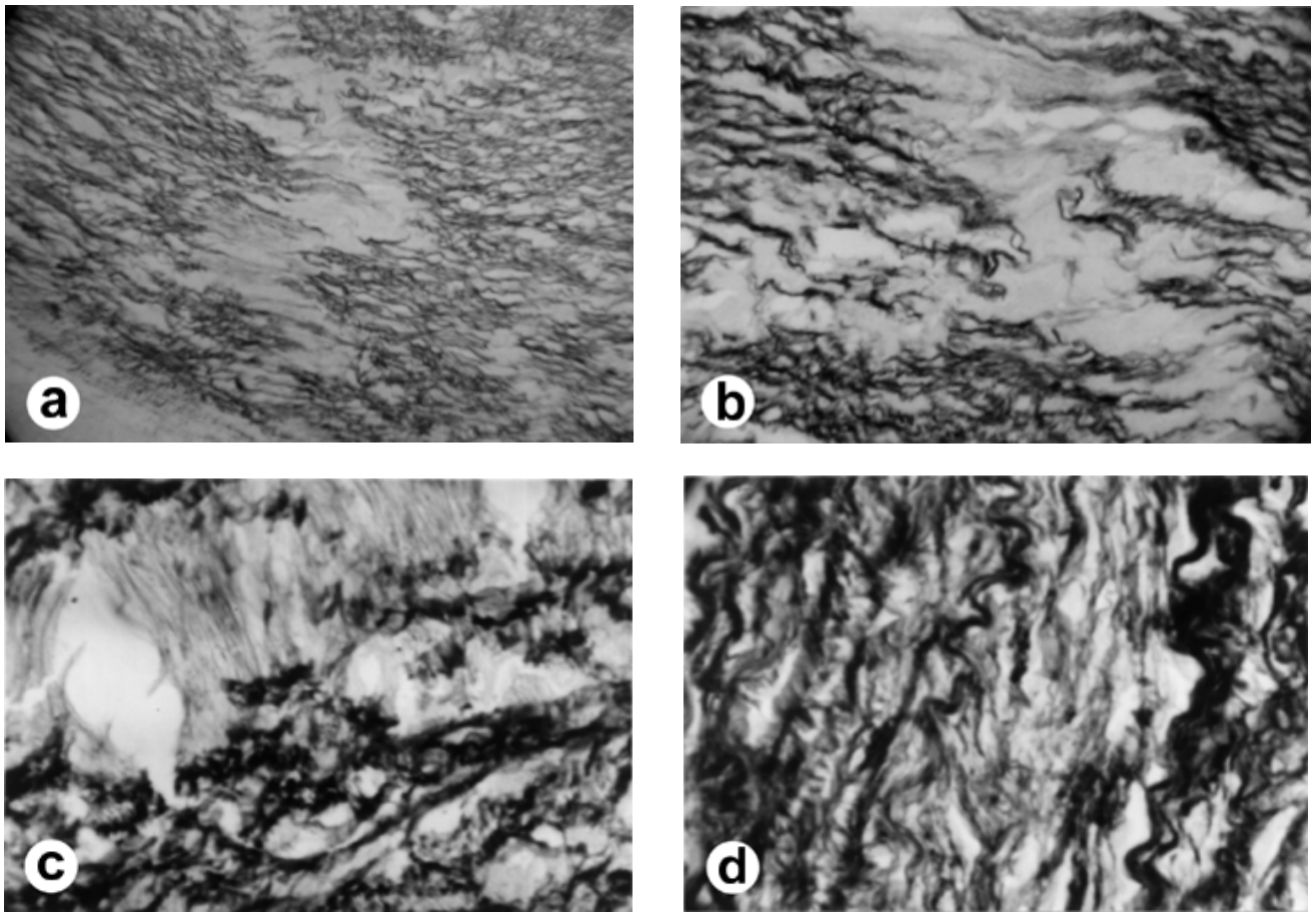

Fig. 2. Gsell-Erdheim syndrome: variants of elastic fibers changes: a – elastic fibers lysis with accumulation of mucopolysaccharides – medianecrosis; areas of dyschromia, thinning, fragmentation of elastic fibers. Resorcin-fuxin. Orig. magn. 100×; b – a fragment of the Figure 2; Orig. magn. 200×; c – fused areas of elastolysis (filled with mucopolysaccharides) and fragmented elastic fibers with signs of hyperelastosis, multiplication and clumping. Resorcin-fuxin. Orig. magn. 100×; d – elastic fibers: hyperelastosis, thinning, areas of elastolysis. Resorcin-fuxin. Orig. magn. 200×.

EF fragmentation [9] occurred in all cases, but grade of the lesions was variable in different parts of the aorta. Classification of the fragmentation by T.J. Schlatman (1977) [9] is used for description of the elastic membranes fragmentation. Three grades of fragmentation may be distinguished: I grade – less than 5 foci of elastic fragmentation (in one field of view, ×200), every focus includes 2–4 adjacent elastic membranes, orientation of SMC is preserved; II grade – 5 or more foci of fragmentation (in one field of view), foci may be dispersed in the media or fused, orientation of SMC is preserved; III grade – fragmentation of more than 5 adjacent elastic membranes, independently of the amount of foci (in one field of view), orientation of SMC is damaged. The highest level – III grade – was seen near the rupture of the aortic wall and was irreversible (Figs. 2a and 2b). In the adjacent areas fragmentation was lower – II or III grade. In other parts of the aorta it was mild – I or II grade – and reversible. Thus, fragmentation in the different parts of the aortic wall was a result of the same process, but with different grades of the severity. Fragmentation of the III grade was combined with the other irreversible lesions – lysis of the collagen and EF (Figs. 2c and 2d). The latter were revealed as an amorphous mass with the signs of hyperelastosis and thinning of EF. Commonly seen fragmented EF were not visible in the areas of lysis or dyschromia, but EF with the signs of loosening, swelling or ribbon-like fibers rather often were fragmented.

Multiplication of EF – presence of multiple thin fibers instead of the normal elastic membrane, independently of the site of dissection – was revealed in 11 cases. Commonly it was seen in the areas of EF lysis.

Some other changes were also seen in the media. Hemorrhage was revealed in the area of rupture and spread to the adventitia. Inflammatory infiltration (leukocytes, plasma cells, lymphocytes, histiocytes), described in some reports [3, 7–9], was not marked. Vascularization was rare (5 cases) when medianecrosis was associated with prolonged arterial hypertension. Nutrient vessels (*vasa vasorum*), forming groups of multiple or single vessels were located in the lower one third of the media, and were associated with focal fibrosis.

In the adventitia were observed: edema, focal sclerosis, *vasa vasorum* with perivascular sclerosis, segmental hypertrophy of the wall, stenosis of the lumen and lymphohistiocytic infiltration. In the area of ruptured adventitia massive hemorrhage was visible, stasis and dilation of *vasa vasorum*.

We revealed three variants of aortic dissection according to its appearance. The first variant – "slit-like" dissection resembled an angle or slit, which expands toward the distal direction. The second variant – "multilayered-multistoried" – dissection includes several layers, separated from one another by slit dissections. Such layers were thin and consisted of several (three-four) fibrillar elements. The third variant – "cystic" dissection consisted of several cystic cavities, which resembled honeycomb with ruptured walls. The most common variant was the first one (18 cases), second and third ones were rarer (4 and 2 cases, respectively).

Discussion

In our research we have carried out complex standardized morphologic examination of aortic wall, which allows us to specify and formulate complex of morphologic changes typical for MNA.

Intimal hyperplasia due to accumulation of extracellular matrix components is the main change in the internal layer of the aortic wall. Such changes may be explained as a vascular wall response to nonspecific injurious stimuli, hemodynamic disorders or as secondary changes, caused by primary lesions in media or adventitia.

The most important changes are revealed in media – 1) medianecrosis and anuclear areas, 2) elastolysis, 3) cystic spaces, accumulation of alcian blue-positive substances.

Elastolysis is the most prominent histological marker. Changes in staining properties (dyschromia) and large-scale loss of elastic membranes are seen in MNA. Medianecrosis is a controversial term, because true necrosis and reactive inflammatory response are absent. Some other terms may be used for definition of these histological findings – cystic medial degeneration, cystic medial necrosis, but none of them explains the real process. So, we prefer to use the oldest one, suggested by Gsell in 1825. Lysis and fragmentation of elastic membranes, anuclear areas and separation of elastic and fibromuscular elements with formation of large spaces filled with amorphous extracellular matrix are revealed in such cases. It is difficult to explain pathogenesis of these changes, but we think that response of smooth muscle cells to injurious stimuli is an important event. Cellular lesions may later cause a complex of various secondary effects in all other components of the vascular wall.

Such pathologic changes are seen not only in the site of rupture and dissection. They may be revealed in the different parts of aorta, but their severity varies from site to site.

Besides these typical changes a group of minor lesions may be revealed in adjacent or distant areas. Such findings include focal thinning, hyperelastosis, swelling, multiplication, fragmentation of elastic fibers, focal accumulations of alcian blue-positive amorphous components of extracellular matrix and formation of multiple small cystic spaces in the site of pre-existing smooth muscle cells. These minor changes are a common finding in elder patients without aortic dissection and may be explained by hemodynamic effects, including hypertension.

Thus, we have described a complex of histopathological changes in the aortic wall. Some of them represent a nonspecific response of the vascular wall to various injurious stimuli (hemodynamic, involutive, metabolic etc.). But medianecrosis and elastolysis are a sign of severe medial lesion, which results in aortic dissection.

Conclusions

1. In aortic medianecrosis pathologic process was revealed in the entire vessel, not only in the area of aneurysm and dissection. Manifestations of variable severity of the same process were seen in different parts of aortic wall.
2. Irregular focal thickening of the intima; focal accumulations of alcian blue-positive mucoid substances, single cystic cavities, focal irregular anuclear zones with disoriented fibers of the media were seen in the areas, distant to the rupture of the aortic wall. Medial lamina elastica interna was partially straightened, fragmented (I–II grade), with the zones of hyperelastosis and multiplication. Adventitial edema, rarely focal sclerosis and perivascular sclerosis of *vasa vasorum* were typical.
3. Signs of total medial disorganization were seen near the area of rupture: focal accumulations of mucoid substances, ribbon-like anuclear zones, chaotic orientation of smooth muscle cells with severe degeneration; irregular sclerosis (collagen fibers). Elastic fibers showed focal hyperelastosis, fragmentation of the lamina elastica interna and medial membranes (I-II grade) with the signs of thinning, straightening or hyperelastosis. Areas of severe elastolysis and zones filled with amorphous masses with altered staining properties and fragmented elastic fibers (II–III grade) were revealed near the rupture of the aortic wall. In adventitia severe hemorrhage and dilated *vasa vasorum* were seen.
4. Aortic medianecrosis – Gsell-Erdheim syndrome – is a disease of the aorta, associated with the lesions of elas-

tic fibers in the media and with some other typical morphologic changes. Clinically it manifests as a dissecting aortic aneurysms.

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