The aorta, the elastic tissue and cystic medial necrosis

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Despite the advances made in diagnostic methods and techniques of surgical correction in recent decades, aortic diseases remain a major cause of mortality and cardiovascular morbidity and an ongoing challenge for cardiologists and cardiovascular surgeons.

To study comprehensively the serious diseases involving the aorta and other elastic arteries, there is need to seek understanding with the scientists who tirelessly studied the phylogenetic evolution of biomolecular and elastic tissue.

It is believed that about 500/600 million years ago during the great burst of the Cambrian period, variant forms of life appeared. Among them were the oxygen-producing cyanobacteria. The progressive enrichment of oxygen in the atmosphere continued during this era. Since most specimens were adapted to a preexisting atmosphere without oxygen, many have disappeared during this phase. New mutations, however, allowed the specimens survivors to adapt to aerobic forms of life, which diversified later.

Vertebrates have been successful in the colonization of all possible ecological niches. Their extraordinary ability to adapt is directly related to the development of a system that allowed access to maximize their cells with oxygen, which is efficiently used for their mitochondria to generate energy. The emergence of an elastic tissue was essencial in developing lungs and cardiovascular system more complex to capture and carry oxygen to the most remote cells of beings of increasing complexity.

According to Leslie Robert [1], from the Laboratory of Cell Biology, University of Paris, "... we consider an extraordinary coincidence that the elastin gene arose during this period. As far as we know, the further development of the elastin gene occurred rapidly, from fish to terrestrial quadrupeds. Elastin, in evolutionary terms, is much newer than most of the collagens." The only similarity between these two types of protein is that both have high proportions of glycine, which ended up confusing the first researchers.

The phylogenetic development of elastin has been crucial for vertebrate develop respiratory and circulatory systems highly efficient. However, these highly specialized systems are malfunctioning related to the aging process by gene determination, causing severe disease in humans. The author concludes his essay by stating that "... this shows once again that the fact of creation of new genes is related to a mechanism to empower each individual species for reproductive success and not to prolong life."

The middle layer of the aorta in humans is comprised of four basic elements: elastic fibers, collagen fibers, smooth muscle cells and amorphous substance, arranged in periluminal disposition in lamellar units. Each unit consists of two lamellar elastic fibers parallel with smooth muscle cells, collagen fibers and amorphous substance between them. Transverse thin elastic fibers connect the larger fibers. This basic pattern is present throughout the length of the vessel, although there are quantitative and qualitative differences between the thoracic and abdominal segments. The thoracic aorta contained 35 to 56 lamellar units, while the abdominal aorta contains around 25 to 28 of these units [2]. The middle layer of elastic arteries has an important role in maintaining the architecture of the vascular wall in response to deformation caused by the pulse wave determined by cardiac systole.

Humans lost the ability to produce elastic fiber early in life, and short synthesis of elastin can be detected in the aortic wall after infancy. Moreover, the number of lamellar units is constant in the aorta of mammals, except humans [3].

Degenerative diseases of the middle layer are the most common causes of aneurysms involving the proximal thoracic aortic. Although most cases are idiopathic, some genetic disorders such as Marfan syndrome, are associated with premature degeneration of the aortic media, and is histologically represented by cystic necrosis (accumulation of mucopolysaccharides), elastic fragmentation and apoptosis of smooth muscle cells. It is believed that cases

of idiopathic dilated of the aortic root may represent fruste form of this syndrome [4,5].

The adventitial layer, which has no external limiting layer, is relatively underdeveloped compared to the average, and contains elastic fibers and collagen. Pereira [6] and White [7] believe the loss of structural integrity of the adventitial layer, not the middle layer would be required for the development of aneurysms. For them, the structural integrity of this layer is critical for the maintenance of the entire aortic wall submitted to intraluminal hemodynamic stress.

The pulse wave determined by cardiac systole, causes in the aorta a localized distension circular and significant longitudinal distension of each elastic strain and of each lamellar unit. It is believed that the internal elastic membrane and the internal lamellar units of the middle layer are proportionally more affected than the outer portions. Cliff [8] suggested that an expansion occurs up to 20% of the diameter of the inner portions and 1% to 4% of the outer portions, although a change of only 10% of radial motion has been proposed [9]. Dobrin [10] reported that the descending thoracic aorta increases longitudinally 1%, while the ascending aorta and pulmonary artery increased from 5 to 11% [11].

In 1986 was identified the **fibrillin-1**, whose involvement in the pathogenesis of Marfan syndrome has been widely accepted. Sakai [12] demonstrated that it is a distinctive structure of collagen, which may be associated or not with elastin in its amorphous form. From then on it became clear that fibrillin-1, and no collagen VI was immunolocalized microfibrillar system component periodically along the microfibrils and that these microfibrils may be aligned in bundles. Fibrillin is described as a collagenase-resistant glycoprotein, monossulphate, with molecular weight estimated at approximately 350 kD and is capable of forming intermolecular disulfide bonds, forming an insoluble aggregate.

In culture media, fibroblasts secrete their precursor, profibrillin in about 4 hours, and processed and deposited into the extracellular matrix with lower weight (320 kD), resulting from a possible proteolytic cleavage. The conversion of the precursor to the final product varies among controls, however, on average, is complete around the twentieth time. The deposition of aggregated protein, alone or together with other proteins, will form a microfibrillar network, associated or not with elastin, thus becoming incorporated into the microfibrils structures [13].

Fibrillin-1 has been proposed as the main component of the system due to its microfibrillar immunolocalization in all tissues where the microfibrils can be structurally identified [12.14]. These microfibrils contain fibrillin molecules that can be identified periodically along its length. It was the fact that fibrillin-1 is a glycoprotein rich in cysteine, which rapidly forms disulfide bonds, which reaffirmed the possibility of it being the main structural component of microfibrils [14,15]. This protein has been recognized as distinct microfibrillar protein elastin, and is believed to have the task of forming a scaffold for subsequent deposition of elastin [16].

Ascending aortic aneurysms are most commonly related to degenerative changes of the middle layer secondary to inherited metabolic disorders. Atherosclerosis is less common in the ascending aorta, the opposite occurring in the descending thoracic aorta. When atherosclerosis is present in the ascending aorta is often associated with those degenerative changes of the middle layer. However, arteriosclerosis as a cause of aortic aneurysms has been intensely debated in the literature [17]. From the biochemical point of view there is a strong affinity for calcium and lipids to the elastic fibers characterizing the aging process [1].

De Sá et al. [18] demonstrated that patients with bicuspid aortic valve (BAV) have more severe degenerative changes in the medial layer of ascending aorta and pulmonary artery than those observed in patients with tricuspid aortic valve, with no relation to age. Later, there was also less fibrillin-1 in the ascending aorta and pulmonary arteries of patients with this congenital malformation. However, the total amount of elastin was similar in both groups [19].

Therefore, it is possible that in certain genetic disorders occurs only reduced fibrillin-1 in the extracellular matrix, since the quantities of elastin and, possibly, elastic tissue, were similar in both groups [19]. Other authors have pointed out that the medial necrosis, elastic fragmentation and alterations in smooth muscle cells in young subjects, ie aged less than 40 years, has a hereditary relationship and result in biochemical defects that are responsible for the loss of cohesive strength of the aortic media [20].

The presence of cystic medial necrosis or accumulation of mucopolysaccharides, although nonspecific, may be a marker of the presence of complex degenerative processes and has assisted in clinical practice to identify patients at higher risk of cardiovascular complications, such as, for example, conduct and monitoring of surgical patients with BAV [21,22]. In an article published in this issue, colleagues will have the opportunity to review the various clinical and pathologic features that involve the cystic necrosis of the aortic media [23].

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