Biomarkers in Acute Aortic Syndrome
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5.1 Introduction

The term acute aortic syndrome (AAS), coined 6 years ago [111], indicates a heterogeneous group of patients presenting one of the following acute aortic pathologies: aortic ulcer, intramural haematoma or classic aortic dissection (Fig. 5.1). More recently, aortitis [109] and intraluminal thrombus [106] were included in this syndrome (Fig. 5.1). Aortic ulcers penetrate the intima through the media; intramural haematoma presents a haemorrhage into the aortic media with the formation of a false lumen; the classic aortic dissection is characterized by the presence of an intimomedial entrance tear. The term aortitis indicates a thickening of the wall owing to different mechanisms such as infections and autoimmune disorders causing systemic vasculitis. Although these alterations appear mostly distinct, the fact that in some cases they coexist demonstrates a possible link between them (Fig. 5.1).

Aortic aneurysms and dissections can be classified on the basis of morphology, aetiology, and anatomic location. Although aneurysms may arise at any site along the aorta, they most frequently occur in the infrarenal abdominal aorta or the descending portion of the thoracic aorta. The ascending thoracic aorta is another common location for aortic aneurysm, which may develop in association with hypertension and spontaneous (type A) aortic dissection, congenital valvar abnormalities (e.g., bicuspid aortic valve, BAV) [98], and inherited connective tissue disorders, e.g., fibrillinopathies type 1 [30, 64] such as Marfan syndrome (MFS) [18, 19], classic, hypermobile and vascular Ehlers-Danlos syndromes (EDS) [78], osteogenesis imperfecta [40], X-fragile syndrome [41], and polycystic kidney disease (PKD) [103]. Aneurysms result primarily from degenerative changes in the aortic wall. Severe intimal atherosclerosis, chronic transmural inflammation, and destructive remodelling of the elastic media are associated with aneurysms dissections that affect primarily the descending thoracic aorta and abdominal aorta (thoracoabdominal aortic aneurysms, abdominal aortic aneurysms, AAAs, and type III dissections) [46, 105].

In contrast, aneurysms and dissections that affect the ascending aorta are primarily due to lesions that cause degeneration of the aortic media, a poorly understood pathological process called cystic medial necrosis (CMN) [26, 73, 75] (Fig. 5.2). CMN is characterized by degeneration and fragmentation of elastic fibres, loss of smooth muscle cells (SMCs), and interstitial collections of basophilic-staining ground substance. Although the pathogenesis of medial necrosis is not understood, it is almost certainly not a single disease entity. Medial necrosis occurs with normal aging of the aorta [88, 89] but it can be accelerated by conditions such as hypertension and it is also associated with genetic syndromes, such as MFS and aortic bicuspid valve (Fig. 5.2).

The specific factors causing aneurismal degeneration in the different locations remain unresolved.

Pathophysiological studies on human and experimental AAAs have focused on increased expression and tissue localization of elastin- and collagen-degrading enzymes, particularly matrix metalloproteinases (MMPs), cysteine proteases, and their respective inhibi-
Fig. 5.1. Acute aortic syndrome. Arrows indicate the possible progression of each of these aortic lesions. (Adapted from van der Loo and Jenni [106]. Classic dissection and intramural haematoma adapted from Vilacosta [110]. Aortitis from Nunn-ninghoff et al. [76]. Aortic ulcer from Eggebrecht et al. [21]. Intraluminal thrombus from Wegener et al. [115]).

Fig. 5.2. Cross sections of ascending thoracic aorta of a control subject (A), of an aortic aneurysm associated with Marfan syndrome (B), and with bicuspid aortic valve (C) stained with Alcian blue and Verhoff-van Gieson. Magnification×250. (From Nataatmadja et al. [73]).

However, the absence of a significant inflammatory response implies alternative mechanisms of aneurysm formation in TAAs with respect to AAAs, related to the different embryologic origin of cells populating the ascending and infrarenal aorta, to the different structural properties and propensities toward atherosclerotic degeneration, or to the distinct haemodynamic conditions in these two areas. Absi et al. [2] in 2003 by using microarray technology showed distinct patterns of gene expression for ascending aortic aneurysms and AAAs.

Clinical manifestation of AAS is aortic pain that affects neck, throat, and anterior chest when the ascending aorta is involved, while descending aorta alteration is associated with back pain and abdominal pain. The aortic pain (chest pain) is probably due to aortic root dilatation and is similar to that caused by ischemic syndromes (angina pectoris). Acute coronary syndromes may result from AAS or be associated with them [109]. Overall, AAS can remain asymptomatic until the initial dissection and also later since the symptoms are common to many pathologies.

The mortality rate of untreated dissection is about 1%/h for the first 48 h increasing up to 80% at 14 days [101]; the gold standard techniques for the diagnosis of AAS are represented by imaging analyses such as computerized tomography, transoesophageal echocardiography, and magnetic resonance. Each of these techniques has some advantages and some limitations; therefore, at least two are required for a diagnosis but the common limit is represented by the fact that the equipment and the personnel with the necessary expertise to perform the tests and interpret correctly the data are not available in all medical set-ups. For these reasons the identification of biochemical and genetic markers able to readily and rapidly diagnose and/or to recognize a predisposition to develop an AAS are highly required, also considering the importance of prophylactic surgery in all patients.