Spontaneous aortic dissection due to cystic medial degeneration. Report of a sudden death case and literature review

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Abstract: A 32 years old woman collapsed during work, after complaining for several minutes of intense diffuse abdominal pains. An emergency team arrived on the spot succeeded in reconverting a ventricular fibrillation and rushed the patient to an Emergency unit. Upon admission the patient was in shock (pulse 110/min, blood pressure 60/40 mmHg), extremely anxious, and continued to complain of intense epigastrial pains. A plain X ray and abdominal echography were irrelevant. Although the ECG suggested an acute myocardial infarction, the enzymatic markers of acute myocardial ischemia were uncharacteristic. The patient died 2 hours after admission, with the presumed diagnostic: “Acute myocardial infarction TOPOL I, possibly with spontaneous reperfusion. Cardiac arrest on ventilatory support”.

The autopsy revealed an almost circumferential aortic dissection initiated at the ostia of the left coronary artery, extending down to right common iliac artery. Microscopic examination revealed a myxoid degeneration between the disrupted elastic lamellae of the aortic media. The paper reviews the incidence of aortic spontaneous dissection, the pathogeny and associated genetic anomalies of aortic media degeneration.

Key words: aortic dissection, cystic medial necrosis, myxoid degeneration, sudden death

Aortic dissection, first described in 1761 [1] remains one of the most severe acute vascular disorders; its low prevalence and great symptoms diversity makes it hard to be diagnosed in the emergency room without a high level clinical suspicion. In order to assess the presentation, management and outcomes of aortic dissection in 1995 was proposed and in 1996 created “The International Registry of Acute Aortic Dissection” which, by the end of 2008 contained more than 2000 patients, from 25 large referral centers in 12 countries [2].

The incidence of aortic dissection is estimated to 5-30/million people/year [3, 4] with a prevalence about 100-250 lower than coronary artery disease [2]. Untreated, aortic dissection has a mortality of 25% at 24 hours, 50% at 48 hours and 80% in two weeks [5, 6]. With medical treatment in-hospital mortality is around 55,9% for Type A and 32,1% in Type B Aortic Dissection; surgical interventions (for Type A) diminishes the mortality to 26,6% and endoscopic interventions (for Type B) diminishes the mortality to 9,6% [2].

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Main causes of death in aortic dissection are: rupture of the aneurysmal sac (80%-86% [7, 8]), usually in the pericardial sac (70% in acute cases, 20% in subacute cases and 25% in chronic cases [7], hemorrhage in left (more often) or right pleural cavity, mediastinum, retroperitoneum, peritoneal cavity, gastrointestinal tract, congestive heart failure (often in chronic aortic dissection), coronary artery involvement/acute myocardial infarction, occlusion of abdominal aorta or its terminal branches, gut malperfusion, carotid hemiplegia, mycotic dissecting aneurysms [7], renal or spinal malperfusion [2]; mortality due to aortic dissection is highest in patients with no back/thoracic pain at initial presentation, hypotension/shock or aortic branches involvement - “the deadly triad” [2]

Classifications of aortic dissection [9, 10]

<table>
<thead>
<tr>
<th>Classification</th>
<th>Svensson</th>
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<tr>
<td>Stanford</td>
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<tr>
<td>A: ascending aorta affected</td>
<td>1: classic dissection with true and false lumen</td>
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<tr>
<td>B: ascending aorta not affected</td>
<td>2: intramural hematoma or hemorrhage</td>
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<tr>
<td>DeBakey</td>
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<tr>
<td>1: entire aorta affected</td>
<td>3: subtle dissection without hematoma</td>
</tr>
<tr>
<td>2: ascending aorta affected</td>
<td>4: atherosclerotic penetrating ulcer</td>
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<tr>
<td>3: descending aorta affected</td>
<td>5: iatrogenic or traumatic dissection</td>
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Aortic dissection is rarely associated to other pathological conditions such as: cocaine use [2, 5, 11], false ecchymoses [7, 12], traumatic dissections [13], bloodless dissection [14], etc.

Case report

While working in a restaurant, a 32 years old woman started to complain of diffuse abdominal pains then collapsed unconscious. An emergency team recorded on the ECG a polymorphic ventricular tachyarrhythmia that rapidly translated into a ventricular fibrillation. After a successful electrical reversion the patient was rushed to an Emergency Unit.

Upon admission the patient was extremely anxious, complained of intense epigastrial pains. The pulse was 110/min, blood pressure 60/40 mmHg. A plain X ray and abdominal echography were irrelevant. Although the ECG suggested an acute myocardial infarction, the enzymatic markers of acute myocardial ischemia were uncharacteristic. A CT scan could not be performed due to the extreme agitation of the patient. The patient died 2 hours after admission, with the presumed diagnostic: “Acute myocardial infarction TOPOL I, possibly with spontaneous reperfusion. Cardiac arrest on ventilatory support”.

The autopsy revealed a moderate haemopericard (120 ml), an almost circumferential aortic dissection initiated at the ostia of the left coronary artery (Fig. 1), extending up to right common iliac artery (Fig 2).

Other circumstantial findings consisted in moderate hipoplasia of LAD, short LCx, predominance of RCA, multiple subendotelial atheroma plaques of RCA with marked luminal stenosis, acute ischaemic areas in the posterior wall of the left ventricle and posterior 1/3 of the interventricular septum. The wall of the right ventricle was thin (<3 mm) with extensive invasion of subendocardial adipose tissue in the myocardial tissue.

Material and methods

Tissue samples of myocardium from the right ventricle and aorta were taken for histopathology investigation. Specimens were selected from the ascending aorta, descending thoracic and abdominal aorta (at renal and iliac level). The selected tissue samples were formalin-fixed and paraffin-embedded. Sections were cut at 5 microns and stained using the standard H&E and van Gieson stains. Special stains such as Weigert (basic resorcin fuxin) for elastic fibers, Gomori (silver impregnation) for reticulin collagen fibers and histochemistry (PAS stain, PAS with diastase and
Alcian blue pH-2.5) for glucidic compounds (glycogen, neutral mucins and acidic mucopolysaccharides) has been carried out. To ensure the reliability of the experimental study, internal quality control of histopathological techniques was performed as a part of an implemented and certified quality assurance system (ISO 9001/2001).

All slides were examined and photographed on a Zeiss AxioImager A1 microscope. Digital images acquired with Zeiss Axio Vision program have been processed and analyzed with ACDSee Pro Photo Manager 3.0, running under Windows XP Professional.

Results

Classic histopathology investigation has revealed an extensive dissection of the ascending and descending aortic wall (restricted to the inner two thirds of the media and adventitia), accompanied by massive hemorrhagic infiltrate beneath the media (fig. 3).

Focal disarrangements of smooth muscle fibers in the aortic wall were also identified.

Van Gieson stain showed fragmentation, a decreased number of collagen fibers and loss of nuclei in the aortic media. Connective tissue fibers in disarray were also observed with Gomori silver stain (fig. 4).

Weigert stain showed disruption of elastic fibers by pools of amorphous ground substance (fig. 5), which was negative to PAS stain and PAS with diastase.

Alcian blue (pH-2.5) stain has revealed an accumulation of acidic mucopolysaccharides (mucoid or myxoid degeneration) between the disrupted elastic lamellae of the media (fig. 6). Other microscopic collateral findings were marked lipomatosis of the heart (fig. 7) and incipient atheromatosis of the major branch of coronary arteries (with foamy cells in the arterial intima). No noticeable histological changes were found in other organs.
Fig. 3 Aortic dissection with hemorrhagic infiltrate between media and adventitia, ascending aorta (HE, 5x)

Fig. 4 Connective tissue fibers in disarray in the media (Gomori stain, 40x)
Fig. 5 Disruption of elastic fibers in the media (Weigert stain, 20x)

Fig. 6 Spaces with blue mucinous ground substance in the media (AB stain pH-2.5, 40x)
Discussions

Degenerative (or dystrophic) artery disease (in particular myxoid / mucoid degeneration of the aortic media) was recognized as an etiology of aortic dissection and has been observed since the sixties. Thus, the presence of big amount of acidic mucinous polysaccharides in the aortic media accompanied by loss and fragmentation of elastic fibers involves some reaction to haemodynamic turbulence, leading to a weakness of the aortic wall, which is susceptible to rupture in time [15].

This lesion is also known as cystic medial necrosis and may be associated with benign intimal hyperplasia, as a substrate of acute coronary syndrome in cocaine abuse [16]. It was described in both Marfan and non-Marfan syndrome, especially in young women [17], followed by non-traumatic, spontaneous wall dissection, mainly in ascending and thoracic aorta [18, 19]. Other localizations involve the circumflex coronary artery [20] and the carotid artery [21], associating aneurisms of the vessels wall at these sites.

The cause of myxoid degeneration is unknown. Areas of cystic medial degeneration could be found in 60% of cases at autopsy, but this is probably secondary ischemic damage due to shearing of the vasa vasorum.

It was suggested, based on the experimental induction of defects in collagen cross linking, that the defect in the media in aortic dissection may have a metabolic basis [22]. In patients with Marfan syndrome, this lesion is caused by point mutations in the fibrillin gene that prevent normal deposition of elastin in the extra cellular matrix [23]. Recent studies suggest that chronic apoptosis of vascular smooth muscle cells promotes medial degeneration and early atherosclerosis in mouse models [24].

An important issue when aortic dissection is found at the autopsy is the genetic screening, especially in young persons with Erdheim lesions (cystic medionecrosis) were
there are no other significant associated comorbidities (atherosclerosis, trauma, etc) [7, 25, 26]. Usually when a genetic predisposition exists, aortic dissection is associated with various genetic syndromes (Marfan – FBN-1 or TGFbR2 mutations [27], Ehlers-Danlos IV – COL3A1 [28], Turner - 45XO [29-31], Noonan – PTPN11, KRAS, SOS1, RAF1 [30, 31], osteogenesis imperfecta - CO1A1,CO1A2 [32], homocystinuria – CBS [31], AD-PKD - PKD1, PKD2 [31], pseudoxanthoma elasticum, Hurler syndrome, Loeys-Dietz syndrome [31], etc) with manifest phenotypes. Very unfrequently aortic dissection predisposition is determined by genes that aren’t responsible for other clinical manifestation.

The genes responsible for non-Syndromic aortic aneurysm and dissection are TAAD1 [33], FAA1 [34], TAAD2 [35], MYH11 [36]; other possible candidates are FBLN2, TIMP4, MMP3, COL1A1, COL1A2 [31, 32]; if they are detected in a patient with aortic dissection genetic counseling must be given to their families.

The importance of these non-Syndromic aortic dissections resides in the fact that they have a higher rate of aortic aneurysms and dissections development, at a lower mean age than Syndromic aortic dissections [31].

References