Case Report

Dissection of the Ascending Aorta in a Patient with HLA-B27 Associated Ankylosing Spondylitis

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ABSTRACT. We describe a 38-year-old patient with ankylosing spondylitis complicated by a non-traumatic dissection of the ascending aorta without concomitant Marfan's syndrome. (First Release Mar 15 2008; J Rheumatol 2008;35:713–6)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS DISSECTION OF THE AORTA HLA-B27

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease with a wide clinical spectrum of articular and extraarticular features that occurs in genetically predisposed persons and is triggered by environmental factors[1]. Cardiovascular involvement in HLA-B27 related spondyloarthropathies is widely described[2-3]. The most common findings include conduction abnormalities and aortic root and aortic valve disease[2-5]. Only 2 patients with AS have been reported to present a non-traumatic dissection of the ascending aorta[6,7] and both of them were HLA-B27 negative. Several authors[8-13] have highlighted the clinical and pathogenic similarities between AS and Marfan's syndrome (MS), suggesting that there could be a common tissue susceptibility factor. There are cases of both MS and AS in the same patient. The clinical similarities of both entities are described in Table 1. We present a new description of this vascular event in a patient with AS positive for HLA-B27 in whom MS was not present.

CASE REPORT

A 38-year-old patient with a recent non-traumatic dissection of the ascending aorta was sent to our rheumatology unit for investigation of recurrent anterior uveitis. His cardiovascular risk factors included obesity, with a body mass index of 31.35 kg/m^2, and recent hypertension. Four months earlier, he presented an acute aortic dissection complicating an 8 cm-diameter aneurysm of the ascending aorta, extending from the right coronary sinus to both iliac arteries. We performed emergency surgery by replacing the aortic root (Bentall procedure), ascending aorta, and aortic arch with a Dacron graft (Figure 1). Pathological findings showed fibrinoid necrosis of the middle media with an intense acute neutrophil polymorphonuclear infiltrate. No other pathological finding was seen in the rest of the aorta and aortic valve.

Our patient did not present a phenotype suggestive of MS, but interestingly, his father had died at the age of 33 due to an unspecified cardiovascular problem. At the examination our patient was asymptomatic, but he had a history of inflammatory back pain and stiffness in early adulthood (from 18 to 25 years old) and recurrent unilateral anterior uveitis (2-3 episodes per year) in the previous 3 years that had responded well to topical treatment.

On physical examination, our patient appeared healthy, with a normal intelligence quotient. Vital signs were normal; height: 175 cm, weight: 96 kg. No joint laxity was observed. He presented a severe limitation of the lumbar spine with Schober test result of 2 cm. Sacroiliac stress tests were negative, and no neurological findings were seen.

Laboratory findings revealed the presence of HLA-B27, an allele of the major histocompatibility complex class I, erythrocyte sedimentation rate: 26 mm/h (reference range: 0-20) and C-reactive protein: 4.7 mg/dl (0–0.8). Antinuclear antibodies, syphilis serology, and plasma levels of cystine and homocysteine were negative. No mutations were detected for exons 1 to 65 of the fibrillin 1 gene. Radiography of the pelvis revealed grade III bilateral sacroiliitis (Figure 2).

We diagnosed AS with related extraarticular features (recurrent unilateral anterior uveitis and dissection of the ascending aorta) according to the modified NY criteria of 1984[18].

Table 1. Clinical points of comparison between ankylosing spondylitis (AS) and Marfan's syndrome (MS).

	AS	MS
Articular	Dorso-lumbar spondylitis, sacroiliitis hip and knee arthritis, enthesitis[1], caudal root sheath ectasia, acetabular osteitis[8]	Scoliosis, joint laxity overgrowth of long bones, acetabular osteitis[14], caudal root sheath ectasia[15]
Ocular	Anterior uveitis	Ectopia lentis
Cardiovascular	Aortitis	Aortic root dilatation
Pulmonar	Apical lung fibrosis	Apical bullae, spontaneous pneumothorax
Retroperitoneal	Retroperitoneal fibrosis[16]	Retroperitoneal fibrosis[17]

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Accepted for publication November 14, 2007.

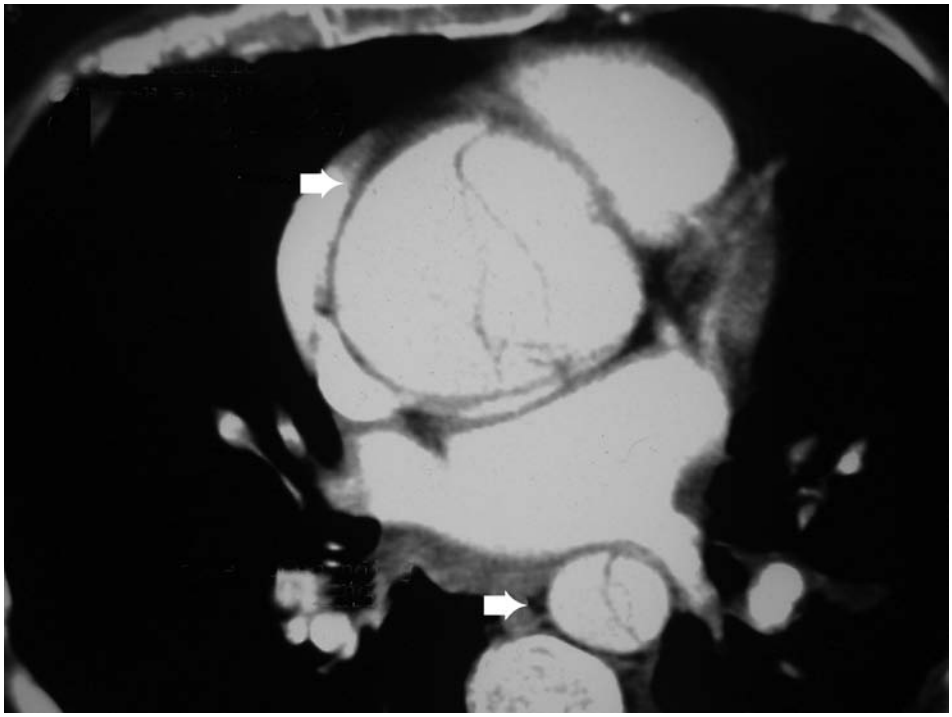

Figure 1. Spiral computed tomography (CT) showed a dilated aortic root (8 cm, arrow at top; intimal flap inside) and dissected descending thoracic aorta (arrow at bottom).

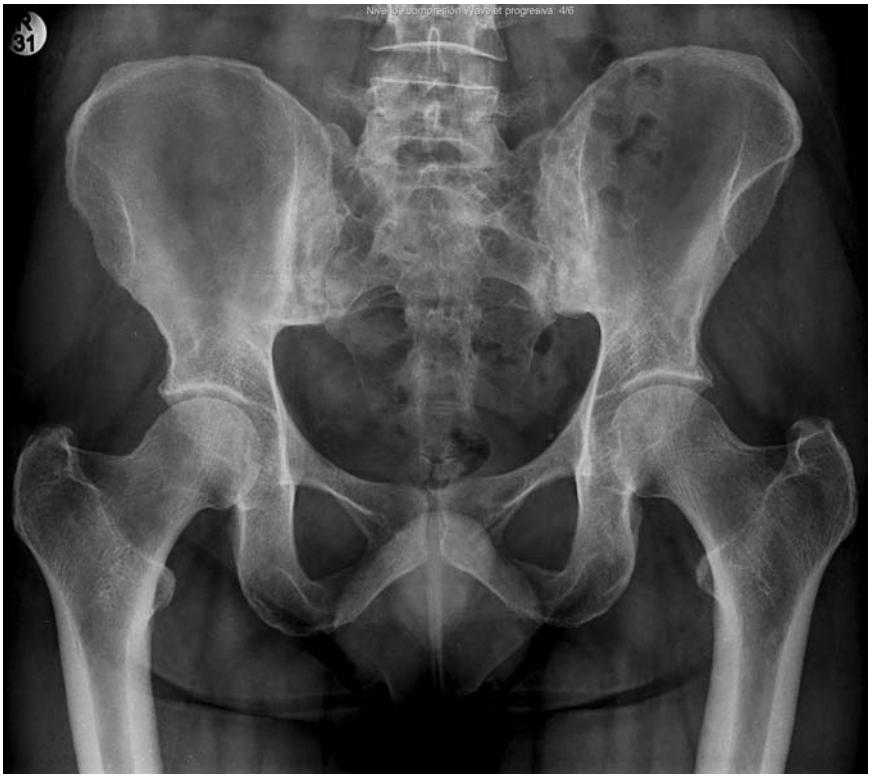

Figure 2. Plain anteroposterior view of the pelvis showed grade III bilateral sacroiliitis.

DISCUSSION

There are different possible cardiovascular complications in AS. The most common are aortic disease (both root and valve) and conduction defects[2-5]. A prevalence of aortic lesions in AS of 82% using transesophageal echocardiography has been reported[5]. Conduction defects cause the most frequent cardiac symptoms in AS[2]. Both these complications are related to HLA-B27[2,19] even without articular symptoms. HLA-B27-associated cardiac syndrome was shown to consist of severe cardiac conduction system abnormalities and lone aortic regurgitation without concomitant arthritis, with HLA-B27 results positive in 66 to 88% of male patients[2]. Another reported cardiac manifestation is myocardial failure, which is mostly a left ventricular dysfunction[3,20]. There are reports of aneurysm of the aorta related to AS, located in the ascending, descending, or entire thoracic aorta,[21-24], and even in the abdominal aorta. Aortic elasticity decreases[25] even without cardiac involvement, and only 2 reports have described a dissection of the ascending aorta[6,7]. Interestingly, and unlike our patient, both reported patients were HLA-B27 negative. Even though HLA-B27 have been present in other AS patients with aortitis and aneurysm[21,23], its importance in aortic dissections still needs to be fully confirmed. Aortic rupture after minor trauma is possible and is probably related to the firm adherence of the aorta to the anterior longitudinal ligament[26]. All of these events are important because cardiovascular events are the leading cause of death in AS patients, with a rate of 35%[27].

MS is a multisystem connective tissue disorder of autosomal dominant inheritance that affects one out of every 5000 individuals[28]. Clinical diagnosis depends on a combination of major and minor criteria defined in the revised 1996 Ghent criteria[29] and the gene for MS is localized to chromosome 15q21 and encodes the microfibrillar protein fibrillin-1[30-31]. Although the presence of a dissection of the aorta in a young patient requires us to rule out MS, considered as a major criterion[29], other entities such as spondyloarthropathies should also be considered; moreso when we take into account the clinical and pathological similarities between AS and MS[8-17] and their possible coexistence[10-13].

Fibrillinopathies represent a wide group of connective tissue disorder groups where mutations of fibrillin or transforming growth factor-ß (TGF-ß) share a clinical spectrum, predominantly in the skeleton, the aorta, and the eyes[32]. A better understanding of fibrillin biochemistry, a 350 kDa glycoprotein, and the role of TGF-ß has led us to consider that fibrillinopathies (especially MS) and AS, could be more closely linked than previously thought[8-13]. Fibrillin-1 is found in the extracellular matrix of tendons, ligaments, periosteum, skin, heart valves, aorta, and ocular lenses and confers biomechanical properties in connecting and maintaining tissues and organs[31]. It also regulates the TGF-ß, latent TGF-ß binding proteins (LTBP), which hold TGF-ß in an inactive complex and bone morphogenetic protein signalling. TGF-ß regulates the proliferation, differentiation, and migration of many cell types, and therefore has an important role in morphogenesis, organogenesis, tissue maintenance, and scarring[32,33]. Overproduction of TGF-ß due to a dysregulation of fibrillin-1 could be one important step in pathology. The mutation or reduction of fibrillin-1 is thought to be secondary to a congenital defect in MS[28,29] and in AS, and could be due to an inflammation target in connective tissue exposed to repetitive biomechanical stress[8,9]. Another point is that fibrillin-1 is rich in cysteine. Even though our patient had normal plasma levels of cysteine, it is thought that a deficiency of cysteine impairs fibrillin-1 deposition[34]. Takagi recently described a patient with AS with aortic dissection and low levels of cysteine in plasma[7]. Further studies are required.

Cardiac involvement in AS patients reveals a tissue-specific modulation towards fibrosis at the sites subjected to stress, such as the ascending aorta. Histological findings reveal adventitial scarring, intimal proliferation, and fibrous thickening of the aortic wall[35] compatible with overproduction of TGF-ß. The finding of TGF-ß in sacroiliac biopsies[36] and in the anterior chamber of the eye[37] supports the hypothesis. Chronic periaortitis is a group that involves inflammatory aneurysm of the abdominal aorta, idiopathic retroperitoneal fibrosis as described in both MS[17] and AS[16], and perianeurysmal retroperitoneal fibrosis[38]. Aortitis in AS has been related to aneurysm formation[21-24] and has been described without it[4]. This is in consonance with the aortic specimen of our patient that showed fibrinoid necrosis of the middle media with an intense acute neutrophil polymorphonuclear infiltrate, being different from the other cases with aortic dissection described by Takagi, *et al*[6,7] that revealed neither aortitis nor cystic medial necrosis.

In summary, different cardiovascular complications in AS are possible. We describe the first case of non-traumatic dissection of the aorta in a young patient with HLA-B27 positive AS. After surgery pathology studies showed features of acute aortitis that may have been related to aneurysm formation.

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