Joint Bone Spine 78 (2011) 451–455

Available online at ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Review

Aortitis and periaortitis in ankylosing spondylitis

Carlo Palazzi[a,*], Carlo Salvarani[b], Salvatore D'Angelo[a,c], Ignazio Olivieri[a]

[a] Rheumatology Department of Lucania, San Carlo Hospital of Potenza and Madonna delle Grazie Hospital of Matera, Potenza and Matera, Italy
[b] Division of Rheumatology, Arcispedale S. Maria Nuova, Reggio Emilia, Italy
[c] Department of Health Sciences, University of Molise, Campobasso, Italy

ARTICLE INFO

Article history:
Accepted 5 November 2010
Available online 24 December 2010

Keywords:
Aortic
Conduction abnormalities
Heart
HLA B27
Retroperitoneal fibrosis

ABSTRACT

Aortic involvement is a potential life-threatening complication of ankylosing spondylitis, usually occurring late in the course of this frequent disease. Inflammatory lesions evolving to fibrosis are primarily localized in the aortic root causing regurgitation, but this process can extend into the left atrium (subaortic bump) involving the mitral valve and the heart conduction system. First, second and third degree atrioventricular blocks are the most common conduction alterations described and they can be temporary. Chronic periaortitis has been described in ankylosing spondylitis patients. This disease is characterized by inflammation evolving to fibrosis and it is localized in the periaortic and peri-iliac retroperitoneum. It causes compressive effects on ureters and venous, arterial and lymphatic vessels. Its treatment employs endoscopic and/or surgical procedures and administration of corticosteroids, even in association with immunosuppressive agents. Both aortitis (with conduction system alterations) and periaortitis should be kept in mind by the physicians because they can significantly influence the prognosis of ankylosing spondylitis patients and they can need a rapid treatment.

Ankylosing spondylitis (AS) is a chronic inflammatory disorder belonging to the SpA (spondyloarthritis) complex which usually starts in young men [1]. It is a common disease because its prevalence varies from 0.1 to 1% of the general population, with the highest prevalence in northern European countries. AS involves the spine and the sacroiliac joints but it can be also localized in the peripheral joints and entheses. SpA can also involve extraarticular tissues such as the skin, the mucous membranes, the eye, the lung and the bowel [2]. Aortitis (with conduction system alterations) and periaortitis are cardiovascular manifestations of AS, less frequently reported in other forms of SpA [3], which should be considered by the physicians because they can strongly influence the prognosis of the disease and can need a rapid treatment.

1. Aortitis

Aortic involvement is a potentially life-threatening complication which may occur both in late and, more rarely, in early evolution phases of AS. Aortitis characteristically involves the aortic root and the ascending aorta leading to valvular insufficiency. The extension of the subaortic fibrotic process into the interventricular septum may cause conduction abnormalities.

1.1. Aortic valve involvement

Aortic valve disease associated with AS typically gives a lone, i.e. without stenosis, aortic insufficiency [5,6]. Macroscopic findings consist of dilatation of valvular annulus and in thickening of the valvular cusps with the free margins rolled inward. Nodularities of the cusps can also be seen [5,6]. The histological examination of the aortic valve reveals both inflammatory and degenerative alterations: proliferation of the cells of the intima, focal infiltrative lesions consisting of aggregates of mononucleate cells in the media with destruction of elastic tissue together with fibrosis, and fibrotic thickening of the adventitia [5–7]. Fibrotic changes can affect the whole cusps from the free margin to the base [7]. Neovascularization in the cups and in the epicardium surrounding the aortic root have also been described [7]. Aortic vasa vasorum are narrowed and surrounded by infiltrates of lymphocytes and plasma cells [5,7]. Fibrosis can extend from the aorta into the left atrium as an excrescence called "sub-aortic bump" that frequently involves the anterior leaflet of the mitral valve causing regurgitation [8,9]. In a recent case described by Krarup et al., the histopathological examination revealed fibrotic lesions in the aortic valve and inflammatory features in the anterior mitral leaflet [10]. A possible explanation is that the inflammatory process was ceased and only cicatricial outcomes remained in the aortic valve.

By a functional point of view, aortic regurgitation may depend on a combination of the thickening and rolling of valve cusps with the enlargement of the valvular annulus and displacement of the cusps due to the subaortic bump [11].

* Corresponding author. Via Potenza 3, 75100 Matera, Italy.
Tel.: +39 083 5253 807; fax: +39 083 5253 807.
E-mail address: kaps57@virgilio.it (C. Palazzi).

1297-319X/$ – see front matter © 2010 Société française de rhumatologie. Published by Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.jbspin.2010.11.003

1.1.1. Disease course

The seriousness of the AS-related AVD (aortic valve disease) is highly variable, ranging from chronic and haemodynamically irrelevant fibrosis to acute and rapidly worsening aortic insufficiency. The most frequent course is characterized by a slow progression towards symptomatic valvular regurgitation. In fact, a diastolic murmur can be audible for several years before dyspnea develops.

Notwithstanding this large amount of abnormalities, bacterial superinfection is very rare in AS-related AVD. However, endocarditis prophylaxis is advisable.

1.1.2. Imaging

Several studies have revealed AVD in many AS patients by using echocardiography. Aortic damage was found by Tucker et al. in eight out of 35 AS subjects [12]. LaBresh et al. described subaortic fibrous ridging or marked leaflet thickening in 11 out of 36 patients suffering from SpA, 25 of whom had AS. In contrast, no changes were found in the age-matched control group consisting of 29 men [13]. More recently, four out of 88 Turkish AS patients were found to have mild to moderate aortic regurgitation [14]. Echocardiographic abnormalities, i.e. aortic and mitral insufficiency, were present in 20 out of 77 German AS patients [15]. In 2006, Brunner et al. did not confirm these data [16]. In this study, the frequency of aortic and mitral valve abnormalities was not different in 100 patients with long-standing AS compared with the normal population.

Transesophageal echocardiography is a better imaging technique to visualize the internal structures of the heart. Forty-four outpatients with AS and 30 age- and gender-matched healthy subjects were studied with this technique by Roldan et al. in 1998 [8]. Twenty-five patients underwent clinical and echocardiographic follow-up evaluation 39 ± 10 months later. Aortic annulus and valve alterations were more commonly found in patients in comparison with controls (82 and 27% respectively; $p < 0.001$). Aortic root thickening, increased stiffness and dilatation were seen in 61, 61 and 25% of patients, respectively. Valvular thickening (41% for the aortic and 34% for the mitral valve) mainly consisted (74%) of nodules of the aortic cusps and basal thickening of the anterior mitral leaflet, as a subaortic bump. Almost 50% of patients suffered from valvular insufficiency, and 40% showed milder lesions. During the follow-up of 25 patients, in 24% new aortic annulus or valve alterations appeared, in 12% existing valve regurgitation significantly worsened and in 20% alterations healed. Twenty percent of the patients showed worsening of the valvular disease with heart failure, valve replacement, stroke or death in comparison with 3% of the control subjects. AS duration was the only feature related to the valvular disease.

1.1.3. HLA B27 and aortic valve disease

The role of HLA B27 in the development of AVD was suggested by Bergfeldt et al. in a study on 91 patients with lone aortic regurgitation [17] The HLA-B27-associated inflammatory disease process was considered the probable underlying cause in 15 to 20% of patients with lone aortic regurgitation of different degrees of severity. Qaiyumi et al. evaluated 100 consecutive cases of lone aortic insufficiency for the prevalence of SpA and found four HLA B27-positive patients with AS and three HLA B27-positive patients with reactive arthritis [18]. They concluded that the HLA-B27 antigen is not specifically associated with AVD in the absence of spondylitis. Recently, a study performed in the Sami populations of Northern Norway, showing a high prevalence of HLA B27 antigen, found that AVD was strongly associated with AS, but not with the HLA-B27 antigen alone [19].

1.1.4. Differential diagnosis

Valves' involvement of AS is characteristic and can be echocardiographically differentiated from other diseases giving a lone aortic insufficiency [11]. Syphilis can cause aortic lesions that are indistinguishable, even histologically, from those of AS but the subaortic tissues and the mitral valve are spared. Marfan disease is characterized by aortic root dilatation without tissue thickening. Aortic endocarditis shows valve vegetations, root abscesses and pseudoaneurisms [10].

1.2. Conduction abnormalities

The probable causative factors of the typical conduction abnormalities of AS include: (1) the inflammatory heart lesions evolving towards fibrosis which start from the aorta and extend to the interventricular septum; (2) the narrowing of the sinus node artery and the atrioventricular node artery [5,8]. Khan found a prevalence of conduction disorders of 3% in AS patients with a disease duration less than 15 years and of 9% in patients with a longer disease [20]. Higher prevalence was reported by others [21–23] while two studies did not find increased conduction disturbance in AS patients [16,24].

First, second and third degree atrioventricular blocks are the conduction alterations most commonly described but intraventricular blocks and bradycardia/pauses caused by sinus node involvement were also reported [6,22,25–27]. In a group of 223 subjects with permanent pacemaker, Bergfeldt found a 15-fold increased prevalence of AS [28].

1.2.1. Disease course

Conduction abnormalities may range from an asymptomatic course, for first grade atrioventricular blocks or presence of an adequate escape rhythm, to complete heart block causing Stokes-Adam's attacks requiring urgent hospitalization. Spontaneous remission of conduction disturbances were observed and attributed to possible amelioration of local inflammatory alterations, for example infiltrative lesions of the vascular wall occurring before the permanent fibrotic damages and causing reduction of blood flow to the physiological pacemakers [22,25].

1.2.2. HLA B27 and conduction abnormalities

A high percentage (12.6%) of patients with permanently implanted pacemakers for severe bradyarrhythmias had a HLA B27-related SpA [27]. But the role played by HLA B27 in the pathogenesis of arrhythmias cannot be exclusive because cases of HLA B27-negative AS with severe conduction disturbances have also been reported [27,29].

1.3. Treatment

There is no specific therapy for conduction disturbances. However, in the presence of symptoms pacemaker implantation is needed.

2. Periaortitis

The term of chronic periaortitis (CP) includes retroperitoneal fibrosis (RPF), inflammatory abdominal aortic aneurysms (IAAA), and perianeurysmal retroperitoneal fibrosis (PRF) that is a combination of the first two disorders [30]. All three entities show similar clinical and histopathologic features.

Idiopathic and secondary forms of RPF have been described in the literature [31]. Secondary RPF can be related to the administration of some drugs (ergot alkaloids, dopaminergic substances, methysergide), neoplastic disorders, trauma, surgery, radiotherapy, and infections. The idiopathic RPF is a rare disorder mainly affecting middle aged males (M/F = 2–3/1) [32]. It has been reported in association with some rheumatic disorders especially AS and other SpA [6] but also with peripheral inflammatory