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Autoimmune aspects of chronic periaortitis

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Abstract

Chronic periaortitis (CP) includes idiopathic retroperitoneal fibrosis, inflammatory abdominal aortic aneurysms and perianeurysmal retroperitoneal fibrosis. These entities are characterised by a fibro-inflammatory tissue which develops around the abdominal aorta and the iliac arteries, and spreads into the surrounding retroperitoneum to entrap adjacent structures such as the ureters. CP often affects patients with advanced atherosclerosis, and several lines of evidence support the view that it could result from a local inflammatory reaction to antigens in the atherosclerotic plaques of the abdominal aorta such as oxidised-low density lipoproteins and ceroid. However, because most CP patients also suffer from constitutional symptoms and show elevated acute-phase reactant levels, positive autoantibodies and, in some cases, autoimmune diseases affecting other organs, CP may also be considered a manifestation of a systemic autoimmune disease.

CP is usually diagnosed using computed tomography or magnetic resonance imaging, but retroperitoneal biopsy may also be necessary; positron emission tomography is useful in assessing the full extent of the disease and the metabolic activity of the retroperitoneal tissue. Ureterolysis and aneurysm repair are frequently performed, but the inflammatory and chronic-relapsing nature of the disease often compels the use of medical therapy, which is based on steroids and immunosuppressants.

Keywords: Chronic periaortitis; Inflammatory aneurysms; Retroperitoneal fibrosis; Autoimmunity; Vasculitis

Contents

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Chronic periaortitis (CP) is a rare clinico-pathological entity characterised by the presence of a retroperitoneal fibro-inflammatory mass which usually surrounds the abdominal aorta and the iliac arteries and may envelop adjacent structures such as the ureters and the inferior vena cava. The term "chronic" derives from the histological appearance of CP: a chronic inflammatory infiltrate consisting mainly of lymphocytes, monocytes, plasma cells and sparse eosinophils is usually found in a background of abundant fibrous tissue and fibroblasts [1–3].

CP involves three main disease entities, namely idiopathic retroperitoneal fibrosis (IRF), inflammatory aneurysms of the abdominal aorta (IAAAs) and perianeurysmal retroperitoneal fibrosis (PRF). In IRF the aortic diameter is normal, and the surrounding retroperitoneal mass may or may not encase the neighbouring structures [4]. In IAAAs and PRF the aorta shows aneurysmal dilatation, and while in the former the periaortic mass does not involve the adjacent structures, in the latter it causes obstructive complications. PRF may thus represent an advanced stage of IAAA. IAAAs and PRF may be referred to as "aneurysmal CP", whereas IRF may be referred to as "non-aneurysmal CP" [2,4].

Table 1
Main proofs of autoimmunity in chronic periaortitis

	Examples
Genetic aspects	Association with HLA-DRB1*03
Histological findings	Small vessel vasculitis of retroperitoneal vessels and aortic vasa vasorum; ectopic lymphoid follicles with germinal centres in periaortic retroperitoneum and aortic adventitia
Clinical manifestations	Constitutional symptoms, systemic involvement of large arteries
Association with autoimmune disorders	Autoimmune thyroiditis (e.g. Hashimoto's, Riedel's), rapidly progressive glomerulonephritis, systemic vasculitis, ankylosing spondylitis, sclerosing pancreatitis
Laboratory tests	High acute-phase reactants, positive auto-antibodies (antinuclear, anti-thyroid microsome, anti-thyroglobulin, ANCA, anti-smooth muscle, rheumatoid factor)
Experimental findings	Anti-fibroblast antibodies

CP has an unclear pathogenesis. An exaggerated local inflammatory reaction to severe atherosclerotic lesions in the abdominal aorta has been purported to be the primum movens of the disease; however, in a number of cases CP may arise in the absence of an advanced atherosclerotic disease [5] and, in addition, most CP patients present with constitutional symptoms, high acute-phase reactant levels and often show positive auto-antibodies and autoimmune/inflammatory diseases involving other organs [6] (Table 1). These findings raise the issue as to whether CP represents a manifestation of a systemic autoimmune disease rather than a consequence of a local reaction to atherosclerosis.

This review will outline the clinical spectrum of CP and will particularly discuss the different clinical, laboratory, genetic and histological aspects which support the "autoimmune hypothesis" of the disease.

1. Epidemiologic and genetic aspects

CP is a rare disorder; although there are no conclusive data concerning its epidemiologic characteristics, a recent study on IRF has demonstrated that its incidence and prevalence are 1/1,000,000 person-year and 1.38 cases/100,000 inhabitants [7]. On the other hand, studies on the aneurysmal forms of CP have shown that they represent about 3% to 10% of the total abdominal aortic aneurysms [8,9].

The male/female ratio is usually 2:1–3:1, with the higher incidence in the male patients being even more pronounced in the aneurysmal forms; the age at disease onset usually peaks between 50 and 60 years [4].

Neither ethnic predisposition nor familial aggregation has clearly been described in patients with CP. However, recent studies have demonstrated that genetic factors may play a role in the pathogenesis of the disease.

In a case-control study involving patients with IAAAs and healthy controls, the prevalence of the HLA alleles HLA-DRB1*15 and HLA-DRB1*0404 was found to be significantly higher in the IAAA group [10].

We have recently performed a case-control study on CP patients and healthy controls in order to investigate the role of HLA in the susceptibility to CP. The results have shown that the frequency of the HLA-DRB1*03 allele was markedly higher in CP patients than in the