IgG4-Related Disease Causing Rapid Evolution of a Severe Aortic Valvular Stenosis

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Immunoglobulin G4-related systemic disease (IgG4-RSD) is a recognized emerging entity characterized by chronic fibroinflammation that can affect every organ but rarely affects the cardiovascular system. We report a rare case of IgG4-RSD involving an aortic valve that resulted in rapid progression of an aortic valvular stenosis and was successfully treated by aortic valve replacement and corticosteroids.


Immunoglobulin G4-related systemic disease (IgG4-RSD) is a recently emerging entity characterized by diffuse lymphoplasmacytic infiltrates rich in IgG4-positive plasma cells, extensive fibrosis, and elevated serum IgG4 [1]. IgG4-RSD has been described in almost every organ system but rarely affects the cardiovascular system [1]. Most reported cases of cardiovascular involvement are of the aorta; only a few reported cases concern cardiac valvular involvement [2]. We report a rare case of IgG4-RSD involving an aortic valve (AV) that resulted in rapid progression of an AV stenosis and was successfully treated by AV replacement and corticosteroids.

Fig 1. (A) Contrast-enhanced computed tomographic (CT) images showing retroperitoneal and right perirenal infiltration (arrows). (B) Positron emission tomographic / CT images showing intense 18F-fluorodeoxyglucose uptake at multiple lymph node sites and adjacent to the right renal hilum (arrows). (C) Hematoxylin and eosin staining of lymph node showing stellar fibrous patches and plasma cell infiltration. Immunoperoxidase staining for immunoglobulin G (IgG) and IgG4 showing (D) numerous IgG-positive plasma cells including (E) a high proportion of IgG4-positive cells. (C, D, and E: original magnification × 200.)
An 82-year old man who had been regularly monitored by a cardiologist for a nonsymptomatic AV stenosis was admitted to the hospital with an initial suspicion of lymphoma. Contrast-enhanced computed tomographic (CT) imaging revealed retroperitoneal and right perirenal infiltration (Fig 1A). In addition, 18F-fluorodeoxyglucose positron emission tomographic / CT (18F-FDG PET/CT) images showed intense FDG uptake at multiple lymph node sites and a node adjacent to the right renal hilum (Fig 1B). Histopathologic analysis showed IgG4 at the level of this infiltration (Figs 1C, 1D, 1E). IgG4-producing plasma cells were detected (22,800 g/L) and were found in lymph node tissue after immunohistochemical analyses and confirmed the diagnosis. After oral steroid administration, the serum IgG4 level decreased (2,790 g/L). At the same time, the patient experienced dyspnea, and a new cardiologic examination revealed progression of the AV stenosis. Echocardiography demonstrated a mean AV gradient of 46 mm Hg and an AV area of 0.7 cm². One year before, echocardiography showed a mean AV gradient of 35 mm Hg and an AV area of 0.9 cm². The patient was referred for an AV operation and underwent uncomplicated AV replacement with a bioprosthesis. The ascending aortic caliber was normal. Pathologic examination of the excised valve leaflets showed infiltration of the valve leaflets by inflammatory mononuclear cells, including plasma cells, and showing immunoreactivity for IgG and IgG4 (Fig 2). Immunohistochemical staining revealed a ratio of IgG4-positive to IgG-positive plasma cells greater than 0.6. However, examination of a biopsy specimen from the ascending aortic wall did not reveal the presence of IgG4. The serum IgG4 level measured postoperatively decreased to 1,140 g/L.

Comment

We describe a rare case of IgG4 involving the heart. To our knowledge, this case is the first resulting in rapid evolution of a severe symptomatic AV stenosis associated with IgG4. Calciﬁc AV disease is an active disease considered to be form of atherosclerosis and so has inﬂammatory features. Steiner and colleagues [3] detailed the pattern of cellular inﬁltrate in calciﬁc AV disease and showed that inﬂammatory cells are the predominant cell type in early AV lesions, with T lymphocytes and macrophages. Diagnosis of IgG4-RSD was established by immunostaining and histopathologic ﬁndings. A ratio of IgG4-positive to IgG-positive plasma cells greater than 0.5 would be suggestive of IgG4-RSD [4]. So, the classic calciﬁc AV disease does not fulﬁll the criteria of an IgG4-RSD. In our case, the ratio of IgG4-positive to IgG-positive plasma cells was greater than 0.6.

The reported therapy for IgG4-RSD includes complete resection of the lesion accompanied by corticosteroid therapy. In most patients, this treatment induces rapid remission of the clinical symptoms and normalization of the IgG4 plasma level.

In conclusion, we postulate that IgG4-RSD may play a role in the rapid progression of AV disease, but prospective clinical studies are needed to establish the exact role of in the progression of an AV stenosis. We and others [2] have proposed an increase in the routine histologic analyses of the surgically excised valves.

References