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Constrictive Pericarditis Caused by Immunoglobulin G4-Related Disease

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Immunoglobulin G4-related disease (IgG4-RD) is a recently recognized systemic fibroinflammatory disease associated with elevated serum level of IgG4. It was initially described as autoimmune pancreatitis; however, in recent years, there have been reports describing a broadening spectrum of organ involvements. We report a case of IgG4-RD manifesting as constrictive pericarditis.

Case Presentation

A 76-year-old former smoker was admitted to an outside hospital with a 2-year history of progressive exertional dyspnea and lower extremity edema. Initial evaluation revealed the presence of bilateral pleural effusions and ascites. He was diagnosed with congestive heart failure. He was treated with diuretics and an afterload-reducing agent. Subsequent hemodynamic cardiac catheterization revealed findings suggestive of constrictive physiology (Figure 1). Despite aggressive management that included multiple paracenteses and thoracenteses, his overall clinical status did not improve. He was referred to our clinic for further evaluation.

Physical examination was notable for blood pressure of 86/64 mm Hg, hepatjugular reflux, a distended abdomen with shifting dullness, and prominent pitting edema in the lower extremities. Heart sounds were unremarkable; however, the lung examination was notable for dullness to percussion over both bases. Chest radiography showed bilateral pleural effusions with a normal heart size. Echocardiography and subsequent cardiac MRI demonstrated abnormal findings consistent with constrictive pericarditis (online-only Data Supplemental Videos I and II). Laboratory data included normal complete blood count and electrolytes with polyclonal hypergammaglobulinemia. During subsequent pericardiectomy, a circumferentially thickened (approximately 2.5 mm) pericardium was noted. Sections of the resected pericardium revealed diffuse fibrous thickening and patchy lymphoplasmacytic infiltration (Figure 2). Immunostaining demonstrated an increased absolute count of IgG4-positive cells (33 per high-power field on average, counted from 3 hot spots) and the ratio of IgG4/IgG-positive cells at 34% (Figure 3). The

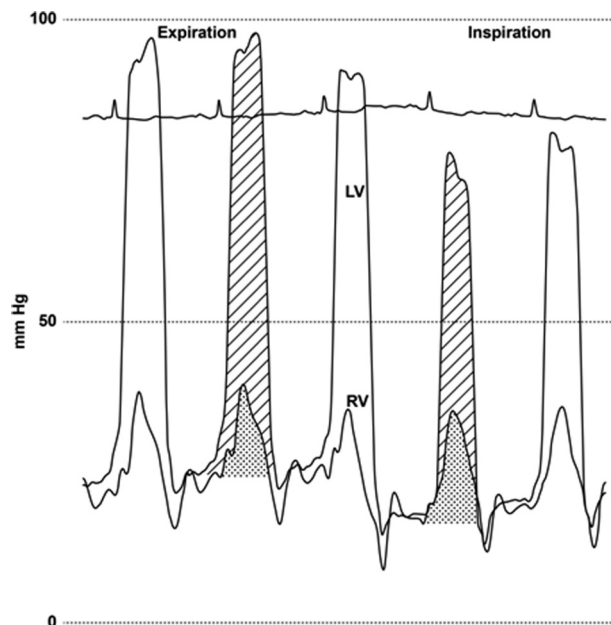


Figure 1. Hemodynamic cardiac catheterization. During inspiration, there was an increase in the area of right ventricular (RV) pressure curve compared with expiration. The area of the left ventricular (LV) pressure curve decreased during inspiration compared with expiration. This ventricular interdependence along with early rapid filling was consistent with constrictive physiology.

specimen was negative on microbial cultures and the diagnosis of IgG4-RD was made. Postoperatively, his symptoms improved significantly and he did not require a corticosteroid therapy. There was no evidence of recurrence or other manifestations attributable to IgG4-RD over the next 2 years.

Discussion

IgG4-RD is a newly recognized systemic fibroinflammatory disease that can affect various organs such as the pancreas, biliary system, salivary glands, periorbital tissues, kidneys, lungs, pleura, lymph nodes, meninges, breast, prostate, thyroid gland, and skin.¹ Very little is known regarding possible cardiovascular manifestations of IgG4-RD; a few cases of

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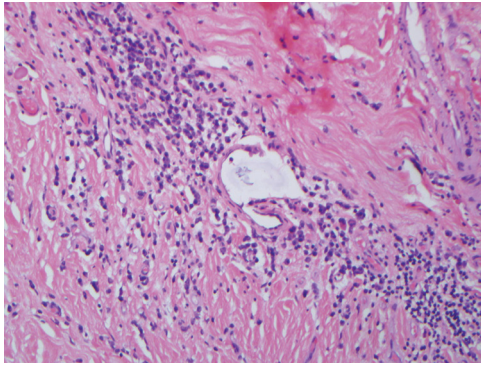


Figure 2. Hematoxylin and eosin, $\times 200$: a resected pericardium demonstrating diffuse fibrous thickening and patchy lymphoplasmacytic infiltration.

aortitis and a case of pericarditis have been reported in the literature.^{2,3} Our patient presented with findings suggestive of constrictive pericarditis without other organ manifestations such as autoimmune pancreatitis. Patients with IgG4-RD typically have high serum IgG4 levels and polyclonal hypergammaglobulinemia. The clinical presentation of IgG4-RD

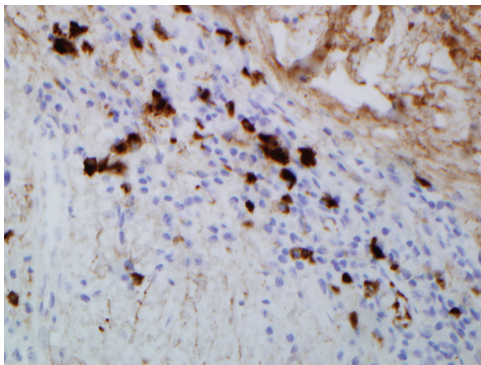


Figure 3. IgG4 staining $\times 400$: immunostaining demonstrating an increased absolute count of immunoglobulin G4 (IgG4)-positive cells (33 per high-power field on average, counted from 3 hot spots). The ratio of IgG4/IgG-positive cells was 34%.

varies widely and depends on the organs affected. Radiological changes in any affected organs can mimic neoplasms, infections, or other inflammatory disorders and its differentiation can be difficult through radiological findings alone. Characteristic histopathologic features include abundant IgG4-positive lymphoplasmacytic infiltration, fibrosis, and obliterative phlebitis or arteritis.¹ Men are approximately 3 times more frequently affected than women with the median age at diagnosis being approximately 60 years.⁴ IgG4-RD is a corticosteroid-responsive disorder, and favorable response is usually observed in 2 to 4 weeks of prednisone therapy, 0.6 mg/kg per day, followed by gradual dose reduction during the following months. Immunosuppressive agents have been used in corticosteroid-refractory disease; however, the data on their efficacy are limited.

Conclusions

IgG4-RD can present with constrictive pericarditis. Cardiovascular manifestations of IgG4-RD have not been adequately explored and this case suggests that other patients with cardiovascular involvement with IgG4-RD have gone unrecognized. Increased awareness of IgG4-RD and measurement of serum IgG4 levels may facilitate diagnosis and minimize morbidity associated with this disease as well as unnecessary diagnostic procedures.

Disclosures

None.

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KEY WORDS: heart failure ■ inflammation ■ pericarditis ■ pericardium

Supplemental Material

Video 1: Breath-held 4 chamber cine balanced steady state free precession magnetic resonance image demonstrates abnormal diastolic septal "bounce" characteristic of constriction.

Video 2: Free-breathing ungated steady state free precession magnetic resonance image demonstrates increased right-to-left shift of the interventricular septum with inspiration. The images are slightly oblique from short axis. When the diaphragm moves down, increased systemic venous return and decreased pulmonary venous pressures cause increased filling of the right ventricle at the expense of the left ventricle and resultant shift in the position of the interventricular septum.

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