Significant Pericardial Involvement of Immunoglobulin G4–Related Disease

Takehiro Morita, MD, Atsushi Izawa, MD, Hideaki Hamano, MD, Naoko Asano, MD, Ayako Kozuka, MD, Hideaki Moteki, MD, Megumi Fuke, MD, Jun Koyama, MD, Jun Amano, MD, and Uichi Ikeda, MD

Department of Cardiovascular Medicine, Second Department of Internal Medicine, and Departments of Pathology, Surgery, and Otorhinolaryngology, Shinshu University School of Medicine, Matsumoto, Japan

A 60-year-old woman was hospitalized with cardiac tamponade due to effusive pericarditis presenting with significant thickening of the pericardium. Serum immunoglobulin G4 (IgG4) level was elevated to 1,800 mg/dL, and an open biopsy specimen from the pericardium revealed massive infiltration of lymphocytes and IgG4-positive plasma cells. She had experienced adenopathies in the lacrimal and parotid glands 6 months earlier, and was diagnosed as having IgG4-related Mikulicz’s disease by similar cell infiltration in the salivary gland biopsy. The significant involvement of the pericardium as a manifestation of IgG4-related disease is described, as well as the successful treatment with oral corticosteroids.


Mikulicz’s disease has been characterized as an immunoglobulin G4 (IgG4)–related plasmacytic exocrinopathy [1, 2]. This report presents an extensive pericardial involvement, which caused cardiac tamponade, in a patient accompanied by Mikulicz’s disease. An open biopsy of the pericardium and IgG4 immunostaining was crucial for the diagnosis. A recent disease category, systemic IgG4-related disease (IgG4-RD) [3] can be a differential diagnosis for pericarditis of unknown etiology.

A 60-year-old woman had cardiac tamponade and was transferred to our hospital after pericardial drainage. A total of 635 mL pericardial effusion contained many lymphocytes and plasmocytes, which were categorized as class III on the basis of cytologic examinations. On admission, the patient was asymptomatic, and physical examinations were unremarkable because the successful pericardial drainage stabilized her hemodynamic status. Her blood pressure was 124/70 mm Hg, and chest auscultation was normal. A 12-lead electrocardiogram showed sinus rhythm at a rate of 62 beats per minute. A chest radiograph showed an enlarged cardiac silhouette. An initial echocardiogram and chest computed tomography scans showed significant thickening of the pericardium (Fig 1A), which was consistent with a hot spot on a 67-gallium scintigram (Fig 1B).

The levels of soluble interleukin-2 receptor and IgG were high (1,470 U/mL and 2,067 mg/dL, respectively). The main subtype of IgG detected was IgG4 (1,800 mg/dL; 34.7% of the total IgG). On the basis of the initial clinical assessment, we made a provisional diagnosis of pericardial lymphoma and performed an open biopsy of the pericardium and mediastinal lymph node. Massive infiltration of lymphocytes and plasma cells with mild atypia was observed in the pericardium (Fig 2A). Follicular hyperplasia, expansion of T-cell zone (Fig 3A), and plasma cell infiltration (Fig 3B) were observed in the mediastinal lymph node. Malignant lymphoma was ruled out with the preserved diversity of T-cell receptors. To characterize immunoglobulin-secreting plasma cells, IgG subtype staining was performed. A remarkably high number of IgG4-positive plasma cells was observed on the tissue sections of the pericardium (Fig 2B) and mediastinal lymph node (Fig 3C). Six months before her admission, she had had symmetrical swelling in the parotid
region and periorbital edema, which were retrospectively diagnosed as adenopathies of the parotid and lacrimal glands. In addition, a computed tomography scan demonstrated enlargement of the bilateral submandibular glands (Fig 4A). Biopsy of the salivary gland revealed similar infiltration of the IgG4-positive plasma cells; therefore, the patient was diagnosed as having IgG4-related sialoadenitis (Mikulicz’ disease).

Oral corticosteroid treatment with prednisolone at 30 mg daily reduced the serum soluble interleukin-2 receptor levels to 161 U/mL, followed by a decrease in size of the bilateral submandibular glands (Fig 4B), and a significant reduction of the pericardial thickness and no recurrence of pericardial effusion (Fig 4C). The patient’s serum IgG4 level at 18 months after the initial diagnosis was 396 mg/dL with maintenance treatment of prednisolone at 2.5 mg daily. The patient was
discharged with no symptoms and remained well for 18 months.

Comment

Clinical manifestations of systemic IgG4-RD include autoimmune pancreatitis, interstitial pneumonia, retroperitoneal fibrosis, tubulointerstitial nephritis, autoimmune prostatitis, sclerosing cholangitis, Riedel’s thyroiditis, and Mikulicz’s disease [1, 2, 4–6]. Recent studies have demonstrated that patients with autoimmune pancreatitis exhibit recurrent pleural and pericardial effusions [7], pericardial thickening [8], and also constrictive pericarditis [9]. Massive pericardial inflammation accompanied by Mikulicz’s disease with no other tissue involvement in this case is unique and demonstrates that lesions of IgG4-RD can occur at different locations and at different times.

The pathologic findings of the pericardium suggested that the inflammation was predominantly mediated by IgG4-positive plasmocytes; therefore, a potential mechanism underlying IgG4-related autoimmunity may play an important role in the development of pericarditis, namely, a potential form of autoimmune pancreatitis. Although Th2-mediated autoimmunity has been suggested to play a role in the pathophysiology of Mikulicz’s disease [10, 11], further investigations are required to elucidate the mechanism of T-cell-mediated or humoral autoimmunity. Serum IgG4 levels should be carefully monitored, because serial levels of serum IgG4 are useful to determine the disease activity, according to a recent report [12].

This report highlights the importance of an open biopsy to diagnose significant pericarditis due to an unknown etiology that can be treated noninvasively. In conclusion, the pericardium can be a target tissue of IgG4-RD; therefore, care should be taken to treat systemic inflammation, including the pericardium, in patients with IgG4-RD.

References