

Case
Report

Immunoglobulin G Subclass 4-Related Lymphoplasmacytic Thoracic Aortitis in a Patient with Acute Type A Aortic Dissection

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Immunoglobulin G subclass 4-related disease (IgG4-RD) is a recently recognized systemic inflammatory disease characterized by an elevated serum IgG4 level and an IgG4-positive lymphocyte infiltrate mainly in exocrine tissues. Previous reports documented IgG4-RD in several cardiovascular disorders. We present a case of type A aortic dissection associated with IgG4-RD. A 52-year-old man diagnosed with a type A aortic dissection was referred for surgical treatment. He underwent emergency hemiarch reconstruction with a prosthetic graft. His postoperative recovery was uncomplicated. Histopathologic examination of his aortic tissue showed marked adventitial thickening with fibrosis and an IgG4-positive plasma cell infiltrate. He was diagnosed with type A aortic dissection incidentally complicated by IgG4-RD. The relationship between IgG4-RD and the pathogenesis of aortic dissection remains unknown and requires further investigation.

Keywords: aortic aneurysm, thoracic, autoimmune diseases, immunoglobulin G, human, plasma cells

Introduction

Immunoglobulin G subclass 4-related disease (IgG4-RD) is a recently recognized systemic disease characterized by consistent histological features including fibroproliferative changes, lymphocyte and plasma cell infiltrates with numerous IgG4-positive plasma cells, and obstructive phlebitis.¹⁾ Although cardiovascular manifestations

of IgG4-RD are considered uncommon, several previous reports have demonstrated IgG4-RD in various cardiovascular disorders.^{2–4)} Some reports described thoracic aortic involvement in IgG4-RD, but the prevalence of this manifestation tends to be underestimated because a biopsy is required for a definitive diagnosis in these cases. We herein present a surgical case of acute Stanford type A aortic dissection incidentally complicated by IgG4-RD diagnosed by histopathologic examination.

Case Report

A 52-year-old man was referred to our hospital for emergent surgical treatment of an acute type A aortic dissection. His medical history was significant only for untreated hypertension.

Upon admission to our emergency department, his blood pressure was stable and his laboratory examination was normal although he complained of persistent back pain. The physical examination revealed sinus tachycardia

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Fig. 1 The preoperative enhanced computed tomography scan shows an ascending aortic dissection. A small amount of pericardial effusion is present.

with no heart murmur. A chest roentgenogram demonstrated marked mediastinal widening. Enhanced computed tomography showed a type A aortic dissection of the ascending aorta and a small pericardial effusion (**Fig. 1**). Transthoracic echocardiography disclosed no evidence of aortic regurgitation. Emergent hemiarch reconstruction with a prosthetic graft was performed under moderate hypothermic circulatory arrest with antegrade selective cerebral perfusion on cardiopulmonary bypass. He was extubated 24 hours after the operation. The patient's postoperative course was uneventful. He was ambulating without difficulty when he was discharged with no complications.

The histopathologic examination showed that the undissected aortic wall was 2.5 mm thick (**Figs. 2a** and **2c**). The adventitia was thickened and a dense lymphoplasmacytic infiltrate and fibrosis were observed (**Fig. 2b**). Immunostaining showed that the IgG4⁺/IgG⁺ plasma cell ratio was over 50% (**Fig. 2d**). The IgG4-positive plasma cell count was 50/high-power field. Atherosclerotic changes, obstructive phlebitis, and cystic medial necrosis were not identified. These findings were considered consistent with a diagnosis of IgG4-RD. The patient's serum IgG4 concentration was not elevated during the postoperative period. During follow-up, the occurrence of IgG4-RD in tissues other than the cardiovascular tissues was not observed. Additionally, no clinically significant systemic inflammation or prosthetic graft problems occurred in the year after the operation.

Discussion

Herein, we report the successful surgical management of a type A dissection complicated by IgG4-RD. The relevance of the IgG4 antibody subclass to the development of fibrous organic diseases was first recognized in Japan in the setting of autoimmune pancreatitis.⁵ Since then, it has become clear that many other organs can also have

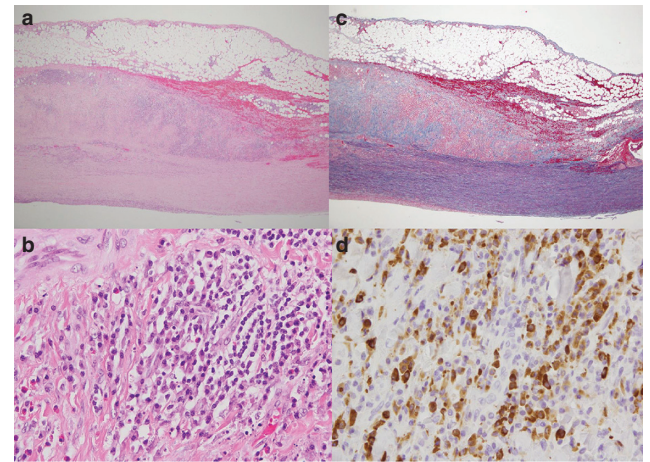


Fig. 2 Histopathologic examination of surgical specimens. (a) The adventitia is markedly thickened due to an inflammatory cell infiltrate accompanied by fibrous proliferation. Obstructive phlebitis is not observed. Hematoxylin–eosin stain, original magnification $\times 2$. (b) A dense lymphoplasmacytic infiltrate is also present. Hematoxylin–eosin stain, original magnification $\times 40$. (c) The adventitia is thickened and a dense lymphoplasmacytic infiltrate and fibrosis are observed. Elastic–Masson stain, original magnification $\times 2$. (d) IgG4 immunostaining shows a ratio of IgG4⁺/IgG⁺ plasma cells over 50%. The IgG4⁺ plasma cell count is 50/high-power field. Original magnification $\times 40$. IgG4: immunoglobulin G subclass 4

similar IgG4-related pathology.⁶ Furthermore, several previous reports have demonstrated IgG4-RD in various cardiovascular disorders.^{2–4}

Kasashima et al.² first described IgG4-related vascular involvement in 2008 in their report of an inflammatory abdominal aortic aneurysm. The first case of IgG4-RD in the thoracic aorta was reported by Stone et al. in 2010.⁷ Several more cases of thoracic aortic aneurysm and dissection have since been reported. A review of the clinical records and radiologic studies of 160 patients with IgG4-RD revealed that 36 (22.5%) had large-vessel involvement.⁸ Of these, two patients had a thoracic aortic dissection requiring surgical treatment. Similarly, Hourai et al.⁴ observed an IgG4-positive plasma cell infiltrate in 9.7% (10/103) of various cardiovascular surgical specimens, especially in the walls of dissecting thoracic aortic aneurysms (2/29, 10%). According to a report by Agaimy et al.,³ 5/175 (2.8%) patients with a type A dissection were diagnosed with IgG4-RD.

IgG4-RD can be diagnosed by comprehensive criteria⁹ or by organ-specific criteria. Currently, there are no cardiovascular-specific diagnostic criteria for IgG4-RD, and most cases involving cardiovascular organs are

diagnosed based on histopathologic findings in tissue obtained during surgery or autopsy. However, vital organ biopsy is associated with considerable risk and is not routinely performed. It is clear that IgG4-RD involving cardiovascular organs is not rare and this entity may be underdiagnosed.^{4,7)} Aortic dissection complicated by IgG4-RD is more common than previously recognized.

Typical pathologic features of IgG4-related aortic disease are adventitial inflammation with significant fibrous thickening and a lymphoplasmacytic infiltrate. In the present case, adventitial fibrosis and a dense lymphoplasmacytic infiltrate with numerous IgG4-positive plasma cells were apparent. Cystic medial necrosis, a typical pathological finding in aortic dissections, and atherosclerotic change were not observed. The relationship between IgG4-RD and the pathogenesis of aortic dissection is still unknown and requires further investigation.

The estimated incidence of IgG4-RD in Japan is 0.28–1.08/100,000, mainly occurring in middle-aged to elderly men.¹⁰⁾ The median age of disease onset is 58 years. The clinical symptoms are usually mild, and damage gradually occurs in various organs. IgG4-RD is a systemic disease and organs may be affected simultaneously or at different times over an extended period.¹¹⁾ In the present case, a lethal aortic event was the first indication of IgG4-RD in our 52-year-old male patient. Previous reports of surgically treated aortic dissection associated with IgG4-RD indicated that the patients had not been diagnosed until the emergent surgery was performed. As patients with IgG4-RD may develop disease manifestations in many organs, close observation is mandatory during postoperative follow-up. Particularly in patients with unexplained signs of systemic inflammation after thoracic aortic surgery, the association of prolonged inflammation and IgG4-RD should be kept in mind.

Conclusion

We report the successful surgical management of a type A dissection complicated by IgG4-RD. Aortic dissection associated with IgG4-RD is not a rare finding and may be underdiagnosed. The significance of IgG4-RD in the pathogenesis of aortic dissection should be investigated in future studies.

Disclosure Statement

The authors have no conflicts of interest to declare.

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