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CLINICAL CASE

Three cases of IgG4-RD complicated by splenic artery aneurysm: a complication of IgG4-RD?

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ABSTRACT

Immunoglobulin 4-related disease (IgG4-RD) is known for its potential to affect nearly every organ, particularly a preference for large and middle-sized arteries when vascular involvement occurs. However, instances of splenic artery aneurysms are exceedingly rare with only two cases reported in the literature. We have summarised the clinical manifestations and laboratory characteristics of the three patients we reported along with the two patients previously reported. It is noteworthy that all five patients had involvement of the salivary glands and only one patient had other arterial involvement. The three patients we reported had no new organ onset or worsening of existing organ involvement and normal or not significantly elevated serum IgG4 levels when the artery aneurysm was identified. These aneurysms may be the result of vascular damage from prior involvement that was not recognised previously. The cases we reported here highlight a potential association between IgG4-RD and concurrent splenic artery aneurysms.

INTRODUCTION

Immunoglobulin 4-related disease (IgG4-RD) manifests as a systemic condition characterised by sclerosing lesions, elevated blood IgG4 levels, storiform fibrosis, obliterative phlebitis and infiltration of IgG4-positive cells in various organs. It affects nearly every organ system within the body. [1] Splenic artery involvement is less common in patients with IgG4-RD. Here, we report three cases of IgG4-RD complicated by splenic artery aneurysm.

CASE PRESENTATION

Case 1

A 51-year-old woman presented with a 14-year history of swelling of the lacrimal gland and an 11-year history of swelling of the submandibular salivary glands. Blood tests revealed a C-reactive protein level of 0.35 mg/L with a serum IgG4 level of 361 mg/dL. A biopsy of the labial gland revealed a dense lymphoplasmacytic infiltrate with IgG4-positive plasma cells. The diagnosis was confirmed according to the American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for IgG4-RD (ACR/EULAR). The patient was initially prescribed prednisolone at a dosage of 40 mg/day to manage the disease activity. During follow-up, the patient also developed involvement of other organs such as the kidneys and we adjusted the dose of prednisolone and prescribed immunosuppressants. Azathioprine was the first immunosuppressant administered followed by cyclophosphamide and methotrexate. Rituximab was subsequently incorporated into the treatment regimen during a relapse of the disease. Enhanced CT identified a newly formed aneurysm (15 mm in diameter) of the splenic artery (figure 1a) with no other vascular abnormalities detected on the scan. The serum IgG4 level was 17 mg/dL and the IgG4-RD responder index (RI) was 5 according to the IgG4-RI V.2018 during the occurrence of splenic artery aneurysm.

Case 2

A 38-year-old woman was hospitalised due to a 3-year history of lacrimal gland swelling and a 2-year history of submandibular and parotid gland enlargement. Blood testing revealed serum IgG4 levels of 1400 mg/dL meeting the ACR/EULAR criteria. Treatment initiation comprised daily prednisone at 35 mg and weekly administration of methotrexate at 10 mg. Two years later, an abdominal CT revealed a newly formed 15 mm splenic artery aneurysm (figure 1b). Serum IgG4 levels were 158 mg/dL at the time of aneurysm detection with an associated IgG4-RD RI of 5.

Case 3

A 74-year-old female patient was diagnosed with IgG4-RD following an 11-year history of salivary gland swelling, pancreatic involvement and markedly elevated blood IgG4 levels (1300 mg/dL) consistent with the

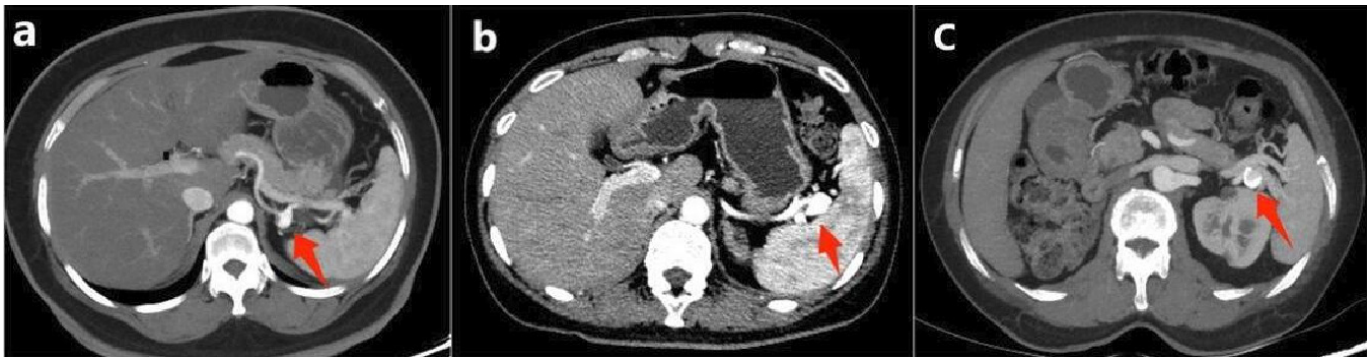

Figure 1 Contrast-enhanced CT on presentation of case 1 (a), case 2 (b) and case 3 (c) showing splenic artery aneurysm (red arrow). Figure 1c shows an aneurysm that developed calcification whereas there is no calcification of the aneurysm in both case 1 and case 2.

ACR/EULAR criteria. Treatment began with 40 mg of prednisolone daily and 1.5 g of mycophenolate mofetil daily. Five years later, CT revealed the development of a splenic artery aneurysm measuring 12 mm in diameter (figure 1c). As with the two patients mentioned above, there was no other cardiovascular involvement. At the time of aneurysm detection, the serum IgG4 level was 121 mg/dL, and the IgG4-RD RI was 8.

DISCUSSION

IgG4-RD is recognised for its potential to affect nearly every organ, particularly a preference for large and medium-sized arteries when vascular involvement occurs.[2] The aorta is the most commonly affected artery followed by the iliac and coronary arteries.[3 4] However, instances of splenic artery aneurysms are exceedingly rare with only two cases reported in the literature. We have summarised the characteristics of the three patients we reported along with the two patients previously reported in table 1. During the follow-up time between the initial diagnosis and the identification of the splenic artery, these three patients underwent one to two abdomen CT scans annually, none of which revealed splenic artery aneurysm formation. The three patients we reported had normal or not significantly elevated serum IgG4 levels and no arterial involvement was found in these three patients at the time of diagnosis. Moreover, other organ involvement was stable when the splenic artery aneurysm was detected. It is noteworthy that all five patients had salivary gland involvement and only one patient had other arterial involvement indicating that splenic artery involvement and other arterial involvement are not parallel in IgG4-RD. All these patients had an IgG4-RD RI of no more than 5 suggesting that splenic artery aneurysm may not indicate disease flare. However, aneurysms may represent a form of damage rather than an active disease. These aneurysms likely represent a late complication of prior vascular involvement that may not have been detected clinically during active disease. Figure 1c shows an aneurysm that developed calcification whereas cases 1 and 2

Table 1 Characteristics of patients with IgG4-RD and splenic artery

Patient	Sex	Age (years)	Duration (years)	Other organ involvement	IgG4 (<135 mg/dL)		IgG (700–1660 mg/dL)		IgE (20–200 IU/mL)		C3 (80–120 mg/dL)		C4 (90–360 mg/dL)	
					a	b	a	b	a	b	a	b	a	b
1	Female	51	14	Lacrimal gland, salivary glands, kidneys, lymph nodes	361	17	1070	1000	39.1	30.54	140	144	30.1	28.8
2	Female	38	3	Lacrimal gland, salivary glands	1400	158	1760	1260	276.6	23.16	65.5	85.2	30.1	12.40
3	Female	74	11	Lacrimal gland, pancreas gland, salivary glands, lymph nodes, kidneys	1300	121	3133	801	381.5	43.29	63.7	85.1	13	20.80
4[5]	Male	68	–	Skin, muscle, salivary glands, periaortitis, and pericoronary arteritis, arteries	–	2390	–	4305	–	9716	–	–	–	–
5[8]	Male	65	1	Pancreatitis, salivary glands	–	472	–	–	–	–	–	–	–	–

Duration: The duration between the occurrence of splenic artery aneurysm and the onset of IgG-4RD manifestation.
a: The laboratory values at the time of initial diagnosis.
b: The laboratory values at the time of discovery of splenic artery aneurysm.
Ig, immunoglobulin; IgG4-RD, immunoglobulin 4-related disease.

show no signs of calcification. On one hand, neither case 1 nor case 2 suffered from any chronic illnesses such as diabetes, hypertension or hyperlipidaemia that might damage the arteries. On the other hand, they abstain from alcohol and smoking.

Considering the risks associated with biopsy, tissue biopsy of the splenic artery aneurysm was not performed in our three patients. It is not certain whether this is a coincidence. Indeed, vascular involvement in IgG4-RD is usually lesions presenting as periarteritis. However, the periarteritis may have been improved when the artery aneurysm formed. One previously reported patient underwent a biopsy and was found to have mild-to-moderate infiltration of plasma cells and lymphocytes in the wall of the splenic artery aneurysm with a maximal plasma cell IgG4+/IgG+ ratio of 40%.[5] Therefore, we hypothesise that the observed aneurysms are probably linked to IgG4-RD. Two out of the three patients we reported underwent embolisation of the splenic artery aneurysm. The follow-up time for the three patients was 7, 12 and 20 months, respectively. The splenic artery aneurysm remained stable with no signs of progression. Currently, the mechanism of vascular involvement in patients with IgG4-RD remains unclear. Notably, a recent study demonstrates elevated absolute T-helper 1 (Th1) cells counts in individuals with IgG4-RD compared with healthy controls.[6] It is interesting to note that Th1 cells typically trigger inflammatory cellular reactions such as macrophage activation which has a direct impact on the development of abdominal aortic aneurysms.[7] The cases we reported here highlight a potential association between IgG4-RD and concurrent splenic artery aneurysms. However, further research is required to elucidate a more comprehensive empirical and theoretical basis for the clinical diagnosis and management of IgG4-RD with splenic artery aneurysms.

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