Immunoglobulin G4-related hepatic artery aneurysm

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ABSTRACT

A 49-year-old man who was a current smoker with a history of hypertension, dyslipidemia, and coronary artery disease after coronary stent placement presented because of abdominal and back pain. Contrast-enhanced computed tomography showed a 30-mm, large hepatic artery aneurysm. Resection of the aneurysm and autogenous vein bypass grafting was performed, which resulted in a successful outcome without any complications. Pathologic examination of the aneurysm confirmed that it was related to immunoglobulin G4 (IgG4). The patient's serum IgG4 level was within the normal range, and no other signs of IgG4-related organ lesions were observed. (J Vasc Surg Cases Innov Tech 2024;10:101377.)

Keywords: Hepatic artery aneurysm; Immunoglobulin G4-related disease; Visceral artery aneurysm

A visceral artery aneurysm (VAA) is a rare vascular disease that can lead to a life-threatening emergency if it ruptures.[1] Hepatic artery aneurysms (HAAs) are the most frequent VAAs, followed by renal and splenic artery aneurysms. Most HAAs are diagnosed incidentally during diagnostic imaging performed for other indications and are most commonly observed during the sixth decade of life, with a 3:2 male predominance.[2]

The relationship between VAAs and IgG4-related aneurysms (RAs) is rarely discussed, because IgG4-RAs primarily affect large and medium arteries, such as the aorta and coronary arteries.[3-6] However, with regard to IgG4-RAs occurring in the visceral artery, only a few patients evaluated with pathologic examination have been reported, especially involving the renal and hepatic arteries.[7-11] Regarding the treatment of IgG4-RAs, steroids can promote sac shrinkage and reduce the thickness of the arterial walls; however, aneurysmectomy has been considered an appropriate treatment because of the risk of aneurysm rupture or dissection during steroid therapy.

Some studies have reported IgG4-related HAAs but none were pathologically evaluated. In the present report, we describe a case of IgG4-related HAA that was confirmed by pathologic examination.

CASE REPORT

A 49-year-old man with a history of hypertension, dyslipidemia, and coronary artery disease, who had previously undergone coronary stent placement, presented to another hospital with sudden abdominal and back pain. He was also a current smoker. Contrast-enhanced computed tomography (CT) revealed a large 30-mm common HAA (Fig 1), and he was subsequently transferred to our hospital. An angiogram confirmed that the aneurysm extended from the common hepatic artery to the bifurcation of the proper hepatic artery, with blood flow originating from the superior mesenteric artery. Due to the aneurysm's saccular shape with a wide neck, endovascular therapy was not feasible, because it would not allow for the preservation of blood flow from the hepatic artery trunk. Thus, we decided to proceed with open surgical repair.

The intraoperative findings showed that the aneurysm extended from the common hepatic artery to the bifurcation of the proper hepatic artery, accompanied by noticeable hyperplasia of the vessel wall (Fig 2, *A*). To address this, we performed an interposition bypass using a great saphenous vein graft, connecting the proximal common hepatic artery to the bifurcation of the proper hepatic artery (Fig 2, *B*). The total duration of clamping was 90 minutes. Additionally, we excised the excess aneurysm wall and wrapped the bypass with the remaining aneurysmal wall.

The pathologic examination of the resected aneurysmal wall confirmed the presence of a significant number of IgG4-positive plasma cells. The density of IgG4-positive plasma cells was >10 per high-power field, and the IgG4-positive/IgG-positive cell ratio was >40% (Fig 3). Immunohistochemistry was performed using the following antibodies and conditions: anti-human IgG (1:30,000, rabbit polyclonal, code no. A0423; DakoCytomation) and anti-human IgG4 (1:20,000, mouse monoclonal, catalog no. 053800, clone HP6025; Invitrogen).

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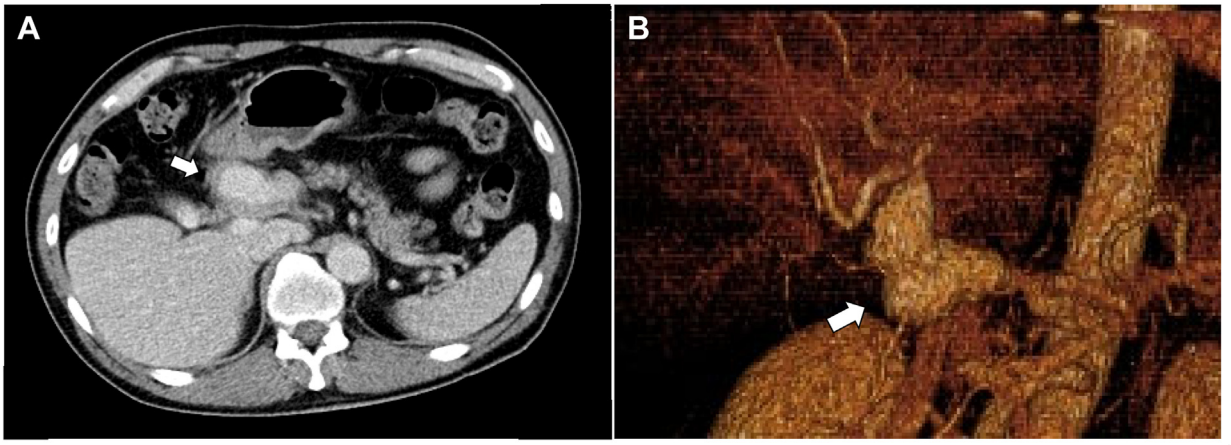

Fig 1. A, Contrast-enhanced computed tomography (CT) scan showing a mass-like lesion with homogenous circumferential enhancement in the late contrast-enhanced phase (*white arrow*). **B,** Volume rendered reconstruction showing a 30-mm giant aneurysm with a wide neck extending from the common hepatic artery and junction of the proper hepatic artery (*white arrow*).

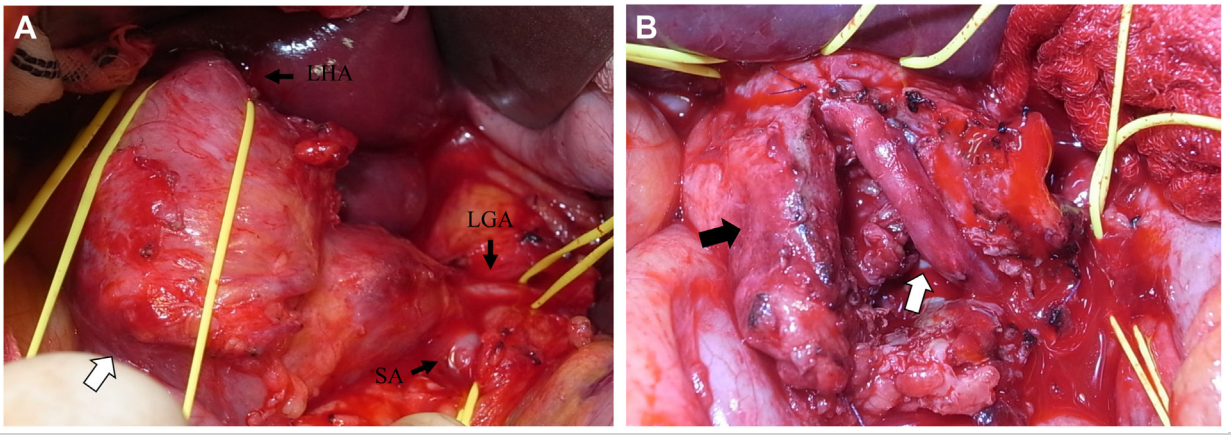

Fig 2. Intraoperative findings. **A,** Photograph showing the hepatic artery aneurysm (HAA) with prominent hyperplasia of the vessel wall (*white arrow*). **B,** Photograph showing the opened aneurysmal sac (*black arrow*) and bypass at origin of the common hepatic artery and junction of the proper hepatic artery with a great saphenous vein graft (*white arrow*). *LGA,* Left gastric artery; *SA,* splenic artery.

Based on these radiologic and pathologic findings, IgG4-RA was diagnosed. The patient's serum IgG4 level, white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level were all within normal limits. Moreover, he did not exhibit any clinical signs of IgG4-related organ dysfunction, including pancreatitis, hypophysitis, or retroperitoneal fibrosis and, thus, did not undergo systemic steroid therapy.

The patient was followed up with CT every 6 months and contrast-enhanced CT annually to evaluate the treated site and any new lesions. At 1 year after surgery, the interposition bypass was occluded. At 5 years and 6 months after the initial surgery, the patient developed a left internal iliac artery aneurysm (36 × 38 mm) and underwent endovascular coil embolization and covered stent placement. Additionally, 6 years and 3 months after the initial surgery, another aneurysm (19 × 20 mm) was detected in the right renal artery, which was also treated with endovascular coil embolization. In both aneurysms, rapid enlargement by >5 mm within 6 months was observed; thus, surgery was indicated for both. During the 7-year period following the initial surgery, the patient never exhibited elevated serum IgG4 levels or developed other organ lesions associated with IgG4-related disease (RD). The patient provided written informed consent for the report of his case details and imaging studies.

DISCUSSION

IgG4-RD is characterized by elevated levels of serum IgG4, and pathologic examination reveals infiltration of IgG4-positive plasma cells, often accompanied by storiform fibrosis.[12,13] This condition is associated with various diseases, including Mikulicz disease, autoimmune pancreatitis, hypophysitis, Riedel thyroiditis, interstitial pneumonitis, interstitial nephritis, retroperitoneal fibrosis, inflammatory aortic aneurysm, and aortitis. In 2008,

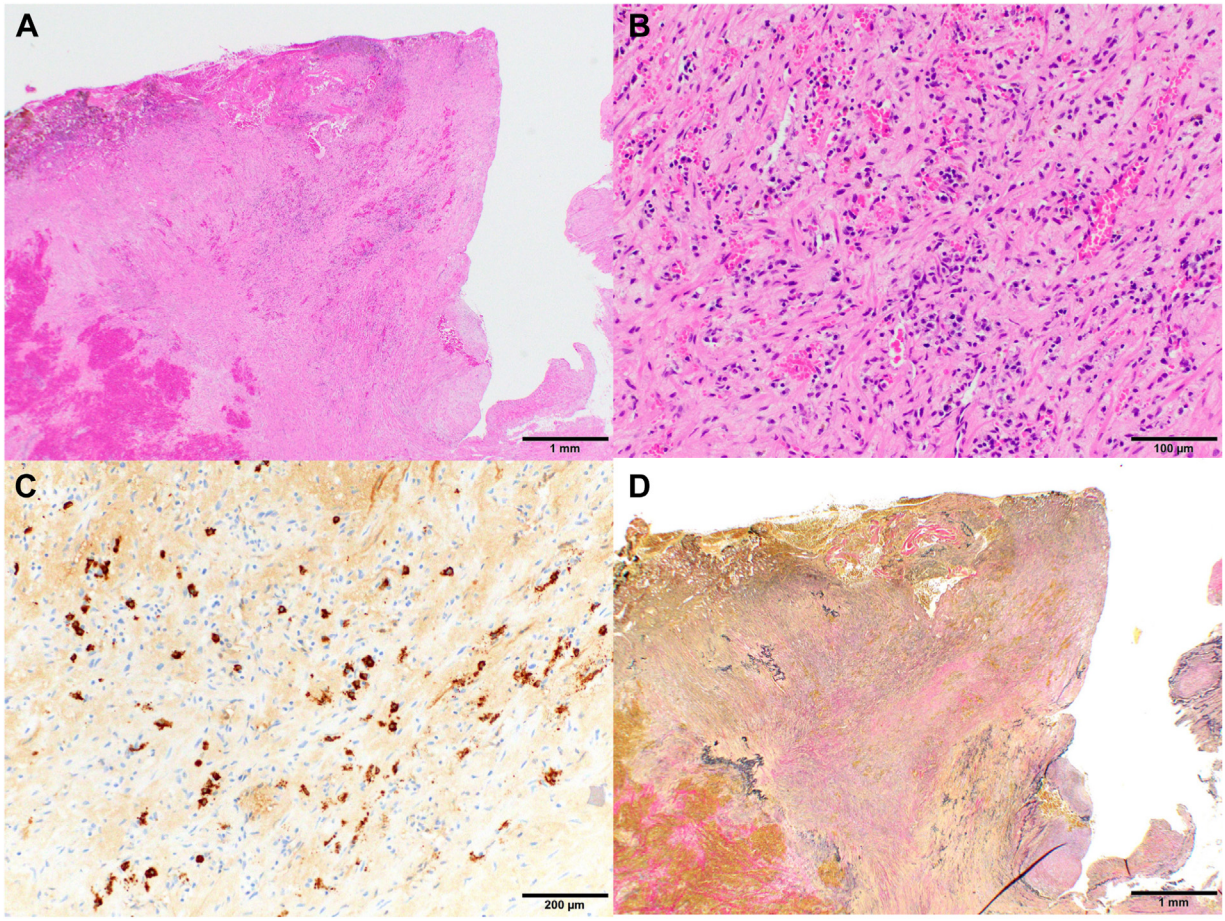

Fig 3. Histologic findings of an immunoglobulin G4 (IgG4)-related hepatic artery aneurysm (HAA). **A,** Hematoxylin and eosin staining showing adventitia thickened due to inflammatory cell infiltration with fibrous proliferation. **B,** Hematoxylin and eosin staining showing crowding by lymphoplasmacytic infiltration with fibrosis. **C,** Immunostaining of IgG4 showing plenty of IgG4-positive plasma cells widely spread. **D,** Elastica van Gieson staining showing storiform fibrosis.

Kasashima et al[14] first reported an IgG4-related inflammatory abdominal aortic aneurysm (IAAA). Since then, multiple cases of IgG4-RD affecting large and medium arteries such as the aorta, iliac artery, and coronary artery have been reported.[3-6] Systemic steroid therapy is commonly used for the treatment of systemic IgG4-RD, including autoimmune pancreatitis and retroperitoneal fibrosis. However, the optimal treatment of localized arterial lesions associated with IgG4-RD, without signs of systemic inflammation, has not yet been well established.[15] For IgG4-related IAAAs presenting with systemic inflammation, hydronephrosis, and abdominal or back pain, systemic steroid therapy can be considered.[16,17] However, unlike other IgG4-related organ lesions, surgical treatment is indicated for IgG4-related aortic lesions due to the potentially catastrophic consequences of rupture.

The incidence of VAAs is generally reported to be between 0.01% and 0.2%, with renal artery aneurysms the most common, followed by HAAs and splenic artery aneurysms. VAAs typically grow slowly, and approximately one in four cases might eventually rupture, leading to critical conditions.[18] Most VAAs are primarily caused by atherosclerosis,[19] and those associated with arteritis are rare. Pathologically diagnosed IgG4-related VAAs are extremely rare, and, to the best of our knowledge, no cases of IgG4-related HAAs with confirmed pathologic evidence have been reported. The treatment options for VAAs include endovascular stenting and surgical repair, and the decision should be determined by individual clinical considerations.[1] Angiography plays a crucial role in assessing the location and morphology of the aneurysm and the need to preserve blood flow in the parent vessel, if applicable. This information helps determine the appropriate treatment option for the patient.[20,21]

The present case fulfilled the criteria for a definitive diagnosis of IgG4-RD based on the radiologic imaging and pathologic study findings.[11] The radiologic features in this case included a thickened arterial wall with severe

periarterial fibrosis and late contrast enhancement of the periarterial tissue. Although the characteristic late contrast enhancement in the entire circumference of the artery, which is one of the organ-specific diagnostic criteria, was not clearly observed in our patient, that could be attributed to the smaller diameter of the vessel compared with the aorta.

Regarding the serum IgG4 levels, multiple studies have reported IgG4-related IAAAs with normal levels of serum IgG4.[6] The possible reason underlying why serum IgG4 levels are not elevated in IgG4-related aneurysms is that the inflammatory response is associated with inflammatory activity. However, because the aneurysmal expansion is influenced by tissue fragility, the inflammatory activity itself is probably low, such as in our patient. In the present case, no evidence of systemic inflammation was indicated by the laboratory data. In contrast, the late contrast enhancement in the perianeurysmal tissue in the CT image and the aneurysm adhesion observed intraoperatively suggested the presence of localized inflammation. This localized inflammation might have extended to the surrounding tissues, potentially causing his abdominal and back pain. However, the extent of this localized inflammation remained speculative, and the etiology of the symptoms remains unclear.

Steroid treatment of IgG4-related arterial disease is controversial.[13] In the literature on steroid therapy for IgG4-related arteritis,[22] no studies have reported the use of steroid therapy after endovascular or surgical treatment or its preventive effects against the development of new aneurysms. In addition, steroid therapy can cause thinning of the arterial walls because the connective tissue becomes more friable. Therefore, we considered the administration of steroids to be based on insufficient evidence and resulting in excessive treatment.

Additionally, four cases from three reports of HAAs in patients with IgG4-RD have been documented in the literature,[8-10] two of which were confirmed in this study. Two of the four patients were asymptomatic and presented with specific findings, such as soft tissue cuffing around the affected arteries and mild narrowing and irregularities on imaging studies, similar to the present case. However, neither of these cases provided pathologic evidence confirming an IgG4-related HAA. The diagnosis of IgG4-related HAAs in those reports was based on the presence of other systemic lesions of IgG4-RD, atypical giant morphology, and multiple lesions. One patient underwent endovascular plug and liquid embolization, and the other patient underwent surgical repair. Pathologic examination of the resected aneurysm was conducted for the second patient; however, it did not meet the diagnostic criteria for IgG4-RD. The second patient received systemic steroid therapy, resulting in significant improvement in the serum IgG4 levels and other inflammatory markers.

Based on these findings, we propose considering IgG4-RA in the differential diagnosis, even in the presence of a symptomatic visceral aneurysm, multiple arterial lesions, and characteristic radiologic findings, despite normal serum IgG4 levels. The presence of a thickened arterial wall with severe periarterial fibrosis and late contrast enhancement of periarterial tissue can support this consideration.

With the widespread adoption of endovascular therapy for aneurysm treatment, the opportunity to obtain surgical specimens has become increasingly rare. It is possible that some of the previously reported atypical VAAs might have been undiagnosed cases of IgG4-RAs.

CONCLUSIONS

To the best of our knowledge, this case report represents the first documented case of an IgG4-related HAA confirmed by pathologic examination. Even in the absence of a history of IgG4-RD or elevated serum IgG4 levels, IgG4-RAs should be considered in the differential diagnosis for patients with symptomatic artery aneurysms with characteristic radiographic imaging findings.

DISCLOSURES

None.

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