

# Arterial-bronchial fistula from ruptured immunoglobulin G4-related subclavian artery aneurysm

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## ABSTRACT

Immunoglobulin G4 (IgG4)-related disease is a systemic chronic inflammatory disease caused by infiltration of IgG4-positive plasma cells into the systemic organs. IgG4-related arterial disease is relatively rare not only in the aorta but also in the small to medium-sized arteries. If IgG4-related vasculitis is suspected on the basis of the preoperative medical history and radiologic and serologic examination findings, a definitive diagnosis can be obtained by open repair and pathologic examination to determine the prognosis and need for additional treatment. Here, we report the successful treatment of arterial-bronchial fistula caused by a ruptured IgG4-related subclavian artery aneurysm. (*J Vasc Surg Cases and Innovative Techniques* 2020;6:84-8.)

**Keywords:** IgG4-related subclavian artery aneurysm; Rupture; Arterial-bronchial fistula

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is a systemic chronic inflammatory disease caused by infiltration of IgG4-positive plasma cells into the systemic organs. IgG4-related vasculitis has been reported in the cardiovascular system, frequently in the aortic region and less frequently in the medium-sized and small arteries. Here, we report a case of IgG4-RD rupture into the main bronchus due to an IgG4-related subclavian artery aneurysm (SAA).

The patient provided consent for publication of this case.

## CASE REPORT

A 68-year-old man underwent open repair of an infrarenal abdominal aortic aneurysm at 62 years of age. He developed sudden hemoptysis, and dynamic contrast-enhanced computed tomography (DCECT) examination revealed a giant right SAA, which was diagnosed as ruptured right SAA with suspected perforation of the main bronchus. The patient was immediately transferred to our hospital. Laboratory data showed mild anemia (hemoglobin level, 12.7 g/dL), white blood cell count of  $8100 \times 10^3/\mu\text{L}$ , and C-reactive protein level of 0.64 mg/dL, indicating no increase in the inflammatory response. IgG4 level was elevated at 466 mg/dL (normal, 4.8-105 mg/dL).

DCECT revealed a right SAA, 56 mm in size, compressing the main bronchus from the right side (Fig 1, A and B). The aneurysm

originated from the bifurcation of the common carotid and brachiocephalic arteries and terminated proximal to the right vertebral artery and bifurcation of the internal thoracic artery. The distal aortic arch showed mild enlargement with a maximum short diameter of 44 mm (Fig 1, B). The descending thoracic aorta was 30 mm in size, and the remaining abdominal aorta exhibited thickened aortic wall, which was circumferentially involved and homogeneously enhanced in the delayed phase of DCECT (Fig 1, C and D).

Resection of the right subclavian artery with extra-anatomic bypass of the right common carotid and right subclavian arteries was performed with omentopexy after considering the possible risk of infection arising from arterial-bronchial fistula (ABF). The approach was through the right suprasubclavian incision and from the median sternotomy to upper laparotomy. Before excision of the SAA, a right common carotid-right subclavian artery bypass was performed with Gelsoft ERS 8 mm (Vascutek, Inchinnan, Scotland). The normal subclavian artery distal to the aneurysm was ligated and dissected from the midline. The proximal part of the aneurysm was transected immediately after the origin of the brachiocephalic artery, and the proximal stump was sutured with 4-0 polypropylene (Fig 2). The SAA showed moderate adhesions to the surrounding tissues but was dissected and completely resected. The omentum was harvested by laparotomy using the right gastroepiploic artery as a feeding artery. The fistula was covered with the omentum through the anterior mediastinum.

The histopathologic findings (Fig 3) showed an aneurysm filled with a laminar organized thrombus (Fig 3, A). The aneurysmal wall showed displacement, thinning, and hyaline degeneration. An atheroma consisting of partial cholesterol deposits, aggregates of foam histiocytes, and calcium deposits was found. The tunica media showed partially decreased, fractured, and absent elastic fibers (Fig 3, B). Dense infiltration of inflammatory cells, mainly plasma cells, was observed predominantly in the outer layer (Fig 3, C). Immunohistochemical staining showed severe infiltration of IgG4-positive plasma cells in the aneurysm wall (Fig 3, D). In the dense inflammatory lesion, more than 300 IgG4-positive cells per high-power field were seen, and

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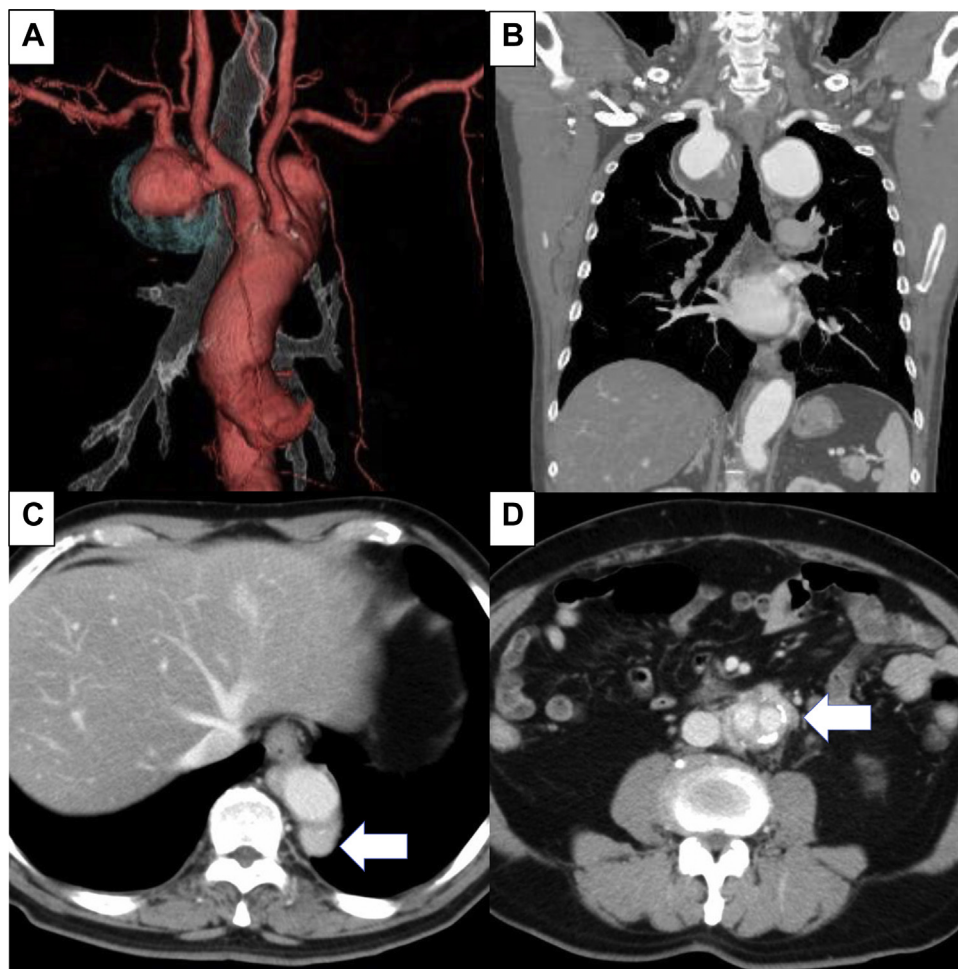
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**Fig 1.** **A** and **B**, A 56-mm subclavian artery aneurysm (SAA). The right side of the trachea was compressed by the aneurysm wall. **C** and **D**, Aortic wall thickening and homogeneous enhancement during the late phase of contrast-enhanced computed tomography in the descending and abdominal aorta.

the IgG4-positive cell/IgG-positive cell ratio was  $>50\%$ . As the IgG4-RD global diagnostic criteria were met (serum IgG4 level, 140 mg/dL or higher; IgG4-positive cell/IgG-positive cell ratio, 40% or higher), aneurysm formation was considered to be caused by IgG-related subclavian arteritis.

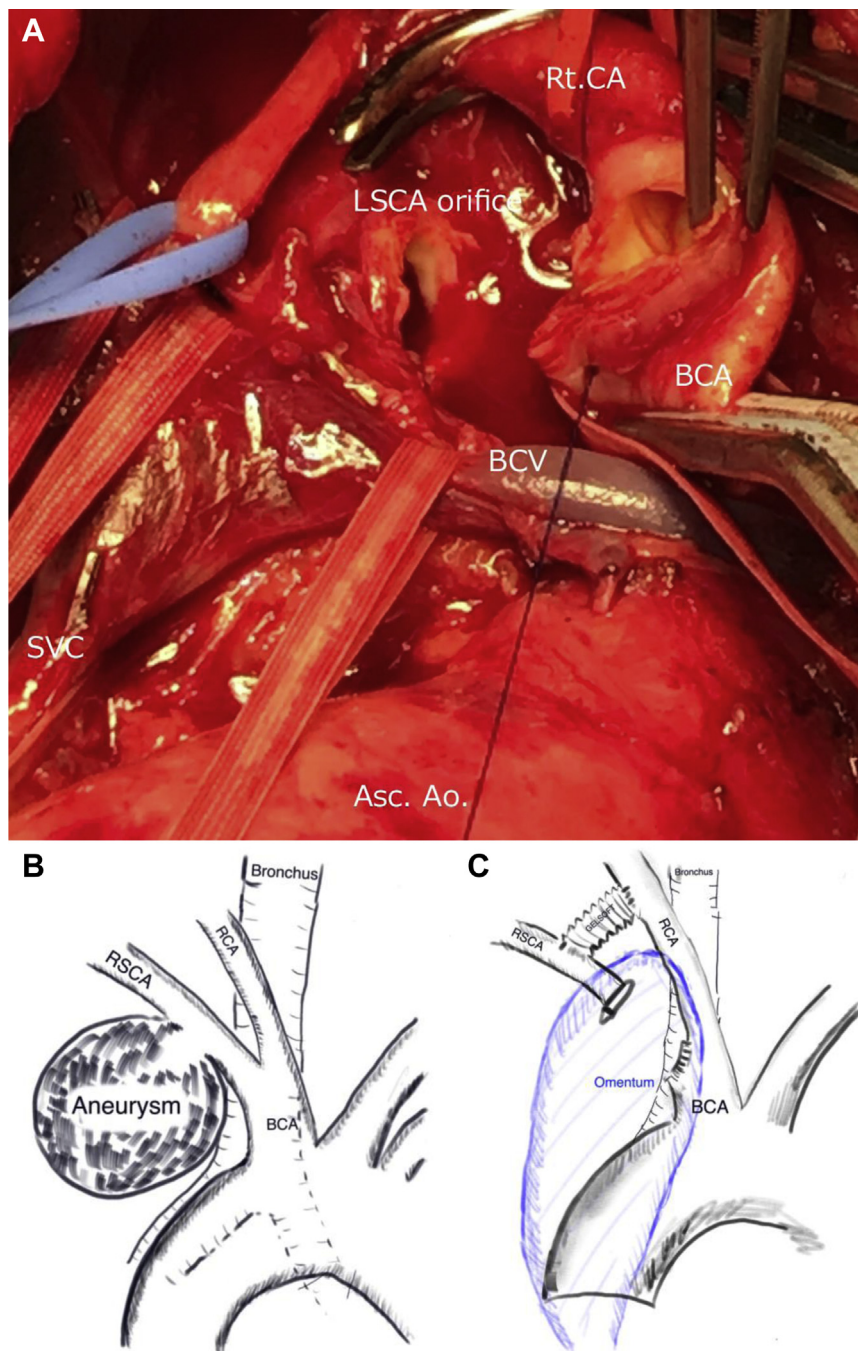
Because of the ABF, antibiotics were administered at a dose of 6 g/d of sulbactam-ampicillin for 6 weeks. Treatment with glucocorticoids (40 mg; 0.7 mg/kg/d) was initiated for vasculitis on postoperative day 30, which was tapered by 5 mg every 4 weeks with continuation of a maintenance dose of 10 mg of oral glucocorticoids. DCECT performed 15 days after initiation of glucocorticoid treatment confirmed the disappearance of the thickened aortic wall with no enlargement of the aortic diameter. On postoperative day 91, blood tests revealed normal IgG4 levels (94.3 mg/dL). The patient is presently alive and well without complications after 6 months of follow-up.

## DISCUSSION

IgG4-RD is a new, widely recognized disease concept reported by Hamano et al.<sup>1</sup> Kasashima et al.<sup>2</sup> in 2008, reported that IgG4-RD is present in inflammatory

abdominal aortic aneurysm. Since then, reports of cardiovascular diseases caused by IgG4-RD have been observed sporadically. The characteristic histopathologic findings are predominant inflammatory sites on the adventitial side of the artery with extensive lymphoplasmacytic infiltration and diffuse and wide distribution of IgG4-positive plasma cells.<sup>3</sup> This strong inflammatory cell infiltration is presumed to weaken the arterial wall or to cause destruction of the elastic fibers in the tunica media, leading to aneurysm formation.

The frequency of IgG4-RD in the small to medium-sized artery (celiac, mesenteric, iliac, coronary artery) region is rarer than that in the aortic region.<sup>4</sup> In the arterial region, the frequency of IgG4-RD is particularly high in the first to second branch from the aorta.<sup>5</sup> The causes of SAA are traumatic, atherosclerotic, thoracic outlet syndrome, and connective tissue disease.<sup>6</sup> The incidence of vasculitis as a cause of SAA is unknown. Although rare, IgG4-related SAA has been described only in a case with multiple IgG4-related aneurysms reported by Tajima et al.<sup>7</sup> Commonly, surgery is indicated for subclavian aneurysms



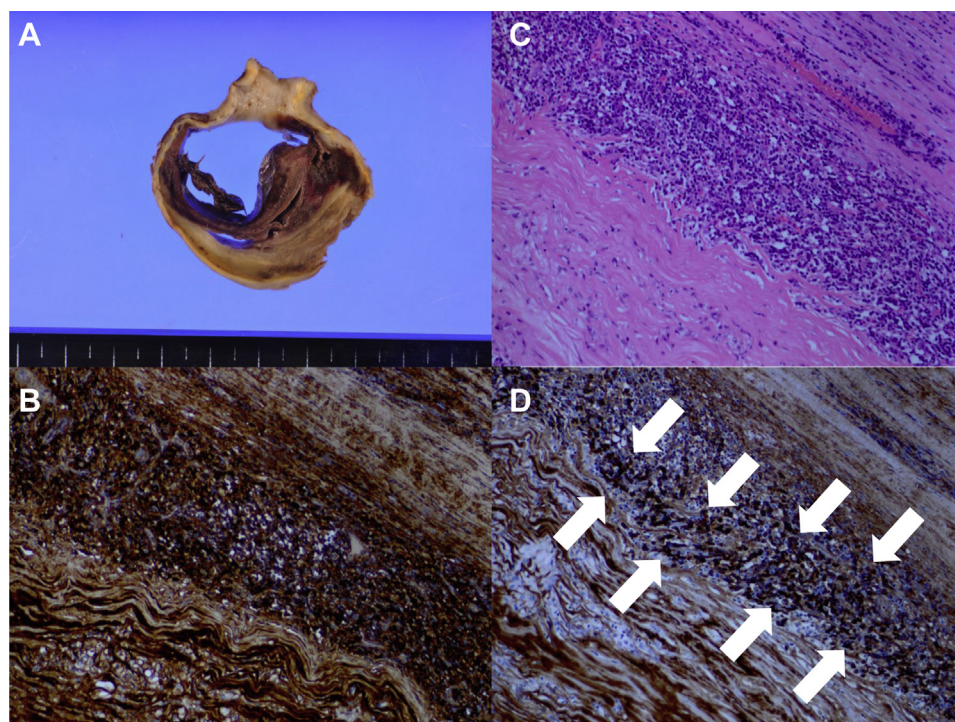
**Fig 2.** **A**, Intraoperative picture. **B**, Preoperative schema. **C**, Postoperative schema. Asc. Ao., Ascending aorta; BCA, brachiocephalic artery; BCV, brachiocephalic vein; LSCA, left subclavian artery; RCA, right common carotid artery; Rt. CA, right carotid artery; RSCA, right subclavian artery.

to prevent rupture and thromboembolism. Although no clear surgical indications exist in terms of aneurysm size, the rupture of such aneurysms can be fatal.

Various surgical procedures, including simple ligation, bypass surgery, and endovascular treatment, have been reported for SAAs. Anatomically feasible hybrid treatment using a stent graft and bypass may be less invasive.<sup>6</sup> In our case, extra-anatomic bypass was considered because of the stable hemodynamics and

for preservation of the blood flow of the right upper limb. Thus, the extra-anatomic route was selected to avoid placing the artificial graft by the anatomic route contaminated by the ABF.

Common carotid-subclavian artery bypass, bilateral axillary artery bypass, and subclavian artery transposition are used to secure blood flow to the subclavian artery. The patency rate of the common carotid-subclavian bypass is 96% at 5 years and 92% at 10 years.<sup>8</sup> Common



**Fig 3.** Immunoglobulin G4 (IgG4)-positive cell invasion of the adventitia-side aneurysmal wall. **A**, Hematoxylin and eosin staining. **B**, Elastic-van Gieson stain. **C**, Immunohistochemical staining for IgG. **D**, Immunohistochemical staining for IgG4.

carotid-subclavian artery bypass, an extra-anatomic bypass technique that does not cross the infected field, was selected in this case. Because the resection of the aneurysm created a large dead space, the greater omentum was used. The patient was treated with antibiotics for 6 weeks according to the Scientific Statement of the American College of Cardiology.<sup>9</sup>

There are no therapeutic guidelines for IgG4-RD arteritis, although an international consensus guidance statement was proposed by experts in 2016. For IgG4-related arteritis, urgent glucocorticoid therapy and maintenance therapy are recommended with an initial dose of prednisolone of 0.5 to 0.6 mg/kg/d and gradual tapering (<0.4 mg/wk), which is important to avoid recurrence. After a successful course of induction therapy, certain patients benefit from maintenance therapy with prednisolone 2.5 to 5 mg.<sup>10</sup> Careful follow-up is essential because some cases show aneurysmal enlargement during steroid therapy.<sup>11</sup>

Treatment with immunodepressants, such as azathioprine and cyclophosphamide, and targeted immunosuppressants, such as rituximab and abatacept, has also been examined, but no evidence has been obtained.<sup>10</sup> Surgical treatment of IgG4-RD vasculitis by open repair rather than by endovascular repair may lower the postoperative level of serum IgG4, sac diameter, and thickness of periaortic fibrosis.<sup>12</sup>

## CONCLUSIONS

Some cases of IgG4-related artery aneurysms might be considered atherosclerotic arterial aneurysms. Careful serologic and histopathologic diagnosis is crucial owing to the possibility of IgG4-related arteritis, especially in patients with multiple aortic and arterial aneurysmal lesions. Appropriate diagnosis-based treatment would improve the clinical outcome in patients with this rare disease entity.

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