Hybrid treatment of an isolated immunoglobulin G4-related internal thoracic artery aneurysm

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ABSTRACT

True aneurysms of the internal thoracic artery (ITA) are rare and are associated with vasculitides, connective tissue diseases, and infections. We report a case of a 3-cm immunoglobulin G4-positive ITA aneurysm that was excised by a hybrid approach involving open ligation of the ITA origin and video-assisted thoracoscopic aneurysmectomy. This novel technique was able to acquire tissue for histopathologic diagnosis through a minimally invasive means. (J Vasc Surg Cases and Innovative Techniques 2018;4:331-4.)

Keywords: Pseudoaneurysm; IgG4; Hybrid; Internal mammary artery; Internal thoracic artery

CASE REPORT

A 43-year-old man presented with hemoptysis in the setting of an upper respiratory tract infection. Initial chest radiography showed an incidental oval opacity in the right superior mediastinum. He had no significant past medical history apart from recurrent urinary tract infections secondary to vesicoureteric reflux. Specifically, there was no history of trauma or surgical intervention to his neck or thorax, autoimmune diseases, connective tissue diseases, or malignant disease.

Further imaging with computed tomography angiography (CTA) showed an isolated 31- × 25-mm well-circumscribed enhancing lesion arising from the proximal right internal thoracic artery (ITA; Fig 1). Given the unusual location of this isolated aneurysm, positron emission tomography (PET) scan was performed to evaluate for an inflammatory cause. This showed that the lesion as well as an anterior mediastinal lymph node was moderately fludeoxyglucose (FDG) avid (Fig 2). An infective and vasculitic screen was unremarkable. Serum inflammatory markers were not elevated, and the immunoglobulin G4 (IgG4) level was normal. The differential diagnosis for the FDG-avid lesion included a mycotic or inflammatory aneurysm and a soft tissue tumor. Given that the lesion appeared highly vascular on CTA, ligation of the ITA was deemed necessary for the complete excision of the lesion.

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The lesion was removed by a hybrid approach with open ligation of the ITA and thoracoscopic excision. The first part of the right subclavian artery was exposed through a supraclavicular approach, and the origin of the right ITA was ligated and divided (Fig 3, *A*). The patient was then repositioned for a three-port video-assisted thoracoscopic approach for the excision of the aneurysm (Fig 3, *B*). The aneurysm and the associated lymph node were dissected from surrounding structures with an ultrasonic dissector, protecting the phrenic nerve, subclavian vein, and brachiocephalic vein.

The histopathologic evaluation of the lesion revealed aneurysmal expansion of the artery by an $IgG4^+$ plasma cell-rich inflammatory pseudotumor (Fig 4). The resected lymph nodes showed reactive changes only. The patient had an uneventful postoperative course. Given that the $IgG4^+$ pseudotumor had been completely excised and there was no evidence of systemic IgG4-related disease elsewhere on PET scan, immunosuppression was not initiated postoperatively. The patient remains under outpatient clinical review. Because the patient's original disease showed positive FDG avidity, we plan to use PET scan surveillance to monitor for local recurrence, which will also offer the opportunity to monitor for distance sites of IgG4-related disease involvement.

Informed consent was obtained from the patient to report this case.

DISCUSSION

ITA aneurysms. ITA aneurysms are uncommon.[1] Pseudoaneurysms are associated with sternotomy, trauma, or endovascular procedures, whereas true aneurysms are associated with vasculitides, connective tissue diseases, and infection.[1-3] Rupture of ITA aneurysms can lead to massive hemothorax and shock, which is often the initial manifestation of such aneurysms, and therefore early treatment has been advocated.[3,4]

The traditional operative management of ITA aneurysm has been ligation and aneurysmectomy through median sternotomy or thoracotomy.[1,5] Recent publications describe endovascular approaches including coil embolization and

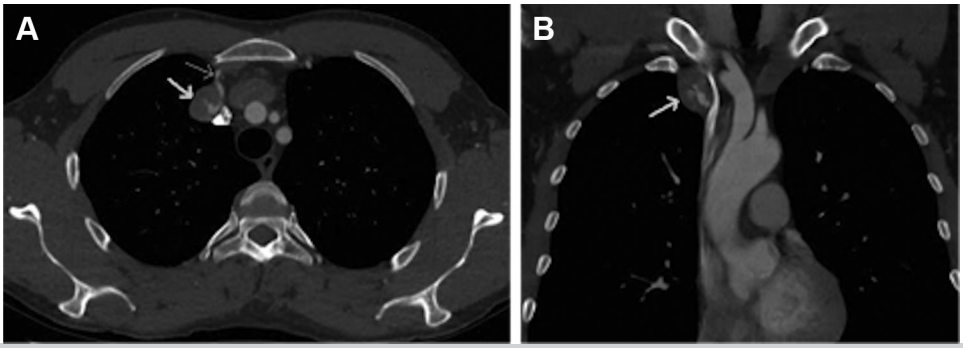

Fig 1. Computed tomography angiography (CTA) showing a 31- × 25- × 25-mm vascular lesion (*thick arrow*) arising from the right internal thoracic artery (ITA; *thin arrow*) on axial **(A)** and coronal **(B)** views.

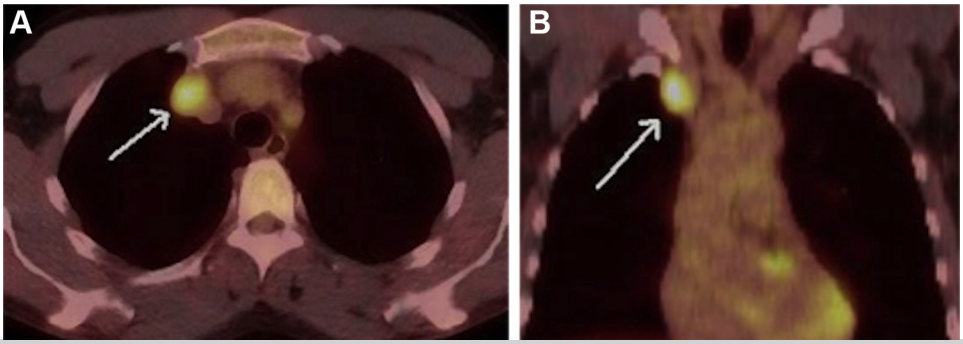

Fig 2. Positron emission tomography (PET) showing a well-circumscribed lesion in the right superior mediastinum with homogeneous moderate fludeoxyglucose (FDG) avidity (*arrows*) on axial **(A)** and coronal **(B)** views.

stent graft implantation.[3,4] Coil embolization allows prompt aneurysm thrombosis and is becoming the treatment of choice, especially for small aneurysms.[4,5] In contrast, stent graft implantation allows preservation of blood flow in the ITA, which may be favorable for coronary bypass conduits.[1] Neither of these endovascular approaches allow tissue diagnosis.

To our knowledge, this is the first case of ITA aneurysm excision by a hybrid open-thoracoscopic technique. Kwon et al[6] reported a case of a ruptured ITA aneurysm with massive hemothorax in a patient with type 1 neurofibromatosis that was treated with an endovascular-thoracoscopic hybrid technique. They performed a staged procedure using coil embolization of the proximal nonaneurysmal ITA segment as a temporizing measure and, 3 days later, returned to the operating room for video-assisted thoracoscopic ligation of the distal ITA for hemostatic control. In this case, the aneurysm was not excised, and histopathologic examination of the aneurysm wall was not performed. Štádler et al[7] described another novel minimally invasive treatment of ITA aneurysm, reporting one case of robot-assisted ligation of an ITA aneurysm in a patient with Marfan syndrome after unsuccessful endovascular treatment.

We performed a hybrid aneurysmectomy to achieve tissue diagnosis and excision of a potentially malignant tumor. The dissection of the aneurysm through a video-assisted thoracoscopic approach allowed an excellent operative view and improved the difficult dissection of adherent tissue surrounding the inflammatory aneurysm. Important adjacent structures, such as the subclavian vein, brachiocephalic vein, and phrenic nerve, were easily identified and preserved. In addition, a sternotomy was not required. Other than the requirement for repositioning, there are few disadvantages compared with an open-only approach. Although endovascular coil embolization was a viable option to achieve proximal and distal control, we thought that the thoracoscopic excision of the lesion was technically easier and that proximal control through open ligation simplified the procedure by partially dissecting the lesion from surrounding structures.

IgG4-related aneurysms. IgG4-related disease is a multiorgan chronic fibroinflammatory condition with classic histopathologic features of lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis. These findings are strongly suggestive of IgG4-related disease if they are accompanied by increased numbers of IgG4-positive plasma cells.[8,9] Although IgG4-related disease affects exocrine organs (most frequently the pancreas) and lymph nodes, it is now recognized to involve a wide variety of organs including the cardiovascular system.[8,10] A raised serum IgG4 level supports the

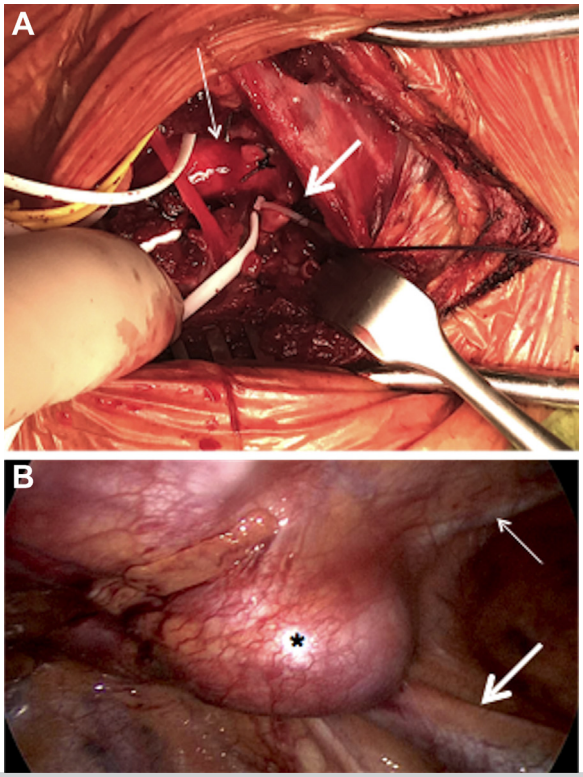

Fig 3. Operative photographs with supraclavicular approach to the right subclavian artery. **A,** exposure and control of the subclavian artery (*thin arrow*) and ligation of the right internal thoracic artery (ITA) origin (*thick arrow*) with a locking ligation clip. **B,** Right ITA aneurysm (*asterisk*) with adjacent distal ITA (*thin arrow*) and phrenic nerve (*thick arrow*) under thoracoscopic view.

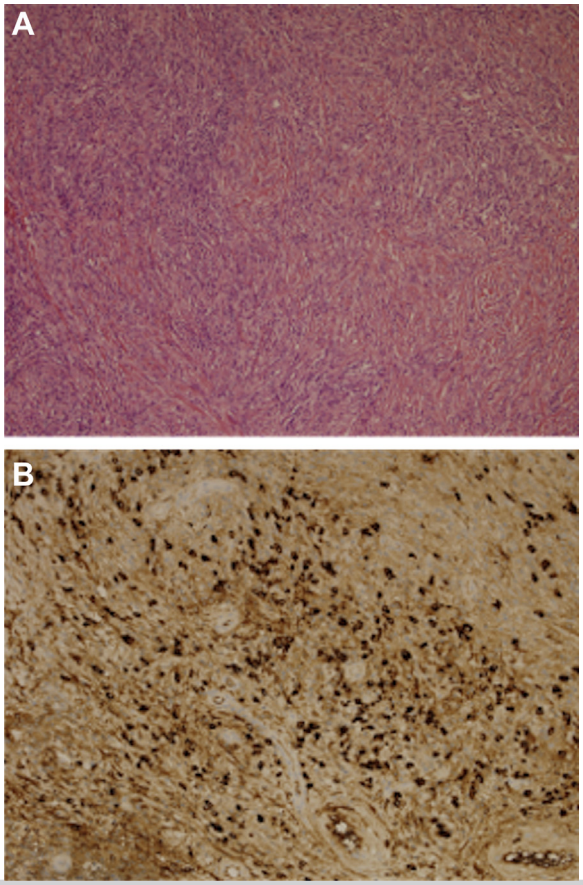

Fig 4. A, Histopathologic features of the excised internal thoracic artery (ITA) aneurysm showing "storiform" fibrosis. **B,** Immunohistochemistry showing preponderance of immunoglobulin G4 (IgG4)-positive plasma cell infiltrate.

diagnosis but is neither a sensitive nor specific test.[11] Approximately 10% of patients with IgG4-related disease have a normal serum IgG4 concentration, and raised IgG4 levels can be found in conditions other than IgG4-related disease, including chronic sinusitis, pneumonia, immunodeficiencies, connective tissue diseases, and interstitial lung disease.[12] PET imaging is a useful tool to determine the extent of IgG4 disease.[13] Tissue biopsy is the "gold standard" for diagnosis and should be pursued where possible.[14]

Manifestations of IgG4-related vascular disease include inflammatory aneurysms, dissections, aortitis, and aortic stenosis.[8,14] Affected arteries may develop periarterial masses, known as pseudotumors, characterized histologically by arterial wall thickening, IgG4-positive plasmacyte-rich inflammation, and adventitial fibrosis.[10] The aorta and its branches are most commonly affected by IgG4-related disease. Only four cases of IgG4-related disease involving medium-sized peripheral limb arteries have been reported.[15] IgG4-related disease has also been reported to involve coronary arteries with pseudotumor or aneurysm formation.[8] To our knowledge, this is the first reported case of IgG4-related disease involving the ITA exclusively.

The optimal treatment of IgG4-related disease has not been established, and no randomized clinical trials have been conducted to date.[16] Corticosteroid therapy is currently the mainstay of pharmacologic treatment of IgG4-related disease and is indicated for active, symptomatic disease. A subset of patients with asymptomatic disease may also require corticosteroids, particularly when organ function is threatened.[8] In addition, rituximab has been used successfully to treat patients with IgG4-related disease. This may be applicable for patients who have a clear contraindication or are unresponsive to steroid therapy.[17] Other agents, such as azathioprine, mycophenolate mofetil, and methotrexate, have been used as well, but their relative efficacy has not yet been studied in prospective trials.[16] Specifically for IgG4-related vascular disease, there are concerns that corticosteroid therapy may cause thinning and weakening of inflammatory aneurysmal wall and increase the risk of vessel rupture.[15,18] IgG4-related inflammatory aneurysms have been treated with surgical resection, embolization, or endovascular stent grafts.[11] Suitability for surgical intervention is governed by anatomic location of lesions and adjacent structures involved.[16]

In this case, given the nondiagnostic CTA and PET characteristics of the aneurysm as well as negative screening test results for infection and vasculitides, surgical resection was necessary for tissue diagnosis and exclusion of malignant disease. This case highlights the diagnostic and therapeutic role of surgical excision for management of IgG4-related vascular disease and the importance of hybrid techniques, depending on anatomy.

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REFERENCES

1. Piffaretti G, Carrafiello G, Franchin M, Ierardi AM, Mariscalco G, Castelli P, et al. Stent-graft repair of a true internal thoracic artery aneurysm. Ann Vasc Surg 2015;29:1452.e11-5.
2. Ohman JW, Charlton-Ouw KM, Azizzadeh A. Endovascular repair of an internal mammary artery aneurysm in a patient with Loeys-Dietz syndrome. J Vasc Surg 2012;55:837-40.
3. Heyn J, Zimmermann H, Klose A, Luchting B, Hinske C, Sadeghi-Azandaryani M. Idiopathic internal mammary artery aneurysm. J Surg Case Rep 2014;2014.
4. Okura Y, Kawasaki T, Hiura T, Seki H, Saito H. Aneurysm of the internal mammary artery with cystic medial degeneration. Intern Med 2012;51:2355-9.
5. Rose JF, Lucas LC, Bui TD, Mills JL Sr. Endovascular treatment of ruptured axillary and large internal mammary artery aneurysms in a patient with Marfan syndrome. J Vasc Surg 2011;53:478-82.
6. Kwon OY, Kim GJ, Oh TH, Lee YO, Lee SC, Cho JY. Staged management of a ruptured internal mammary artery aneurysm. Korean J Thorac Cardiovasc Surg 2016;49:130-3.
7. Štádler P, Dvořáček L, Vitásek P, Matouš P. Robot assisted aortic and non-aortic vascular operations. Eur J Vasc Endovasc Surg 2016;52:22-8.
8. Tajima M, Nagai R, Hiroi Y. IgG4-related cardiovascular disorders. Int Heart J 2014;55:287-95.
9. Perugino CA, Wallace ZS, Meyersohn N, Oliveira G, Stone JR, Stone JH. Large vessel involvement by IgG4-related disease. Medicine (Baltimore) 2016;95:e3344.
10. Matsumoto Y, Kasashima S, Kawashima A, Sasaki H, Endo M, Kawakami K, et al. A case of multiple immunoglobulin G4-related periarteritis: a tumorous lesion of the coronary artery and abdominal aortic aneurysm. Hum Pathol 2008;39:975-80.
11. Hao M, Liu M, Fan G, Yang X, Li J. Diagnostic value of serum IgG4 for IgG4-related disease: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e3785.
12. Carruthers MN, Khosroshahi A, Augustin T, Deshpande V, Stone JH. The diagnostic utility of serum IgG4 concentrations in IgG4 related disease. Ann Rheum Dis 2015;74:14-8.
13. Yabusaki S, Oyama-Manabe N, Manabe O, Hirata K, Kato F, Miyamoto N, et al. Characteristics of immunoglobulin G4-related aortitis/periaortitis and periarteritis on fluorodeoxyglucose positron emission tomography/computed tomography co-registered with contrast-enhanced computed tomography. ENJMMI Res 2017;7:20.
14. Hourai R, Kasashima S, Sohmiya K, Yamauchi Y, Ozawa H, Hirose Y, et al. IgG4-positive cell infiltration in various cardiovascular disorders—results from histopathological analysis of surgical samples. BMC Cardiovasc Disord 2017;17:52.
15. Kasashima S, Kawashima A, Endo M, Matsumoto Y, Kasashima F, Zen Y, et al. A clinicopathologic study of immunoglobulin G4-related disease of the femoral and popliteal arteries in the spectrum of immunoglobulin G4-related periarteritis. J Vasc Surg 2013;57:816-22.
16. Khosroshahi A, Wallace ZS, Crowe JL, Akamizu T, Azumi A, Carruthers MN, et al. International consensus guidance statement on the management and treatment of IgG4-related disease. Arthritis Rheumatol 2015;67:1688-99.
17. Hart PA, Topazian MD, Witzig TE, Clain JE, Gleeson FC, Klebig RR, et al. Treatment of relapsing autoimmune pancreatitis with immunomodulators and rituximab: the Mayo Clinic experience. Gut 2013;62:1607-15.
18. Inoue D, Zen Y, Abo H, Gabata T, Demachi H, Yoshikawa J, et al. Immunoglobulin G4-related periaortitis and periarteritis: CT findings in 17 patients. Radiology 2011;261:625-33.

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