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CASE REPORT

Immunoglobulin G4-related sclerosing disease invading the trachea and superior vena cava in mediastinum

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Abstract

It is well known that immunoglobulin G4 (IgG4)-related sclerosing disease usually occurs in the pancreas, bile duct and gall bladder, but not in the mediastinum, trachea or superior vena cava (SVC). In this case, a patient underwent mediastinal mass excision and trachea resection and repair for a mediastinal and intratracheal mass 15 years ago. This mass was diagnosed postoperatively as an inflammatory pseudotumour (plasma cell granuloma). Subsequently, a mass was found to have recurred in the SVC. We performed a mass excision and innominate vein to the right atrium auricle bypass operation. The mass was diagnosed as IgG4-related sclerosing disease. This patient is now disease and recurrence free.

Keywords: Immunoglobulin G4-related sclerosing disease • Superior vena cava • Trachea

CASE REPORT

A 70-year old female patient was admitted to our institute for dyspnoea and facial oedema. She was medicated with a bronchodilator, regularly given to her due to bronchial asthma for the last 20 years. She underwent computed tomography (CT) for dyspnoea 15 years ago. There was a mediastinal mass in the intratracheal and right lower paratracheal area (Fig. 1A); she therefore underwent a resection operation for the mediastinal mass through right posterolateral thoracotomy. An irregular solid and partially cystic mass was noted, which was measured to be 4.0 × 5.0 cm around the lower paratrachea and adhered to the superior vena cava (SVC) and azygos vein. We performed mediastinal mass excision, tracheal resection and end-to-end anastomosis, as well as partial resection and repair of the SVC. Microscopic findings of the mass from the first operation showed diffusely fibrosclerotic change with proliferation of the fibroblasts and infiltration of chronic inflammatory cells. The mass was diagnosed as an inflammatory pseudotumour (plasma cell granuloma) at that time. She took a bronchoscope for dyspnoea and haemoptysis 6 years later. There was a smooth polypoid mass at the lower trachea. The mass was again diagnosed as an inflammatory pseudotumour (plasma cell granuloma). In addition, she received LASER treatment. After the LASER treatment, she had been doing well with no specific symptoms, and there was no specific finding on the bronchoscope. However, she repeatedly complained of dyspnoea and facial oedema 2 years later. There was no abnormal finding on her laboratory examination. The chest X-ray showed elevated right hemi-diaphragm and subsegmental atelectasis at the right upper lobe and right lower lobe. On chest CT examination, there was a 4.7 cm sized enhanced mass in the SVC without obstruction (Fig. 1B). We performed a resection of the mass for symptom relief through median sternnotomy. The mass was resected, and innominate vein to right atrium auricle bypass was performed. She was relieved of the SVC syndrome and seems to be recovering well. Gross findings of the mass showed it to be relatively well-encapsulated, pale tan and solid, measuring 2.4 × 2.2 × 1.0 cm (Fig. 2A). Microscopic findings of the mass revealed features similar to the previous tumours, with markedly increased lymphoid follicles, fibrosclerotic change of the stroma and a heavy infiltration of the plasma cells (Fig. 2B and C). In addition, immunohistochemical staining for immunoglobulin G4 (IgG4) antibody demonstrated diffusion with strong positivity at the increased plasma cells (Fig. 2D). The mass was diagnosed as IgG4-related sclerosing disease, according to the histological and immunohistochemical features. The plasma IgG4 level was 0.15 g/l postoperatively.

DISCUSSION

It is very rare that inflammation and immune-related fibrosclerosis invade the cardio-vascular system and other organs. Since the discovery of autoimmune disease in the pancreas in 1995 by Yoshida *et al.* [1], autoimmune disease has been found in other organs. Immunohistochemically, IgG4-positive plasma cells are abundant in the involved organs; therefore, we called these diseases IgG4-related disease, IgG4 syndrome, IgG4-related sclerosing disease or IgG4-related multifocal fibrosclerosis.

The pathogenesis is still poorly understood, but it is considered an autoimmune or allergic disorder. The pathological features of considering IgG4-related sclerosing disease are variable, such as diffuse lymphoplasmacytic infiltration, irregular fibrosis, frequent eosinophilic infiltration, obliterative phlebitis and numerous

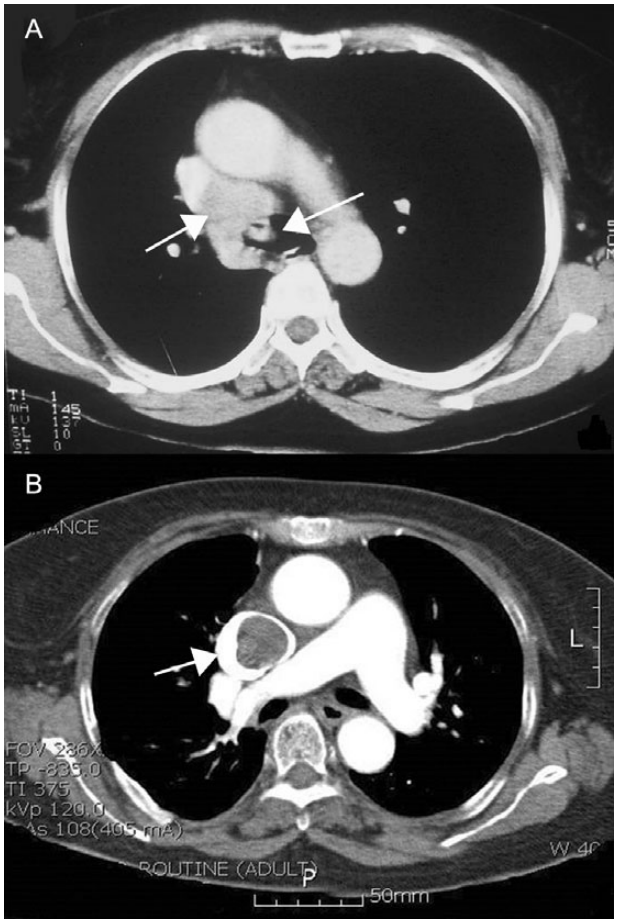

Figure 1: (**A**) Computed tomogram of the patient showed mediastinal mass in the intratracheal and right lower paratracheal area. (**B**) Computed tomogram of the patient showed enhanced mass on the SVC wall.

IgG4-positive plasmacytic infiltrations. In addition, the clinically characteristic finding of this disease is high serum IgG4 concentrations [2]. IgG4 is the least common of the four subclasses of IgG, with a normal constitution of only 3–6% of the entire IgG fraction. High serum IgG4 concentrations are found in only a limited number of conditions, such as atophic dermatitis, asthma or some parasitic disease [2, 3].

IgG4-related sclerosing disease is a disorder that can involve one or multiple organs. This disease often involves the pancreas, bile duct, liver, orbit, lacrimal grand and rarely the aorta, lung or skin. In this case, this disease involved the trachea and SVC, which caused dyspnoea and SVC syndrome.

Often, the radiological features resemble sarcoidosis. The serum angiotensin converting enzyme level would be useful for distinguishing this disease. Also, this disease is rarely associated with granuloma, and is histologically different from the granuloma that is typically observed in sarcoidosis. In addition, this disease resembles Castleman disease, but interleukin-6 or IgG4 would be useful for a different diagnosis [4].

The diagnosis of IgG4-related sclerosing disease is based on biopsy findings, demonstrating the characteristic histopathological findings and immunohistochemical straining of the IgG4 antibody. The serum IgG4 level would be elevated, and this is a significant aid in the diagnosis; however, this is not diagnostic. This elevated serum IgG4 level is related to disease activity and the involved organs [2].

The optimal treatment for IgG4-related sclerosing disease has not been established yet. Most patients respond to glucocorticoids in the early periods, typically with symptomatic improvement, reductions in the size of masses or organ enlargement and improvement in organ function; besides, serum IgG4 levels decrease. However, there are some patients who relapse and others who respond less or even not at all initially. Also, immunosuppressive therapy, such as azathioprine or cyclosporine, would be another alternative treatment [5]. However, unfortunately, the long-term follow-up for IgG4-related sclerosing disease is not sufficient.

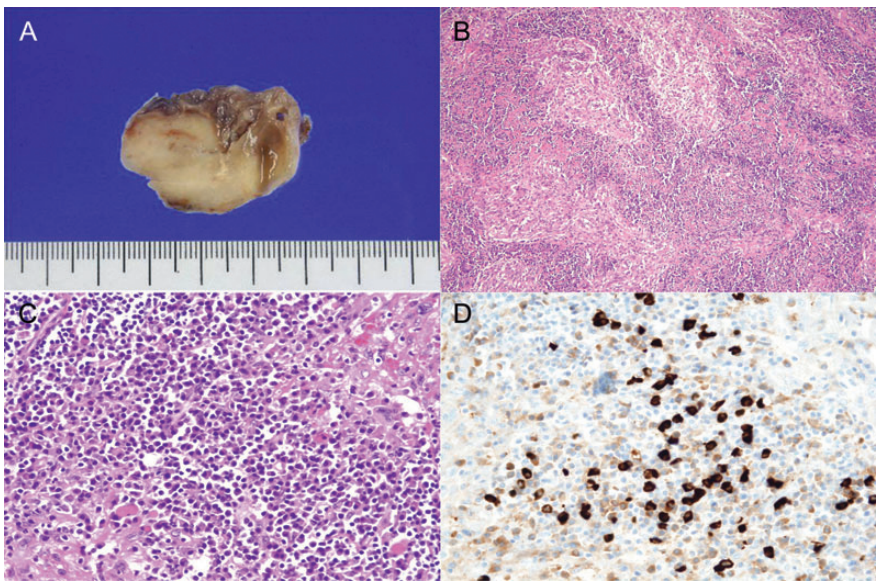

Figure 2: (**A**) Gross finding of the mass reveals a well-encapsulated, pale tan and solid mass. (**B**) Microscopic finding of lower power field of the mass reveals a marked infiltration of the inflammatory cells with diffusely fibrosclerotic change (H&E, X40). (**C**) Microscopic finding of high power field shows a heavy infiltration of the plasma cells (H&E, X400). (**D**) Immunohistochemical staining of IgG4 antibody demonstrates strong positivity at the plasma cells (IgG4, X400).

In this paper, we report a successful management of an IgG4-related sclerosing disease, which involved the trachea and the SVC.

Conflict of interest: none declared.

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