

## IgG4-Related Sclerosing Mediastinitis: Report of a Case with Distinct Ultrasound Findings

### Introduction

Sclerosing mediastinitis is a rare disease characterized by an aggressive fibroinflammatory process within the mediastinum. It may result in the compression and functional impairment of vital mediastinal structures. The precise etiology and pathogenesis of the disease are unknown. Several cases in North America are considered to be caused by *Histoplasma capsulatum* infection. Most cases in Europe seem to be idiopathic. Occasionally sclerosing mediastinitis is associated with a large number of immunoglobulin-G4 (IgG4)-positive plasma cells and is then referred to as IgG4-related sclerosing mediastinitis. We present a case of IgG4-related sclerosing mediastinitis in which percutaneous ultrasound revealed distinct signs because the disease extended into the neck on the left side.

### Case Description

A 44-year-old man was referred to an ultrasound examination of the neck because of a globus sensation for 4 weeks. He had lost 5 kg in two months, and had a history of malignant melanoma. The melanoma was located on the back, had a thickness of 0.5 mm and had been surgically removed seven years earlier. There had been no evidence of lymph node metastasis, other metastasis or tumor recurrence in the meantime. High-resolution ultrasound revealed a homogeneous solid mass with sharp margins, circumferentially encasing the lower part of the left common carotid artery (► Fig. 1a). The intima-media of the encased carotid artery seemed to be preserved and the thickness was normal (► Fig. 1a). Also included in the mass was the lower part of the jugular vein, which showed marked symmetrical mural thickening and occlusion (► Fig. 1b,c). Contrast-enhanced ultrasound revealed moderate and homogeneous vascularization within the lesion (► Fig. 1d). The caudal end of the mass was not visible on ultrasound because it extended into the mediastinum. The subsequent CT examination revealed a huge solid tumor with sharp margins in the superior mediastinum,

surrounding the aortic arch and the supraaortic vessels (► Fig. 2a). The tumor extended also into the left neck and the hilum of the right lung. FDG-PET showed intense uptake in the mass, but no further lesions (► Fig. 2b,c). Histology and immunohistochemistry of the ultrasound-guided 18G core needle biopsy specimen revealed multiple fibrocollagenous bundles containing focally dense, predominantly lymphoplasmacytic infiltrates (► Fig. 3). An average of 50 IgG4-positive plasma cells per high power field (HPF) was present and the ratio of IgG4 to IgG was about 1:1 (more than 40% of IgG-positive cells expressed IgG4) (► Fig. 3), thus suggesting the diagnosis of IgG4-related sclerosing mediastinitis. In fact, in accordance with the histological diagnosis, the patient's serum IgG4 level was markedly increased (473 mg/dl; normal value: up to 201 mg/dl), confirming the definite diagnosis of IgG4-related disease. CRP (C-reactive protein) was slightly elevated at 0.81 mg/dl (normal range 0.00–0.50) and ESR (erythrocyte sedimentation rate) was moderately elevated at 32 mm/h (normal range 6–12). All other assessed parameters including blood cell count, liver function, urea, creatinine, IgA, IgM, IgE, IgG1, IgG2, IgG3, ANA, ANCA, AMA, LKM, SMA, ACPA, rheumatoid factor, and complement C3 and C4 were normal.

Three months after initiating treatment with corticosteroids (initial dose of 80 mg methylprednisolone per day, gradually decrements to a lowest dose of 4 mg methylprednisolone per day as long-term therapy) and rituximab (1 000 mg rituximab IV infusion on day 1 and day 15), the patient's globus sensation had disappeared, the IgG4 serum level decreased to a normal value and the mass was reduced in size by 30% at the follow-up CT examination (► Fig. 4).

### Discussion

IgG4-related sclerosing mediastinitis, also known as IgG4-related fibrosing mediastinitis, is regarded as an idiopathic fibroinflammatory disorder. It is characterized by the expansion of IgG4-producing plasma cells. Serum IgG4 levels are also frequently

elevated, but the absence of such elevated values does not rule out the disease. The exact role of IgG4 in these patients has not been elucidated so far. The triggers and pathogenesis of IgG4-related disease are still unknown. Interestingly, in contrast to autoimmune diseases which often occur in women, IgG4-related disease predominantly affects middle-aged and elderly men (I. Novotny et al. *Dig Dis* 2010; 28: 334–338).

In our patient the presence of a tumorous lesion, typical pathohistological findings including IgG4:IgG cell ratio > 0.4 and > 10 IgG4-positive cells/HPF and serum IgG4 > 135 mg/dl allowed the definite straightforward diagnosis of IgG4-related disease (H. Umehara et al. *Mod Rheumatol* 2012; 22: 21–30, M. Yamamoto et al. *Nat Rev Rheumatol* 2014; 10: 148–159).

IgG4-related sclerosing mediastinitis may cause extrinsic stenoses of the great mediastinal vessels, trachea or esophagus (M. Ferrer Galvan et al. *Clin Respir J* 2015; 9: 125–128). In our patient the lower part of the left common carotid artery showed slight compression, the lower part of the internal jugular vein was thickened and obstructed, and the trachea and esophagus were slightly displaced to the right side due to the mediastinal mass.

The mediastinum is not the only site of IgG4-associated sclerosing disease. The disease may involve various organs and may occur at locations distant from the mediastinum, namely the retroperitoneum, parotid, submandibular and lacrimal glands, thyroid, hypophysis, pancreas, bile ducts, lung, liver, kidney, breast, pleura, pericardium, lymph nodes, or seminal vesicle. It may also occur at several locations simultaneously (I. Novotny et al. *Dig Dis* 2010; 28: 334–338, Y. Zen et al. *Human Pathol* 2005; 36: 710–717). Therefore, whole-body imaging should be performed to identify sites of potential manifestation. In our case the upper mediastinum was the only affected area on the imaging investigations.

While sclerosing mediastinitis is difficult to cure, IgG4-associated cases were reported to respond to corticosteroid therapy. This was also true of our patient (Y. Zen et

al. *Human Pathol* 2005; 36: 710–717, M. Inoue et al. *Gen Thorac Cardiovasc Surg* 2007; 55: 431–433). For type I autoimmune pancreatitis, which by definition is an IgG4-related disease, corticosteroid thera-

py is the treatment of choice (I. Novotny et al. *Dig Dis* 2010; 28: 334–338).

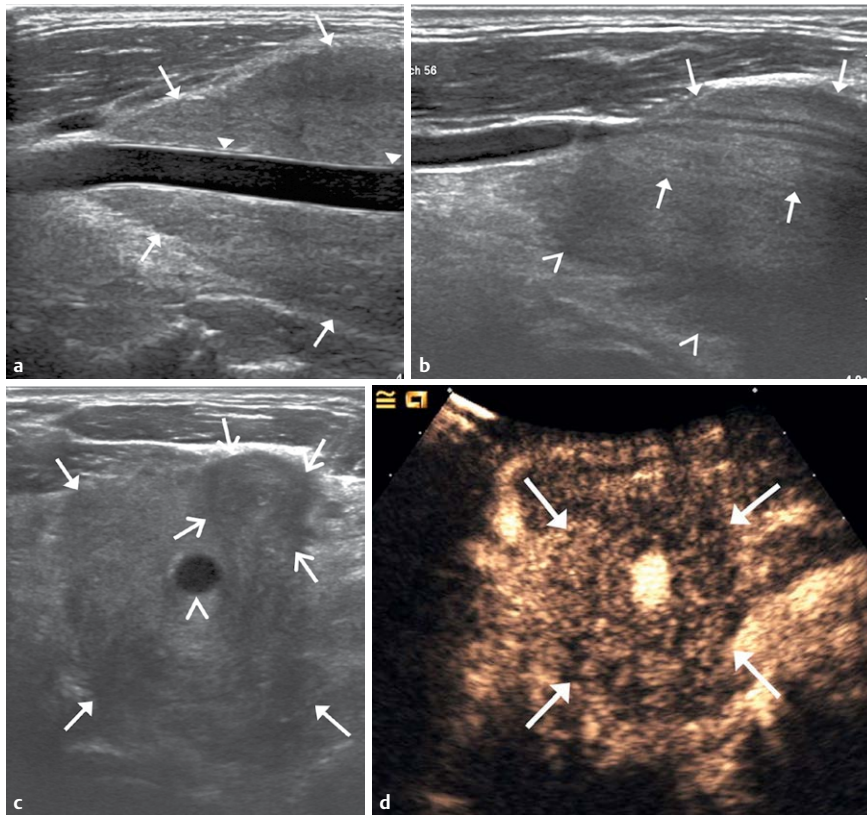
In our patient the huge and solid mass with sharp margins resembled a neoplasm rather than an inflammatory process. Hence the foremost differential diagnoses

included malignant lymphoma (M. Taki et al. *Intern Med* 2013; 52: 2645–2651), melanoma metastasis in our patient with a history of malignant melanoma, other neoplasms, tuberculosis or sarcoidosis (M. Ferrer Galvan et al. *Clin Respir J* 2015; 9: 125–128). It was mandatory to obtain tissue samples. An ultrasound-guided core needle biopsy was performed because the mass extended into the lower part of the left neck. Since the nodular sclerosing type of Hodgkin's disease may be difficult to distinguish from sclerosing mediastinitis on histological investigation, it is important to obtain a sufficient amount of tissue.

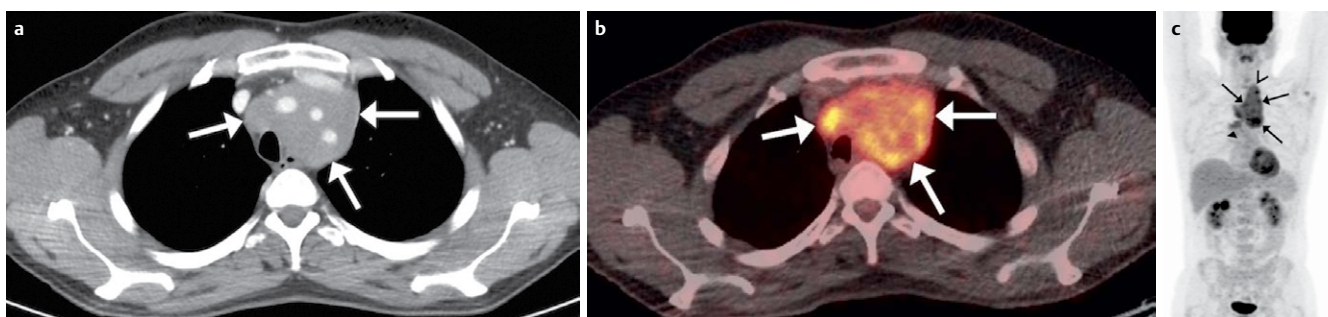
In patients with an IgG4-related sclerosing disease, signs of obliterative phlebitis are frequently found on histological investigation (I. Novotny et al. *Dig Dis* 2010; 28: 334–338, Y. Zen et al. *Human Pathol* 2005; 36: 710–717). To the best of our knowledge, corresponding radiological findings have not been described previously in the published literature. Due to its superficial position, high-frequency ultrasound was an ideal modality to show inflammatory wall thickening and obliteration of the jugular vein, which could not be demonstrated by CT or MRI in our patient (► **Fig. 1b,c**).

The intima-media of the encased common carotid artery was not thickened and was preserved in our patient (► **Fig. 1a**). In contrast, cases with arterial vasculitis are usually associated with marked thickening of the arterial wall.

In conclusion, a solid mass with sharp margins, circumferentially encasing the great vessels, with a preserved wall of the common carotid artery, considerable wall thickening and obstruction of the internal jugular vein, were the distinct ultrasound findings in our

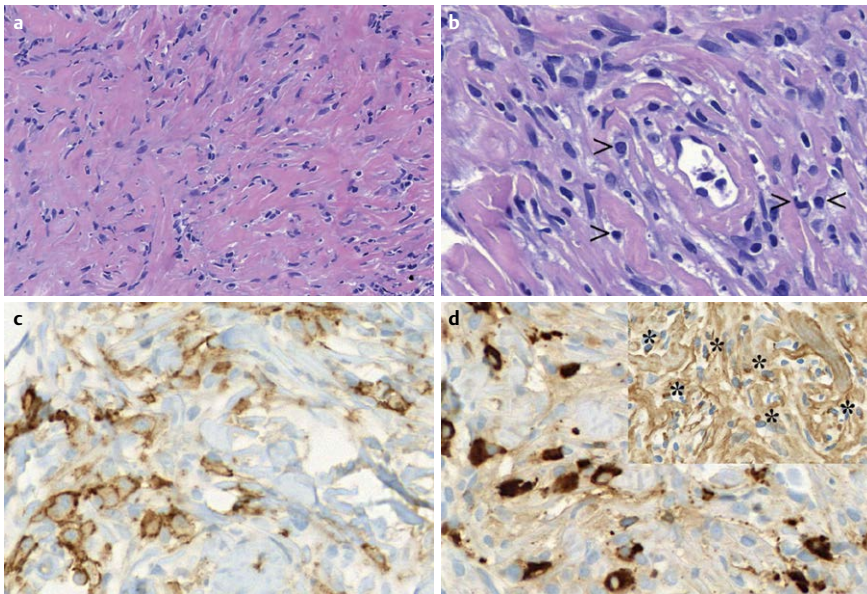


► **Fig. 1** Ultrasound images on the lower level of the left neck. **a** Longitudinal section showing a homogeneous hypoechoic mass with sharp margins (arrows), surrounding the common carotid artery. The vessel wall (intima-media) is preserved (arrowheads). **b** Longitudinal section showing the mass (arrowheads) and wall thickening of the occluded internal jugular vein within the mass (arrows). **c** Transverse section of the mass (arrows with closed head) with the common carotid artery in the center (arrowhead) and the thickened wall of the occluded internal jugular vein on the periphery of the mass (arrows with open head). **d** Transverse section of the mass (arrows) with moderate homogeneous vascularization on contrast-enhanced ultrasound, with the common carotid artery in the center (late arterial phase).

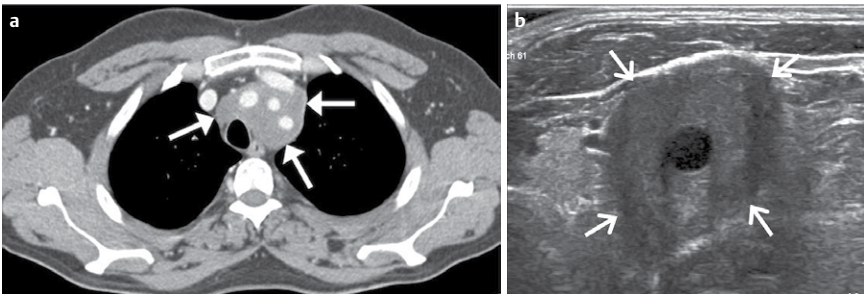


► **Fig. 2** **a** Axial CT image on the level of the upper thorax, showing a homogeneous mass with sharp margins, surrounding the great supraaortic arteries (arrows). **b** FDG PET-CT image on the same level, revealing intense uptake into the mass (arrows). **c** Whole-body FDG PET image showing marked uptake within the mediastinal lesion (arrows) extending into the left neck (open arrowhead) and the right hilum of the lung (closed arrowhead). Focal uptake in projection to the left shoulder is located at a small calcification at the dorsal aspect of the humeral head probably due to a degenerative inflammatory change.





► **Fig. 3** The lesion was composed of dense collagenous bundles with entrapped inflammatory cells **a**, many of them being plasma cells **b**, see arrowheads) as highlighted by CD 138 **c**. IgG4-positive plasma cells comprised a significant proportion (>40%) of the IgG-positive plasma cells **d**, see inset with asterisks).



► **Fig. 4** Three months after the initiation of treatment, the mass was reduced in size by 30% at the follow-up CT examination **a** and ultrasound examination **b**.

patient with IgG4-related sclerosing mediastinitis extending into the left neck.

### Conflict of Interest

The authors have no conflict of interest to disclose.

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### Bibliography

DOI <https://doi.org/10.1055/s-0043-110477>  
 Ultrasound Int Open 2017; 3: E125–E127  
 © Georg Thieme Verlag KG Stuttgart ·  
 New York  
 ISSN 2199-7152

