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Spinal Bony Involvement of IgG4-related Disease Treated by a Spondylectomy

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Abstract

Immunoglobulin G4-related sclerosing disease (IgG4RD) is an emerging immune-mediated fibro-inflammatory disorder which can involve any organ. We describe the first IgG4-RD spondylitis treated with total en-bloc spondylectomy (TES). A 55-year-old man presented with back pain. Magnetic resonance imaging (MRI) of the thoracic spine revealed a pathologic compression fracture on T11 vertebral body and both pedicles suggestive of primary bone tumor or bone metastasis. We conducted TES of T11, because we could not exclude the possibility of primary bone tumor including giant cell tumor. Immunohistochemical examination of the pathology specimens from pleura around the pedicle demonstrated diffuse infiltration of IgG4-bearing plasma cells. Six weeks later from the surgery, a delayed serologic test was done and his serum IgG4 concentration was 45 mg/dL. The final diagnosis was probable IgG4RD on the basis of serological, imaging, histopathological findings. After 6 weeks of oral prednisolone treatment, patient's back pain improved dramatically. IgG4RD is very rare systemic disease and its paraspinal soft tissue like pleura involvement with vertebra body invasion was absent until now. Our experience indicated that surrounding soft tissue biopsy would be helpful when a percutaneous vertebra bone biopsy mismatched with the image studies, even though vertebra body was main pathological lesion considering the possibility of IgG4RD.

Keywords: immunoglobulin G4-related disease, spinal bony involvement

Introduction

Immunoglobulin G4-related sclerosing disease (IgG4RD) is an emerging immune-mediated fibro-inflammatory disorder which can involve any organ, and pancreas is the most frequently affected organ.[1)] IgG4RD is characterized by elevated serum IgG4 levels and by painless swelling and inflammation of affected organs and IgG4-positive plasma cells are abundant in the affected tissues. Histologically characteristic features include lymphoplasmacytic infiltration, dense storiform fibrosis, and alveolar phlebitis.[2)] Diagnosis can be made on the basis of serology, image including computed tomography (CT) scan, magnetic resonance imaging (MRI), particularly histopathological findings. Glucocorticoid is the first-line therapy for patients with multiple organ dysfunction and clinical symptoms.[3)]

There have been several reports of patients with IgG4RD involving a wide range of extrapancreatic tissues.[4–7)] However, involvement of the spinal bony lesion is still exceptional. We describe the first

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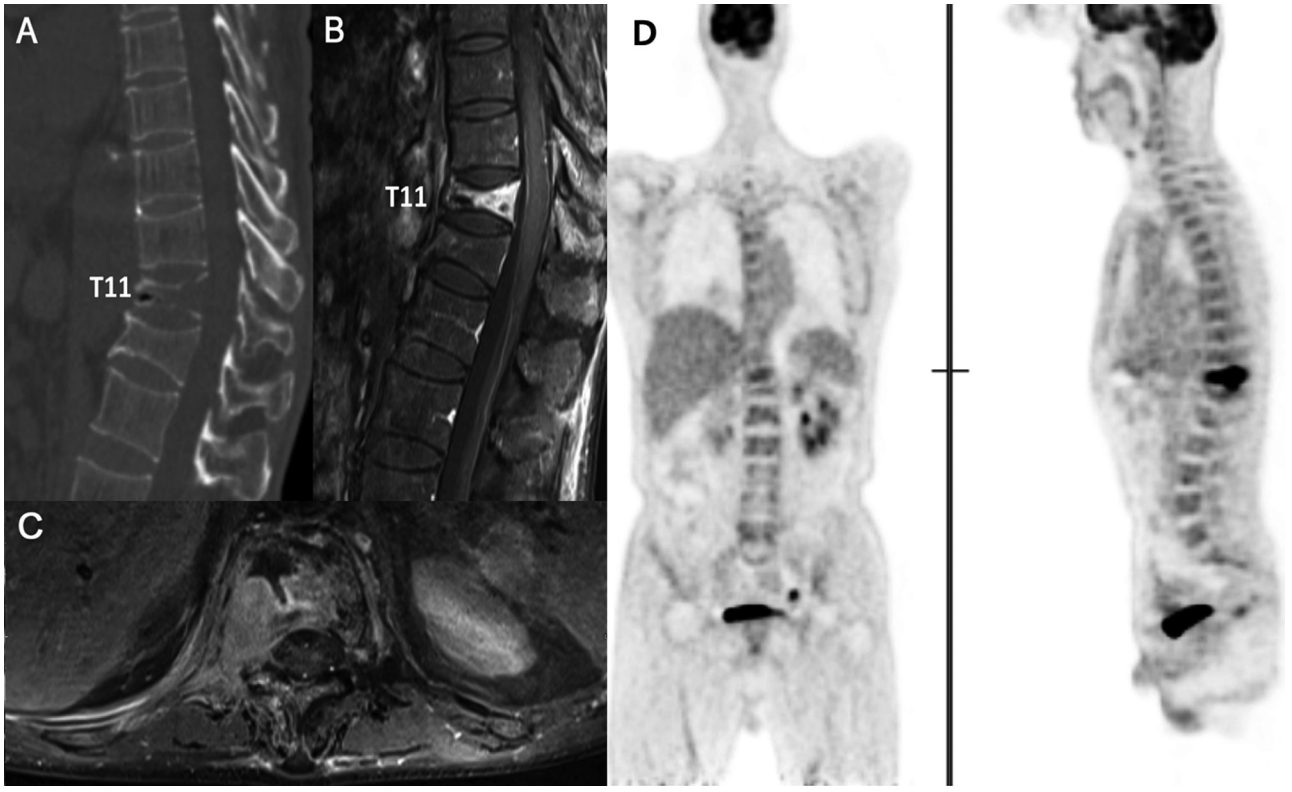

Fig. 1 Lumbar CT (A), sagittal (B), and axial (C) T1-weighted MRI obtained after gadolinium infusion showing collapsed T11 vertebral body with soft tissue thickening around right pedicle and costovertebral junction area, involving right neural foramen of T10-11-12 level and adjacent pleural thickening. (D) Whole-body 18 F-fluorodesoxyglucose PET/CT showing hypermetabolic osteolytic mass with compression fracture in T11 suggesting bone metastasis from unknown primary origin or plasmacytoma. CT: computed tomography, MRI: magnetic resonance imaging, PET: positron emission tomography.

spinal bone involved IgG4RD treated with total en-bloc spondylectomy (TES) methods.

Case Report

A 55-year-old, male patient presented with back pain with numeric rating scale (NRS) 10. A CT scan and MRI of the thoracic spine showed collapsed T11 vertebral body with soft tissue thickening around right pedicle and costovertebral junction, involving adjacent pleural thickening and those lesions showed high enhancement after gadolinium enhancement (Fig. 1). These radiological findings revealed a pathologic compression fracture on T11 vertebral body. We performed positron emission tomography (PET)-CT and bone scan for differential diagnosis of these lesions. PET-CT revealed hypermetabolic osteolytic mass with compression fracture on T11 vertebra (Fig. 1D). Thus, a percutaneous biopsy was performed and the presumptive pathologic diagnosis was a low-grade spindle cell lesion with giant cell components. After multidisciplinary team discussion, we planned radical excision of T11 and adjacent pleura, because we could not exclude the possibility of primary bone tumor including giant cell tumor from imaging and biopsy results.

Angiography was performed before surgery, but an additional embolization was not necessary due to a lack of high vascular staining. During surgery, both T11 and T12 level bilateral ribs were resected and bilateral dearticulation of costovertebral joints was done. The detachment of T11 vertebral body from pleura was attempted and right side adhesive pleura was included in the T11 vertebra side due to the invasion of some portion of lesion to the right side pleura. A pedicle screw fixation was done and a temporary rod was applied. After ventral dissection of the vertebral body from the heart and aorta, both pedicles of the T11 level were cut and the posterior elements including lamina and spinous process were removed with an en-block passion. After cutting T10-11 and T11-12 level disc with a Tomita saw, the T11 vertebral body was removed with en-block passion. A new vertebra reconstruction was done

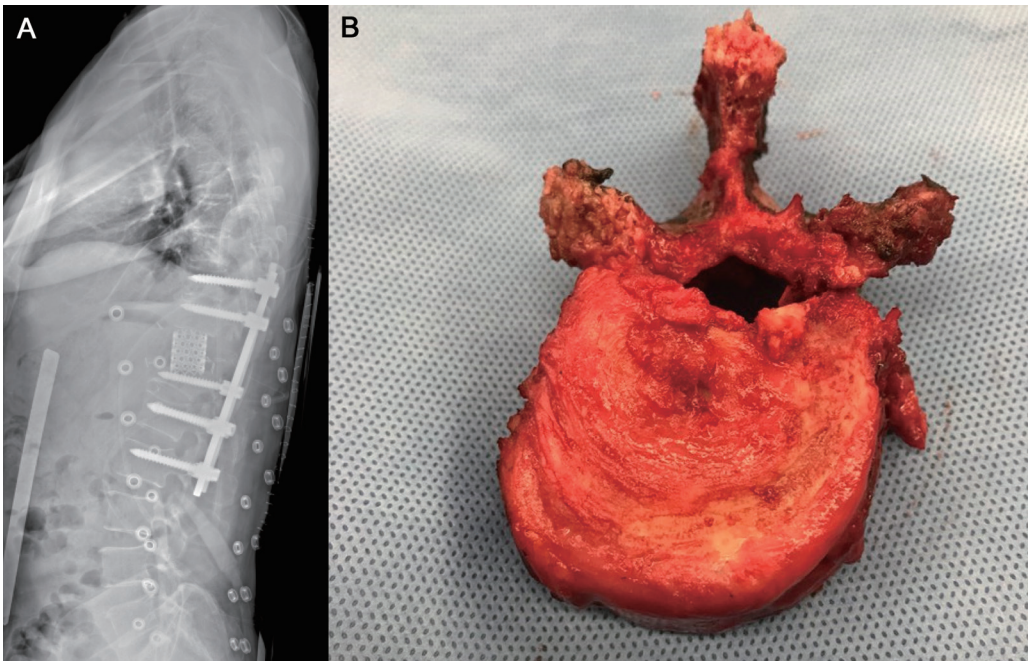

Fig. 2 (A) Postoperative standing lateral X-rays. (B) Gross specimen of the T11 vertebra.

with a mesh cage filled with a harvested and lesion uninvolved ribs (Fig. 2).

The pathologic specimen of T11 vertebra showed lymphoplasmacytic infiltration to the lesion favor with spondylitis. Thus, an immunohistochemical examination from the pleura was followed and final diagnosis was probable IgG4RD (IgG4/IgG = 76.0% in hotspot) (Fig. 3).

Six weeks later from the surgery, a delayed blood serologic test could be done after the multidisciplinary discussion because of a rarity of this disease. Although the serum IgG concentration was abnormally elevated (2020 mg/dL), the IgG4 concentration was 45 mg/dL (within the normal range of 8–140 md/dL) which might be related with delayed serologic test after 6 weeks lesion resection. The final diagnosis was probable IgG4RD on the basis of serological and histopathological findings. Despite 6 weeks passed after surgery, back pain of patient was same with preoperative status (NRS 10). Treatment was started with oral prednisolone 50 mg per day for 3 weeks, followed by oral prednisolone 30 mg per day for 3 weeks.

Thereafter, patient's back pain improved dramatically and NRS was 4. A laboratory tests including routine blood tests and inflammatory markers also decreased. C-reactive protein (CRP) decreased from 1.0 mg/dL to 0.1 mg/dL (within the normal range of 0–0.6mg/dL) and erythrocyte sedimentation rate (ESR) decreased from 74 mm/hr to 3 mm/hr (within the normal range of 0–9mm/hr).

Discussion

IgG4RD can affect any organ with multiple clinical manifestations that makes the diagnosis a challenge. The differential diagnosis of IgG4-related disease is broad and usually depends upon the specific site of involvement and clinical presentation. IgG4RD should be suspected in patients with one of the characteristic patterns of organ or tissue involvement. The diagnosis should be confirmed by biopsy of an involved organ whenever this is possible, but histopathology findings are never diagnostic alone of IgG4RD and must be interpreted in the context of clinical, serologic, and radiologic data. Comprehensive diagnostic criteria are shown in Table 1,[8] therefore, according to the this criteria, our patient was diagnosed with probable IgG4RD.

Our patient's CT scan, MRI, bone scan, and PET-CT suggested malignant tumor such as primary bone tumor and bone metastasis. However, bone biopsy results were reported as relatively benign lesions. Thus, there was no involvement of other organs commonly invaded by IgG4RD, such as pancreas, retro-peritoneum, aorta, lung, and eyes, in the chest CT and abdominal CT of the patient. Given this inconsistent findings, we had to consider other diagnosis including soft tissue origin tumor. If biopsy was performed again at the pleura, IgG4RD could have been diagnosed before surgery.

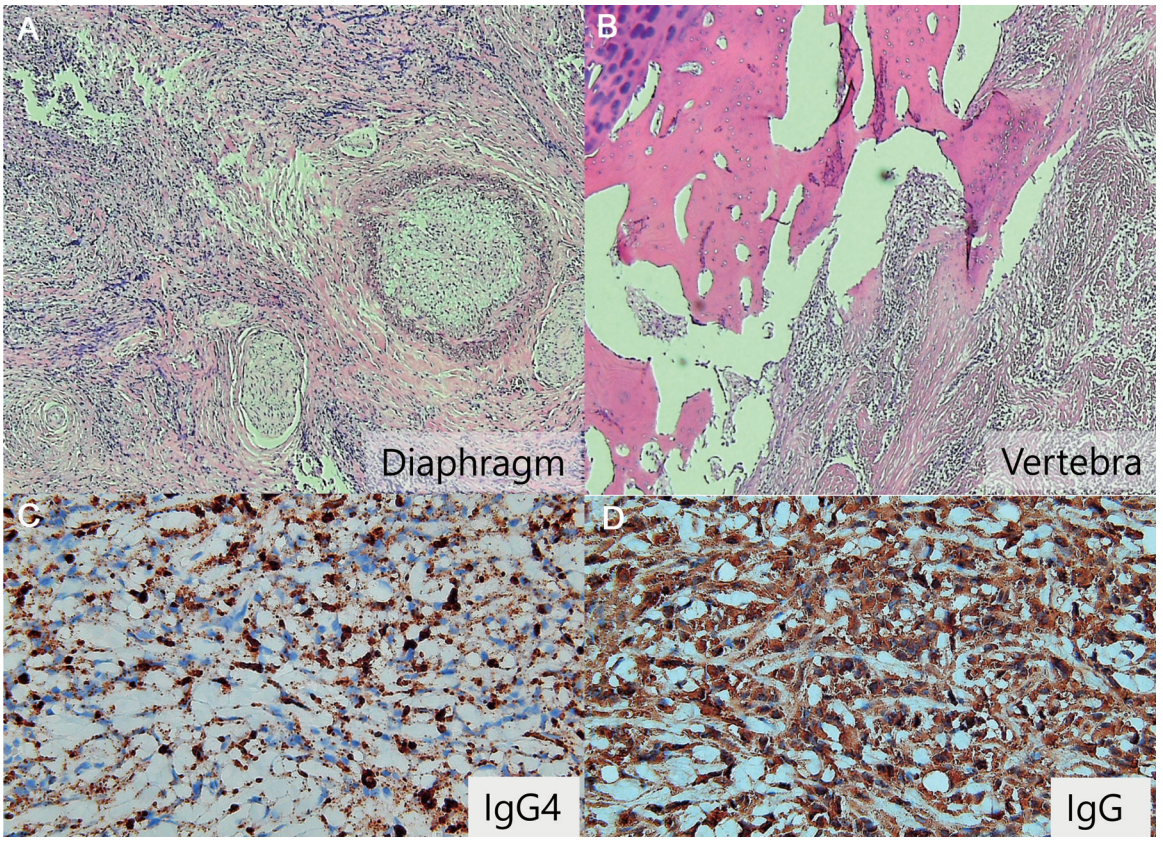

Fig. 3 Pathologic specimen of pleura and diaphragm (A) showed lymphoplasmacytic infiltration with fibrosis and obliterative phlebitis. Pathologic specimen of vertebra showed lymphoplasmacytic infiltration with fibrosis in peri-spinal soft tissue (B). IgG4 immunohistochemistry (C) and IgG immunohistochemistry (D) showed prominent IgG4-positive plasma cells and the proportion of IgG4/IgG-positive plasma cells is 76%.

Because we could not exclude the possibility of primary bone tumor through those results before surgery, we believed a radical excision was necessary. During the surgery, adhesive pleura was also included in the resected vertebra through the detachment from the normal structure like uninvolved pleura and lung. Because of this pathological pleura resection, IgG4RD was successfully diagnosed in this patient. Usually, it might be too difficult to think that percutaneous biopsy should be taken on this highly enhanced pleura only with images. Because the pathological pleural enhancement was minimal comparing to the obvious gadolinium enhancement on all three columns of T11 vertebra, the origin of tumor may be commonly believed from the bone not from the pleura. However, it was definitely pathological looking because the bone and normal pleura detachment was easy but the pathological pleura showed whitish, thicker, and adhesion to the vertebra. Thus, our experience indicated that surrounding soft tissue biopsy would be helpful when a percutaneous vertebra bone biopsy mismatched with the image studies, even though vertebra body was main pathological lesion considering the possibility of IgG4RD.

In addition, the preoperative angiography also supported the mismatched result, which might be second chance not to do an unnecessary surgery. Because primary bone tumors usually a highly vascularized lesion,[9–11] the lack of high vascular staining on our patient suggested also other inflammatory disease than tumor. However, if we suspected inflammatory disease before surgery, IgG4RD could not be diagnosed with the serology because of its rarity.

The reason the patient's back pain did not improve immediately after surgery is that IgG4RD is a systemic inflammatory disease. In the case of spinal bone tumors including metastasis, vertebrae cortex and periosteum are invaded and this invasion induce spinal axial pain, but IgG4RD causes a global inflammatory reaction. Although solid components of disease including T11 were totally removed by TES, it was thought that back pain persisted even after surgery due to the inflammatory reaction of the remaining surrounding soft tissue, and it was believed that it improved dramatically after steroid administration.

Table 1 Comprehensive diagnostic criteria of immunoglobulin G4-related sclerosing disease

Diagnosis	Criteria
Definitive	Diffuse or local swelling in single or multiple organs Serum IgG4 levels >135 mg/dL Histology • Lymphoplasmacytic infiltration and fibrosis • IgG4-positive plasma cells: ratio of IgG4/IgG-positive cells >40%, and >10 IgG4-positive plasma cells/high-power field
Probable	Diffuse or local swelling in single or multiple organs Histology • Lymphoplasmacytic infiltration and fibrosis • IgG4-positive plasma cells: ratio of IgG4/IgG-positive cells >40%, and >10 IgG4-positive plasma cells/high-power field
Possible	Diffuse or local swelling in single or multiple organs Serum IgG4 levels >135 mg/dL

We suggest that if there were low-grade spindle cells with inflammation on percutaneous vertebra bone biopsy, increased uptakes on images, and lower vascularity, IgG serology followed by surrounding soft tissue biopsy should be mandatory to differentiate this rare IgG4RD.

Nevertheless, the precise pathogenesis of IgG4RD is still not well understood, systemic steroid has been shown to have the favorable response.[10,11] Although we only diagnosed probable IgG4RD according to the guideline[8] because we could not do serological test before the resection of the lesion, the dramatic response of systemic steroid on the patient also add the evidence to the probable IgG4RD diagnosis according to the previous studies.

Conclusion

IgG4RD is very rare systemic disease and its paraspinal soft tissue like pleura involvement with vertebra body invasion was absent until now. Our experience indicated that surrounding soft tissue biopsy would be helpful when a percutaneous vertebra bone biopsy mismatched with the image studies, even though vertebra body was main pathological lesion considering the possibility of IgG4RD.

Conflicts of Interest Disclosure

The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

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