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CASE REPORT

Cervicothoracic spinal cord compression caused by IgG4-related sclerosing pachymeningitis: a case report and literature review

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Abstract
Purpose To report a case of cervicothoracic spinal cord compression caused by IgG4-related sclerosing pachymeningitis (IgG4-RSP).
Methods A 43-year-old male patient presented with 'neck pain for 15 days, exacerbated accompanying motor and sensory dysfunction of lower limbs with bowel and bladder dysfunction for 4 days' was admitted to our department. Combined with the history of 'acupuncture treatment', MRI results and rapid-developing progression, we considered the great possibilities of spinal cord compression by intradural hematoma and timely performed the emergency operation of cervical double-door laminoplasty and thoracic decompression with internal fixation.
Results After combined therapy of dexamethasone, mannitol and neurotrophic drugs, sensory recovery of lower limbs started at the fifth day after operation and the sensory function became normal at the fourteenth day after operation with still complete loss of muscle strength. Pathological examination strongly suggested the diagnosis of IgG4-related sclerosing pachymeningitis (IgG4-RSP).
Conclusions IgG4-related sclerosing pachymeningitis (IgG4-RSP) is a newly recognized disease. This case of cervicothoracic spinal cord compression caused by IgG4-related sclerosing pachymeningitis (IgG4-RSP) has never been reported in China with merely three case reports worldwide. Prompt surgical decompression is recommended and pathological examination is essential for diagnosis and comprehensive treatment.

Keywords IgG4-related sclerosing pachymeningitis · Spinal cord compression · Immunohistochemical staining · Diagnosis · Surgery

Introduction

The most common lesions which could lead to spinal cord compression are intraspinal primary or metastatic tumor and hematoma [1]. To the best of authors' knowledge, spinal cord compression caused by IgG4-related sclerosing pachymeningitis (IgG4-RSP) has never been reported in China with merely three case reports worldwide. There is one case of spinal cord compression caused by cervicothoracic IgG4-related sclerosing pachymeningitis reported as follows.

Materials and methods

A 43-year-old male patient presented with 'neck pain for 15 days, exacerbated accompanying motor and sensory dysfunction of lower limbs with bowel and bladder dysfunction for 4 days' was admitted to our department. Though the patient underwent splenectomy for ruptured spleen 15 years ago, he was otherwise healthy and denied history of hypertension, diabetes, heart diseases or infectious diseases. Due to the neck pain which had no obvious incentive, the patient received 'acupuncture treatment' which was one of the traditional Chinese Medicine

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treatment (the specific condition is not clear) at a local clinic 15 days before admission, which made the neck pain exacerbate. Then the patient was presented with motor and sensory dysfunction below navel with bowel and bladder dysfunction 4 days before admission. MRI at the local hospital showed intraspinal strip-like lesion at C4–T2 level, C4–5 and C5–6 disc herniation with spinal stenosis for corresponding segments. Then the patient was admitted to our department with preliminary diagnosis of intraspinal space-occupying, highly suspected to be hematoma compression. During the course, the patient underwent indwelling catheter and dry stool without significant short-term weight loss. The patient was wheeled into the ward with clear consciousness and suffered numbness below the navel straight two transverse fingers and slight muscular hypertonia of lower limbs. Upper limbs' muscle strengths were as follows: deltoid Class IV, biceps brachii Class V, triceps brachii Class III and grip strength Class III. Major lower limbs' muscle strengths were Class II. Bilateral biceps reflexes were normal with bilateral radioperiosteal and triceps hyperreflexia. The left knee and Achilles jerks were normal with right knee and Achilles hyperreflexia. Both Eaton sign and Spurling sign were positive while Hoffmann sign and Babinski sign were not drawn out. Bilateral patellar clonus and ankle clonus were not elicited. CRP and leukocytes were both in the normal range. Serum IgG level was 9.76 g/L which was in the normal range (8.00–16.00 g/L). MRI at our hospital showed intraspinal strip-like lesion with hypointensity on T1WI and slight hyperintensity on T2WI at C4–T2 level, C4–5 and C5–6 disc herniation with spinal stenosis for corresponding segments (Fig. 1). During the preoperative preparation time, the patient's sensory level rose to bilateral nipple plane with complete loss of muscle strength and superficial sensation of lower limbs. After further questions about the patient's history of 'acupuncture treatment' combined with rapid-developing progression, we considered great possibilities of spinal cord compression by intradural hematoma. The emergency operation of cervical double-door laminoplasty and thoracic decompression with internal fixation was timely performed. The fish-meat like rubbery lesion adhered tightly to the dura mater at C2–T3 level with the absence of normal epidural space and no apparent hematoma. We removed the lesion like tearing the bark using scalpel and spatula (Fig. 2). The entire resected lesion received pathological examination and intraoperative diagnosis might well be epidural metastatic tumor.

Results

The patient's sensory level was in bilateral nipple plane with complete loss of muscle strength and superficial sensation of lower limbs shortly after surgery. Sensory recovery of lower limbs started at the fifth day after operation and the sensory function became normal at the fourteenth day after operation with still complete loss of muscle strength. Pathological examination (Fig. 3) showed large numbers of lymphocytic infiltration in the collagenous and adipose tissues with diffused focal distribution and many mature plasma cells. Proliferative active fibrotissue cells could be seen in the mesenchyme. The immunohistochemical staining showed CD3 (+) CD20 (+) CD38 (+) CD138 (+) LCA (+) Ki67 (30 %) Pax5 (+) S-100 (+) Kappa (+) Lambda (+). In this case, large numbers of proliferative plasma cells expressed IgG4 abundantly, accounted for over 40 % of all the IgG-positive cells. Moreover, IgG4-positive cells were more than 50/HPF. All of these strongly suggested the diagnosis of IgG4-RSD. Unfortunately, the patient refused to accept ultrasound and whole body MRI although we strongly recommended the examinations. As a result, we were not

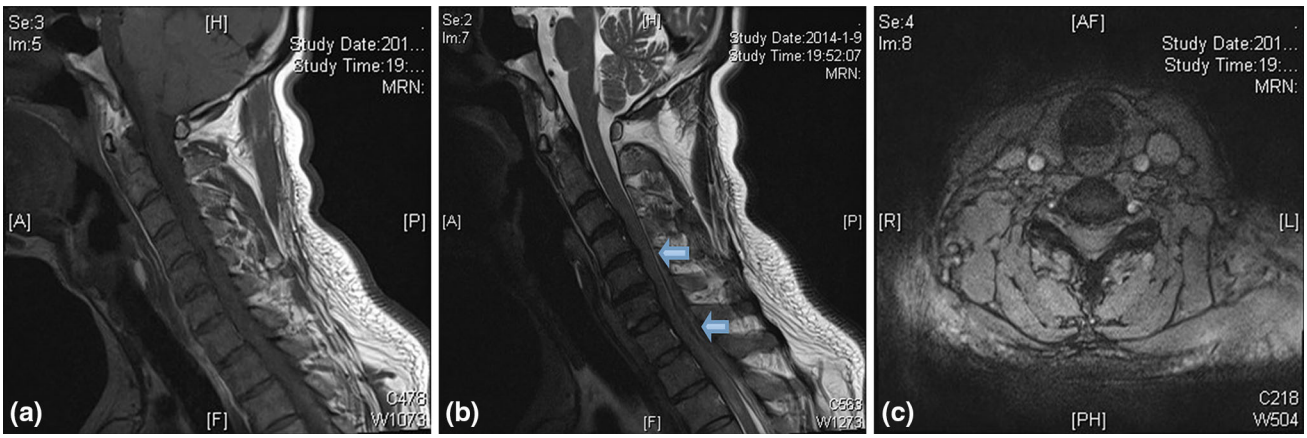


Fig. 1 Preoperative MRI showed intraspinal strip-like lesion at C4–T2 level. **a** Lesion presented with hypointensity on T1WI. **b** Lesion presented with slight hyperintensity on T2WI. **c** Transverse image showed lesion with even signal

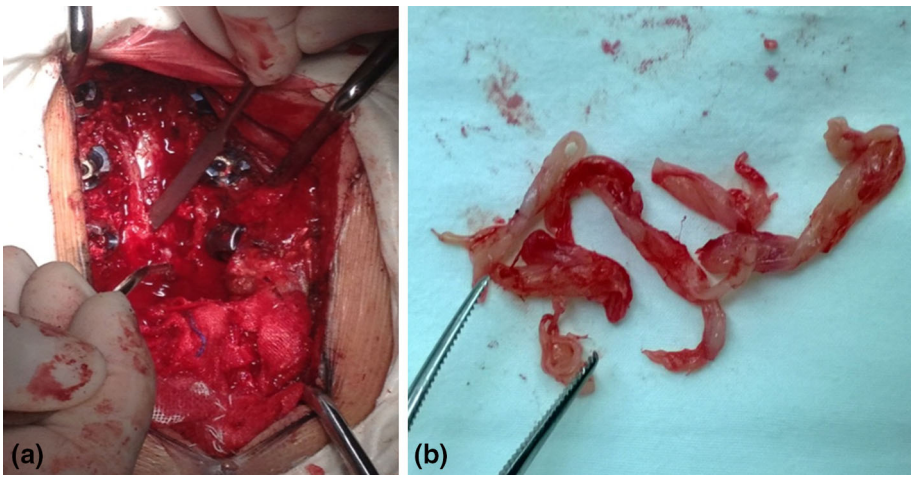


Fig. 2 **a** The lesion adhered tightly to the dura mater at C2–T3 level with absence of normal epidural space and no hematoma compression. **b** Fish-meat like rubbery lesion

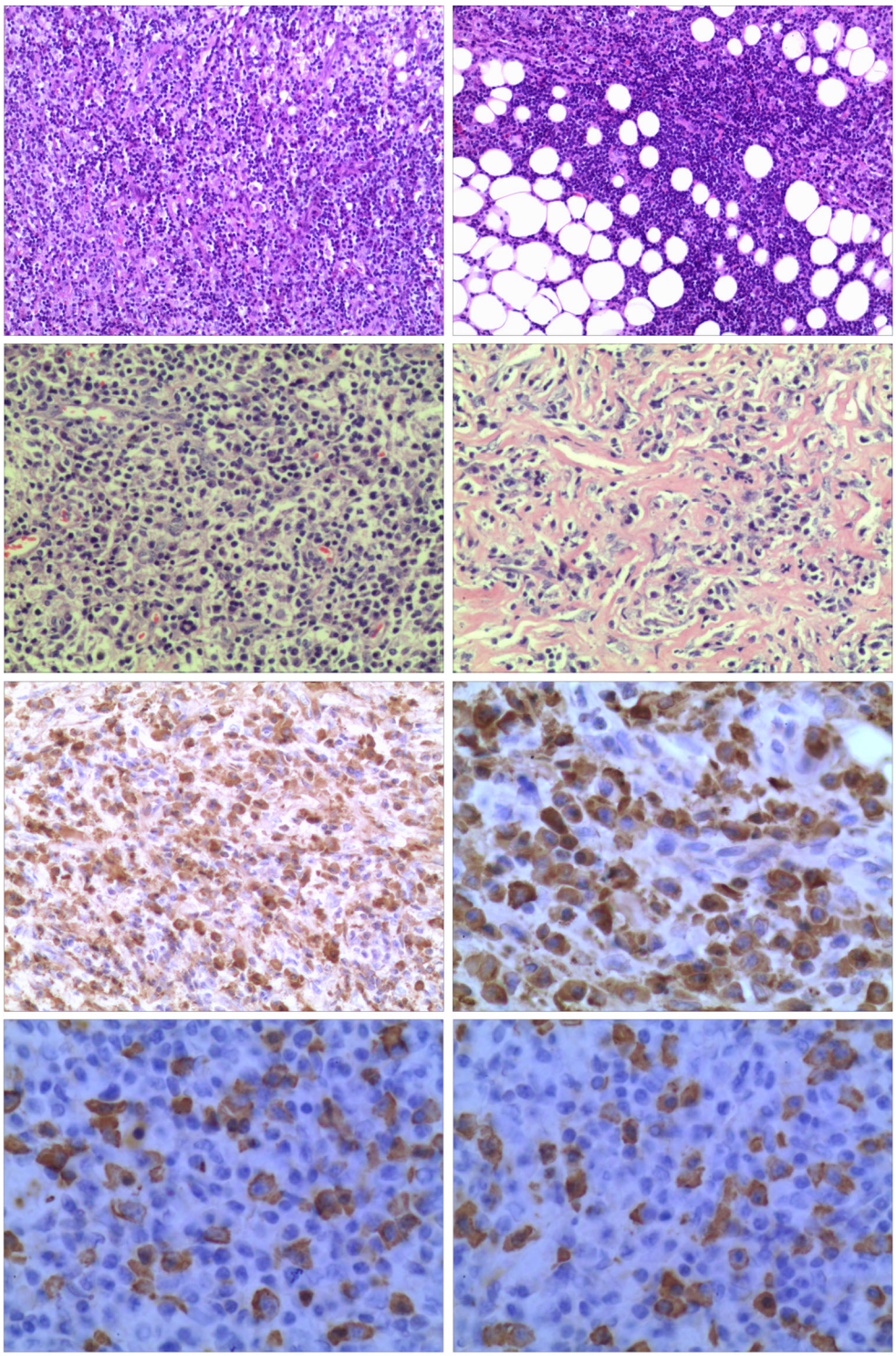
sure if other organs were simultaneously affected. Since the patient went back home, we only got in touch with him on postoperative 6 months for the follow-up. On postoperative 6 months of follow-up, patient's motor and sensory function of upper limbs returned to normal. Major lower limbs' muscle strengths were Class IV with sensory function returning to normal.

Discussion

The discovery of the IgG4-related disease could be dated back to the research of autoimmune pancreatitis (AIP). Yoshida [2] first proposed the concept of AIP in 1995 and considered that the pathogenesis of the disease was associated with autoimmune factors. The relationship between AIP and IgG4-positive plasma cells was first introduced in 2001: AIP is often associated with other organ involvement (such as salivary glands, bile ducts, retroperitoneal tissues, etc.). And pathologic specimens showed diffuse IgG4-positive plasma cell infiltration [3]. Kamisawa [4] confirmed IgG4-positive plasma cells, CD4-positive and CD8-positive T cell infiltration in AIP patients' pancreas, biliary tract, portal area of liver, lymph nodes in 2003; he also pointed out that AIP is not simply pancreatitis but a systemic disease and named it as IgG4-related autoimmune disease or IgG4-related disease (IgG4-RD). In recent years, the concept of IgG4-RD has been widely recognized and was released in the journal of *Autoimmun Rev* in 2010 [5].

IgG4-RD patients are usually older than 50 years with male predominance [6, 7]. So far no large-scale epidemiological data have ever been reported. Only Japanese scholars reported that the overall incidence was (2.8–10.8)/1,000,000 [8]. It is characterized by IgG4-positive plasma cell infiltration accompanied by storiform fibrosis and phlebitis. Pancreas and bile duct are the most commonly affected. Lacrimal gland, salivary gland, retroperitoneal, thyroid, kidney and lung could be involved as well [9]. The patients are usually accompanied by elevated serum IgG4 levels. Glucocorticoid therapy may have some relief but is easy to recur [3, 4]. IgG4-RD has non-specific clinical manifestations, mainly the involvement of local compression and corresponding organ or tissue dysfunction. Patients may also be presented with fever, fatigue, weight loss and other non-specific systemic manifestations. The main clinical features are as follows: (1) one or more organ/tissue swelling as the shape of tumor; (2) IgG4-positive plasma cells proliferated causing lymphoproliferative infiltration; (3) serum IgG4 levels rise significantly (>1350 mg/L) and a ratio of IgG4 + cells/total lymphocyte count >50 %; (4) respond well to glucocorticoid therapy [10, 11].

In consideration of the low incidence and deficient knowledge of IgG4-RD, the clinical diagnostic criteria have not been unified yet. Japanese scholars put forward the comprehensive IgG4-RD diagnostic criteria in 2011 [12] (proposed by the Japanese Research Committee for "Systemic IgG4-related Sclerosing Disease"): (1) clinically, diffuse/focal enlargement, or mass-forming, nodular/thickened lesions in one or more organs; (2) elevated levels of serum IgG4 (>135 mg/dL); (3) histopathological findings: ① prominent infiltration of lymphocytes and plasmacytes with fibrosis, but no neutrophilic infiltration; ② abundant infiltration of IgG4-positive plasmacytes (>10/hpf) and/or a ratio of IgG4/IgG-positive cells of >40 %; ③ storiform/swirling fibrosis; ④ obliterative phlebitis. Diagnosis of IgG4-related disease: (1)+(2), (1)+(3) ①②, (2)+(3) ①② or (3) ①②③④. Other scholars found that some non-IgG4-RD patients may also have IgG4-positive plasma cell infiltration or elevated serum IgG4 levels, while some patients with typical IgG4-RD histological features were not associated with elevated serum IgG4 levels [13]. IgG4-positive plasma cell infiltration or elevated serum IgG4 levels are likely to conduce to the diagnosis; however, they



Figs. 3, 4 (×100) HE staining showed more lymphocytes and plasma cells in the fibrous connective tissue and adipose tissue; **Figs. 5**(×100)**, 6** (×100): HE staining showed infiltration of lymphocytes and plasma cells. The infiltrated plasma cells were well differentiated with eccentric nucleus and eosinophilic cytoplasm; **Figs. 7** (×200), **8** (×400): immunohistochemical staining showed IgG-positive cytoplasm with the positive rate more than 40 %; **Figs. 9** (×400), **10** (×400): immunohistochemical staining showed IgG4-cytoplasm with IgG4-positive cells >50/hpf

are not necessarily the only indicator. The diagnosis of IgG4-RD requires a comprehensive assessment of clinical manifestations, laboratory tests, imaging and histologic features. The abundant infiltration of IgG4-positive plasmacytes (>50/hpf) and a ratio of IgG4/IgG-positive cells of >40 % of our case supported the diagnosis of IgG4-RD.

However, spinal cord compression caused by IgG4-related sclerosing pachymeningitis (IgG4-RSP) is extremely rare and has never been reported in China with merely three case reports worldwide [14–16]. Chan [13] reported one case of a 37-year-old male patient in 2009. Magnetic resonance imaging (MRI) revealed an elongated dural mass extending from the fifth to tenth thoracic vertebra. Postoperative pathological examination showed dura expanded by a dense lymphoplasmacytic infiltrate accompanied by stromal fibrosis and phlebitis. IgG4-positive plasma cells were increased and the proportion of IgG4+/IgG+plasma cells was 85 %. This is also the world's first case of IgG4-RD-induced spinal cord compression and thus named as IgG4-related sclerosing pachymeningitis (IgG4-RSP), which represents a new member of the IgG4-RD family affecting the central nervous system. Choi [14] reported one case of 46-year-old female IgG4-RSP patient in 2010. MRI revealed a mass in the epidural space between T9 and T11 with circumferential spinal cord compression suggestive of malignancy. The pathologic specimen showed non-specific lymphoplasmacytic infiltration and fibrosis. Immunohistochemical examination demonstrated diffuse infiltration of IgG4-positive plasma cells (>20/hpf). Sakai [15] reported one case of a 32-year-old female IgG4-RSP patient in 2014. On examination, she revealed diabetes insipidus, retrobulbar neuritis, hyperreflexia and limb weakness. MRI showed cranial, cervical and lumbosacral hypertrophic pachymeningitis associated with infundibulo-hypophysitis. Pathological findings revealed lymphoplasmacytic inflammatory cell infiltrate with dense fibrosis. Such disease with rapid progression often results in serious neurological damage and prompt surgical decompression is vital to prognosis [17].

In summary, because of its varied organ involvement and non-specific clinical manifestations, there are still many difficulties in the diagnosis of IgG4-RD. With the gradual deepening awareness of the disease, clear diagnostic criteria and more effective treatments are urgent for accurate assessment of the long-term prognosis.

Compliance with ethical standards

Conflicts of interest None of the authors has any potential conflict of interest.

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