Clinical Case Report

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Isolated extradural Rosai–Dorfman disease causing the spinal cord compression

A case report

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Abstract

Rationale: Rosai-Dorfman disease (RDD) is a rare benign histiocytic disease that is commonly characterized by massive painless cervical lymphadenopathy and systemic manifestations. Isolated extranodal involvement, especially spinal involvement, is extremely rare.

Patient concerns: A 28-year-old man presented with intermittent dorsodynia and bilateral lower-limb weakness and numbness. A magnetic resonance scan (MRI) showed an extradural lesion of the T6-T9 thoracic spine that lead to cord compression.

Diagnoses: Histopathological findings showed distinctive emperipolesis and immunohistochemistry results that were positive for cluster of differentiation CD68 and S100. Therefore, we diagnosed the Rosai-Dorfman disease.

Interventions: we performed a nearly total surgical resection and a limited T6-T9 laminectomy.

Outcomes: Postoperatively, the patient's symptoms were partially relieved and experienced no recurrence during the 6-month follow-up. The preoperative diagnosis of isolated spinal RDD still remains challenging.

Lessons: Thus, we should consider RDD in the differential diagnosis of the central nervous system. Besides surgical resection, the treatment also included radiation, chemotherapy or monoclonal antibodies. However, the optimal treatment remains controversial. Therefore, we should exert all our energies on the exploration of etiology and adjuvant therapy for this disease.

Abbreviations: ^{18}F-FDG PET/CT = ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography, CNS = central nervous system, EMA = epithelial membrane antigen, MRI = magnetic resonance imaging, RDD = Rosai–Dorfman disease.

Keywords: Rosai–Dorfman disease, sinus histiocytosis, spine involvement

1. Introduction

Rosai–Dorfman disease (RDD), also referred to as sinus histiocytosis, was first documented by Rosai and Dorfman in 1969.[1] This disease mainly affects the lymph nodes, with its hallmark being massive, painless, and cervical lymphadenopathy. Other systemic symptoms that may occur include fever, weight loss, anemia, increased erythrocyte sedimentation rate and serum levels as well as leukocytosis. Extranodal involvement is present in about 30% of cases of RDD, including the upper respiratory tract, skin, and bone.[2] Central nervous system (CNS) involvement is very uncommon, accounting for <5% of all cases with extranodal disease. Even rarer is the occurrence of isolated spinal RDD, which makes up appropriately 20% to 25% of all RDD patients with CNS disease.[3] Spinal RDD predominantly afflicts children and young adults with a slight male preponderance. Spinal RDD is novel to the clinical doctor. This case reports documents a rare instance of isolated spinal RDD with a summary of its clinical presentation.

2. Case report

A 28-year-old man presented to the Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medicine Sciences & Peaking Union Medical College, Beijing province, China in June with a one-year history of back pain in the mid-thoracic region, accompanied with bilateral lower limb numbness and weakness for the last 3 months. He denied bowel or bladder incontinence, fever, weight loss, or night sweats. There was no history of trauma, palpable lymph nodes, or skin lesions. A review of personal and family medical history was unremarkable. His physical examination was positive for markedly reduced distal muscle strength of the lower extremities (power graded 3/5) but had intact proximal muscle strength of the lower extremities (power graded 5/5). The patient was unable to walk in a straight line and was Romberg sign positive. Muscle tone was normal, with no pathological reflexes present. There were no

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Ethical statement: Ethics committee approval is not included as it is commonly accepted that case reports do not require such approval. Our work did not use patients' data that would allow identifying them, thus no ethical approval is required.

Informed consent: The patient has consented to submission of this case report to the journal.

The authors have no conflicts of interest to disclose.

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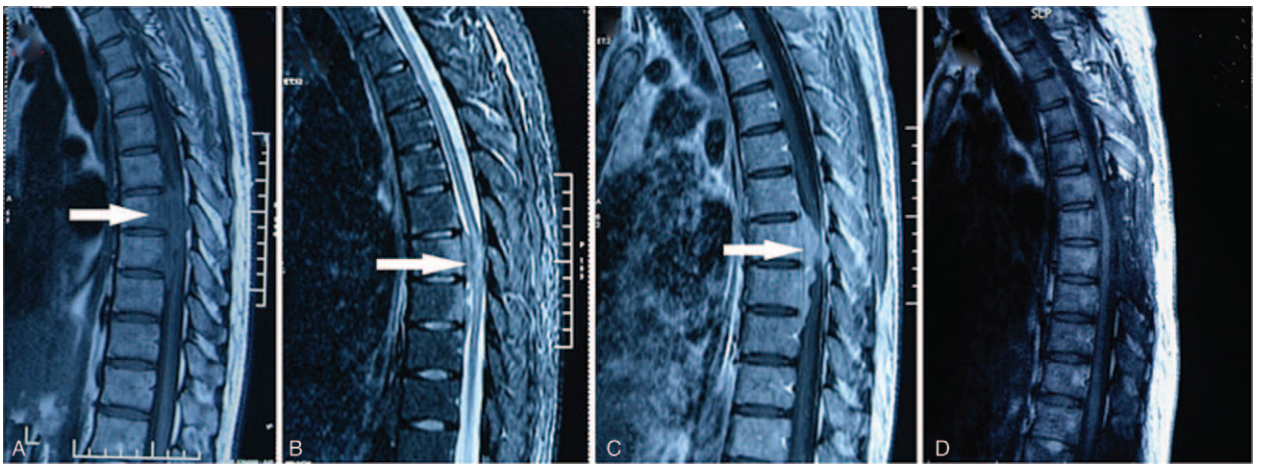

Figure 1. Thoracic magnetic resonance imaging scans of a 28-year-old man with a 1-year history of mid-thoracic back pain and 3-month history of bilateral lower-limb weakness and numbness. (A) Sagittal T1-weighted magnetic resonance imaging (MRI) shows a lesion of isointense located in the T6-9 spinal cord (arrow). (B) Sagittal T2-weighted MRI shows the lesion is slightly hyperintense (arrow). (C) Sagittal-enhanced T1-weighted scanning shows that it was distinctly and homogenously enhanced after contrast (arrow). (D) Postoperative (6-month after surgery), MRI demonstrates that the lesion experienced no recurrence.

findings of massive lymphadenopathy in the axillary, supra-clavicular or cervical regions. No abnormalities were revealed in subsequent routine laboratory investigations.

A magnetic resonance imaging (MRI) scan of the thoracic spine revealed an oval shaped/Long flake epidural lesion in the thoracic spine (T6-T9) that appeared to be causing cord compression. Upon T1-weighted imaging, the mass was isointense, appearing slightly hypointense upon T2-weighted imaging and was enhanced diffusely with the addition of gadolinium (Fig. 1). Possible differential diagnosis based on these radiological findings included infections (e.g., tuberculosis) or neoplasms (e.g., metastasis, lymphoma or meningioma).

In order to confirm the diagnosis, the patient consented to a T6-T9 decompressive laminectomy. Surgical exposure of the spine revealed a firm, pinkish-gray mass that appeared to have a soft, "fish-flesh" appearance. The mass was adherent to the anterior extradural space. We also found that the bone behind the vertebral body was destroyed and that some of the lesions had infiltrated the cancellous bone. Frozen section analysis revealed diffuse infiltration of plasmocytes and lymphocytes in the lesion. Due to the wide surface area and tough texture of the tumor, combined with intraoperative frozen pathological features, we removed most of the occupying lesions to protect the spinal cord nerve function.

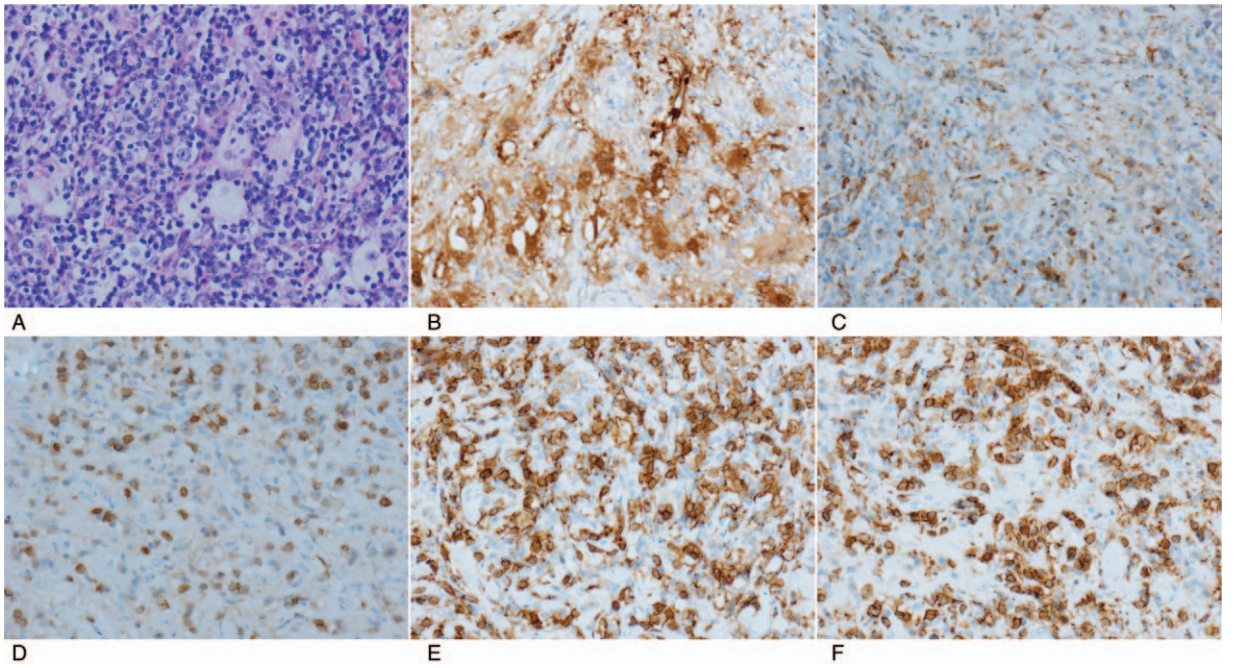

Figure 2. Pathological examination showed fibrous hyperplasia, accompanied by a large number of lymphocytes and plasma cell infiltration. Some of the cytoplasm is rich and transparent, and the typical emperipolesis is observed (A 200×). Photomicrographs showing positive immunohistochemical staining of neoplastic cells for cluster of differentiation S-100 protein (B, 200×), CD68 (C, 200×), CD3(D, 200×), CD20(E, 200×), CD21(F, 200×).

Postoperative histopathological examination found that the specimen was rich with inflammatory cells including histiocytes, plasma cells, and lymphocytes. Plasma cells and lymphocytes were found in the cytoplasm of histiocytes, a phenomenon known as "emperipolesis." Immunological testing found the lesion positive for CD68, CD21, CD21, CD3, and the S-100 protein (Fig. 2). However, the lgG4 was <5/HPF, lgG4/LgG was <10%, and AE1/AE3 was negative. Based on the pathological and immunological results, the patient given the diagnosis of RDD.

The patient obtained partial relief of symptoms after the surgery, with resolution of numbness in the right limb and full recovery of power (graded 5/5) in the right lower limbs. However, the left lower limb symptoms persisted and remained unchanged in comparison to his preoperative state. Nevertheless, the patient appeared clinically well at follow-up 6 months after the surgery. No disease recurrence was present, as confirmed with a repeat MRI scan (Fig. 1).

3. Discussion

This case report presents a rare instance of spinal cord compression attributed to isolated RDD of the thoracic spine. Upon its discovery in 1965, RDD was originally thought to be a disorder of lipid storage.[4] In 1969, it was reclassified as a sinus histiocytosis with massive painless lymphadenopathy by Rosai and Dorfman.[1] Current understanding of RDD deigns it to be a self-limiting and benign disease of uncertain etiology, which occurs predominantly in lymph nodes on both sides of the body. Clinical symptoms vary widely because of involvement of different organs. Therefore, diagnosis is dependent on pathological examination. However, sometimes there are nonspecific clinical manifestations and atypical histological morphology. Current literature suggests that isolated RDD of the CNS occurs in <5% of all RDD patients.[5,6] Moreover, spinal RDD occurring without involvement of any other organs is even rarer. A retrospective analysis on clinical records dated from 1969 to 2016 revealed that only 60 cases of isolated spinal RDD were reported during this time period.[7] Of these 60 cases, a significant majority of them (58 cases) were extramedullary dura-based lesions with intramedullary lesions affecting only 2 patients.[7] Interestingly, Chhabria et al[8] has reported RDD presenting as Conus–Cauda syndrome in which the mass lesion extended from the cauda equina to the sacral level. Our case report is of a 28-year-old patient who presented with an isolated epidural mass at the level of the thoracic vertebra, in the absence of intracranial lesions.

The cause of RDD remains controversial. Infectious or unexplained immune disorders may be behind this condition. Some authors have suggested that Epstein-Barr virus, human immunodeficiency virus and human herpes virus type 6 may be associated to this disease,[9,10] while others believe that this disease may be related to lgG4. However, previous analysis of IgG4 expression levels in 9 cases of RDD failed to provide clear evidence of the involvement of IgG4 in the pathogenesis of the disease.[11] Our patient did not have any alterations in IgG4 expression levels (lgG4:405 mg/L, ref:80–1400 mg/L). We are unable to conclude with certainty the etiology of the lesion in our patient.

Classic RDD symptoms include painless lymphadenopathy and neurological symptoms such as hypesthesia, numbness, unstable walking, paraparesis, or paraplegia which are closely related to the size and location of the lesion. Given that the lesion was as the level of the thoracic vertebrae in our patient, his symptoms of constant back pain and progressive bilateral lower extremity weakness and paresthesia can be attributed to spinal cord compression at this level.

The radiological examinations for RDD are often nonspecific and inconclusive, rendering a definitive diagnosis. Extracranial RDD masses are usually isointense on T1-weighted (T1WI) imaging but mildly hyperintense on T2-weighted imaging (T2WI). Similarly, intracranial masses are typically isointense on T1WI but hypo- to isointense with distinct edema on T2WI.[12] The currently patient possessed a homogenously enhancing extradural lesion that was isointense on T1WI imaging but only slightly hyperintense on T2WI imaging. Nevertheless, MRI imaging of RDD are often more difficult to distinguish from other more frequently encountered extradural spinal lesions, including meningioma, metastases, lymphoma and plasma cell granuloma.[6,13] Meningioma and RDD share similar features such as homogenous contrast enhancement in a dural-based lesion, although meningiomas typically have the distinct dural tail sign. Metastases are often T1WI hypo-intense and T2WI hyper-intense. Lymphomas tend to be iso-intense on T1WI and on T2WI, and they are usually iso- or hyper-intense. Plasma cell granuloma is isointense or hypo-intense on T1WI and hyper-intense on T2WI, which can present homogenous or inhomogeneous enhancement. Unfortunately, this disease lacks characteristic imaging findings. On the other hand, Dhull et al[14] reported the successful use of ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography (^{18}F-FDG PET/CT) to diagnose RDD with multiple enlargements. PET/CT may be a useful means of diagnosing RDD that warrants further investigation.

Histopathological features remain the most definitive way of confirming RDD. Typical RDD features on histopathology are a histiocytic proliferation as well as unusually large cells (not unlike the Langerhans giant cell) with large oval or round nuclei and nucleoli with sporadic signs of mitosis. Emperipolesis, or lymphagocytosis is a diagnostic criteria of RDD and represents the findings of intact lymphocytes inside macrophages.[15] RDD-specific cell immunohistochemical profiles are the absence of CD1a and epithelial membrane antigen (EMA) as well as the positive expression of S-100 protein and CD68.[5] CD1a is the marker of Langerhans cell histiocytosis.[2] In addition, CD163, CD4, CD8, CD45RO, CD20, CD79a, C38, CD138, κ and λ can also be positive. Unfortunately, CD1a immunohistochemistry was not performed in our cases which is a limitation of our study.

Given its rarity, there are no uniform guidelines for the treatment of the RDD. In general, surgical excision of systemic RDD is preferred in patients suffering from symptomatic lesions that affect functional abilities and are diminishing quality of life.[6] Given the benign nature of spinal RDD, surgical resection is considered to be the first line treatment and has been documented to impart positive clinical outcomes.[12] Surgery is able to relieve the compression, limit local damage, and preserve neurological function. Most patients usually have no recurrence after resection. If total excision is successful, adjuvant treatments with steroids or radiotherapy are not recommended. In a series of 29 patients who were followed up for an average of 10.1 years, Petzold et al[16] reported only a 14% symptom recurrence rate and instances of intracranial tumor regrowth. Radiosurgery and chemotherapy (etoposide, methotrexate, 6-mercaptopurine) have been effective in recurrent cases and are recommended for recurrence or residual after surgery.[17,18] So far, it is not clear whether these adjuvant treatments are beneficial. Since our patient underwent successful total surgical resection, no

chemotherapy or radiotherapy regimens were instituted. Furthermore, our patient experienced restoration of motor and sensory function on his right side upon removal of the mass. Plans have been made to follow-up this patient annually. In most cases, RDD carries an excellent prognosis. However, rare fatalities have been reported, most of which includes intracranial disease.[5] Emergent prescription of multiple treatment regimens will provide more options during treatment of the early phases of this disease, but require support from more research findings.

4. Conclusion

Spinal RDD occurring in isolation is an extremely rare benign histiocytic disease. Diagnosing this disease remains a daunting task that depends mainly on histological investigations and immunophenotyping. Surgical resection is an effective treatment approach for relieving spinal compression. However, given its unclear etiology and lack of evidence on the efficacies of other adjuvant therapies, further research in these areas is necessary.

Author contributions

Conceptualization: Yongning Li, Xin Wang, Jun Gao, Zhimin Li.
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Methodology: Jun Gao.
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Writing – review & editing: Yongning Li, Xin Wang, Jun Gao.

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