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CASE REPORT

Spinal Rosai–Dorfman disease: case report and literature review

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Abstract
Objective Sinus histiocytosis with massive lymphadenopathy or Rosai–Dorfman disease (RDD) is a rare benign disease of dubious etiology that arises predominantly in lymph nodes with generalized fever and malaise. Isolated intraspinal involvement has its unique characteristics. The purpose of this study is to present the largest series of cases in the spinal Rosai–Dorfman disease literature to increase familiarity with its clinicopathologic features, diagnosis, and treatment of RDD from spine.
Methods We present the case of a 34-year-old man who presented with paraplegia secondary to an isolated thoracic vertebral lesion. On physical exam, the patient displayed progressive weakness and tendon hyperreflexia of the lower limbs. After a totally section, symptoms of the patient were obviously relieved and the patient remained asymptomatic and no signs of recurrences were observed after follow-up for 5 months. We also retrospectively analyzed 60 cases of patients with spinal RDD published in English since 1969. Clinical date, histopathology, and radiological feature were retrospectively analyzed.
Results Spinal RDD should no longer be considered rare and it may occupy an increasingly prominent place in the list of differential diagnoses for intraspinal lesions. Only elaborate histopathology was diagnostic for RDD. Most of the patients were surgically treated and marked improvements were observed in their clinical conditions.
Conclusions RDD with spinal involvement is uncommon and it is challengeable in making a certain diagnosis. Histopathologic characteristics and immunohistochemical findings are considered as the key points for the diagnosis of this disease. The optimal treatment remains controversial, and more efforts should be focused on the investigation of etiology and adjuvant therapy for relapsing cases or subresected lesions.

Keywords Rosai–Dorfman disease · Sinus histiocytosis with massive lymphadenopathy · Spinal involvement

Introduction

Sinus histiocytosis with massive lymphadenopathy (SHML), also known as Rosai–Dorfman disease (RDD), was first reported by Rosai and Dorfman in 1969 [1]. It is a rare idiopathic lymphoproliferative disorder of uncertain etiology that is generally characterized with bilateral, painless, massive, peripheral cervical lymphadenopathy. Patients with RDD may also have other constitutional symptoms, such as fever, neutrophilia, increased serum erythrocyte sedimentation rate, leukocytosis, lymphopenia, polyclonal hyperglobulinemia, and anemia. Extranodal involvement can be found in 43% cases sustained with RDD, and the primary extranodal sites include skin, orbit, upper respiratory tract, and bones [2]; however, central nervous system (CNS) involved was reported in less than 5% of extranodal RDD cases [3], and furthermore, spinal RDD was only described in 20–25% of CNS RDD patients [4, 5]. We report a case of spinal RDD and review the relevant identified manuscripts. In conclusion, spinal RDD

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is very unfamiliar to the clinical doctor, so it is necessary to conduct a systematic review and summarize the clinical features of spinal RDD.

Case report

A 34-year-old man presented with 4 weeks of girdle-like pain in chest and 2 weeks of progressive bilateral lower extremity paresthesia. He denied fever and weight loss. On physical exam, he had hypesthesia below T10 and weakness of the lower limbs (left 3/5 and right 4/5) with normal muscular tension was observed. No lymph nodes were palpated in cervical, supraclavicular, or axillary regions.

At hospitalization, he developed bladder and bowel dysfunction with depraved neurologic examination. Muscle strength of the left lower limbs was grade 2/5 with active knee and ankle reflex and that of the right lower limbs was grade 3/5 with active knee and ankle reflex. Laboratory data were entirely normal except mildly increased erythrocyte sedimentation rate (ESR) of 17 mm/h (ref: 0–15 mm/h).

As his neurologic symptoms progressed, myelopathy was probably indicated, thoracic magnetic resonance imaging (MRI) was performed, and a dorsal epidural mass with clear borders extending from the T9–T10 levels was observed which caused spinal cord compression (Fig. 1). The lesion was iso-intense to the spinal cord on T1-weighted (T1WI) sequences and heterogeneously hypo-intense on T2-weighted (T2WI) sequences with obviously enhancement after gadolinium application.

To decompress the spinal canal and obtain tissue for pathologic diagnosis, laminectomy from T8 to T10 was performed and a 2.0 cm × 1.5 cm × 1.0 cm sized, firm and well-encapsulated mass was found in the epidural space. Complete resection was realized, and the mass was grossly with a "fish flesh" soft appearance (Fig. 2). The frozen section showed a diffuse infiltration of lymphocyte and considered as lymphoid and hematological system tumor. Post-operatively, both bilateral lower extremity paresthesia and bladder and bowel dysfunction were obviously relieved.

Histopathologic examination revealed histocytosis with an infiltrate of lymphocyte and plasma cell. These histiocytes demonstrated emperipolesis (Fig. 3). The immunohistochemistry confirmation reported lymphocytes that were positive for CD68 and S-100 (Fig. 4). These findings were consistent with a diagnosis of Rosai–Dorfman disease. Throughout a follow-up period of 5 months, the patient remained asymptomatic and no signs of recurrences were observed (Fig. 5).

Discussion

Rosai–Dorman disease

RDD was initially described in the French literature as a lipid storage disorder possibly developing after inflammation (adénites avec surcharge lipidique) by Destombes in 1965 [6], and was recognized as a unique histiolymphproliferative disease of the lymph nodes by Rosai and Dorfman in 1969 [1]. In general, it is a benign, non-neoplastic histiocytic proliferative disease characterized by prominent cervical lymph node enlargement, hence the initial name of SHML. However, cases also illustrated the RDD might involve multiple organ systems and be indeed fatal [7]. Extranodal involvement was subsequently recognized and an analysis of the RDD registry was published in 1990 showing that 43% of cases were extranodal. The

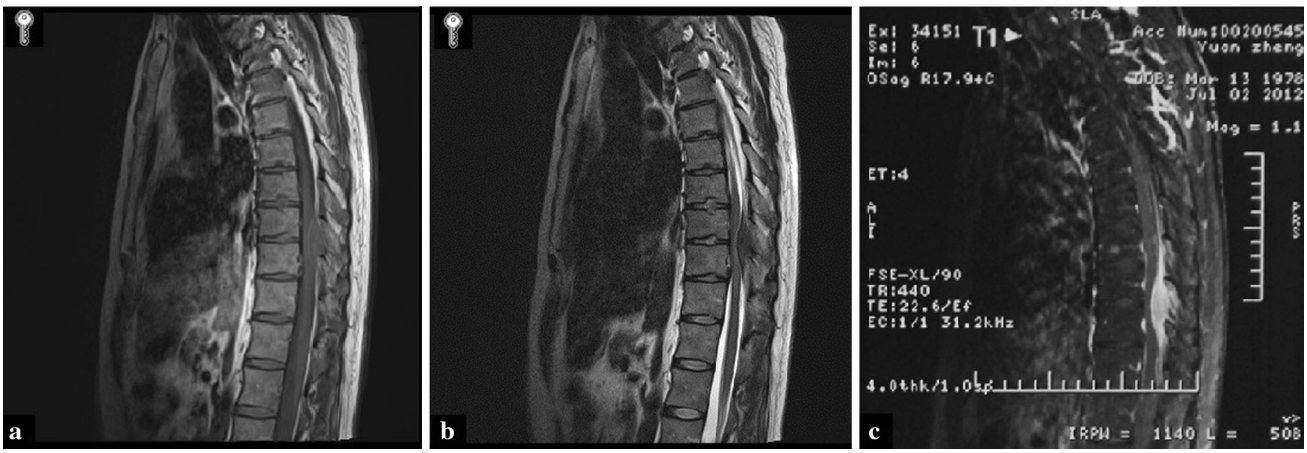

Fig. 1 Magnetic resonance imaging of the thoracic spine demonstrating a well-defined epidural mass extending from the T9–T10 levels. **a** Sagittal T1-weighted images demonstrating a iso-intense mass. **b** Sagittal T1-weighted images demonstrating a heterogeneously hypo-intense mass. **c** Homogenous gadolinium enhancement is evident

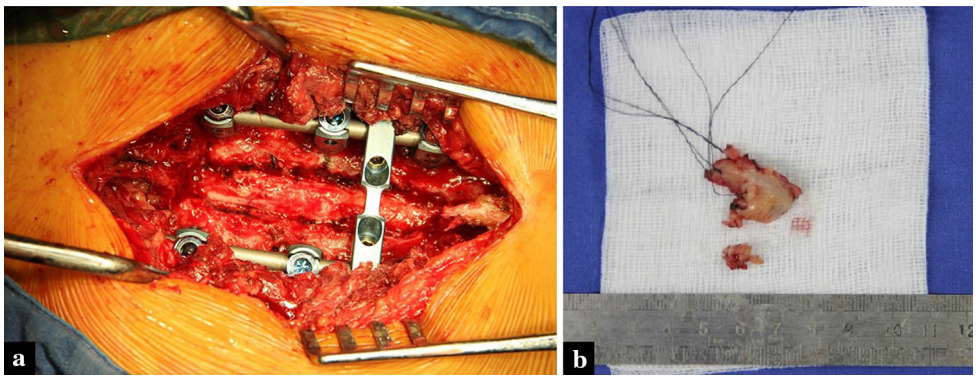

Fig. 2 **a** Laminectomy from T8 to T10 was performed; **b** with a "fish flesh" soft appearance, a 2.0 cm × 1.5 cm × 1.0 cm sized, firm, and well-encapsulated mass was found and realized complete resection

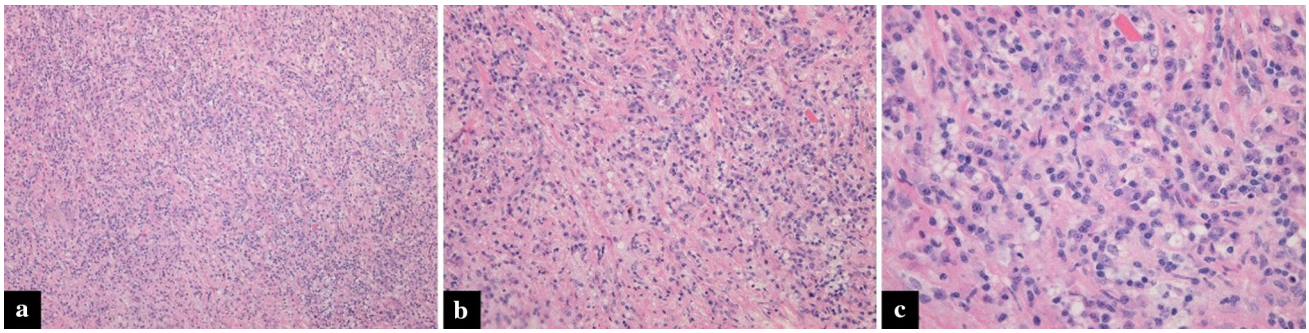

Fig. 3 Histopathologic: the HE staining results showed histiocytes with large vesicular nuclei and abundant pale eosinophilic cytoplasm. Emperipolesis is displayed in some histiocytes with intact lymphocyte or plasma cell engulfed within histiocyte cells. **a** 10 × 10, **b** 20 × 10, **c** 40 × 10

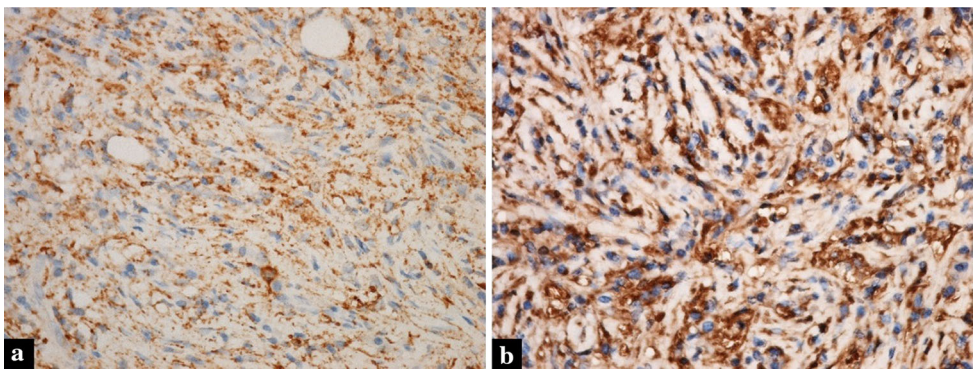

Fig. 4 Immunohistochemistry: **a** lesion was positive for CD68. **b** Lesion was positive for S-100

most common sites of extranodal involvement were skin, upper respiratory, orbits, testes, and bones [2].

Rosai–Dorman disease in the spine

In less than 5% of the extranodal RDD cases, central nervous system (CNS) involvement was previously reported [3], and by the year 2014, a total of 210 cases of RDD involving the CNS had been reported with a mean age of 39 years (range 2–79 years), and present a strong male predominance (M/F = 1.8). In detail, 167 (79.5%) of those cases sustained with intracranial lesions, 24 (11.4%) with spinal involvement and 19 (9.0%) with both intracranial and spinal involvement [8]. The disease was usually suspected according to a typical clinical presentation which was massive painless lymphadenopathy, and the diagnosis of RDD was confirmed by biopsy. However, 65.5% cases of RDD with CNS involvement were isolated, which mean that no lymphadenopathy or other extronodal sites involved [8]; as a result, it was more difficult to make an accurate diagnosis. Actually, spinal surgeon should be aware of this kind of disease, because spinal RDD was a potential reason to cause spinal compression and raise neurological symptoms [8]; however, there was limited reports describing

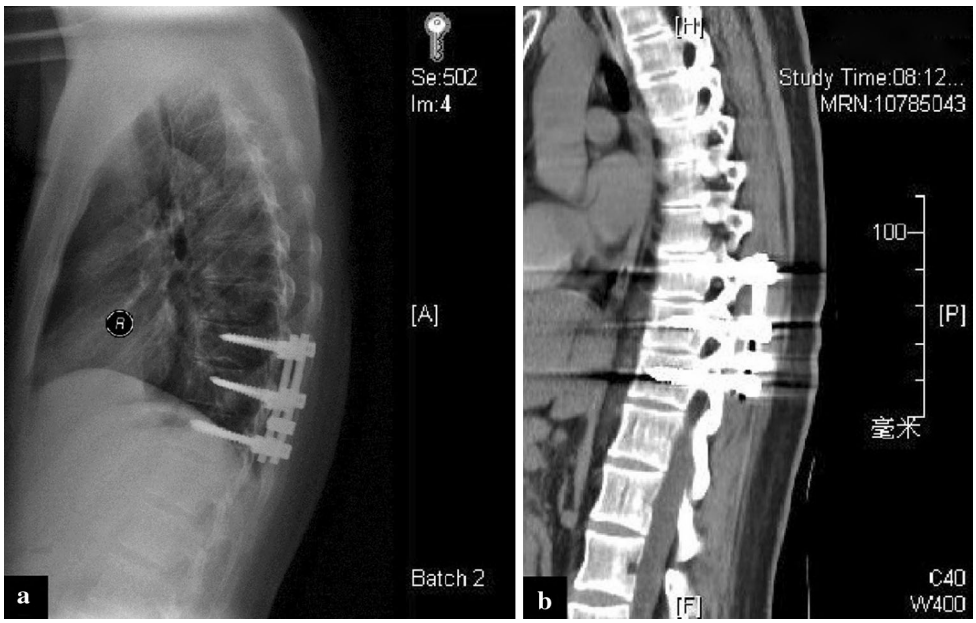

Fig. 5 Imaging examination after follow-up for 5 months. **a** Plain film demonstrated the internal fixator was still in good condition. **b** No signs of recurrences were observed on computed tomography

spinal RDD to our knowledge, and therefore, it is necessary for use to conduct a systemic review and summarize the clinical features of spinal RDD.

In our updated review, totally 60 patients with spinal RDD, including our current case, were found and the mean age of spinal RDD was 34.7 years (range 2.5–78 years) with a male predominance (M/F = 1.48). 28 (45.9%) cases presented with epidural mass, 18 (29.5%) cases presented with intradural extramedullary mass, 4 (6.6%) cases presented with intramedullary mass, 1 (1.6%) cases presented with both epidural mass and intradural extramedullary mass, and 1 (1.6%) cases presented with both epidural mass and intramedullary mass. Under the double counting of cases with different segments involvement, we find that the distribution of spinal RDD in cervical vertebra, thoracic vertebra, lumbar vertebra, and sacral vertebrae is 26:37:7:5. 71.4% cases of spinal RDD are isolated; 21.4% cases have lymphadenopathy and 19.7% patients have intracranial lesions simultaneously (Table 1) [2–5, 7–55]. In our case, the 34-year-old patient presented with an epidural thoracic vertebra mass, which is isolated and without intracranial involved.

Etiology

The etiology of RDD remains unclear since the recognition of this disease in 1969. Infectious etiology is the aspect that attracts most of the attentions. Human herpes virus-6 (HHV-6) genome has been demonstrated to present in lymph nodes affected by RDD [56]. The presence of elevated titers of antibodies to the Epstein–Barr virus (EBV) in some individuals also led to the hypothesis on EBV [2]. Nevertheless, some experts doubted that increased serological titers might be the result of a non-specific host immune response, because there was no evidence of latent or lytic EBV carriage in histiocytes and lymphocytes [48]. In addition, parvovirus B19 (Parvo B19) was also implied to be the causative agents [57]. Some authors also reported that abnormal immunologic response was another etiology, such as Becroft et al., ever demonstrated a defect in cellular immunity which promotes monocyte recruitment from the circulation into the nodal or extranodal sites and expressed that it was important in the histiocytic reaction [58]. Moreover, RDD is a sporadic disease, with occasional clusters, which suggests the role of either infection or heredity in the pathogenesis [39]. Despite all these assumptions, the exact pathogenesis of RDD remains doubtful. In the current case, we have no concrete evidence on what causes the lesion.

Symptom

The typically symptom is massive, painless, peripheral, bilateral lymphadenopathy, especially in the cervical region [59], which has also been described as “bull neck” [60]. Axillary, inguinal, and mediastinal nodes are also affected although less frequently than cervical nodes [14]. Other constitutional symptom includes fever and weight loss. Patients with spinal involvement are often free from the systemic symptoms mentioned above and may exhibit with only neurological symptoms, such as paraparesis or paraplegia. Our case sustained with girdle-like pain in chest and progressive bilateral lower extremity paresthesia and displayed progressive weakness and tendon hyperreflexia of the lower limbs, indicating typical thoracic vertebral spinal cord compression.

Table 1 Clinical features of 60 cases with spinal RDD published in English since 1969 and our current study

No	Authors/year	Age	Sex	Symptom	LN	Isolated	Location	Segment/type	Treatment	Improvement	Recurrence	Follow-up (M)
1	Rozman et al. (1974)	NA	NA	Paresthesia	NA	NA	Intraspinal	T8: epidural	NA	NA	NA	NA
2	Kessler et al. (1975)	53	M	Spastic paraparesis	✔	✖	Intraspinal	C7–T3: epidural	OPS	✔	✖	2
3	Hass et al. (1978)	11	F	Weakness, ptosis, hypacusis, tongue atrophy, palatoplegia	✔	✖	Intraspinal	C2: epidural C5–T2: epidural	CT	✔	✔	4
4	Buchino et al. (1982)	13	M	Progressive muscular weakness	✔	✖	Intraspinal and intracranial	C1–C6: intradural C6–T12: epidural	OPS and RT	death	✔	50
5	Chan et al. (1985)	7	F	Progressive quadriparesis, torticollis	✖	✔	Intraspinal	C5–C7: intradural	OPS	✔	✖	6
6	Unni (1988)	19	F	Pain in the sacral area, right knee, and both wrists	✖	✖	Intraspinal	S: bone mass	Steroids	✔	✖	12
7	Foucar et al. (1990)	NA	NA	Paraparesis	NA	NA	Intraspinal	T3–T9: epidural L5–S1: epidural	NA	NA	NA	NA
8	Foucar et al. (1990)	NA	NA	Paraparesis	NA	NA	Intraspinal	C1–C3: epidural	NA	NA	NA	NA
9	Foucar et al. (1990)	NA	NA	NA	NA	NA	Intraspinal	T: epidural	NA	NA	NA	NA
10	Katz et al. (1993)	20	M	NA	✔	✖	Intraspinal and intracranial	Upper C: intradural	NA	NA	NA	NA
11	Osenbach (1996)	35	M	Paraplegia	✖	✔	Intraspinal	T4–T5: intramedullary	OPS	✔	✖	12
12	Bernard et al. (1999)	10	F	Paraparesis	✔	✖	Intraspinal	L5: intradural	Steroids and CT	✔	✖	NA
13	Kelly et al. (1999)	45	F	Progressive weakness and numbness	✔	✖	Intraspinal	T2: intradural	OPS and RT	✔	✖	9
14	Hollowell et al. (2000)	78	M	Left arm pain, loss of sensation and strength and legs weakness	✖	✔	Intraspinal	C4–T4: epidural L2: epidural	OPS	✔	✖	18
15	Andriko et al. (2001)	51	M	Acute onset of paraplegia	✖	✔	Intraspinal	T: epidural	OPS	✔	✖	3
16	Andriko et al. (2001)	42	M	Weakness and numbness of lower extremities	✖	✔	Intraspinal	T6–T8: epidural	OPS	✔	✖	38
17	Yip et al. (2002)	65	M	Progressive backache and lower extremity weakness	✖	✖	Intraspinal	T12: epidural	OPS	✔	✖	75
18	Sato et al. (2003)	59	F	Bilateral visual impairment and sensory disturbance	✖	✔	Intraspinal and intracranial	C5: intramedullary	OPS and RT	✔	✖	24
19	Bhaskar et al. (2003)	2.5	M	Paraplegia	✔	✖	NA	NA	OPS and RT and CT	✔	✖	NA
20	Chen (2003)	62	M	Cauda equina syndrome	✖	✔	Intraspinal	S: NA	NA	NA	NA	NA

Table 1 continued

No	Authors/year	Age	Sex	Symptom	LN	Isolated	Location	Segment/type	Treatment	Improvement	Recurrence	Follow-up (M)
21	Hargett et al. (2005)	29	F	Progressive paraplegia and leg pain	✖	✔	Intraspinal	T5–T9: extradural	Steroids and OPS and RT	✔	✔	48
22	Tubbs et al. (2005)	13	M	Neck discomfort	✖	✖	Intraspinal	C1–C2: cervical mass	Steroids and OPS and CT	✔	✖	12
23	Purav et al. (2005)	18	M	Spastic quadriparesis with left hand paraesthesia	✖	✔	Intraspinal and intracranial	C2–C3: extradural	OPS	✔	✖	10
24	Al-Saad et al. (2005)	17	M	Backache, leg numbness, and clumsiness on walking	✖	✔	Intraspinal	T8–T10: epidural	Steroids and OPS	✔	✔	8
25	Kidd et al. (2006)	37	F	Increasing weakness of both upper limbs	✖	✔	Intraspinal and intracranial	C5: NA	RT	✔	NA	NA
26	Robert et al. (2006)	23	F	Progressive left leg pain and foot dorsal and plantar flexion weakness	✖	✔	Intraspinal	S: bone mass	OPS	✔	✖	12
27	Bhandari et al. (2006)	23	F	Quadriparesis and incontinence of urine and stool	✖	✔	Intraspinal	C3–C6: intradural T1–T4: intradural T5: intradural	OPS	✔	✖	5
28	Seyednejad et al. (2007)	43	F	Progressive quadriplegia and leg paresthesia	✖	✔	Intraspinal and intracranial	C5–C6: intradural T3–T7: paravertebral	Steroids and RT	✔	✖	10
29	Huang et al. (2007)	31	F	Mid-thoracic back pain, legs weakness, numbness below umbilicus	✖	✔	Intraspinal	T6–T8: epidural	OPS	✔	✖	12
30	Dauendorffer et al. (2007)	30	M	Hyposensitivity of the lower extremities	✖	✖	Intraspinal	NA: epidural	Steroids and CT	✔	✖	NA
31	Mitra et al. (2007)	18	M	Paraplegia	✔	✖	Intraspinal	T6–T7: epidural	OPS	NA	NA	18
32	Dran et al. (2008)	17	M	Progressive weakness with unsteadiness of gait	✔	✖	Intraspinal	T1–T4: intradural	OPS	✔	✖	12
33	Ma et al. (2008)	44	M	Low-back pain and progressive weakness of both lower limbs	✖	✔	Intraspinal	T12–L4: intradural	OPS	✔	✖	8
34	Raslan et al. (2008)	50	M	Loss of strength in the right foot	✖	✔	Intraspinal and intracranial	L1: intradural	OPS	✔	✔	9
35	Konca et al. (2009)	36	M	Weakness and back pain	✔	✖	Intraspinal	T6–T7: epidural T12: epidural	Steroids and CT	✔	✖	7
36	Wang et al. (2010)	58	M	Leg weakness	✖	✔	Intraspinal	T8–T10: epidural	OPS	✔	✖	6
37	Abou-Zeid et al. (2010)	24	M	Thoracic back pain and paraparesis	✖	✔	Intraspinal	T4–T7: epidural	OPS	✔	✔	18
38	Maiti et al. (2011)	19	F	Progressive quadriparesis	✖	✔	Intraspinal	C2–C7: epidural	OPS	✔	doubtful	NA

Table 1 continued

No	Authors/year	Age	Sex	Symptom	LN	Isolated	Location	Segment/type	Treatment	Improvement	Recurrence	Follow-up (M)
39	Ambekar et al. (2011)	37	F	asymmetric spastic quadriparesis with graded sensory loss	✖	✔	Intraspinal and intracranial	C1–T2: NA	OPS	✔	NA	NA
40	Zhu et al. (2012)	58	M	Back pain and hypnalgia	NA	NA	Intraspinal	T8–T10: NA	OPS	NA	NA	24
41	Chen et al. (2012)	16	F	Right leg cramps and weakness, progressive numbness of both legs	✖	✔	Intraspinal	T4–T5: intradural	OPS	✔	✖	24
42	Ramos et al. (2012)	10	F	Spastic paraparesis	✖	✔	Intraspinal and intracranial	T6–T7: intradural T9–T10: intradural T10–T11: intradural	OPS	death	✔	5
43	Zhu et al. (2012)	53	M	Weakness and paresthesia of both lower extremities	✔	✖	Intraspinal	T3–T4: NA	Anti-inflammatory	✔	✖	12
44	Roy et al. (2012)	NA	M	Progressive paraparesis	✖	✔	Intraspinal	T11–L2: epidural	OPS and RT	NA	NA	NA
45	Parmar et al. (2013)	64	M	Neck pain and cervical radicular pain	✖	✔	Intraspinal and intracranial	C5–C6: intradural	OPS	✔	✖	9
46	Yao et al. (2013)	12	F	Numbness and weakness in her right extremities	✖	✔	Intraspinal	C1–T6: intramedullary	OPS	✔	✖	18
47	Molla et al. (2014)	76	M	Progressive right arm weakness and right footdrop	✖	✔	Intraspinal	C2–C3: intramedullary	OPS	✔	✖	12
48	Sandoval-Sus et al. (2014)	53	M	Progressive unsteadiness, recurrent falls, and generalized body aches	✖	✔	Intraspinal and intracranial	C5–C6: intramedullary T1–T2: epidural T5–T6: epidural	Steroids and RT	✖	NA	22
49	Sandoval-Sus et al. (2014)	18	M	Quadriparesis	✖	✔	Intraspinal and intracranial	Upper C: epidural	OPS and RT and CT	✔	✔	84
50	Wu et al. (2014)	43	M	Upper back pain and progressive numbness in bilateral hands	✖	✔	Intraspinal	C5–C6: intradural	OPS	✔	✖	18
51	Fu et al. (2015)	25	F	Progressive neck pain and upper limbs weakness and numbness	✖	✔	Intraspinal	C3–C6: intradural	OPS	✔	✖	12
52	Sciacca et al. (2015)	75	F	Lower limbs spastic paraparesis and saddle paraesthesia	✖	✔	Intraspinal	T10: epidural	Steroids and OPS	✔	✔	2
53	Tian et al. (2015)	40	M	Neck and left shoulder pain with unsteady gait	✔	✖	Intraspinal	C3–C5: epidural C6: epidural	OPS	✔	✖	18
54	Tian et al. (2015)	43	M	Numbness in both hands	✖	✔	Intraspinal	C5–C6: epidural	OPS	✔	✔	22
55	Huang et al. (2016)	55	M	Numbness of upper and lower limb	✖	✔	Intraspinal	T1–T9: intradural	OPS	✔	✖	6
56	Huang et al. (2016)	14	F	Bilateral leg pain	✖	✔	Intraspinal	S1–S2: epidural	OPS	✔	✖	12
57	Huang et al. (2016)	12	F	Right-limb numbness and weakness	✖	✔	Intraspinal	C4–C5: intradural	OPS	✔	✖	12

Table 1 continued

No	Authors/year	Age	Sex	Symptom	LN	Isolated	Location	Segment/type	Treatment	Improvement	Recurrence	Follow-up (M)
58	Lima et al. (2016)	50	F	Spastic paraparesis	✖	✔	Intraspinal	T4: intradural L1: intradural	OPS	✔	✖	NA
59	Rocha-Maguey et al. (2016)	27	F	Progressive strength loss on both legs	✖	✔	Intraspinal	C7–T1: intradural	OPS	✔	✖	6
60	Kozak et al. (2016)	26	M	Bilateral lower extremity numbness, weakness, and gait difficulty	✖	✔	Intraspinal	T1–T5: epidural	OPS	✔	✖	18
	Current study	34	M	Back pain, weakness and paresthesia of both lower extremities	✖	✔	Intraspinal	T9–T10: epidural	OPS	✔	✖	5

M male, *F* female, *NA* not applicable, *OPS* operations, *CT* chemotherapy, *RT* radiotherapy

Laboratory test and imaging finding

Laboratory findings are generally non-specific. The erythrocyte sedimentation rate (ESR) is elevated in most of the patients and normocytic or microcytic anemia is not uncommon [2]. Many patients demonstrated a polyclonal gammopathy on serum immunoelectrophoresis of IgG [2]. Similar findings may be found for IgA and IgM, although less consistently [17]. Furthermore, rheumatoid factor (RF) may be inconsistently positive, although the significance of this is not clear [33]. With the exception of elevated ESR, no other abnormal laboratory data could be found, which are similar to the cases we reviewed. In other words, spinal-RDD patients rarely presented with systemic disease.

There are also no specific marks in the radiologic examinations for RDD. On images of computed tomography, the lesions appear as homogeneous, hyperdense mass with no calcification and may be associated with bone erosion [59, 61, 62]. Lesions present as homogeneous, isointense mass with clear borders and have obvious enhancement after contrast administration according to T1-weighted magnetic resonance images, whereas on T2-weighted images, these lesions appear to be heterogeneously hypo- to iso-intense mass [63]. In addition, significant perifocal edema was also associated with the masses [39]. As a matter of fact, because the presentation of RDD lesion on CT and MRI is similar to that of meningiomas, spinal dura-based RDD is frequently misdiagnosed, especially when some spinal RDD demonstrated characteristic dura tail sign of meningioma [47].

Pathology and differential diagnosis

Histologically, typical nodal RDD has pathognomonic cytoarchitecture. Massive expansion of the sinusoids is full of numerous large histiocytes with large vesicular nuclei and abundant pale eosinophilic cytoplasm. Emperipolesis is displayed in some histiocytes with intact lymphocytes or erythrocytes engulfed within histiocyte cells [60], which is often noted as the most remarkable diagnostic feature but not pathognomonic as this phenomenon also reported in a case of B-cell lymphoma [64]. In addition, there is a pronounced lymphoplasmacytic inflammatory cell infiltrate in the background with displayed a storiform pattern in many areas [4]. In addition, Russell bodies can be found in some cases, which are eosinophilic, large, homogenous immunoglobulin-containing inclusions that are usually found in a plasma cell undergoing excessive synthesis of immunoglobulin [18, 59]. Immunologically, the large histiocytes are immunoreactive for protein S100 and CD68, but negative for CD1a and CD15. In spinal RDD, the gross specimen is lobular, firm, whitish gray, or yellowish tan in

Table 2 Possible factors affecting the prognosis of spinal RDD

	Eusemia	Not improve or recurrence	*p* value
Isolated spinal RDD	28	10	
Non-isolated spinal RDD	10	4	0.871
Intraspinal cases	6	5	
Intraspinal and intracranial cases	32	9	0.119
Totally section	22	10	
Subtotally section	5	3	0.736
Surgery	28	6	
Surgery and adjuvant therapy	3	6	0.004

color and adherent to the dura [63], and the pathological section exhibits more fibrosis, fewer typical histiocytes, and a lesser degree of lymphocytophagocytosis than nodal RDD [2]. Spinal RDD was usually misdiagnosed on intraoperative frozen section, or even on permanent paraffin-embedded section, indicating that spine surgeon should be familiar with this disease and differential diagnoses, including meningioma, Langerhans cell histiocytosis, and plasma cell granuloma. The reason that RDD is often mistaken as meningioma is not only due to its mimicking radiological features, but also because of its positive S-100 protein histiocytes. As a result, comprehensive histological analysis is of great importance for a final confirmed diagnosis. For instance, Langerhans cell histiocytosis (LCH) can also present as a dura-based mass; however, pathologic examination always shows the absence of emperipolesis and negative for CD68; Plasma cell granuloma, characterizing a mixed inflammatory infiltrate with polyclonal plasma cells, is also usually confused with RDD; however, emperipolesis and expression of S-100 protein are negative in the pathology of plasma cell granuloma [51]. The pathology of our case showed histiocytes with emperipolesis and positive for S-100, which was the characteristic performance of RDD and leads to an accurate diagnosis.

Treatment and prognosis

As RDD was considered as a benign disease, in cases without CNS involved, spontaneous resolution and stable asymptomatic disease are observed in about of 90% cases [2]; however, surgical resection was still considered to be optimal for those spinal-RDD patients, because not only complete resection and CNS decompression, but also getting mass for histologically diagnostic purpose is necessary. 46 of 60 cases in our review performed a surgery and symptoms of 34 patients (73.9%) were obviously relieved and they remained asymptomatic and no signs of recurrences were observed during the follow-up period. However, in some cases, complete surgical excision is not possible and further adjuvant therapeutic modalities are still required, though limited evidence can be found due to the rare incidence of RDD. Corticosteroid application has shown some therapeutic benefit when was used in patients with systemic RDD, but the problem of recurrence should be considered when steroids are tapered [65, 66]. For inoperable masses, radiotherapy can be used for local control of the disease. In addition, various chemotherapy regimens were used to treat progressive systemic RDD, the responses were not uniform, and some of the therapies could not be used in patients with intradural involvement because of reduced blood–brain barrier permeability. Newly reported therapies, including tyrosine kinase inhibitor imatinib and the anti-CD20 monoclonal antibody rituximab, have also been used in systemic RDD [67–69]. In our review, we found that complete resection or partially resection was not associated with prognosis ($p = 0.736$). On the basis of surgery, the use of adjuvant therapy would not only lead to improved prognosis, but also contribute to be much poorer ($p = 0.004$). We assumed that the reason of this result was that the patients who utilize adjuvant therapy had subtotally excision or complicated condition (Table 2).

The prognosis of RDD is ideal in most cases. However, multisystem involvement and, indeed, fatal outcomes were also previously described [7]. Long-term prognosis is believed to be associated with the number of nodal groups and extranodal systems involved [2], indicating that patients with extranodal lesions will probably a poorer prognosis than those with nodal diseases [61]. According to our analysis, there is no difference in the prognosis between cases with isolated CNS RDD or those with intracranial lesions and cases with isolated spinal RDD ($p = 0.871$, $p = 0.119$) (Table 2).

Conclusion

61 spinal-RDD cases have been reported by far and spinal RDD may occupy an elevated prominent position in the list of differential diagnosis for spinal dural-based lesions. Spinal RDD always presents with neurological deficits and

its radiologic features are similar to those of many dura-based masses especially meningioma. The diagnosis of spinal RDD mainly depends on the characteristic histiocytes, which presents with emperipolesis and positive for S-100. For the express purpose of relieving the compression and conducting pathological diagnosis, surgical resection is supposed to be the best treatment, which has revealed satisfactory therapeutic effects. The etiology and other adjuvant treatment options for spinal RDD are still dubious, and a great deal of further investigation is necessary.

Compliance with ethical standards

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

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Rosai J, Dorfman RF (1969) Sinus histiocytosis with massive lymphadenopathy. A newly recog-nized benign clinicopathological entity. Arch Pathol 87(1):63–70
2. Foucar E, Rosai J, Dorfman R (1990) Sinus histiocytosis with massive lymphadenopathy (Ro-sai-Dorfman disease): review of the entity. Semin Diagn Pathol 7(1):19–73
3. Ma J, Xiao J, Wang L (2008) Extranodal Rosai-Dorfman disease with multilevel lumbar spinal lesions. J Neurosurg Spine 9(1):55–57
4. Hargett C, Bassett T (2005) Atypical presentation of sinus histiocytosis with massive lymphade-nopathy as an epidural spinal cord tumor: a case presentation and literature review. J Spinal Disord Tech 18(2):193–196
5. Raslan O et al (2008) Intracranial Rosai-Dorfman disease with relapsing spinal lesions. J Clin Oncol 26(18):3087–3089
6. Destombes P (1965) Adenitis with lipid excess, in children or young adults, seen in the Antilles and in Mali. (4 cases). Bull Soc Pathol Exot Fil 58(6):1169–1175
7. Buchino JJ, Byrd RP, Kmetz DR (1982) Disseminated sinus histiocytosis with massive lym-phadenopathy: its pathologic aspects. Arch Pathol Lab Med 106(1):13–16
8. Sandoval-Sus JD et al (2014) Rosai-Dorfman disease of the central nervous system: report of 6 cases and review of the literature. Medicine (Baltimore) 93(3):165–175
9. Kessler E et al (1976) Sinus histiocytosis with massive lymphadenopathy and spinal epidural involvement: a case report and review of the literature. Cancer 38(4):1614–1618
10. Haas RJ, Helmig MS, Prechtel K (1978) Sinus histiocytosis with massive lymphadenopathy and paraparesis: remission with chemotherapy. A case report. Cancer 42(1):77–80
11. Chan KW et al (1985) Rosai-Dorfman disease presenting as spinal tumor. A case report with ultra-structural and immunohistochemical studies. J Bone Jt Surg Am 67(9):1427–1431
12. Unni KK (1988) Case report 457. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease) presenting as lesion in the sacrum. Skelet Radiol 17(2):129–132
13. Katz DS, Poe LB, Corona RJ (1993) Sinus histiocytosis with massive lymphadenopathy: a case of simultaneous upper respiratory tract and CNS disease without lymphadenopathy. AJNR Am J Neuroradiol 14(1):219–222
14. Osenbach RK (1996) Isolated extranodal sinus histiocytosis presenting as an intramedullary spinal cord tumor with paraplegia. Case report. J Neurosurg 85(4):692–696
15. Bernard F et al (1999) Sinus histiocytosis (Destombes-Rosai-Dorfman disease) revealed by extran-odal spinal involvement. Arch Pediatr 6(2):173–177
16. Kelly WF, Bradey N, Scoones D (1999) Rosai-Dorfman disease presenting as a pituitary tumour. Clin Endocrinol (Oxf) 50(1):133–137
17. Hollowell JP et al (2000) Rosai-Dorman disease causing cervical myelopathy. Spine (Phila Pa 1976) 25(11):1453–1456
18. Andriko JA et al (2001) Rosai-Dorfman disease isolated to the central nervous system: a report of 11 cases. Mod Pathol 14(3):172–178
19. Yip CC et al (2002) Orbital, adnexal, and unusual systemic involvement in Rosai-Dorfman disease. Ophthal Plast Reconstr Surg 18(3):223–227
20. Sato A et al (2003) Rosai-Dorfman disease presenting with multiple intracranial and intraspinal masses: a case report. No Shinkei Geka 31(11):1199–1204
21. Bhaskar V et al (2003) Sinus histiocytosis with nodal and extranodal involvement—a case report. J Indian Med Assoc 101(1):28–30
22. Chen KT (2003) Crush cytology of Rosai-Dorfman disease of the central nervous system. A report of 2 cases. Acta Cytol 47(6):1111–1115
23. Tubbs RS et al (2005) Spinal cord compression as a result of Rosai-Dorfman disease of the upper cervical spine in a child. Childs Nerv Syst 21(11):951–954
24. Purav P et al (2005) Rosai-Dorfman disease of the central nervous system. J Clin Neurosci 12(6):656–659
25. Al-Saad K et al (2005) Extranodal Rosai-Dorfman disease with multifocal bone and epidural involvement causing recurrent spinal cord compression. Pediatr Dev Pathol 8(5):593–598
26. Kidd DP, Revesz T, Miller NR (2006) Rosai-Dorfman disease presenting with widespread intra-cranial and spinal cord involvement. Neurology 67(9):1551–1555
27. Robert EG, Fallon KB, Tender GC (2006) Isolated Rosai-Dorfman disease of the sacrum. Case illustration. J Neurosurg Spine 4(5):425
28. Bhandari A, Patel PR, Patel MP (2006) Extranodal Rosai-Dorfman disease with multiple spinal lesions: a rare presentation. Surg Neurol 65(3):308–311
29. Seyednejad F et al (2007) Presumed recurrence of intracranial Rosai-Dorfman disease as a cervical spine tumor. Acta Neurochir (Wien) 149(4):425–427
30. Huang YC et al (2007) Spinal epidural Rosai-Dorfman disease preceding by relapsing uveitis: a case report with literature review. Spinal Cord 45(9):641–644
31. Dauendorffer JN et al (2007) Cutaneous and epidural Rosai-Dorfman disease. Ann Dermatol Venereol 134(3 Pt 1):257–260
32. Mitra S et al (2007) A young male with paraplegia, massive cervical adenopathy and nondiagnostic biopsy specimens. J Assoc Phys India 55:238–241
33. Dran G et al (2008) Rosai-Dorfman disease causing spinal cord compression: case report. Neurosurgery 62(4):E977–E978 **(discussion E978)**

34. Konca C et al (2009) Extranodal multifocal Rosai-Dorfman disease: response to 2-chlorodeoxyadenosine treatment. Int J Hematol 89(1):58–62
35. Wang Y et al (2010) Rosai-Dorfman disease isolated to the central nervous system: a report of six cases. Neuropathology 30(2):154–158
36. Abou-Zeid AH et al (2010) Isolated extradural Rosai-Dorfman disease of the thoracic spine: a rare cause of spinal cord compression: case report. Neurosurgery 67(2):E514–E515
37. Maiti TK et al (2011) Rosai-Dorfman disease presenting as cervical extradural lesion: a case report with review of literature. Neurol India 59(3):438–442
38. Ambekar S et al (2011) Isolated cranio-spinal involvement of Rosai-Dorfman disease: case report. Br J Neurosurg 25(2):297–299
39. Zhu H et al (2012) Imaging characteristics of Rosai-Dorfman disease in the central nervous system. Eur J Radiol 81(6): 1265–1272
40. Chen CW et al (2012) Rosai-Dorfman disease presenting as a thoracic intradural extramedullary spinal tumor but without extraspinal manifestations. Acta Neurochir (Wien) 154(2): 367–368
41. Antuna RA et al (2012) Multiple involvement of the central nervous system in Rosai-Dorfman dis-ease. Pediatr Neurol 46(1):54–56
42. Zhu F et al (2013) Rosai-Dorfman disease: a retrospective analysis of 13 cases. Am J Med Sci 345(3):200–210
43. Roy C et al (2012) Extranodal Rosai-Dorfman disease presenting as spinal extradural lesion: a case report with a review of the literature. J Cancer Res Ther 8(4):647–649
44. Parmar V et al (2013) Rosai-Dorfman disease presenting as cervical radiculopathy. Clin Neurol Neurosurg 115(6):808–810
45. Yao K et al (2013) An intramedullary cervical cord lesion in a 12-year-old girl. Neuropathology 33(5):582–585
46. El MM et al (2014) Rare presentation of Rosai-Dorfman disease mimicking a cervical intramedullary spinal cord tumor. World Neurosurg. 81(2):442.e7–442.e9
47. Wu L, Xu Y (2014) Rosai-Dorfman disease: a rare lesion with dura tail sign mimicking spinal meningioma. Spine J 14(12):3058–3059
48. Fu X et al (2015) Isolated spinal Rosai-Dorfman disease misdiagnosed as lymphoplasmacyte-rich meningioma by intraoperative histological examination. Brain Tumor Pathol 32(1):72–75
49. Sciacca S et al (2015) Rosai-Dorfman disease with spinal cord compression: a diagnostic challenge. Eur Spine J 24(Suppl 4):S529–S535
50. Tian Y et al (2015) Rosai-Dorfman disease involving the central nervous system: seven cases from one institute. Acta Neurochir (Wien) 157(9):1565–1571
51. Huang BY et al (2016) Rosai-Dorfman disease of rare isolated spinal involvement: report of 4 cases and literature review. World Neurosurg 85:367.e11–367.e16
52. Huang BY, Liu HL, Yu CJ (2016) Isolated intramedullary spinal Rosai-Dorfman disease: a case report and literature review. World Neurosurg 88:694.e11–694.e15
53. de Oliveira LG et al (2016) Double compression caused by isolated spinal Rosai-Dorfman disease. Spine J 16(8):e521–e522
54. Rocha-Maguey J et al (2016) A new case of cervical intramedullary sinus histiocytosis causing para-plegia and review of the literature. Surg Neurol Int 7:9
55. Kozak B et al (2015) Rosai-Dorfman disease isolated to the thoracic epidural spine. J Radiol Case Rep 9(11):6–16
56. Levine PH et al (1992) Detection of human herpesvirus 6 in tissues involved by sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). J Infect Dis 166(2):291–295
57. Mehraein Y et al (2006) Parvovirus B19 detected in Rosai-Dorfman disease in nodal and extranodal manifestations. J Clin Pathol 59(12):1320–1326
58. Becroft DM et al (1973) Benign sinus histiocytosis with massive lymphadenopathy: transient immunological defects in a child with mediastinal involvement. J Clin Pathol 26(7):463–469
59. Udono H et al (1999) Rosai-Dorfman disease presenting multiple intracranial lesions with unique findings on magnetic resonance imaging. Case report. J Neurosurg 91(2):335–339
60. McAlister WH, Herman T, Dehner LP (1990) Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). Pediatr Radiol 20(6):425–432
61. Geara AR et al (2004) Rosai-Dorfman disease mimicking neurofibromatosis: case presentation and review of the literature. Clin Radiol 59(7):625–630
62. Toh CH et al (2005) Rosai-Dorfman disease with dural sinus invasion. Report of two cases. J Neurosurg 102(3):550–554
63. Adeleye AO et al (2013) Diagnosis and management of Rosai-Dorfman disease involving the central nervous system. Neurol Res 32(6):572–578
64. Lopes LF et al (2003) Emperipolesis in a case of B-cell lymphoma: a rare phenomenon outside of Rosai-Dorfman disease. Ann Diagn Pathol 7(5):310–313
65. Sita G et al (1996) Rosai-Dorfman syndrome with extranodal localizations and response to glucocorticoids: a case report. Haematologica 81(2):165–167
66. Raveenthiran V et al (2003) Rosai-Dorfman disease: report of a 3-year-old girl with critical review of treatment options. Eur J Pediatr Surg 13(5):350–354
67. Alqanatish JT et al (2010) Rituximab treatment in a child with rosai-dorfman disease and systemic lupus erythematosus. J Rheumatol 37(8):1783–1784
68. Pagel JM et al (2007) Therapeutic use of Rituximab for sinus histiocytosis with massive lymphade-nopathy (Rosai-Dorfman disease). Am J Hematol 82(12):1121–1122
69. Utikal J et al (2007) Imatinib as a treatment option for systemic non-langerhans cell histiocytoses. Arch Dermatol 143(6): 736–740