

# World Journal of *Clinical Cases*

*World J Clin Cases* 2021 July 26; 9(21): 5754-6177



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**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: Ji-Hong Lin; Production Department Director: Xiang Li; Editorial Office Director: Jin-Lei Wang.

**NAME OF JOURNAL**

*World Journal of Clinical Cases*

**ISSN**

ISSN 2307-8960 (online)

**LAUNCH DATE**

April 16, 2013

**FREQUENCY**

Thrice Monthly

**EDITORS-IN-CHIEF**

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

**EDITORIAL BOARD MEMBERS**

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

**PUBLICATION DATE**

July 26, 2021

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<https://www.wjgnet.com/bpg/GerInfo/288>

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<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Rosai-Dorfman disease in the spleen of a pediatric patient: A case report

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**Informed consent statement:** Written informed consent was obtained from the patient's parents for the publication of this report and any accompanying images.

**Conflict-of-interest statement:** The authors declare that they have no conflicts of interest.

**CARE Checklist (2016) statement:** The authors have read the CARE

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### Abstract

#### BACKGROUND

Rosai-Dorfman disease (RDD) is a rare histiocytic proliferation of unknown etiology commonly found in children and adolescents. The common manifestation of RDD is massive and painless bilateral cervical lymphadenopathy with extranodal disease. While extranodal involvement in RDD is common, the spleen is an infrequent site of disease.

#### CASE SUMMARY

We report a 10-mo-old female infant with RDD presenting multiple splenic masses without cervical lymphadenopathy. She had fever, and blood tests showed leukocytosis, anemia, and elevated erythrocyte sedimentation rate and C-reactive protein. Ultrasound, computed tomography, and magnetic resonance images demonstrated multiple splenic masses. Despite antibiotic therapy, her symptoms were not relieved. She underwent diagnostic splenectomy and was discharged with recovery.

#### CONCLUSION

In pediatric patients with refractory infectious symptoms or hematological abnormalities, clinicians should suspect RDD, even in patients without significant lymphadenopathy.

**Key Words:** Rosai-Dorfman disease; Sinus histiocytosis with massive lymphadenopathy; Ultrasonography; Computed tomography; Magnetic resonance imaging; Case report

Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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**Manuscript source:** Unsolicited manuscript

**Specialty type:** Radiology, nuclear medicine and medical imaging

**Country/Territory of origin:** South Korea

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): 0  
Grade C (Good): C  
Grade D (Fair): 0  
Grade E (Poor): 0

**Received:** March 15, 2021

**Peer-review started:** March 15, 2021

**First decision:** April 4, 2021

**Revised:** April 14, 2021

**Accepted:** May 24, 2021

**Article in press:** May 24, 2021

**Published online:** July 26, 2021

**P-Reviewer:** Wen J

**S-Editor:** Zhang H

**L-Editor:** A

**P-Editor:** Wang LYT



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**Core Tip:** Rosai–Dorfman disease (RDD) is a rare histiocytic proliferation of unknown etiology, characterized by massive and painless bilateral cervical lymphadenopathy accompanied by fever, commonly found in children and adolescents. The spleen is an infrequent site of extranodal involvement in RDD. We report a 10-mo-old girl with RDD with extranodal involvement of the spleen without significant cervical lymphadenopathy.

**Citation:** Ryu H, Hwang JY, Kim YW, Kim TU, Jang JY, Park SE, Yang EJ, Shin DH. Rosai–Dorfman disease in the spleen of a pediatric patient: A case report. *World J Clin Cases* 2021; 9(21): 6032-6040

**URL:** <https://www.wjgnet.com/2307-8960/full/v9/i21/6032.htm>

**DOI:** <https://dx.doi.org/10.12998/wjcc.v9.i21.6032>

## INTRODUCTION

Rosai–Dorfman disease (RDD), also called sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic proliferation of unknown etiology, usually occurring in children and adolescents. It is characterized by massive and painless bilateral cervical lymphadenopathy accompanied by fever, leukocytosis, elevated erythrocyte sedimentation rate, and polyclonal hypergammaglobulinemia[1]. More than 40% of patients have an extranodal involvement, and commonly affected sites are the upper respiratory system, skin, eyes, bones, genitourinary system, oral cavity, central nervous system, and soft tissue[2,3]. The spleen is an infrequent site of disease, and if involved, combined nodal and extranodal disease is more frequent. Here we report a case of a 10-mo-old female infant with RDD with extranodal involvement of the spleen and provide a review of the available literature on extranodal RDD involvement in pediatric patients.

## CASE PRESENTATION

### Chief complaints

A 10-mo-old female infant visited our hospital due to fever.

### History of present illness

The patient had persistent fever during the previous 10 d. Her body temperature was elevated to 39 °C. The patient did not have any respiratory or gastrointestinal symptoms, except for mild rhinorrhea.

### History of past illness

The patient had a free previous medical history.

### Personal and family history

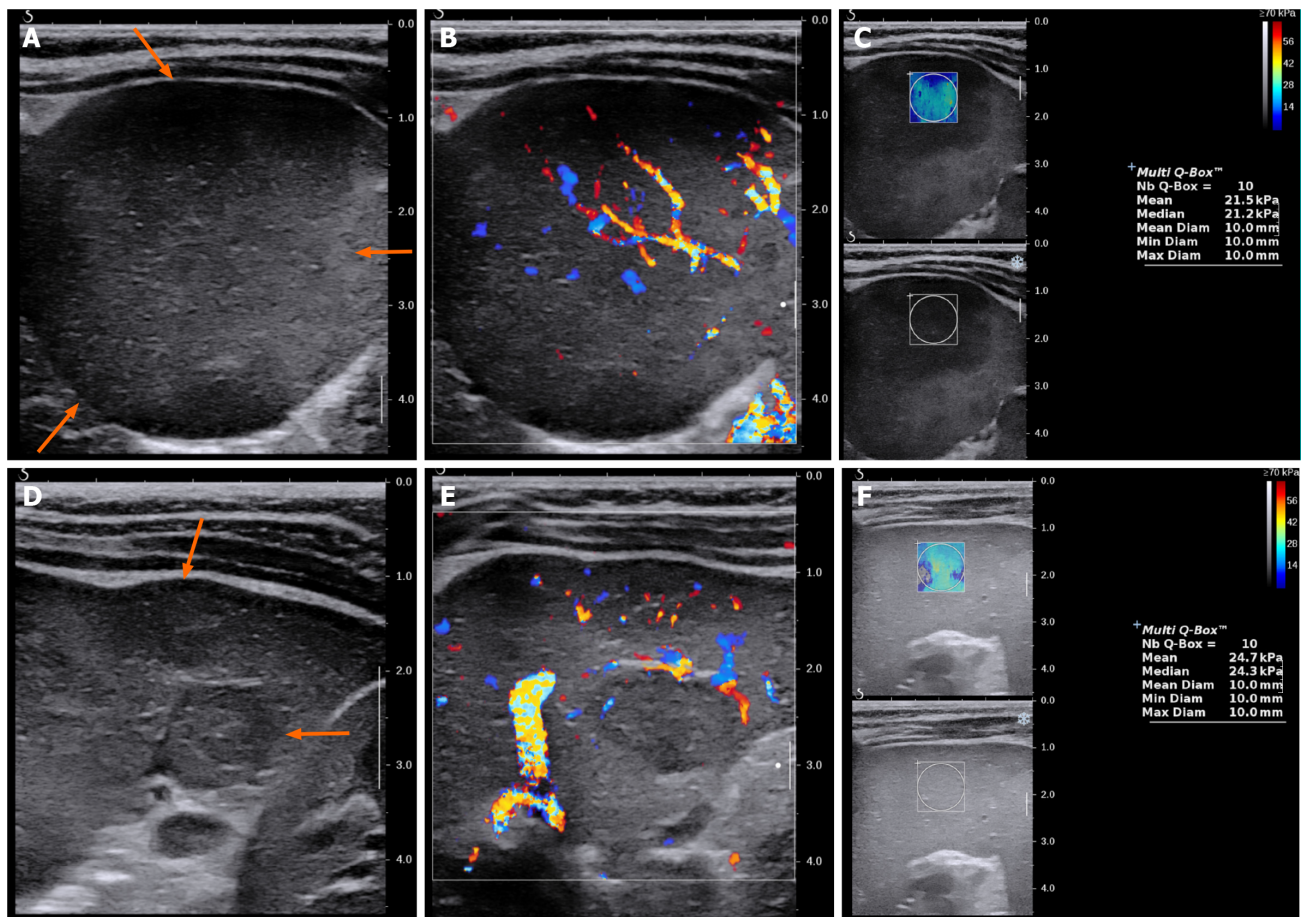
No notable family history was found.

### Physical examination

Physical examination showed no abnormal findings.

### Laboratory examinations

At presentation, blood tests showed leukocytosis (leukocyte count,  $25.29 \times 10^6/L$ ), anemia (hemoglobin, 9.3 g/dL), a high erythrocyte sedimentation rate (ESR) (72 mm/h), and an elevated C-reactive protein level (CRP) (11.04 mg/dL). Peripheral blood smear showed normocytic normochromic anemia with spherocytes and tear drop cells and leukocytosis with monocytosis, basophilia, and neutrophilia.



**Figure 1** Ultrasound images of two solid spleen masses. A and D: B-mode images demonstrated irregular and hypoechoic masses; B and E: Color Doppler images showed similar mass vascularity to that of a normal area of the spleen; C and F: Shear wave elastography showed similar shear wave velocity to that of a normal area of the spleen.

### Imaging examinations

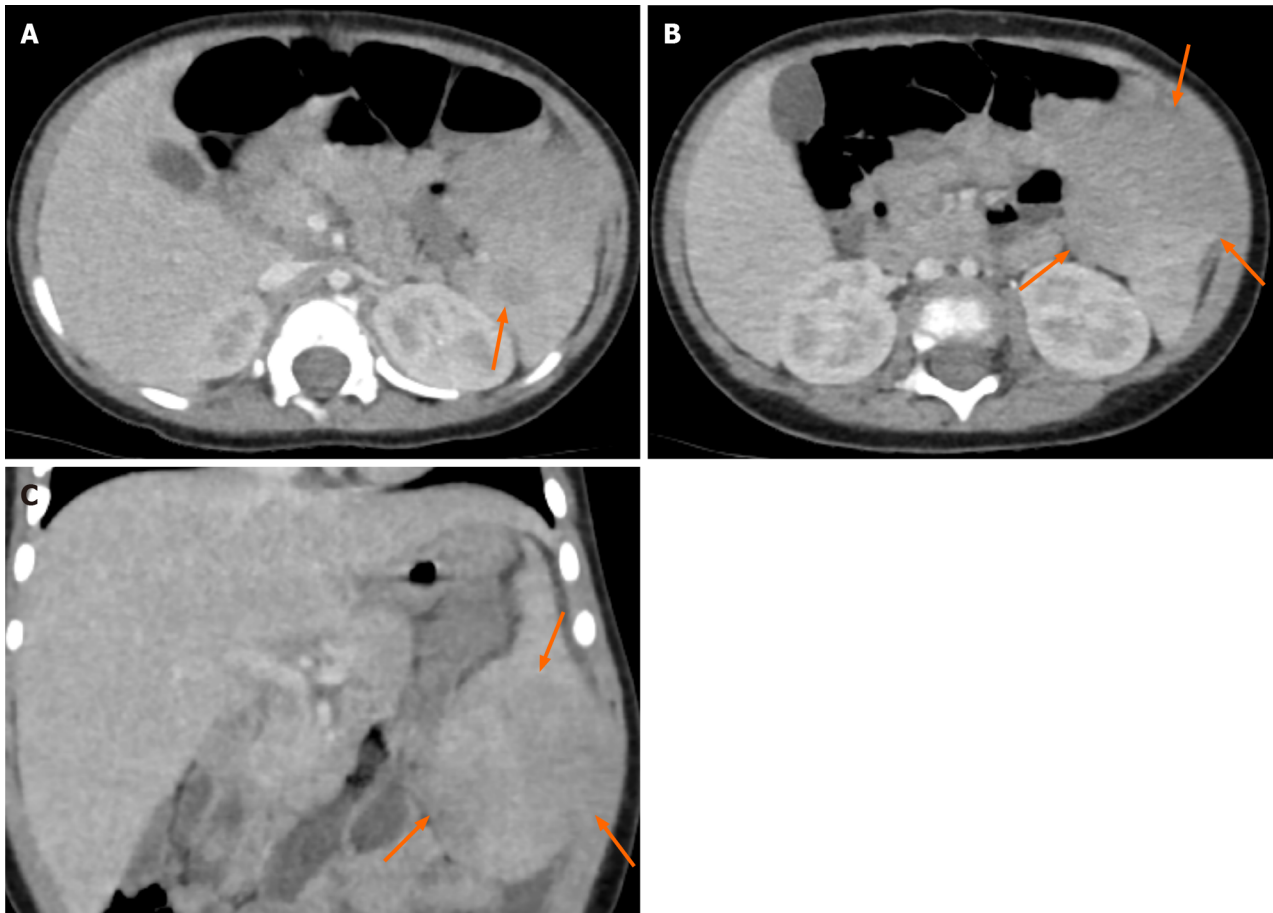
On plain radiography, an approximately 4-cm mass was observed in the left upper quadrant of the abdomen with displacement of the bowel loops. Ultrasonography showed two hypoechoic solid masses in the spleen with diameters between 1 cm and 1.5 cm. The lower pole of the spleen was enlarged, forming a 4.5-cm solid lump, which contained irregular and well-defined hypoechoic areas with intervening normal spleen tissue. The lesions did not show cystic portions or necrotic changes, but showed similar vascularity to the spleen on both color Doppler study and superb microvascular imaging and showed comparable shear wave velocity to a normal area of the spleen with a median value of 21.5 kPa on elastography, which was repeatedly measured 10 times (21.5 kPa for the lesion vs. 24.7 kPa for the normal spleen) (Figure 1).

Contrast-enhanced computed tomography (CT) of the abdomen obtained in the portal venous phase showed hypo-enhanced splenic masses. The exophytic lesion at the inferior pole of the spleen showed heterogeneous enhancement with low attenuation and isoattenuation to the spleen. No significant lymphadenopathy was observed in the abdominal and pelvic cavities (Figure 2). Magnetic resonance imaging (MRI) was performed for further characterization of the masses. On T2-weighted images, the lesions showed low signal intensity to the spleen. However, on T1-weighted images, the lesions showed variable signal intensities: three lesions showed low signal intensity, one lesion showed iso signal intensity, and two lesions showed high signal intensity. After gadolinium administration, the lesions showed low signal intensity with peripheral enhancement in both the arterial and portal venous phases. The lesions showed persistent low signal intensity until 5 min after gadolinium administration (Figure 3).

### Pathological findings

Histopathology showed histiocytic proliferation with emperipolesis in an ill-defined





**Figure 2** Computed tomography images of two solid splenic masses. A: Axial image showed smaller hypodense mass; B: Axial image demonstrated larger exophytic hypodense mass; C: Coronal image revealed larger exophytic hypodense mass.

ovoid splenic mass and splenic hilar lymph nodes. Immunohistochemistry revealed that the proliferating histiocytes were positive for CD68 antigen and S-100 protein, but negative for CD1a (Figure 4). These findings were consistent with RDD. Epstein-Barr virus (EBV) was not detected in the specimen using EBV *in situ* hybridization for EBV-encoded RNA.

## FINAL DIAGNOSIS

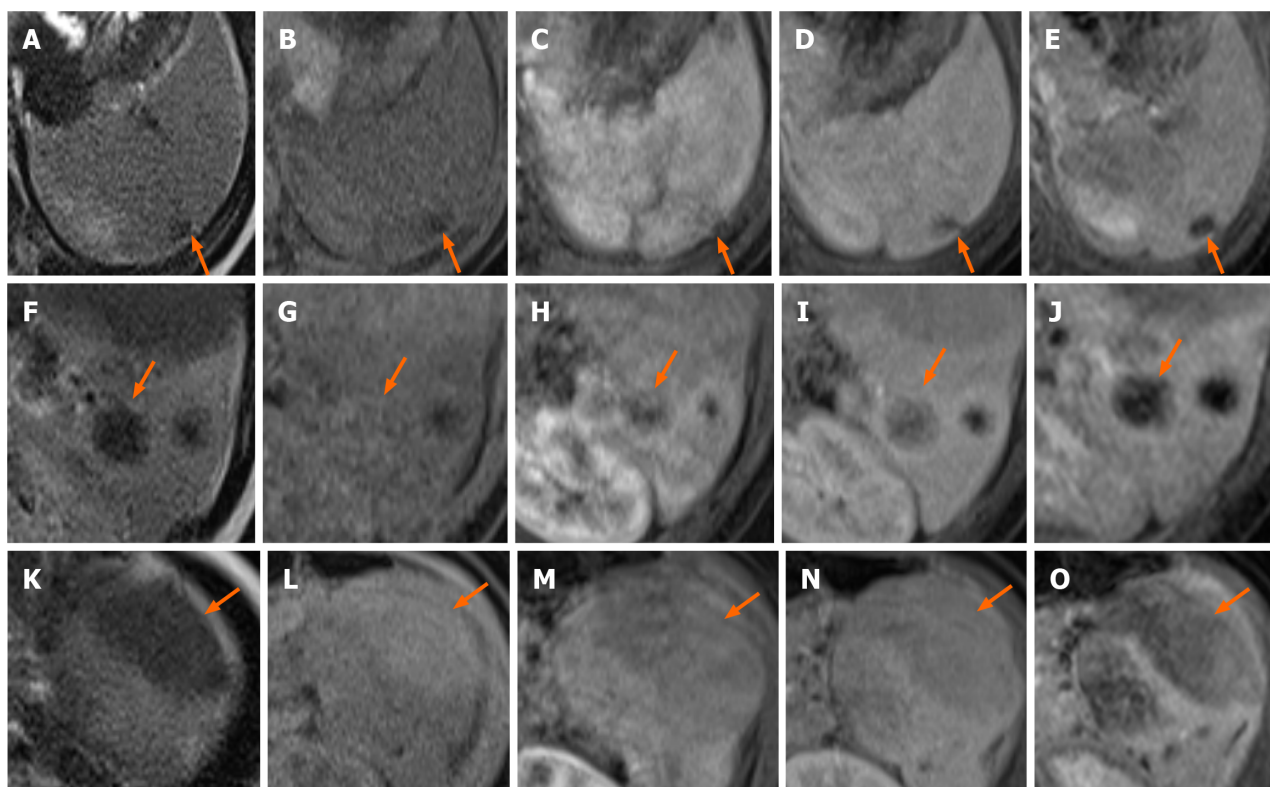
The patient was diagnosed with extranodal involvement of RDD in the spleen.

## TREATMENT

Although 1 mg of piperacillin-tazobactam were administered three times daily for five days, the patient had persistent fever and anemia. Considering laboratory and radiological findings, diagnostic splenectomy was performed. Following a laparotomy, a slightly hard and round-shaped exophytic mass approximately 6 cm in size was found at the inferior pole of the spleen, and a few enlarged lymph nodes around the splenic hilum and pancreas tail and along the gastroepiploic vessels were found. After splenectomy, one accessory spleen and a few enlarged lymph nodes along the gastroepiploic vessels were found and retrieved.

## OUTCOME AND FOLLOW-UP

The patient's symptoms, including fever, anemia, and leukocytosis, improved after splenectomy. The patient was discharged 14 d after the operation. At one month



**Figure 3 Magnetic resonance images of splenic masses.** A-E: Magnetic resonance imaging (MRI) images demonstrated mass in upper level of spleen; F-J: MRI images showed mass in middle level of spleen; K-O: MRI images illustrated mass in lower level of spleen. A, F and K: Splenic masses showed low signal intensity on T2-weighted images; B, G and L: Splenic masses demonstrated various signal intensities on T1-weighted images; C, H and M: Splenic masses showed low signal intensity in the late arterial phase; D, I and N: Splenic masses showed persistent low signal intensity in the portal venous phase; E, J and O: Splenic masses showed still low signal intensity in the 5-min delayed phase.

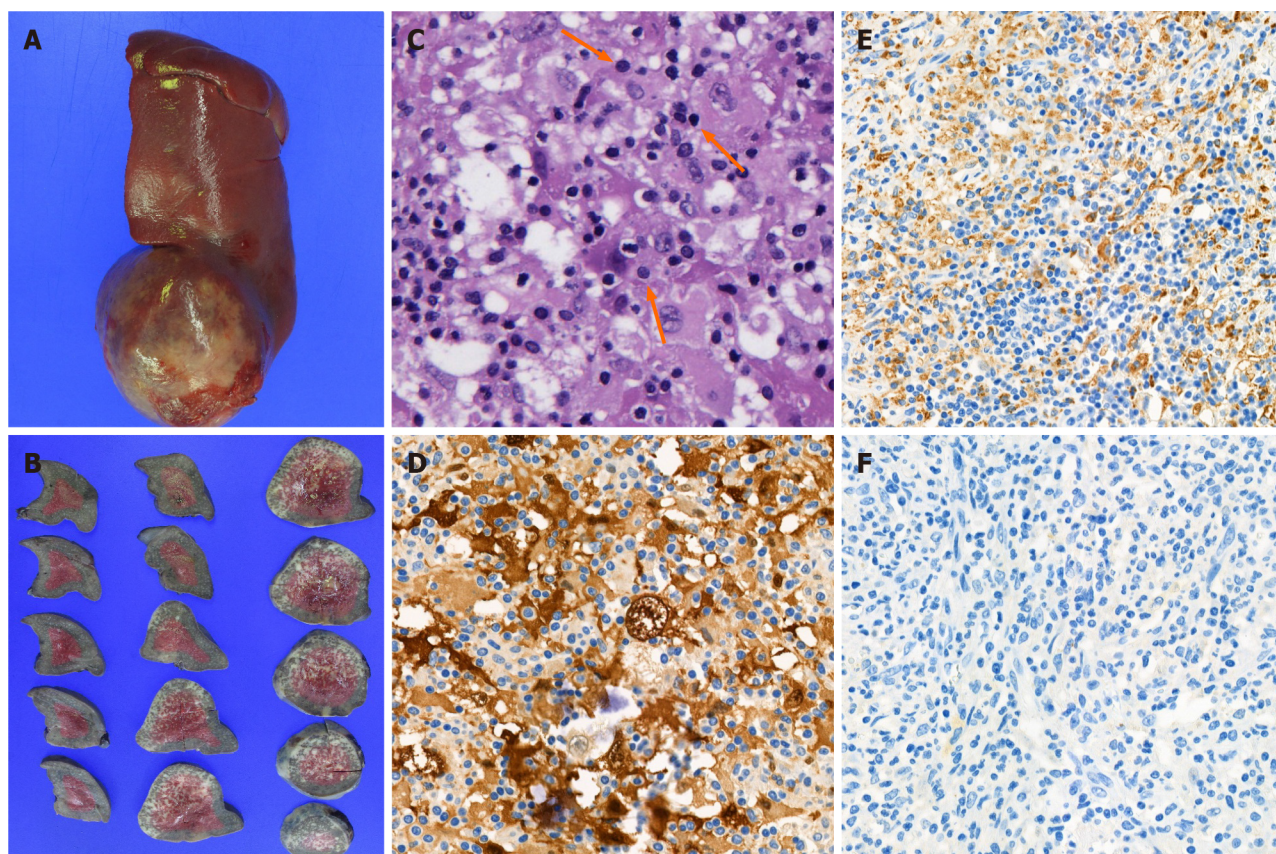
follow-up, the patient had no fever or other discomfort. The lab findings including leukocyte count, hemoglobin, ESR and CRP were within normal limit. The patient underwent contrast-enhanced CT exams one month, six months, and two year surgery. Those examinations demonstrated no abnormal finding except splenectomy state.

## DISCUSSION

Histiocytoses are a group of hematological disorders characterized by pathological mononuclear phagocytic cell infiltration of normal tissues. Mononuclear phagocytes can be classified into two major classes: macrophages and dendritic cells. The World Health Organization has classified histiocytic disorders into three classes based on pathological cells: dendritic cell histiocytoses, non-dendritic cell histiocytoses, and malignant histiocytoses[4]. RDD, originally named sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic disorder, but is the most common non-dendritic cell histiocytosis[5]. RDD was initially described by Rosai and Dorfman in 1969; however, its exact etiology and pathogenesis remained unknown. Some studies have proposed that RDD is a type of chronic inflammatory lymphoid hyperplasia due to antigenic stimuli, such as malignant tumors and acute lymphadenitis disorder[6,7]. Lu *et al*[8] have reported four cases in which RDD and malignant lymphoma were confirmed in the same lymph node. di Dio *et al*[9] have reported one case in which RDD and EBV infection were diagnosed in the same biopsied cervical lymph node specimen. In addition, Arakaki *et al*[5] have reported human herpesvirus 6 detection in a biopsied RDD renal sample. However, here, the patient had no simultaneous hematological disorder or definite infection.

RDD affects males more frequently than females[10] and commonly occurs in the first two decades of life[11]. The most commonly affected site is the lymph nodes, and the most common clinical symptom is painless and isolated lymphadenopathy[12]. Over 90% of patients with RDD present with cervical lymphadenopathy, but any group of lymph nodes can be invaded. Axillary, inguinal, mediastinal, hilar, and





**Figure 4 Pathologic images of splenic masses.** A: Resected specimen showed contour bulging splenic mass; B: Cut surface of the resected specimen; C: Hematoxylin and eosin-stained section (200 ×) showed histiocytic proliferation with emperipolesis (arrows); D: Proliferating histiocytes were positive for S-100 protein stained section (400 ×); E: Proliferating histiocytes were positive for CD68 antigen stained section (400 ×); F: proliferating histiocytes were negative for CD1a stained section (400 ×).

retroperitoneal lymph node involvements have been reported[9,10]. Extranodal involvement of RDD has been reported in up to 40% of all cases[2]; however, few cases are available in the literature. The most commonly affected extranodal sites are the skin and soft tissue. The involvement of the upper respiratory tract, eyes, salivary gland, central nervous system, bones, lungs, urogenital and gastrointestinal tracts, breast, thyroid, and heart has also been described[9,11-16]. Concurrent involvement of nodal and extranodal sites is more commonly observed. According to some studies, no correlation was observed between the type of RDD and clinical outcomes, but a significant difference was observed between the mean age of children and the type of RDD, with younger children more frequently affected by purely nodal RDD[9,17]. We summarized further case reports of RDD in pediatric patients in Table 1[4,5,7,9,12,14-16,18].

Few cases of splenic involvement of RDD have been reported to date. In the English literature, all patients were middle-aged women and presented with hematological symptoms, such as anemia and thrombocytopenia that improved after splenectomy [19,20]. To the best of our knowledge, splenic involvement of RDD in pediatric patients is extremely rare.

Imaging examinations are not pathognomonic in the diagnosis of RDD because of their nonspecific findings. Furthermore, the appearance of extranodal RDD on imaging studies often mimics malignancy[12]. Therefore, biopsy is necessary to establish diagnosis[12,18]. In our case, CT images showed multiple hypodense masses in the spleen in accordance with other studies[19,20].

The definitive diagnosis of RDD can only be made by histological analysis. One of the pathognomonic findings is emperipolesis defined as the presence of phagocytized cells in a histiocyte. In immunohistochemical analysis, positivity for CD68 antigen and S-100 protein, but negativity for CD1a antigen is diagnostic for RDD. Emperipolesis can also be found in Langerhans cell histiocytosis (LCH), but the absence of Birbeck granules and negativity for CD1a antigen help differentiate RDD from LCH[9,12].



**Table 1 Literature review of pediatric Rosai–Dorfman disease**

Ref.	Age	Gender	Symptoms	Underlying disease	Nodal disease	Extranodal disease	Radiologic findings			
							Location	US	X-ray/CT	MRI
di Dioet al[9], 2016	14M	(-)	Swelling of the right parotid gland	Recent EBV infection	Bilateral cervical, hilar	Bilateral parotid gland	Multiple intraparotid LNs	Cystic and solid	(-)	Enhancement: Irregular
Rasool <i>et al</i> [4], 2015	15M	F	Pain and swelling of distal forearm	Not described	No	Physis of distal radius	Well-defined intramedullary lesion	(-)	Radiolucent lesion with scalloping and thin rim	(-)
Mantilla <i>et al</i> [12], 2016	2	F	Proptosis, headache	H syndrome (SLC29A3 mutation)	No	Bilateral orbit	Numerous well-circumscribed intraorbital masses	(-)	(-)	T2WI: Moderately hyperintense; enhancement: Mild
Nandi <i>et al</i> [7], 2008	5	M	Painless huge neck swelling, fever	HHV-6 infection	Bilateral cervical	No		(-)	(-)	(-)
Nandi <i>et al</i> [7], 2008	5	M	Bilateral proptosis, swelling over the mandibular area	No	Preauricular, mandibular	Bilateral orbit	Ill-defined irregular masses involving mainly intraconal parts	(-)	Enhancement: heterogeneous	(-)
Rodriguez-Galindo <i>et al</i> [14], 2004	6	F	Orbital swelling, proptosis, and blindness	No	Ipsilateral cervical	Orbit	Retroconal and preseptal mass extended to cavernous sinus	(-)	(-)	Enhancement: Mild
Arakaki <i>et al</i> [5], 2012	7	M	Abdominal pain and diarrhea	HHV-6 infection	No	Kidney	Mass at anterior portion of kidney	Homogeneous echogenicity	Soft tissue density; enhancement: Homogeneous	Enhancement: Homogeneous
Rodriguez-Galindo <i>et al</i> [14], 2004	9	F	Left frontal swelling and tenderness	No	No	Skull	Well-defined lesions in frontal bone		Radiolucent lesions without sclerotic margin	(-)
Sridhara <i>et al</i> [15], 2012	11	M	Painless bilateral neck swelling	Recent EBV infection	No	Bilateral submandibular gland	Enlarged submandibular glands	(-)	Enhancement: Homogeneous	(-)
Tubbs <i>et al</i> [16], 2005	13	M	Neck pain, headache, blurred vision	No	No	Right parietal bone	Intraosseous lesion	(-)	(-)	(-)
						Suboccipital musculature		(-)	(-)	Enhancement: Mild
Rittner <i>et al</i> [18], 2012	15	M	Fever, back and left hip pain	No	No	Multiple bone lesions (cranial bone, spine, pelvis, upper/lower extremities)		(-)	Lytic lesions	T1WI: Hypointense; T2WI: Hyperintense; enhancement: Strong
Rodriguez-Galindo <i>et al</i> [14], 2004	15	F	Headache, proptosis	Recent EBV infection	Mediastinal	Brain	Anterior and posterior falx	(-)	(-)	T1WI and T2WI: Isointense; Enhancement: Strong
						Bilateral orbit	Retroconal, preseptal space			

T1WI: T1-weighted image; T2WI: T2-weighted image; US: Ultrasound; CT: Computed tomography; MRI: Magnetic resonance imaging; EBV: Epstein–Barr virus; HHV: Human herpesvirus.

The clinical course of RDD is benign and may regress spontaneously. Given that fact, observation may be a good treatment option. However, treatment is required in cases of significant extranodal disease because locoregional recurrence or even dissemination can be possible. Compression of vital organs or severe constitutional symptoms, such as fever, is also indications for therapy[7,9]. Although there is no consensus for the optimum treatment option, surgery is probably the best curative treatment if complete resection is possible. In addition, medical therapy, including corticosteroids, antibiotics, antiviral agents, chemotherapy, and radiotherapy, is available[9].

## CONCLUSION

In conclusion, although splenic involvement is rare, especially in pediatric patients with RDD, RDD should be considered a differential diagnosis, even in patients without significant lymphadenopathy, especially in the setting of hematological abnormality or infectious symptoms.

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