



# Extranodal Rosai-Dorfman disease presenting as an isolated glenoid lesion in a high school athlete

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Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), was first described as a clinical entity by Rosai and Dorfman in 1969.<sup>15</sup> The first description of the disease reported a rare non-neoplastic disorder involving the proliferation of histiocytes predominantly involving the lymph nodes. "Sinus histiocytosis" refers to histiocytosis that occurs in the distended sinuses of lymph nodes, but since its initial description, RDD has been reported to involve a wide variety of organ systems and has been found in numerous locations throughout the body.<sup>6</sup>

RDD most commonly presents in young patients in the second or third decade of life, with an increased prevalence in men.<sup>6</sup> RDD generally presents as bilateral, nontender, painless adenopathy in the neck, which may be accompanied by fever, elevated erythrocyte sedimentation rate, weight loss, and immunologic abnormalities such as leukocytosis and polyclonal hypergammaglobulinemia. Less frequently involved nodal sites are mediastinal, hilar, retroperitoneal, axillary, and inguinal.<sup>3,4,12,18</sup> Extranodal RDD occurs in 42% of patients, with 23% having isolated extranodal disease.<sup>6</sup>

Of the nearly 1000 patients with documented RDD,<sup>3,4,18</sup> less than 3% have presented with isolated osseous involvement.<sup>6</sup> In the 423 RDD cases presented by Foucar et al,<sup>6</sup> 7.8% had osseous involvement, 2% had osseous involvement without lymphadenopathy, and 0.5% had isolated osseous

involvement. The skull is the most commonly cited location of solitary bone lesions and often presents with pain and headaches.<sup>1</sup> In another series by Sundaram et al,<sup>19</sup> 15 patients had isolated bone lesions and 3 had multiple bone lesions as the sole presentation of RDD. Pain at the involved site was the most commonly cited symptom among patients.

In this case report we present a 16-year-old male patient with an extranodal lesion within the glenoid found incidentally and misdiagnosed as osteomyelitis and later Langerhans cell histiocytosis before finally being diagnosed as RDD through immunohistochemical staining. A primary isolated extranodal intraosseous lesion of the glenoid is an extremely rare presentation of RDD and this is the only report in the literature to date of this presentation. We obtained informed written consent from the patient's guardian for publication of this report.

## Case report

A 16-year-old African American high school football player presented to his primary care provider 1 week after sustaining a mild impact injury to the anterior portion of his right shoulder during practice. The patient reported pain with overhead activities and associated weakness. There was no numbness or tingling or any radiation of pain down the affected arm. His medical history was positive only for attention deficit hyperactivity disorder treated with methylphenidate. On examination, there was no overlying skin erythema, warmth, or swelling. Range of motion testing showed forward flexion was 180° with a painful arc of motion during the last 40°, abduction to 160° with pain, external rotation with the elbow at the side to 35° with pain, and internal rotation to L1 with anterior shoulder pain.

Investigational Review Board approval is not required for a case report.

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Three-view plain radiographs of the right shoulder showed a cystic-appearing glenoid with a slightly enlarged appearance and sclerotic rim (Fig. 1). No evidence of fracture, dislocation, or involvement of the proximal humerus was seen. The patient diagnosed with rotator cuff strain and was referred for a magnetic resonance imaging (MRI) study to further evaluate the shoulder pain and incidental cystic glenoid lesion.

The MRI showed an abnormal multilobulated, expansile, destructive lesion of the right glenoid with isointense signal to muscle on T1-weighted images (Fig. 2). The lesion extended beyond the cortical margins of the bone anteriorly into the subscapularis muscle, and posteriorly into the scapular neck and infraspinatus muscle. No fluid-fluid levels were present, and the rotator cuff muscles and labrum were all intact without evidence of tears.

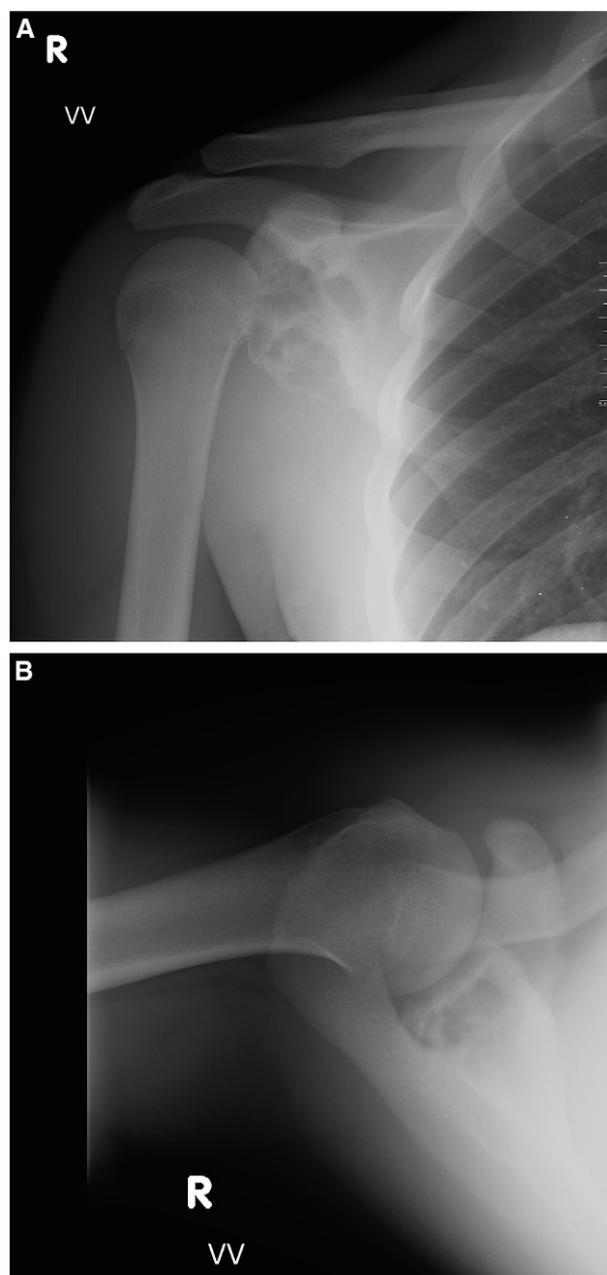
The patient then underwent a computed tomography-guided biopsy of the lesion. The specimen showed numerous neutrophils, lymphocytes, and plasma cells and was diagnosed osteomyelitis despite normal inflammatory laboratory values for C-reactive protein, erythrocyte and sedimentation rate, a negative gram stain, and negative biopsy cultures (Fig. 3). At that point, the patient was referred to our Orthopaedic Oncology clinic for further work-up and management.

On secondary examination, the patient had full range of motion of the right shoulder without instability and skin was clean, dry, and intact over the shoulder. He had sharp pain with compression of the humerus into the glenoid that recreated his original symptoms. There were no palpable lymph nodes and the remainder of the examination was unremarkable. There was concern at this time that the diagnosis of infection was not accurate given the normal laboratory findings, imaging results, and clinical examination. As a result, the patient was scheduled for a one-stage open biopsy procedure with an orthopaedic oncology and orthopaedic shoulder specialist to check intraoperative frozen section pathology and cultures.

A posterior approach to the right shoulder was used with the patient in the lateral decubitus position using a beanbag positioner. A 6- to 7-cm incision 1-cm medial to the posterolateral border of the acromion towards the posterior axillary line was used for exposure. Minimal skin flaps were raised, and the deltoid was split beginning 4 cm medial from the posterolateral corner of the acromion to the scapular spine distally. The fascia of the infraspinatus was then lysed and the raphe between the teres minor and infraspinatus was identified and bluntly dissected down to the neck of the humerus providing a small window into the posterior glenoid.

A reddish-purplish material ballooning out of the bony defect in the medullary cavity of the glenoid was curetted and sent for cultures and frozen section pathology. The initial pathology diagnosis was Langerhans cell histiocytoma (LCH), based on findings of numerous histiocytes, at which time the bony defect was fully curetted and packed with 30 mL of crushed cancellous allograft. The wound was irrigated before and after grafting and was closed in layers. The patient was discharged successfully the following day in a long-arm postmold splint with non-weight-bearing restriction.

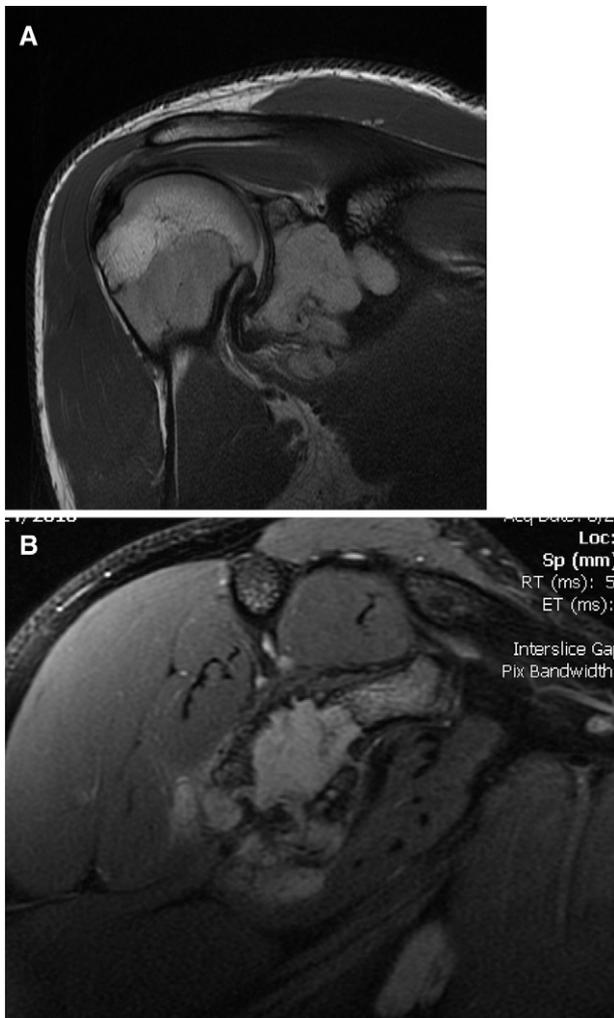
Two days later, a second pathology opinion was obtained for further hematoxylin and eosin (H&E) analysis and immunohistochemical (IHC) staining before the final diagnosis. H&E staining of the specimen showed histiocytes with lymphocytic nuclei in the cytoplasm and on IHC staining were CD68 (PGM1)-positive,



**Figure 1** A large cystic lesion with a sclerotic rim in the right glenoid vault is shown on (A) anteroposterior and (B) axillary radiographs taken during the initial work-up.

CD4-positive, S-100-positive, CD30-negative, and CD1a-negative (Fig. 4). This excluded LCH, which was favored originally but is CD1a-positive. The final diagnosis was then changed to RDD.

At the 2-week follow-up, the patient had a significant decrease in pain and had good passive range of motion with pain at extremes. He was started on physical therapy for increased range of motion with no heavy lifting and no contact sports. At the 6-week follow-up, the patient had no pain, a well-healed incision, no tenderness to palpation, and good passive range of motion in all directions with good strength throughout his rotator cuff and deltoid. A clinical examination showed no developing lymph node involvement and radiographs showed no further lesions.

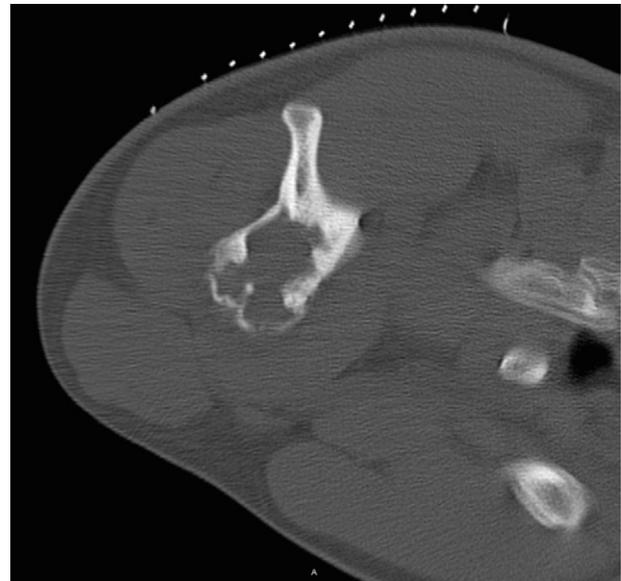


**Figure 2** A multilobulated, expansile lesion of the right glenoid with extension outside of the cortical bone margins into the scapular neck is shown on (A) coronal and (B) sagittal T1-weighted magnetic resonance images.

The patient had progressively improving range of motion and range of motion at the 6-month follow-up. Radiographs showed no glenoid fracture with good fill of the glenoid defect with mild remaining bone loss in the superior aspect with moderate consolidation of the lesion (Fig. 5). Physical therapy was discontinued and he was instructed to return to activities with shoulder range of motion, excluding contact sports. At 9 months after the procedure, there was no disease recurrence, and the patient was pain-free, with normal range of motion.

## Discussion

RDD is an idiopathic histiocytosis of unknown etiology that is rare and generally self-limited. RDD can present infrequently with isolated osseous involvement, with locations reported in the skull, spine, femur, radius, ulna, metacarpals, and talus.<sup>9,11,16</sup> RDD is often called a “pseudolymphomatous” disorder because presentations often include enlarged



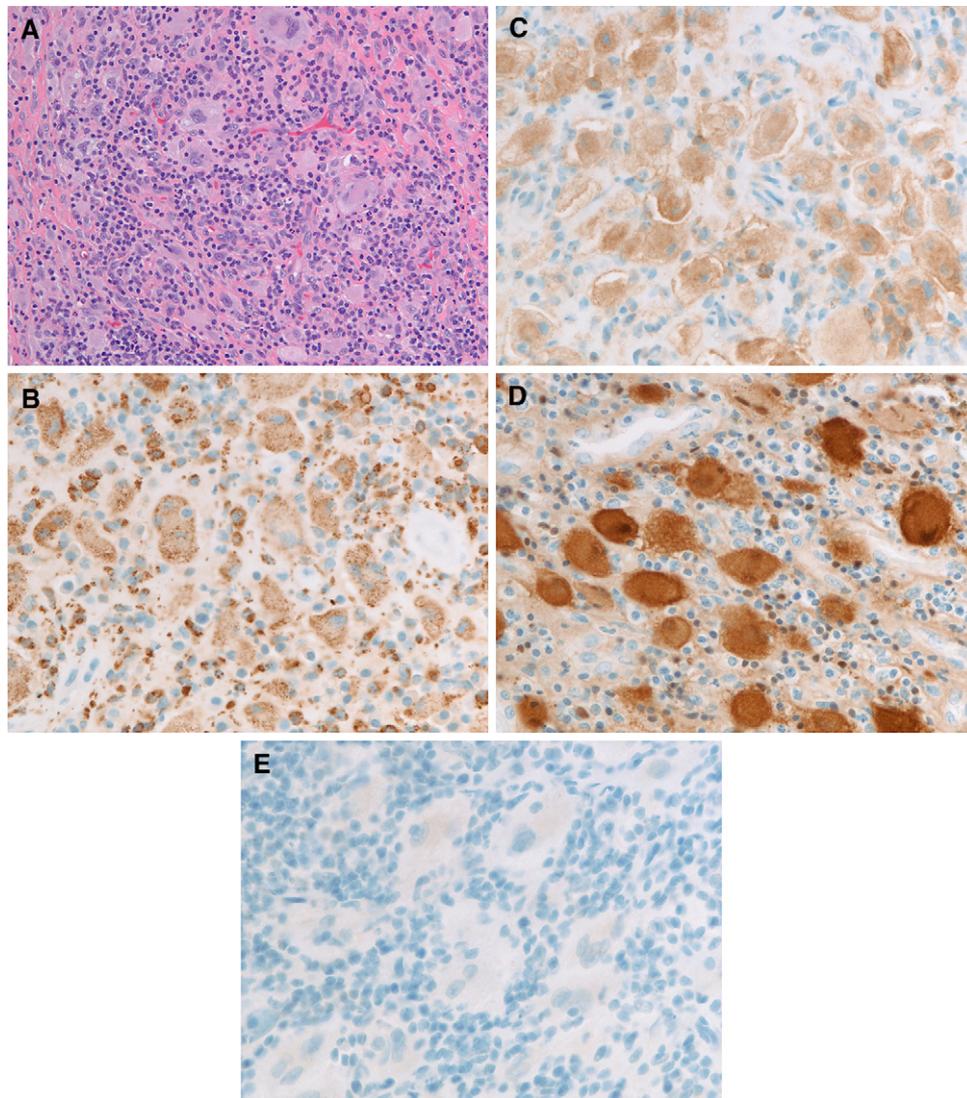
**Figure 3** An axial image from computed tomography-guided aspiration of a right shoulder lesion demonstrates extensive bony destruction of the glenoid.

lymph nodes and histopathology of proliferations of lymphoid cells but are benign. One of the main problems with RDD is that it is commonly misdiagnosed, thus leading to improper patient treatment and subsequent complications.

Histiocytes are part of the mononuclear phagocytic system and are sometimes referred to as tissue macrophages. They have an eosinophilic cytoplasm and have a number of lysosomes, and their main functions involve phagocytosis and antigen presentation. An important disease characterized by histiocytosis is LCH, also referred to as eosinophilic granuloma. Clinical manifestations of LCH may include single or multiple bone lesions, exophthalmos, visceral or skin lesions, fever, hepatosplenomegaly, anemia, bacterial infections, or lymphadenopathy. The histologic appearance of LCH includes an eosinophilic cytoplasm, polymorphous mix of inflammatory cells, and Langerhans histiocytes, cells with bean-shaped nuclei, crisp nuclear membrane, finely stippled chromatin pattern, and abundant eosinophilic (pale) cytoplasm.

Achieving a definitive diagnosis of RDD, as initially described by Goel et al,<sup>7</sup> is accomplished through H&E and IHC analysis and detection of histiocytes positive for CD68 (PGM1) and S-100 protein. CD68 is a stain for monocytes and macrophages, whereas S-100 is a stain for a variety of cells, including neural crest cells, chondrocytes, adipocytes, myoepithelial cells, macrophages, Langerhans cells, dendritic cells, and keratinocytes. Compared with its presentation in lymph nodes, osseous RDD has less pronounced lymphophagocytosis and more fibrosis.<sup>20</sup>

The differential diagnosis of a solitary lesion of the glenoid causing pain and decreased range of motion in a teenager may include osteomyelitis, LCH, aneurysmal bone cyst,



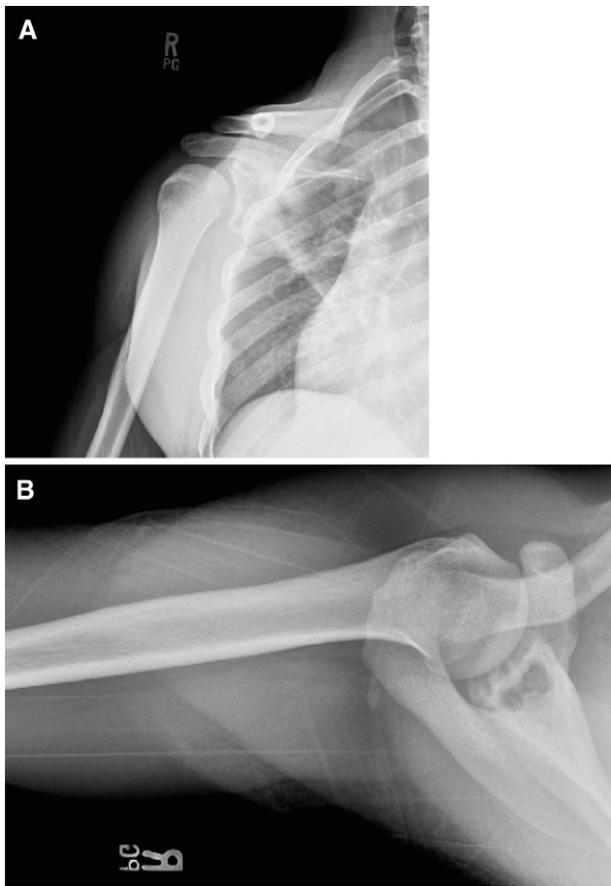
**Figure 4** (A) Hematoxylin and eosin staining of intraoperative biopsy shows abundant cytoplasm and mixed inflammatory infiltrate, including lymphocytes, neutrophils, plasma cells, and histiocytes, with lymphocytic nuclei in the cytoplasm, histiocytes positive for (B) CD68 (PGM1), (C) CD4, and (D) S100 immunohistochemical staining, but negative for (E) CD1a staining (original magnification  $\times 400$ ).

unicameral bone cyst, giant cell tumor, fibrous dysplasia, plasmacytoma, and lipoidosis, among others. In adults with a similar lesion it is important to consider metastatic malignancy as an additional diagnosis.<sup>6,20</sup> The bony lesions in RDD typical appear on radiographs as small, medullary, lytic lesions with sharply or poorly defined borders. However, they can also appear as large, mixed lytic, and sclerotic, with cortical involvement and periosteal reaction with or without soft tissue involvement.<sup>6,17,20</sup>

Our intraoperative biopsy specimen had evidence of intracellular engulfment of lymphocytes by histiocytes, a phenomenon known as emperipolesis, which is a characteristic feature of RDD. The initial preoperative diagnosis of osteomyelitis can easily be confused with RDD due to the nature of the mixed chronic inflammatory infiltrate and accompanying fibrosis and focal osteonecrosis seen in both

diseases. Our first intraoperative diagnosis of LCH was confused with RDD because the histiocytic cells in both diseases express S-100. However, LCH usually contains abundant eosinophils, which are unusual in RDD, and LCH is CD1a-positive whereas RDD is CD1a-negative. Our case demonstrates the critical role that IHC analysis can play in cases of RDD that are difficult to diagnose.

RDD is often benign and has a high rate of spontaneous remission; therefore, nonsurgical management is usually adequate. In a review by Pulsoni et al,<sup>14</sup> complete remission resulted in 32 of 40 patients (80%) who were not treated with surgery, radiotherapy, or chemotherapy. Of the remaining patients without remission, 5 had persistent disease, 1 had partial remission, and 1 died of renal failure. A more aggressive surgical approach may be recommended when there are clinical symptoms or when the location of the lesion threatens major



**Figure 5** At 6 months after the surgery, (A) anteroposterior and (B) axillary radiographs of the right shoulder showed no glenoid fracture, with good fill of the bony defect and moderate consolidation of the lesion.

complications such as spinal cord compression. Persistent cases requiring therapy have been treated with combinations of surgical resection, steroids, radiotherapy, or chemotherapy.<sup>8,10</sup> Surgical curettage or resection has been found to have the best overall outcomes, followed by radiotherapy alone and chemotherapy, which has been largely ineffective.<sup>14</sup>

In a recent case series of primary intraosseous RDD, the mean age of presentation was 27 years, and lesions were found in the tibia, femur, clavicle, skull, maxilla, calcaneus, pharynx, metacarpal, and sacrum.<sup>5</sup> Of the 12 patients available for follow-up, 5 developed additional extraosseous manifestations, including testicular, lymph node, and subcutaneous lesions, and 1 patient developed additional bony lesions. A recent case report by Bachmann et al<sup>2</sup> also found osseous RDD in the ilium in a 71-year-old patient, which is far beyond the typical age of presentation.

In the published literature, there are no other cases of solitary osseous RDD involving the glenoid. If our initial computed tomography-guided biopsy diagnosis of osteomyelitis had not been questioned within the context of the clinical and laboratory findings, the diagnosis and appropriate treatment would have been missed. A similar case

progression was published by Abdelwahab et al,<sup>1</sup> in which a 63-year-old woman who complained of progressive pain in her left ankle underwent a biopsy and was misdiagnosed with osteomyelitis and given long-term intravenous antibiotics. She presented 25 years later on crutches with progressive swelling and intermittent flares of pain without lymphadenopathy. MRI revealed a heterogeneous low intensity signal on T1-weighted image of the talus with extension into the calcaneus, navicular bone, and surrounding soft tissue. Ultimately, the correct diagnosis of RDD was given after analysis of an open biopsy specimen, but remaining follow-up details were limited.

The etiology of RDD remains largely unknown, and there has been evidence to suggest that an infectious origin may be possible, with parvovirus B19 as a culprit.<sup>13</sup> The association of RDD with clinical fever, elevated erythrocyte sedimentation rate, and appearance of lytic lesions on radiographs supports this theory. Our patient, who was just 16 years old during the initial presentation, is one of the younger reported cases and is unique in its isolated glenoid location of RDD. There have been only 4 reported cases in the literature of osseous RDD in patients aged younger than 16, none of which were in the shoulder region.<sup>5</sup>

The rarity of isolated osseous RDD and its dense inflammatory component that can be mistaken for other diseases, such as osteomyelitis, granulomatous disease, LCH, storage disease, and malignancy, can make the correct diagnosis difficult to obtain. We present this case to increase awareness of this disease so that it can be included in the differential diagnosis of atypical glenoid lesions.

## Conclusions

A primary isolated extranodal intraosseous lesion of the glenoid, especially in a teenager, is an extremely rare presentation of RDD. This is the only report in the literature to date of a documented isolated RDD lesion of the glenoid. The rarity of isolated osseous RDD and its dense inflammatory component that can be mistaken for other diseases, such as osteomyelitis, granulomatous disease, LCH, storage disease, and malignancy, can make the correct diagnosis difficult to obtain. We present this case to increase awareness of this disease so that it can be included in the differential diagnosis of atypical glenoid lesions.

## Disclaimer

The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

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