

A rare case of Rosai-Dorfman disease presenting as solitary lesion of distal femur: A case report

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Abstract

Introduction: Rosai-dorfman disease (RDD) or sinus histiocytosis with massive lymphadenopathy is a rare histiocytic proliferative disorder of unknown etiology first identified and characterized by Rosai and Dorfman in 1969. The disease is characterized by painless cervical lymphadenopathy, fever, leukocytosis, elevated erythrocyte sedimentation rate, and hypergammaglobulinemia. <500 patients have been reported worldwide. Osseous involvement without lymphadenopathy occurs in <10% of patients and is usually multifocal. Extranodal solitary osseous lesions are just 4% of this subpopulation, no more than 50 such cases have been described in the literature. Here, we report a rare case of RDD presenting as solitary lesion of the distal femur without any evidence of lymphadenopathy and normal laboratory work up.

Case Report: We report the case of a 29-year-old female who presented with pain and swelling of distal femur of 2-month duration without any evidence of lymphadenopathy, with a normal laboratory workup. Radiographical evaluation showed an epiphyseal, osteolytic, and well-defined lesion with cortical break over the medial femoral condyle and soft-tissue extension into the medial patellar recess abutting the medial patellar retinaculum. Whole body positron emission tomography did not show any other sites of abnormal increased uptake. Intralesional extended curettage, bone grafting, bone cementing, and pinning were done. Histologically, the biopsied lesion demonstrated the classic histiocyte proliferation which exhibited emperipoiesis (engulfment of lymphocyte or plasma cells by large histiocyte) which are CD-68, S-100 positive, and CD-1a negative on immunohistochemistry. At 2-year follow-up, the patient is symptom free, without any new osseous/extranodal/nodal lesions.

Conclusion: RDD rarely affects bone as a primary or even secondary form of the disease. It has relatively non-specific radiological appearance causing diagnostic challenges and may lead to erroneous diagnosis of a malignancy. Biopsy and histological examination by an experienced pathologist is mandatory for the final diagnosis. The ideal treatment ranges from wait and see policy to surgery, chemotherapy, and radiotherapy.

Keywords: Rosai-Dorfman disease, Extranodal, Osseous, Histiocytosis, Emperipoiesis

Introduction

Rosai-dorfman disease (RDD) also known as sinus histiocytosis with massive lymphadenopathy is a rare benign entity first identified and characterized by Rosai and Dorfman in 1969 [1]. Classically, the disease causes painless bilateral cervical lymphadenopathy often accompanied by fever, leukocytosis, increased erythrocyte sedimentation rate, weight loss, and immunological abnormalities such as hypergammaglobulinemia [2]. Extranodal involvement occurs in 33–43% of patients; bone involvement occurs in <5–10% of patients and skeletal cases are usually multifocal. Extranodal solitary

lesions of bone without nodal involvement or additional clinical manifestations are exceedingly rare; only a few case reports have been noted in the literature, as well as a larger series describing 15 cases [3].

The rarity of osseous RDD and its complicated inflammatory component often causes diagnostic difficulties, which leads it to be confused with other lesions such as lymphoma, osteomyelitis, Langerhans cell histiocytosis, storage diseases, and malignancies [3].

Here, we report a case of primary, extranodal, and solitary RDD of the distal femur, in a young lady who had severe knee pain, whose radiographs initially suggested metastatic

carcinoma, Langerhans cell histiocytosis, and giant cell tumor as differentials. Results of needle biopsy followed by excision biopsies confirmed the diagnosis of RDD.

Case Report

A 29-year-old female presented to the orthopedic clinic with a 2-month history of pain and swelling over the right knee. She had no history of fever or swelling anywhere else in the body. No comorbidities or positive family history noted. The pain was of insidious in onset, gradually progressing, intermittent, aggravated on activity, and relieved on rest with no diurnal variation. On physical examination, she had a tender

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Figure 1: Right knee radiography at presentation. Anteroposterior (a) and Lateral (b).

medial femoral condyle, with fullness over the medial patella, severe painful restriction of knee movements. No lymph node enlargement, hepatosplenomegaly, or any other bone involvements were noted.

Her blood parameters (complete and differential counts, erythrocyte sedimentation rate, C-reactive protein, and liver function test) were within normal limits. Radiographs (Fig. 1) showed a well-defined, eccentric, epiphyseal, and lytic lesion over the right medial femoral condyle with and cortical break and narrow zone of transition over the medial femoral condyle. No periosteal reaction and joint involvement seen or soft-tissue effacement noted.

Magnetic resonance imaging (Fig. 2) with contrast showed well defined, osteolytic, and epiphyseal lesion with subarticular extension involving the medial femoral condyle, with narrow zone of transition, destruction of cortex, and mild soft-tissue extension into the medial patellar recess closely abutting the medial patellar retinaculum. Differential diagnosis of giant cell tumor, Langerhan cell histiocytosis, lymphoma were made.

Whole body positron emission tomography (PET) (Fig. 3) was done to look for any occult nodal or extranodal lesions. Abnormal increased uptake was limited to the right



Figure 2: Magnetic resonance image T1-weighted coronal image (a) and sagittal image (b).

medial femoral condyle.

She underwent needle biopsy of the lesion which showed florid histiocytosis admixed with inflammatory cells without any evidence of neoplasm. After multidisciplinary tumor board meeting, she underwent intralesional extended curettage, bone grafting, bone cementing, and pinning of the medial femoral condyle (Fig. 4). The curetted specimen was sent for histopathological examination which showed florid histiocytosis exhibiting emperipolesis (Fig. 5a) and in immunohistochemistry, these histiocytes expressed CD-68 (Fig. 5b), S-100 positive staining (Fig. 5c), and negative staining for CD-1a (Fig. 5d).

She was followed up in the outpatient at 6-week, 3-month, and 1-year post-surgery. She is now symptom free, ambulating normally without any clinical or radiographic (Fig. 6) evidence of local recurrence or any new nodal or extranodal lesions.

Discussion

Since rosai and dorfman [1] identified and characterized RDD in 1969, more than 400 patients have been reported with this rare condition. Fewer than half of these cases involved extranodal sites, including the skin, nasal cavity, paranasal sinuses, eye orbit bone,

salivary gland, central nervous system, oral cavity, kidney, respiratory tract, liver, tonsil, breast, gastrointestinal tract, and heart [2, 4, 5]. About 20% of these cases presented with extranodal involvement alone [4]. Presentation of RDD with a solitary bone lesion is exceptionally rare and typically occurs in children. Solitary bone involvement without lymphadenopathy is an extremely rare clinical situation and has been reported in only a handful of cases [6, 7, 8].

Bone involvement occurs in <10% of patients and is usually multifocal. Extranodal solitary lesions are even rarer, representing just 4% of this subpopulation [3]. No more than 50 cases of primary intraosseous RDD have been described in the literature [3, 9].

RDD is an idiopathic histiocytosis that has been postulated to be of neoplastic, immunologic, or infectious origin [2]. The leading hypothesis is that of Parvovirus infectious origin [10].

On radiographs, RDD bone lesions typically appear multifocal, lytic, and intramedullary and have poor or sharp margins. Some lesions



Figure 3: 18FDG-whole body positron emission tomography showing metabolically active lesion in the right medial femoral condyle (circle).



Figure 4: Post-operative radiograph of right knee showing post curettage bone cement, bone graft substitute, and smooth pins. Anteroposterior view.

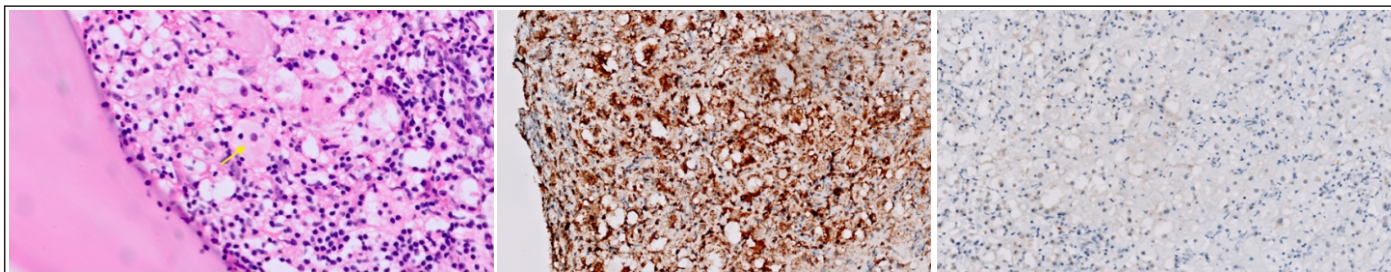


Figure 5: ×200 magnification, H&E staining showing florid histiocytosis exhibiting emperipolesis (a) (arrow), CD-68 positive (b), S-100 positive (c), and CD-1a negative (d).



Figure 6: 1-year follow-up Right Knee radiography – no recurrence of tumor. Anteroposterior.

are sclerotic, particularly when healing. In most cases, there is no periosteal reaction with cortical defects [6, 11]. Signature histologic features of RDD include emperipolesis (lymphophagocytosis), or presence of intact lymphocytes within the cytoplasm of histiocytes and CD-68, S100 protein positive, and CD-1a negative on immunostaining [12, 13].

Our patient demonstrated an osteolytic, epiphyseal, and well defined bone mass with soft-tissue extension, metabolically active on whole body PET; it was concerning for

aggressive giant cell tumor, Langerhan cell histiocytosis, or malignancy. Due to the ambiguous nature of radiographic findings, RDD diagnosis requires biopsy and histopathological examination by an experienced pathologist to identify emperipolesis and immunohistochemistry. Throughout literature, initial biopsies frequently caused diagnostic challenges due to common findings of mixed chronic inflammatory infiltrate, as was the case with our patient.

The clinical course is usually self-limiting; more than 70% patients achieve spontaneous resolution [1, 2, 4]. The prognosis of RDD depends on the extent, extranodal involvement, and comorbidities (immunological diseases). Prognosis is worse with disseminated involvement. No malignant transformations have been reported. However, with osseous RDD, most patients experience a chronic course, with spontaneous resolution rarely reported [4, 9]. In the literature, only four patients were reported to die of the disease. Three of those patients had involvement of bone [1, 4, 9]. Thus, the ideal treatment is unknown and ranges from a conservative wait-and-see policy to treatment consisting of modalities such as surgery, chemotherapy (Prednisone and Interferon alpha), and radiotherapy.

Our patient proceeded with surgical intervention due to severe pain, affecting her

activities of daily living. She is remaining asymptomatic till date (20 months) with intralesional extended curettage. We present this case to raise awareness of the disease and to include in differential diagnosis of osteolytic lesions.

Conclusion

Primary RDD involving the bone without lymphadenopathy is extremely rare. It has a long clinical course attributed to difficulties with radiological and histopathological diagnosis. The non-specific radiological features cause diagnostic challenge and can lead to an erroneous diagnosis of a malignancy. Thus, biopsy and histopathological examination by an experienced pathologist is required for final diagnosis. Most cases of RDD undergo spontaneous and complete remission. Prognosis typically is good and the disease course is not aggressive. However, treatment depends on the extent of nodal and extranodal involvement.

Clinical Relevance

Despite its low incidence, RDD can be included in the differential diagnosis of unifocal and multifocal skeletal involvement caused by granulomatous diseases, infection, pseudogranulomatous lesions, and malignancy.

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