Extranodal Rosai-Dorfman Disease as Solitary Lesion of the Tibia in a 56-Year-Old Woman

Nathan D. Orvets, MD, Joel L. Mayerson, MD, and Paul E. Wakely Jr, MD

Abstract

We report the case of a 56-year-old woman who had severe leg pain and whose radiographs initially suggested metastatic carcinoma, lymphoma, osteogenic sarcoma, or adamantinoma. Results of multiple biopsies confirmed a diagnosis of Rosai-Dorfman disease, which typically presents in children and young adults (mean age at onset, 20 years).

Rosai-Dorfman disease (RDD), or sinus histiocytosis with massive lymphadenopathy (SHML), is a rare, acquired, idiopathic, proliferative histiocytic disorder that was first described by Destombes in 1965 and officially classified by Rosai and Dorfman in 1969.[1-3] SHML typically affects children and young adults (mean age at onset, 20 years). Patients most commonly present with painless adenopathy but may also report fevers, pharyngitis, pain, tenderness, malaise, night sweats, or weight loss.[1,4,5] On laboratory evaluation, many patients have an elevated erythrocyte sedimentation rate and immunologic abnormalities, such as autoimmune hemolytic anemia or polyclonal hypergammaglobulinemia. Some patients present with extranodal disease, most commonly involving the skin, upper respiratory tract, and bone.[1]

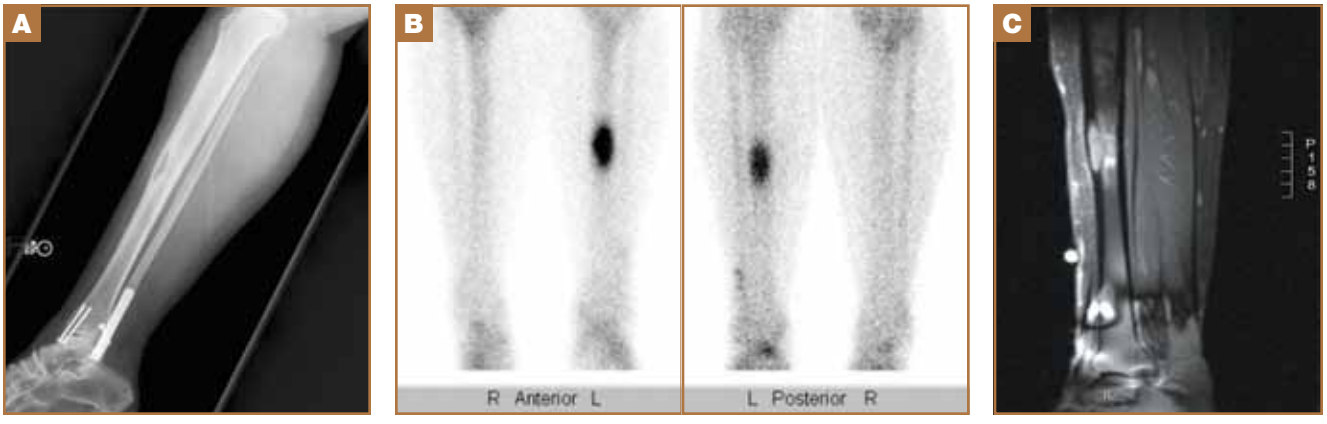
We report the case of a 56-year-old woman who had severe leg pain and whose radiographs initially suggested metastatic carcinoma, lymphoma, osteogenic sarcoma, or adamantinoma. Results of multiple biopsies confirmed a diagnosis of RDD.

The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 56-year-old woman with diabetes and hyperthyroidism presented with a 6-month history of increasing left leg pain. It included pain at rest and occasional night pain, as well as forcing her to ambulate with a walker. She had no other symptoms or appreciable lymphadenopathy. She had a surgical history of multiple obstetric procedures, appendectomy, cholecystectomy, and a left ankle fracture repair. Left lower extremity musculoskeletal and neurological examinations were

Figure 1. (A) Anteroposterior radiograph of left leg shows 6×31×8-mm osteolytic lesion of anterior tibial cortex without sclerotic margins. (B) Bone scan shows distinct focus of increased uptake in left tibia. There were no other abnormalities in axial or appendicular skeleton. (C) T_1-weighted sagittal magnetic resonance imaging of left leg shows lesion, centered within midtibial diaphysis, associated with pronounced cortical thinning and focal cortical breakthrough.



Authors' Disclosure Statement: The authors report no actual or potential conflict of interest in relation to this article.

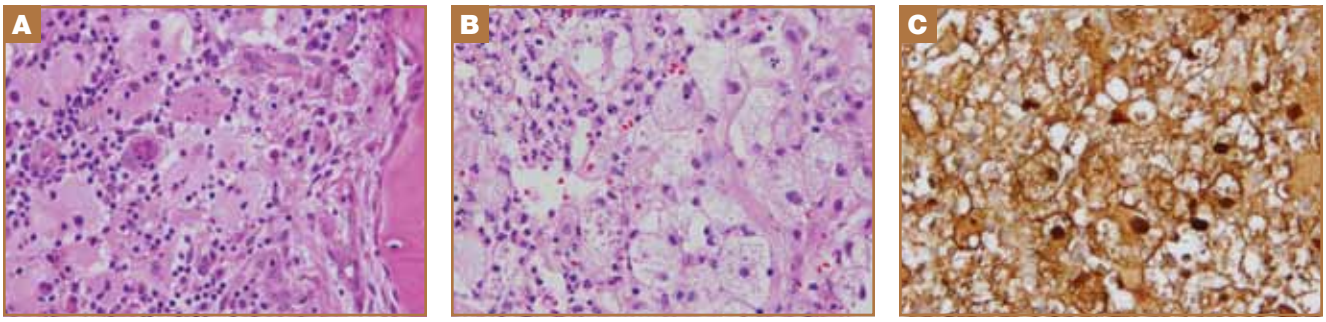


Figure 2. (A) Histiocytes contain intact inflammatory cells within abundant eosinophilic cytoplasm. Bone spicule at extreme right is unremarkable (hematoxylin-eosin, original magnification ×60). (B) Histiocyte cytoplasm appears foamier or more granular in this field. Enlarged nuclei and nucleoli are appreciated (hematoxylin-eosin, original magnification ×60). (C) S-100 stain shows intense positive nuclear and cytoplasmic staining of histiocytes.

normal, with the exception of tenderness to palpation over the mid-left tibia. There was no palpable mass or overlying skin changes on the leg.

Radiographs showed a lytic, destructive lesion without a sharp border, in the left anterior tibial cortex in the midshaft. There was no surrounding soft-tissue mass. Bone scan revealed isolated left tibial uptake. Magnetic resonance imaging showed a cortically based lesion extending into the medullary cavity and involvement of the anterior tibial cortex (**Figures 1A-C**). Computed tomography of the chest, abdomen, and pelvis was performed for preoperative evaluation of systemic nodes.

The initial presentation was concerning for metastatic carcinoma, lymphoma, osteogenic sarcoma, or adamantinoma. Fluoroscopy-guided open biopsy of the lesion was performed. The biopsy specimen consisted of a 2.2-cm aggregate of tissue containing a solid proliferation of inflammatory cells composed primarily of lymphocytes and plasma cells, with a minor population of neutrophils. Admixed with these was a population of larger histiocytes containing a moderate amount of eosinophilic and foamy cytoplasm, slightly enlarged nuclei, and distinct, rounded macronucleoli. Histiocyte cytoplasm contained 1 or more inflammatory cells without cell degradation—so-called emperipolesis (**Figures 2A-C**). These cells showed diffuse cytoplasmic staining with vimentin, CD68 antibodies, and both cytoplasmic and nuclear staining with S-100 antibody. Staining was completely negative with pan-cytokeratin and CD1a antibodies. Histochemical stains for fungi and acid-fast bacilli were also negative. Based on these findings, patient was diagnosed with RDD.

Two weeks after the biopsy, the patient returned to clinic with severe left leg pain, which continued to impair ambulation. She elected to proceed with definitive curettage, bone grafting of the left tibia, and prophylactic internal fixation. A 4×3.4×1.8-cm aggregate of tan-pink tissue was removed during surgery, which, along with a repetition of most of the stains that had been performed on the biopsy specimen, confirmed the diagnosis of RDD.

The patient recovered well, resumed full-time work, and was able to ambulate normally, without the use of a walker. Two years after surgery, she was pain-free, and there were no radiographic signs of local recurrence.

Discussion

More than 400 patients with RDD have been identified in the Yale University School of Medicine registry since the disease was first characterized in 1969.[1] 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.[1,6,7] About 20% of these cases presented with extranodal involvement alone.[1] Presentation of RDD with a solitary bone lesion is exceptionally rare and typically occurs in children. Almost all cases with bone involvement are associated with lymphadenopathy and disease of other organs.[1,8-10] Similar presentations of bone RDD without lymphadenopathy have been described in the literature.[3,5,10-15] Solitary bone involvement without lymphadenopathy is an extremely rare clinical situation and has been reported in only a handful of cases.[11,16,17] Most cases of RDD involve the long bones, but there are reports of the condition affecting the skull, vertebral bodies, pelvis, phalanges, metacarpals, and ribs.[3,18] Overall, RDD of the bone without lymphadenopathy accounts for approximately 2% of all RDD cases.[19]

On radiographs, RDD bone lesions typically appear multifocal, lytic, and intramedullary and have poor or sharp margins. Some lesions are sclerotic, particularly when healing. In most cases, there is no periosteal reaction with cortical defects.[5,11] Recent literature has suggested using fine-needle aspiration cytology to diagnose extranodal RDD without lymphadenopathy.[14,15] Signature histologic features of RDD include emperipolesis (lymphophagocytosis), or presence of intact lymphocytes within the cytoplasm of histiocytes and S100 protein positivity on immunostaining.[15,20] RDD is pathologically defined by a predominance of distinctive histiocytes with large round or oval vesicular nuclei, well-defined delicate nuclear membranes, and a single prominent nucleolus.[1] Other pathologic entities in the differential diagnosis of histiocytic proliferations in bone include granulomatous inflammation secondary to fungal or acid-fast

bacilli, eosinophilic granuloma of bone, and Erdheim-Chester disease. The positive S-100 staining and the negative staining for organisms and CD1a are useful in excluding these entities.

Most cases of RDD undergo spontaneous and complete remission.[1] The disease is seldom fatal, even in cases with poor prognostic indicators, including RDD involvement of the kidneys, lower respiratory tract, and liver; immunologic abnormalities; and anemia.[1,6] Despite its low incidence, RDD can be included in the differential diagnosis of unifocal and multifocal skeletal involvement caused by granulomatous diseases, infections, pseudogranulomatous lesions, and malignancy.[19] Recommended treatment, when possible, consists of clinical observation. As in our patient's case, in the rare case of vital organ compression or extranodal localization presenting with important clinical signs, surgical debulking may be necessary.[6]

Dr. Orvets is Resident Physician, Department of Orthopaedic Surgery, Boston University Medical Center, Massachusetts. Dr. Mayerson is Associate Professor of Orthopaedics and Program Director or Orthopaedics Residency Prgram, Ohio State University College of Medicine, Columbus; Director of Musculoskeletal Oncology, Arthur James Cancer Hospital at Ohio State University, Columbus; and Co-Director of Bone Tumor Clinic, Nationwide Children's Hospital, Columbus, Ohio. Dr. Wakely is Professor of Pathology and Otolaryngology, Ohio State University Wexner Medical Center, Columbus.

Address correspondence to: Joel L. Mayerson, MD, Arthur James Cancer Hospital at Ohio State University, 725 Prior Hall, 376 W 10th Ave, Columbus, OH 43210 (tel, 614-293-4420; fax, 614-293-3747; e-mail, joel.mayerson@osumc.edu).

Am J Orthop. 2013;42(9):420-422.

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