Orthopaedic Case of the Month

A 50-year-old Woman with Persistent Knee Pain

Brian E. Walczak DO, MPT, Dorothy M. Halperin MD,
Rabei W. Bdeir MD, Ronald B. Irwin MD

Received: 18 February 2011 / Accepted: 25 August 2011 / Published online: 20 September 2011
© The Association of Bone and Joint Surgeons® 2011

History and Physical Examination

A 50-year-old woman presented with a 7-month history of spontaneous onset of pain in her right knee. She complained of joint-line pain without instability that often radiated from medial to lateral and had become increasingly constant. On examination her knee was tender over only the medial joint line and she had a positive medial McMurray test. She had no signs of instability of the cruciate or collateral ligaments. There was no lymphadenopathy. She reported experiencing

several falls during the past year, aggravating her pain. She had no significant medical history and denied tobacco use.

Her chest radiograph was unremarkable, and comprehensive metabolic panel, serum and urine protein electrophoresis, c-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were within normal limits.

She was referred to our institution after imaging studies were performed for suspicion of a medial meniscus tear (Fig. 1, Fig. 2, Fig. 3).

Based on the history, physical examination, laboratory studies, and imaging studies, what is the differential diagnosis?

Imaging Interpretation

Initial AP and lateral radiographs were interpreted as normal. The oblique radiograph of her distal femur showed a subtle lucency with a sclerotic-appearing border involving the lateral femoral condyle measuring approximately 7×3 cm (Fig. 1). MR images confirmed a tear of the posterior horn of the medial meniscus. An incidental marrow signal abnormality was present in the lateral femoral condyle. On T1-weighted sequences the lesion was primarily hypointense compared with the surrounding marrow and approximately 7 cm in greatest length involving the lateral portion of the distal femur. T2-weighted fat saturated sequences showed a multilobulated mildly heterogeneous but primarily hyperintense lesion compared with the surrounding marrow that did not involve the subchondral bone or show cortical expansion (Fig. 2). A triple-phase Tc-99 bone scan revealed increased activity in the lateral distal right femur and medial aspect of the proximal right tibia on the delayed static images (Fig. 3).

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research* editors and board members are on file with the publication and can be viewed on request. Each author certifies that his or her institution approved the reporting of this case report, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

B. E. Walczak (✉), R. B. Irwin
Department of Orthopaedic Oncology, Mount Clemens Regional
Medical Center and Great Lakes Cancer Institute/Ted B. Wahby
Cancer Center, 1000 Harrington Street,
Mount Clemens, MI 48043, USA
e-mail: bewalczak@gmail.com

D. M. Halperin, R. W. Bdeir
Department of Pathology,
Mount Clemens Regional Medical Center,
Mount Clemens, MI, USA

Differential Diagnosis

Metastatic carcinoma
 Plasmacytoma/multiple myeloma
 Leukemia/lymphoma
 Langerhans cell histiocytosis (LCH)
 Erdheim-Chester disease (ECD)
 Rosai-Dorfman disease (RDD)
 Osteomyelitis

Open biopsy of the lateral femoral condyle was performed (Fig. 4).

Based on the history, physical examination, laboratory studies, imaging studies, and histologic picture, what is the diagnosis and how should the patient be treated?

Histology Interpretation

Microscopic examination under low power revealed a background of infiltrative mixed chronic inflammatory processes that destroyed the bone. The cells included histiocytes, plasma cells, and small lymphocytes (Fig. 5A). The large histiocytes had ample pale cytoplasm and some contained evidence of phagocytosis of lymphocytes and plasma cells (emperipolesis) (Fig. 5A). Immunohistochemical staining revealed proliferation of S-100, CD68, and CD163-positive histiocytes that were negative for

CD1a expression (Fig. 5B-D). CD138-positive immunostaining confirmed numerous plasma cells, and kappa and lambda chain studies showed the plasma cells were polyclonal. Lymphocytes stained strongly for CD3 and weakly for CD20 and CD79A without expression of CD5 and CD43.

Diagnosis

Primary Rosai-Dorfman disease of bone (RDD)

Discussion and Treatment

Diagnosis was made by histology and confirmed with immunostaining. Emperipolesis (histiocytic phagocytosis), best seen with a touch preparation of bone, was identified with routine hematoxylin and eosin staining. Proliferation of S-100, CD68, and CD163-positive histiocytes and negative CD1a expression confirmed the diagnosis (Fig. 5).

Microscopic evaluation was inconsistent with metastasis. The patient's normal urine and serum protein electrophoresis and CD138 immunostaining showed polyclonal plasma cells, which excluded plasmacytoma/myeloma. A mixed population of T and B lymphocytes and immunostaining excluded a chronic lymphocytic leukemia/small lymphocytic lymphoma. Immunostaining ruled out Langerhans cell histiocytosis (CD1A positive) and Erdheim-Chester disease (CD1a and S-100 negative) [1, 2, 6, 7, 9]. Infection was ruled out by normal serum testing, MRI showing no reactive edema or discrete fluid collection, and negative cultures.

RDD (sinus histiocytosis with massive lymphadenopathy) is a nonneoplastic condition of the lymph nodes in association with systemic inflammation [11], however, cases of primary osseous lesions have been reported [2]. Foucar et al. reviewed the extranodal manifestations of RDD [3]. Thirty-three of 423 patients had osseous involvement and nine had no associated lymphadenopathy [3]. Approximately 8% of extranodal cases involve bone with less than 1% having isolated osseous involvement [3]. Bone lesions may be seen anywhere, but the skull, femur, and tibia are the most commonly involved [2, 3, 9, 10]. The mean age of patients at onset is between 20 to 28 years [2, 3].

Patients typically present with unimproved pain after antecedent injury, but RDD may be found incidentally [1, 6, 7, 9]. Palpable pain and notable swelling are often apparent [2]. Lesions presenting in the axial skeleton might produce neurologic symptoms, whereas skull involvement might initially present with headache, neck pain, and seizure [2].

Fig. 1 A faint lytic lesion with surrounding sclerosis in the lateral femoral condyle is seen on the oblique radiograph of the distal femur.

Fig. 2A–C (A) The T2-weighted sagittal image shows a tear (arrow) of the medial meniscus. (B) The T1-weighted coronal image shows a somewhat heterogeneous but primarily low intensity lesion of the distal portion of the lateral femoral condyle without extension into the

subchondral bone. (C) A T2-weighted fat-saturated coronal image shows a multilobulated primarily hyperintense signal involving the lateral femoral condyle.

Radiographs commonly show a lytic medullary lesion, but a sclerotic border is not uncommon [1, 2, 6, 7, 9]. To our knowledge, all reported patients for whom a bone scan was reported showed increased uptake [6, 9]. Computerized tomography or MRI might help with evaluation of the extent of the lesion [6, 9].

RDD might be confused histologically with granulomatous disease or osteomyelitis [2]. Emperipolesis and S-100-positive histiocytes distinguish RDD from other mixed chronic inflammatory diseases [2, 4]. An adequate tissue sample might obviate a diagnostic delay or misdiagnosis [1, 2, 6, 7, 9].

The pathogenesis of RDD is unknown. Infection, genetic associations, and immune-mediated processes have

been postulated, but not substantiated [7–9, 12]. Others have suggested including RDD in the histiocytic spectrum of disorders (eg, LCH, ECD) because the disease findings are similar and variations in locations might help to explain the type of histiocytes involved [3, 6, 7]. Some studies support malignancy, infection, storage diseases, and histiocytic disorders in the initial differential diagnosis [1, 2, 6, 7, 9].

The disease course is unpredictable [2, 3] and no standard treatment approach has been established. Studies that have focused on the skeletal manifestations have documented high success rates with surgical resection or curettage [2, 10]. Demicco et al. reviewed 17 patients with primary bone disease who were treated surgically (eight

Fig. 3 The Tc-99 bone scan shows increased uptake of the lateral right distal femur.

Fig. 4 A postoperative AP radiograph shows the extent of the lesion and treatment after curettage and cementation.

with curettage, eight with resection, one with radiation then resection), with 11 patients having no evidence of disease (longest followup, 108 months) [2]. Pulsoni et al. reported success with surgical treatment in eight of nine patients [10]. An anecdotal report of extraosseous RDD remission with low-dose oral corticosteroid treatment exists [8], but to our knowledge, no available information pertains to primary osseous disease. Radiation therapy has proven less successful [7, 10]. Pulsoni et al. reported only three of nine patients treated with radiotherapy had resolution of their disease [10]. Furthermore, they suggested chemotherapy was ineffective [10]. Spontaneous regression also has been reported by Demicco et al. [2] and Pulsoni et al. [10], however, prognostic indicators that differentiate lesions that need to be treated from those that should be observed are not known.

The development of subsequent osseous lesions, recurrence, lymph node involvement, and external manifestations such as testicular involvement have been documented [2] and therefore, continued followup is important. Demicco et al. reported 21 of 32 (66%) patients had stable or no evidence of disease at followup and 11 of 32 (34%) had new or recurrent lesions develop [2]. Surveillance with imaging

Fig. 5A–D (A) A histologic section shows a substantial number of histiocytes with abundant cytoplasm and evidence of emperipolesis (arrow) (Stain, hematoxylin and eosin; original magnification, $\times 40$). (B) The histiocytes are CD1a negative (original magnification, $\times 20$).

(C) The S-100 protein immunostain shows positive staining of the histiocytes (original magnification, $\times 20$). (D) The histiocytes are also positive for CD163 (original magnification, $\times 20$).

or routine physical examination might help to identify future relapsing disease.

Consideration was given to an image-guided needle biopsy, but because of the broad differential diagnosis, we believed an open biopsy would improve the diagnostic yield. Treatment was discussed with the patient and she elected to undergo curettage and cementation owing to the advantages of immediate full weightbearing, reduced risk of postoperative fracture, and early identification of recurrence. An arthroscopic partial meniscectomy was performed secondary to persistent joint pain. The patient was asymptomatic 22 months after her initial biopsy.

Acknowledgments We thank Scott Dumas in multimedia services and Monroe Adams, DO in the Department of Pathology for help with preparation of the figures for this manuscript.

References

1. Chan KW, Chow YY, Ghadially FN, Stansfeld AG, Woo CH. Rosai-Dorfman disease presenting as spinal tumor: a case report with ultrastructural and immunohistochemical studies. *J Bone Joint Surg Am.* 1985;67:1427–1431.
2. Demicco EG, Rosenberg AE, Bjornsson J, Rybak LD, Unni KK, Nielsen GP. Primary Rosai-Dorfman disease of bone: a clinicopathologic study of 15 cases. *Am J Surg Pathol.* 2010;34:1324–1333.
3. Foucar E, Rosai J, Dorfman R. Sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): review of the entity. *Semin Diagn Pathol.* 1990;7:19–73.
4. Goel MM, Agarwal PK, Agarwal S. Primary Rosai-Dorfman disease of bone without lymphadenopathy diagnosed by fine needle aspiration cytology: a case report. *Acta Cytol.* 2003;47:1119–1122.
5. Komp DM. The treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease). *Semin Diagn Pathol.* 1990;7:83–86.
6. Loh SY, Tan KB, Wong YS, Lee YS. Rosai-Dorfman disease of the triquetrum without lymphadenopathy: a case report. *J Bone Joint Surg Am.* 2004;86:595–598.
7. Miyake M, Tateishi U, Maeda T, Arai Y, Sugimura K, Hasegawa T. Extranodal Rosai-Dorfman disease: a solitary lesion with soft tissue reaction. *Radiat Med.* 2005;23:439–442.
8. Oka M, Kamo T, Goto N, Nagano T, Hirayama Y, Nibu K, Nishigori C. Successful treatment of Rosai-Dorfman disease with low-dose oral corticosteroid. *J Dermatol.* 2009;36:237–240.
9. Patterson FR, Rooney MT, Damron TA, Vermont AI, Hutchison RE. Sclerotic lesion of the tibia without involvement of lymph

- nodes: report of an unusual case of Rosai-Dorfman disease. *J Bone J Surg Am.* 1997;79:911–916.
10. Pulsoni A, Anghel G, Falcucci P, Matera R, Pescarmona E, Ribersani M, Villiva N, Mandelli F. Treatment of sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease): report of a case and literature review. *Am J Hematol.* 2002;69:67–71.
 11. Rosai J, Dorfman RF. Sinus histiocytosis with massive lymphadenopathy: a newly recognized benign clinicopathological entity. *Arch Pathol.* 1969;87:63–70.
 12. Yetiser S, Cekin E, Tosun F, Yildirim A. Rosai-Dorfman disease associated with neurosensorial hearing loss in two siblings. *Int J Pediatr Otorhinolaryngol.* 2004;68:1095–1100.