

A Rare Case of Rosai-Dorfman Disease in Calcaneum and Study of Literature

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ABSTRACT

Background: Pain and osteolytic lesions on X-rays with non-specific changes on histopathology and negative culture are common scenarios; patients often treated with empirical antibiotics or anti-tuberculosis therapy (ATT), especially in regions where tuberculosis (TB) is endemic. The policy of "Diagnosis before treatment" should be the dictum in such cases. We report a rare case of Rosai-Dorfman disease (RDD) of calcaneum diagnosed by following these guidelines.

Case description: A 17-year-old female presented with left heel pain for 1 year. She was diagnosed with Brodie's abscess of calcaneum at another facility on imaging. Empirical antibiotics were started after debridement, as cultures were negative and histopathology was not done. Symptoms recurred in 2 months. At presentation, careful clinical evaluation, the site of tenderness was found to be 2–3 cm distal to the prior incision. MRI revealed a large lesion with post-contrast enhancement. CT-guided biopsy from an appropriate site at our facility was inconclusive as there were no signs of infection or malignancy. Subsequently, thorough debridement was done using a different incision excising the biopsy scar. Tissue cultures were negative. Histopathology showed areas of dense lymphohistiocytic infiltrate with lymphocytic emperipolesis within their cytoplasm. There were no granulomas. On immunohistochemical staining, the macrophages strongly expressed S100 but not CD1a. Accordingly, a diagnosis of RDD was made. The surgical site healed with an uneventful postoperative period. She was advised protected weight-bearing for 6 weeks. Pain resolved and no further treatment had to be given. The patient was asymptomatic at a 3-year follow-up and the radiograph showed complete consolidation of the cavity with no evidence of recurrence.

Conclusion: Primary intraosseous RDD is an unusual manifestation of a rare disease. Careful assessment of clinical details, inputs and help from imaging consultants, sending adequate tissue samples from appropriate sites for both culture and histopathology, and specialized staining techniques helped accurately diagnose this condition.

Clinical significance: The case highlights the challenges faced in diagnosing a lytic lesion in the foot and the importance of avoiding empirical medication before obtaining a diagnosis despite negative percutaneous image-guided biopsies.

Keywords: Brodie's abscess, Calcaneal osteomyelitis, Case report, Foot tumors, Heel pain, Histiocytosis, Immunohistochemical staining, Lytic, Osteoarticular tuberculosis-foot and ankle tuberculosis.

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BACKGROUND

The most common causes of pain with osteolytic lesions in the foot are Brodie's abscess and tuberculosis (TB) osteomyelitis, especially in India which has a high burden of TB.¹ Primary or secondary tumors with lytic lesions are extremely rare in foot and ankle. Very often, empirical antibiotics or anti-tuberculosis therapy (ATT) are initiated without deep tissue biopsy or if the biopsy shows non-specific changes and cultures are negative. Instead of initiating empirical therapy, the surgeons must re-evaluate the diagnostic process. If the team of treating surgeon, radiologist, and histopathologist are convinced that adequate representative sample of the diseased tissue has been procured, further studies like immunohistochemical (IHC) staining should be initiated. "Establishing a Diagnosis prior to treatment" should be the dictum in every case.

CASE DESCRIPTION

A 17-year-old female presented to our Orthopaedic Outpatient Department with left heel pain for 1 year, aggravated since past 3 months. The pain was intermittent in nature and increased on weight-bearing. It was not associated with any constitutional symptoms.

She was diagnosed with Brodie's abscess of the left calcaneum at another facility 1 year before presentation based on imaging (Fig. 1). She did not have any constitutional symptoms, prior history

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of Koch's or Koch's contact. Exploration and debridement was done, however tissue cultures were negative. Histopathology was not done. She was given 6 weeks of empirical antibiotics.

The symptoms recurred 2 months after surgery, with intermittent episodes of pain relieved with rest and pain killers. Initiation of ATT was also considered by the primary surgeon on account of recurrence of symptoms.



Figs 1A to C: Preoperative images before 1st surgery



Fig. 2: Clinical image showing area of tenderness distal to the previous scar

On presentation to our institute, a scar of previous surgery was noted along the posteromedial aspect of the ankle. Tibialis posterior tendon and posterior tibial artery pulsation were deep to the scar. Tenderness and minimal swelling were found to be distal to the scar along the calcaneum (Fig. 2). There was no warmth, redness or



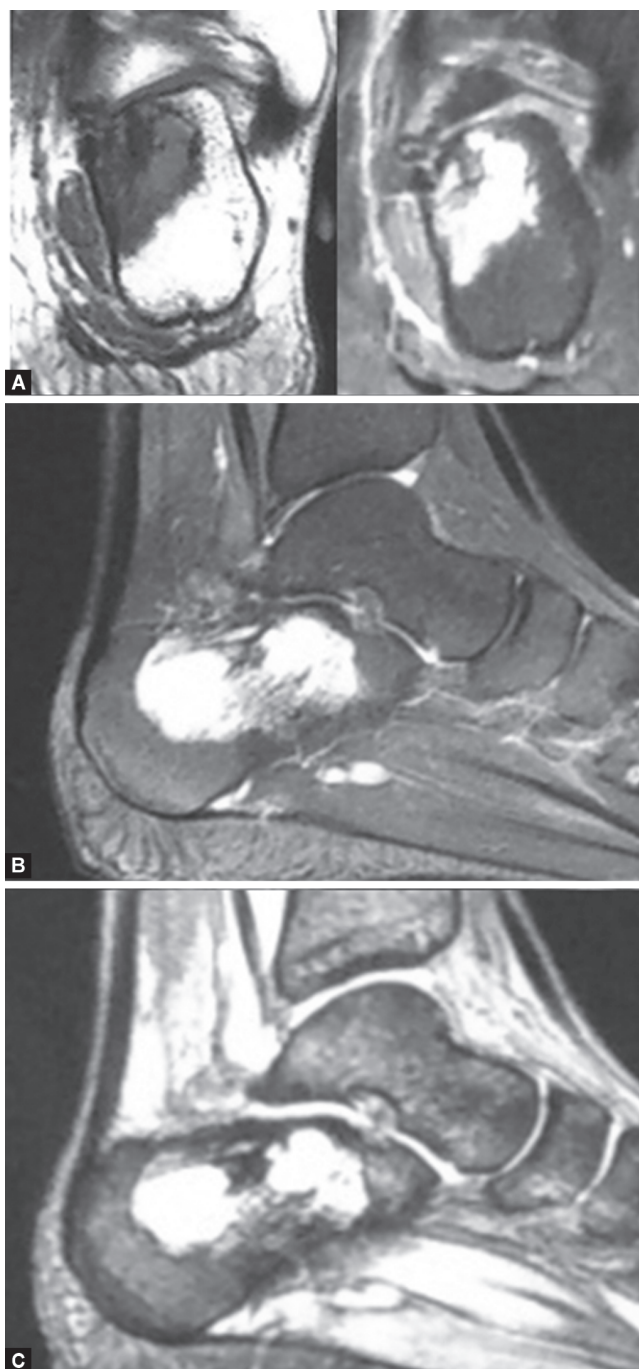
Fig. 3: Preoperative radiograph showing a lytic area in the calcaneum

discharging sinus. Ankle movements were painless and full. A digital radiograph showed an osteolytic lesion in the calcaneum (Fig. 3).

Contrast MRI done before presentation described a large necrotic cavity with postoperative changes in the left calcaneum. There was evidence of residual intraosseous lesion showing heterogeneous post-contrast enhancement with cortical defect and mild intraosseous edema (Fig. 4).

CT-guided biopsy at our institute revealed acute on chronic inflammation with negative tissue cultures. There was no evidence of malignancy or granulomas.

Having ruled out malignancy, the lesion was explored through a new incision 2 cm distal to the previous surgical scar overlying the site of maximum tenderness along the medial aspect of the



Figs 4A to C: Preoperative MRI images

calcaneum as there was no definitive diagnosis on cultures/histopathology. The cavity was scraped completely with adequate samples for frozen section, tissue cultures (bacterial, fungal, TB, TB gene Xpert), and histopathology (Fig. 5). Acute on chronic inflammation with granulation tissue was seen on frozen sections. There were no granulomas or malignant cells. All tissue cultures were negative.

Destruction of bone with moderately dense lymphohistiocytic infiltrate in the inter-trabecular spaces with fibrosis was seen on histopathology. There were areas of dense lymphohistiocytic infiltrate alternating with pale areas showing sheets of large macrophages with pale cytoplasm and small vesicular nuclei separated by lymphocytes and plasma cells with neutrophils. Some of the macrophages showed phagocytosis of intact lymphocytes-emperipolesis (arrow) (Fig. 6). There were no granulomas.

Further studies were conducted on the tissue samples by the histopathologist based on the pathological findings as described above. The macrophages strongly expressed S100 but not CD1a on IHC staining.

Accordingly, a diagnosis of Rosai-Dorfman disease (RDD) was made.

The surgical site healed with an uneventful postoperative period. She was advised protected weight-bearing for 6 weeks, her pain slowly disappeared. Patient refused bone grafting of the lytic cavity and was closely observed at 6 monthly intervals for signs of recurrence/pathological fracture. No further treatment was given.

The patient was asymptomatic at a 3-year follow-up (Figs 7 and 8). The radiograph showed complete consolidation of the cavity as compared to the postoperative radiographs with sclerosis representing walls of the original lytic lesion (Fig. 9). There was no evidence of recurrence.

DISCUSSION

Lytic lesions of the foot are most commonly infective. MRI and deep tissue biopsy remain the gold standard in identifying the causative microorganism as well as differentiating between an infective and tumorous lesion.²

This patient was apparently diagnosed with Brodie's abscess based on MRI, but without characteristic features of subacute osteomyelitis like "Penumbra" sign. Though characteristic, it is not pathognomic.³ The penumbra sign represents a rim of vascularized granulation tissue around a bone abscess cavity that has a higher T1 signal intensity than the cavity itself.

The patient was operated on for the same and treated with empirical antibiotics as the deep tissue cultures were negative and samples were not sent for histopathology. However, the symptoms recurred.



Figs 5A to C: Intraoperative images

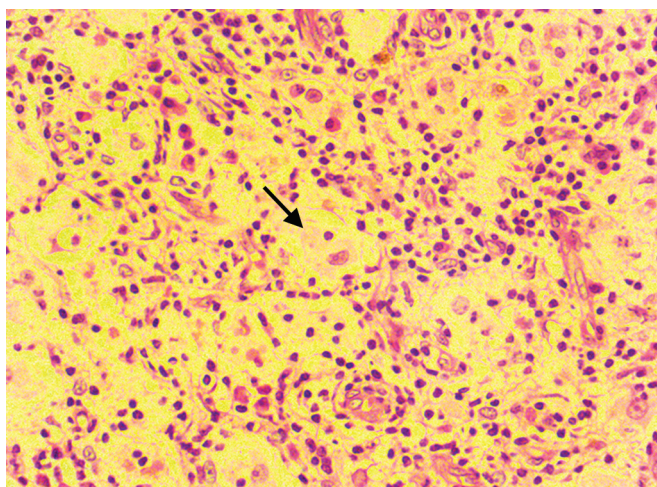
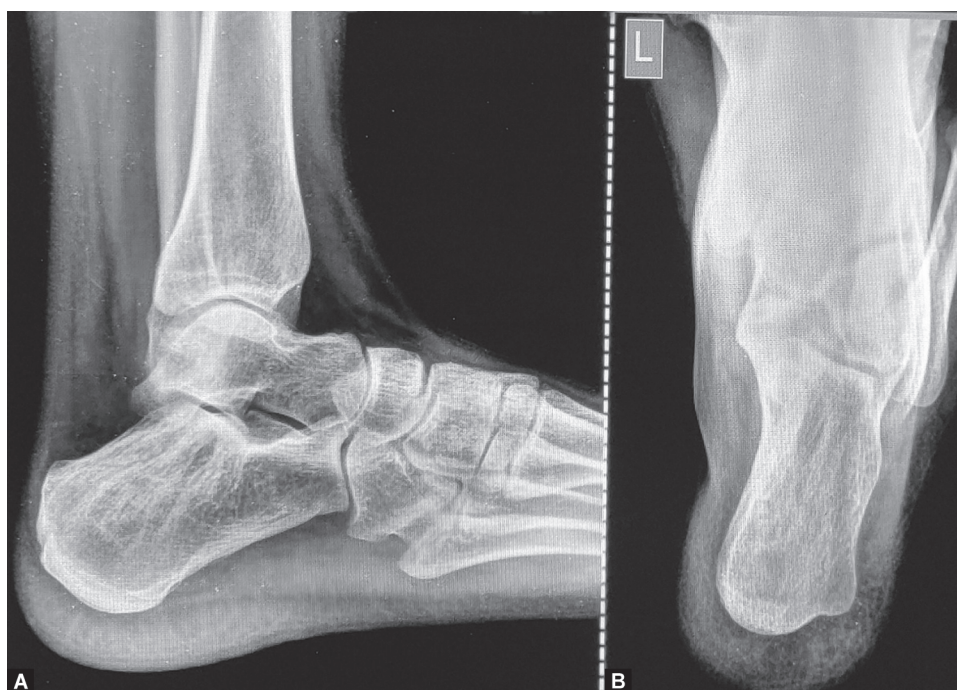


Fig. 6: Histopathology images



Fig. 7: Clinical image at a 3-year follow-up



Figs 8A and B: X-ray at a 3-year follow-up

The most common differential diagnoses of Brodie's abscess are benign and malignant tumors.³ The calcaneus is a rare location for primary tumors. Most clinicians are unfamiliar with calcaneal tumors, resulting in delayed or missed diagnosis.^{4,5} The radiographic and MRI features of tumors may overlap with osteomyelitis in the younger patient, among other differential diagnostic possibilities.⁶

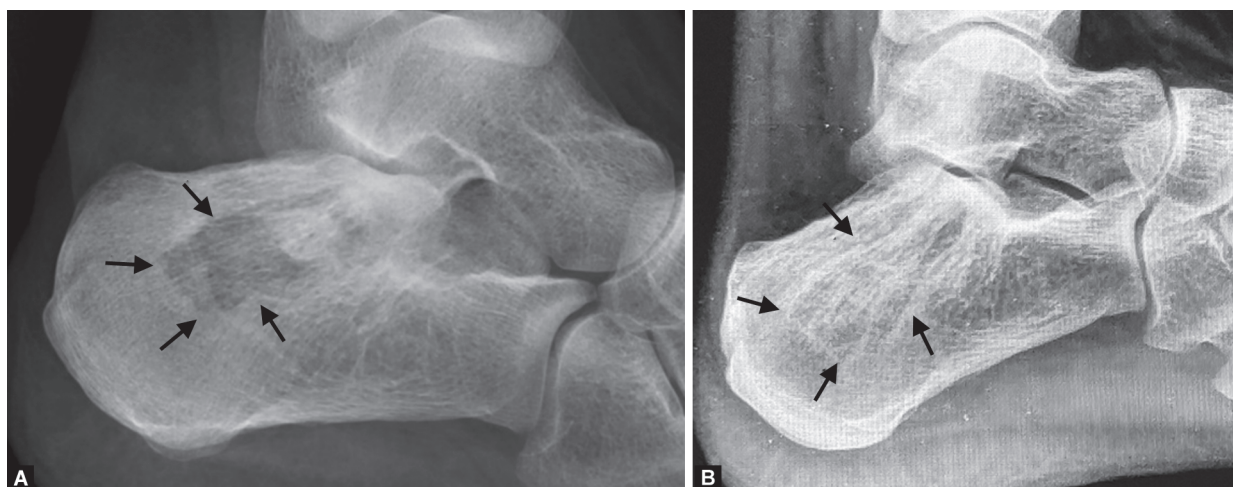
Moreover, the imaging manifestations of intraosseous RDD are not specific. Radiographs show a lytic appearance with variably defined margins ranging from sclerotic to permeative.⁶ Cortical thinning and focal breakthrough, as seen in our case are common.

Sending tissue for histopathology in the first surgery could have helped diagnose RDD at an earlier stage. However, CT-guided biopsy at our center also missed the diagnosis, highlighting the fact that a tumor may not have the diagnostic cells all across the lesion. Biopsy of the correct area within a lesion is essential to avoid

missing the primary pathology. A dense inflammatory infiltrate may be more prevalent within the lesion than the characteristic histiocytes leading to sampling error and complicating histologic diagnosis from percutaneous biopsy specimens.⁶ If RDD or any other tumor is contemplated in the differential, care must be taken to obtain adequate tissue for diagnosis during any percutaneous biopsy attempt.

The patient presented to us when she was advised ATT at another facility. We insisted on attempts (percutaneous and open) to diagnose the lesion and this perseverance helped diagnose this rare condition.

Rosai-Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a rare histiocytic non-malignant (benign) disorder typically presenting as painless cervical lymphadenopathy in adolescents and young adults.^{7,8} Constitutional symptoms and laboratory signs of inflammation



Figs 9A and B: Comparative X-ray showing consolidation of a lytic cavity

may exist but are not seen in all cases. Histiocytes in RDD exhibit emperipolesis, the non-destructive phagocytosis of lymphocytes and erythrocytes, which is the hallmark of the disease and required for diagnosis.^{9,10} Immunohistochemical staining of RDD histiocytes is positive for CD68, CD14, HLA-DR, fascin, CD163, and S100 and typically negative for CD1a, distinguishing it from Langerhans histiocytosis, a similar yet malignant pathology.

The clinical course of RDD is often benign, though lethal outcomes are also possible when associated with vital organ involvement.⁶ Extranodal involvement is common and may occur in >40% of patients, sometimes without associated lymphadenopathy.^{7,11} The most frequent affected extranodal sites include the skin, nasal cavity and paranasal sinuses, eye and orbit, and the central nervous system. Bone involvement occurs in <10% of cases.⁷

There are reports of primary RDD of the bone without lymphadenopathy as in our case; the largest series describes 15 cases.¹² But there is only one previous report of RDD with a solitary bony lesion in the calcaneus.¹²

Clinical presentation includes pain or swelling but bone lesions may also be an incidental finding. On radiographs, skeletal lesions are typically lytic and intramedullary,¹³ sometimes with surrounding sclerosis. Pure sclerotic lesions are rare.¹⁴ Due to the rarity of the disease, diagnosis, and treatment are challenging. There is no consensus treatment algorithm for primary RDD of bone. In general, most authors agree that asymptomatic cases do not require treatment and may spontaneously regress in as many as 80% of cases.⁶

Primary intraosseous RDD is not thought to pose a mortality risk with a focus on palliating sites of painful disease or preventing complications such as pathologic fracture. Bone grafting may be contemplated for large lytic cavities.

Based on the literature, surgery remains the most effective treatment modality for symptomatic osseous RDD, as most healed completely after curettage or resection.^{6,12} Similar outcome was seen in our case with complete consolidation of the cavity at a 3-year follow-up.

There is no consensus on disease surveillance and many patients are managed expectantly with further imaging obtained if symptoms recur or new symptoms develop.

Overall, the prognosis of primary intraosseous RDD is very good, the disease course is not aggressive and curettage or resection are generally effective for local control.¹²

CONCLUSION

Tumors of the foot are extremely rare. Non-specific symptoms and radiological features result in delayed diagnosis. A combination of good clinicoradiological assessment, sending adequate tissue samples from appropriate site for both culture and histopathology are the main stay for accurate diagnosis and further management.

Moreover, primary intraosseous RDD is an unusual manifestation of a rare disease. Accurate diagnosis rests on the identification of the characteristic large S-100 positive histiocytes that demonstrate prominent emperipolesis.

Knowledge of this uncommon entity may assist the clinicians to take appropriate treatment decisions.

CLINICAL SIGNIFICANCE

The case highlights the challenges faced in diagnosing a lytic lesion in the foot and the importance of avoiding empirical medication before obtaining a diagnosis despite negative percutaneous image-guided biopsies.

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