Ulcerating Nodule on the Foot

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A 59-year-old woman with a history of joint pain presented with a foot nodule that developed over the course of 2 years. Physical examination revealed a firm, mobile, mildly tender, 3-cm, deep red nodule on the dorsal aspect of the left foot (top [inset]) with an overlying central epidermal defect and thick keratinaceous debris. The remainder of the physical examination was unremarkable. Empiric treatments with oral antibiotics and intralesional corticosteroids were unsuccessful. Incisional biopsy was performed for histologic review, and tissue culture studies were negative.

THE BEST DIAGNOSIS IS:

a. epithelioid sarcoma
b. necrobiosis lipoidica
c. necrobiotic xanthogranuloma
d. perforating granuloma annulare
e. perforating rheumatoid nodule

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The authors report no conflict of interest.

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doi:10.12788/cutis.0494
**THE DIAGNOSIS:**

**Perforating Rheumatoid Nodule**

Perforating rheumatoid nodule (RN) is a variant of RN that demonstrates necrobiotic material extruding through the epidermis via the process of transepidermal elimination. The necrobiotic material contains fibrin and often harbors karyorrhectic debris. The pathogenesis of RN remains unclear; possible mechanisms include a small vessel vasculitis or mechanical trauma inciting a localized aggregation of inflammatory products and rheumatoid factor complexes. This induces macrophage activation, fibrin deposition, and necrosis. The majority of patients with RNs have detectable rheumatoid factor and anticyclic citrullinated protein in the blood. Rheumatoid nodules are the most common cutaneous manifestations of rheumatoid arthritis (RA) and will develop in 30% to 40% of RA patients. They typically are associated with advanced RA but may precede the onset of clinically severe RA in 5% to 10% of patients. Rheumatoid nodules generally range in size from 2 mm to 5 cm and are slightly more prevalent in men than in women. They present as firm painless masses typically on the extensor surfaces of the hands and olecranon process but can occur over any tendinous or ligamentlike structure. Perforating RNs are most common on areas subjected to pressure or repeated trauma, such as the sacrum.

The diagnosis usually is clinical; however, in cases of diagnostic uncertainty, RN can be distinguished by its histologic appearance. Rheumatoid nodules demonstrate granulomatous palisading necrobiosis with a central zone of highly eosinophilic fibrinoid necrobiosis surrounded by palisading mononuclear cells, and an outer zone of granulation tissue. There may be a mixed chronic inflammatory infiltrate predominantly composed of lymphocytes and histiocytes in the background.

Rheumatoid nodules typically do not require treatment; however, perforation is known to increase the risk for infection, and surgical excision generally is indicated for prophylaxis against infection, though nodules may recur in the excision area. Alternatively, disease-modifying antirheumatic drugs and intralesional corticosteroids may effectively reduce the size of RNs. The differential diagnosis for perforating RNs includes epithelioid sarcoma, perforating granuloma annulare, necrobiotic xanthogranuloma, and necrobiosis lipoidica.

Epithelioid sarcoma is a malignant soft tissue tumor typically found on the upper extremities of adolescent or young adult males. They usually present as hard tender nodules that commonly ulcerate. Epithelioid sarcoma makes up less than 1% of soft tissue sarcomas. Although rare, they present a diagnostic pitfall, as the histology may mimic an inflammatory palisaded granulomatous dermatitis similar to RN and granuloma annulare, thus a high index of suspicion is required to not overlook this aggressive malignancy. Histology is typified by nodular aggregates of epithelioid cells with abundant eosinophilic cytoplasm and often with central zones of necrosis (Figure 1). Epithelioid sarcoma displays immunoreactivity to cytokeratin, CD34, and epithelial membrane antigen, but loss of integrase interactor 1 expression. Cytologic abnormalities such as pleomorphism and hyperchromatism can be helpful in distinguishing between epithelioid sarcoma and RN.

Perforating granuloma annulare is a rare subtype of granuloma annulare that presents with flesh- to red-colored papules that develop central crust or scale. Perforating granuloma annulare may develop on any region of the body but...
has an affinity for the extensor surfaces of the extremities. It most frequently occurs in young women and rarely presents as a single lesion.\(^\text{10}\) Granuloma annulare typically is not associated with joint pain, and thus it differs from most cases of RNs. Histologically, it presents with an inflammatory palisading granuloma. There may be overlying epidermal thinning or parakeratosis, which can progress to perforation and extrusion of necrobiotic material. In comparison with RN, perforating granuloma annulare displays mucin deposition in the necrobiotic zones in lieu of fibrin (Figure 2).\(^\text{10,11}\)

Necrobiosis xanthogranuloma is a rare chronic form of non-Langerhans histiocytosis that characteristically presents with yellow or violaceous indurated plaques and nodules in a periorbital distribution. It often is associated with monoclonal gammopathy of IgG-κ. Lesions will ulcerate in 40% to 50% of patients.\(^\text{12}\) The mean age at presentation is in the sixth decade of life, and it is moderately predominant in females.\(^\text{13}\) Histopathology demonstrates palisading granulomatous formations with a lymphoplasmacytic infiltrate and zones of necrobiosis in the mid dermis extending into the panniculus. Characteristic histologic features that are variably present in necrobiotic xanthogranuloma but typically absent in RN include neutrophilic debris, cholesterol clefts, and Touton or foreign body giant cells (Figure 3).\(^\text{13}\)

Necrobiosis lipoidica is a rare chronic granulomatous disease characterized by well-demarcated, atrophic, yellow-brown plaques on the pretibial surfaces. It typically presents in the third decade of life in women, and most cases are associated with diabetes mellitus types 1 or 2 or autoimmune conditions.\(^\text{14}\) Necrobiosis lipoidica begins as asymptomatic papules that enlarge progressively over months to years. They can become pruritic or painful and often develop ulceration. Histopathology shows horizontal zones of palisading histiocytes with intervening necrobiosis. An inflammatory infiltrate containing plasma cells also may be present (Figure 4).

REFERENCES