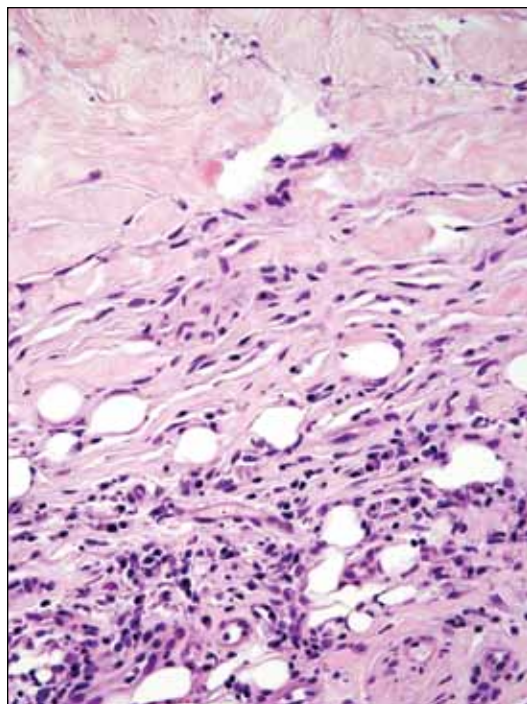


H&E, original magnification $\times 20$.



H&E, original magnification $\times 200$.

The best diagnosis is:

- a. cutaneous Rosai-Dorfman disease
- b. granuloma annulare
- c. juvenile xanthogranuloma
- d. necrobiosis lipoidica diabetorum
- e. necrobiotic xanthogranuloma

PLEASE TURN TO PAGE 265 FOR DERMATOPATHOLOGY DIAGNOSIS DISCUSSION

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The authors report no conflict of interest.

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Necrobiosis Lipoidica Diabeticorum

Necrobiosis lipoidica diabeticorum (NLD) is a rare granulomatous skin manifestation that is strongly associated with diabetes mellitus. Necrobiosis lipoidica diabeticorum is more common among females and occurs primarily in the pretibial area.¹ Necrobiosis lipoidica diabeticorum may clinically manifest as single or multiple lesions that begin as small red papules and progress into patches or plaques. Lesions ultimately develop into areas of yellowish brown atrophic tissue with central depression and telangiectasia. The etiology of NLD is not completely understood, but it is thought to be a presentation of diabetic microangiopathy.¹ Histologically, NLD demonstrates broad horizontal zones of necrobiosis with a surrounding inflammatory infiltrate that is principally composed of histiocytes but also may contain multinucleated giant cells, lymphocytes, and plasma cells (Figures 1 and 2). Occasionally, sarcoidal granulomas are seen in NLD. There also may be thickening of vessel walls and edema of the endothelial cells.¹

Cutaneous Rosai-Dorfman disease (RDD) is characterized by the presence of diffuse, large, pale histiocytes

(commonly known as Rosai-Dorfman cells) with an admixed infiltrate of lymphocytes and plasma cells (Figure 3).² Additionally, Rosai-Dorfman cells display emperipolesis. They stain positively for S-100 protein and CD68 and negatively for CD1a.² Clinically, cutaneous RDD has a myriad of manifestations but most commonly presents as cutaneous nodules that can be tender or pruritic. It also may be associated with systemic symptoms. Patients with cutaneous RDD often have an elevated erythrocyte sedimentation rate and concomitant anemia.²

Granuloma annulare demonstrates necrobiosis and palisaded granulomatous dermatitis similar to NLD; however, the necrobiotic foci in granuloma annulare usually are more focal than in NLD and typically are surrounded by well-formed palisaded granulomas. There also is an increase in dermal mucin (Figure 4), which can be highlighted on colloidal iron or Alcian blue staining.¹ Granuloma annulare also typically has scattered eosinophils rather than plasma cells as seen in NLD. Granuloma annulare also may present in an interstitial pattern, with scattered histiocytes,

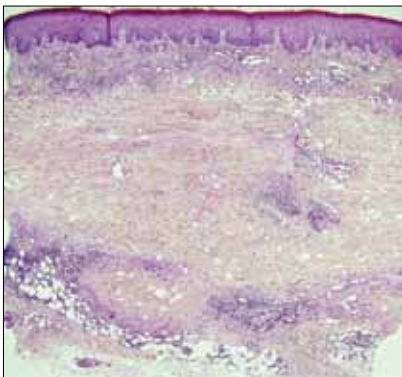


Figure 1. Broad horizontal arrangement of necrobiotic collagen with a surrounding inflammatory infiltrate of histiocytes and lymphocytes seen in necrobiosis lipoidica diabeticorum (H&E, original magnification $\times 20$).

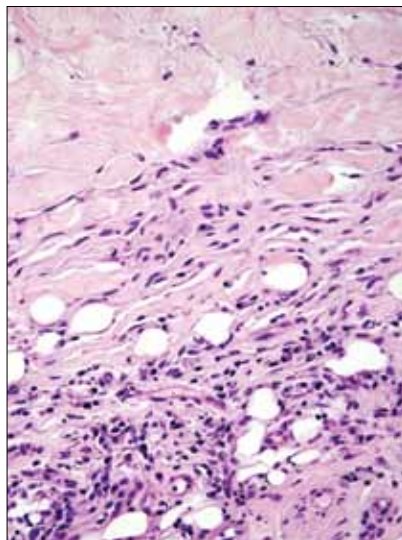


Figure 2. High-power view demonstrating lymphocytes and plasma cells at the inferior border of the necrobiotic collagen seen in necrobiosis lipoidica diabeticorum (H&E, original magnification $\times 200$).

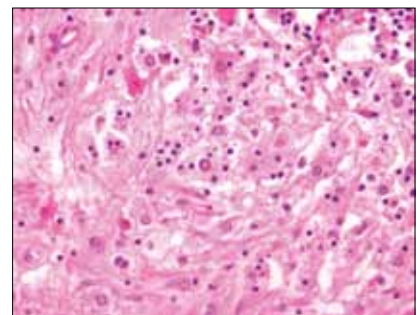


Figure 3. Sea of pale histiocytes with a patchy infiltrate of lymphocytes and plasma cells seen in cutaneous Rosai-Dorfman disease. Lymphocytes are seen within the cytoplasm of the histiocytes (emperipolesis) (H&E, original magnification $\times 200$).

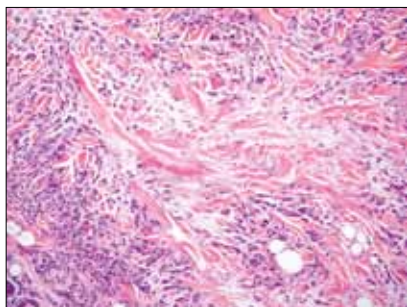


Figure 4. Necrobiotic collagen with abundant mucin surrounded by palisaded histiocytes, often with eosinophils characteristic of granuloma annulare (H&E, original magnification $\times 100$).

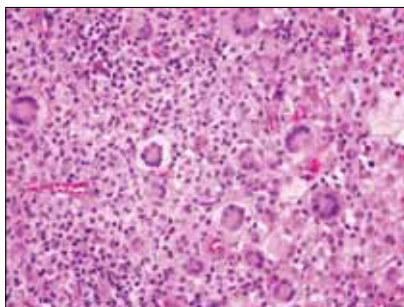


Figure 5. Touton giant cells and occasional eosinophils in a sea of histiocytes and lymphocytes characterize juvenile xanthogranuloma (H&E, original magnification $\times 200$).

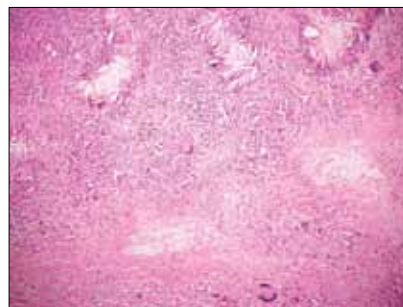


Figure 6. Necrobiotic xanthogranuloma is distinguished by the nodularity of the infiltrate, with necrobiotic collagen, palisaded histiocytes and giant cells, and the presence of cholesterol clefts (H&E, original magnification $\times 40$).

mucin, and eosinophils between collagen bundles. Granuloma annulare clinically presents as variably colored papules arranged in an annular pattern on the distal extremities but also can present as widespread papules or plaques.

Juvenile xanthogranuloma (JXG) is a benign condition typically seen in children that is characterized by the presence of 1 or more pink or yellow nodules, most commonly presenting on the head and neck. Histologically, JXG demonstrates a dermal collection of histiocytes, lymphocytes, eosinophils, and characteristic Touton giant cells, which contain nuclei that are arranged in a wreathlike pattern and exhibit peripheral xanthomatization (Figure 5).³ The histiocytes in JXG typically stain positive for CD68 and negative for S-100 protein, though occasional S-100–positive cases are reported.³

Necrobiotic xanthogranuloma presents as yellowish to brown plaques and nodules most commonly in the periorbital area. Necrobiotic xanthogranuloma

is strongly associated with monoclonal gammopathy, typically IgG κ monoclonal gammopathy. Necrobiotic xanthogranuloma is histologically similar to NLD but is distinguished by a nodular pattern of inflammation and the frequent presence of cholesterol clefts (Figure 6).⁴

REFERENCES

1. Kota SK, Jammula S, Kota SK, et al. Necrobiosis lipoidica diabetorum: a case-based review of literature. *Indian J Endocrinol Metab.* 2012;16:614-620.
2. Khoo JJ, Rahmat BO. Cutaneous Rosai-Dorfman disease. *Malays J Pathol.* 2007;29:49-52.
3. Cypel TK, Zuker RM. Juvenile xanthogranuloma: case report and review of the literature. *Can J Plast Surg.* 2008;16:175-177.
4. Inthasotti S, Wanitphakdeedecha R, Manonukul J. A 7-year history of necrobiotic xanthogranuloma following asymptomatic multiple myeloma: a case report. *Dermatol Res Pract.* 2011;2011:927852.