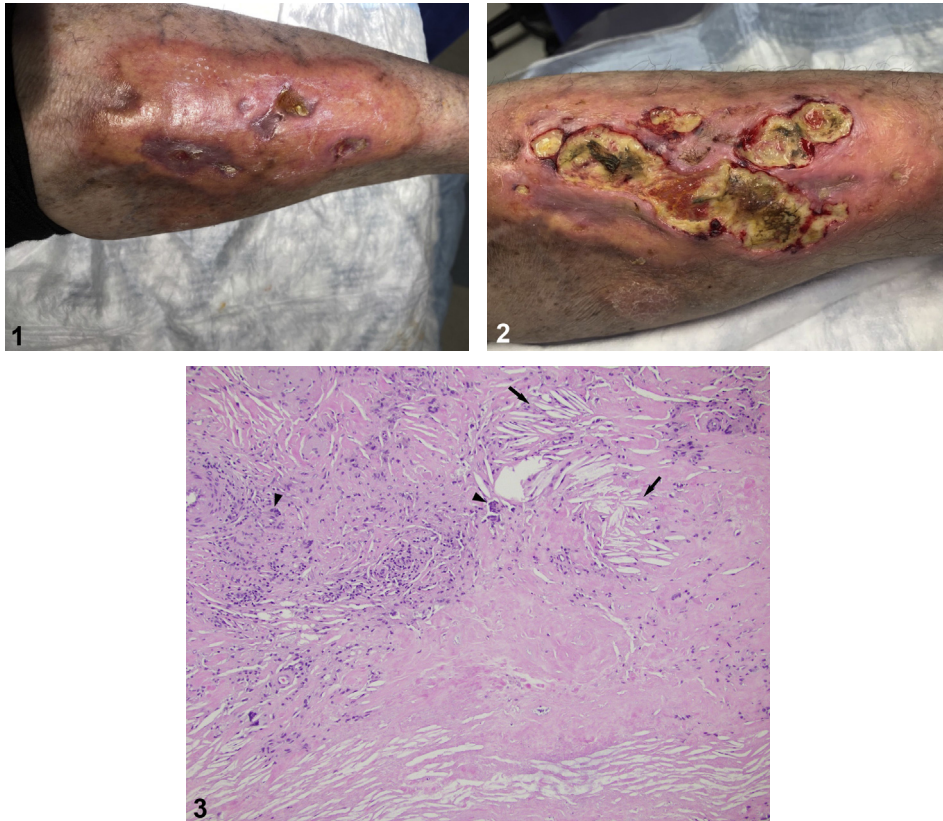


## Ulcerating yellow plaques on the legs



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A woman in her sixties with a 25-year history of multiple myeloma presented with yellow-orange plaques on her lower extremities. The plaques waxed and waned for years without associated pain or pruritus, but recently they became painful and ulcerated, thus prompting evaluation by dermatology (Figs 1 and 2). Treatments previously administered for multiple myeloma, including corticosteroids, stem cell transplantation, immunotherapy, and chemotherapy, had variable effects on the lesions. Treatment for multiple myeloma had been suspended because her disease was stable and there was concern that the skin progression could represent an adverse effect. An incisional biopsy for histologic examination was performed, with representative sections shown (Fig 3).

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**Question 1: What is the correct diagnosis?**

- A. Necrobiotic xanthogranuloma (NXG)
- B. Cholesterol emboli
- C. Necrobiosis lipoidica (NL)
- D. Pyoderma gangrenosum (PG)
- E. Plane xanthoma

**Answers:**

**A.** Necrobiotic xanthogranuloma (NXG) — Correct. NXG is a rare non-Langerhans cell histiocytosis, the histologic features of which include palisading necrobiotic granulomas of the dermis and subcutis, in addition to cholesterol clefts, foamy histiocytes, and prominent touton and bizarre, foreign body multinucleated giant cells (Fig 3).<sup>1</sup> Due to sampling error, this entity can be mistaken for NL when the cholesterol clefts and bizarre giant cells are not present.

**B.** Cholesterol emboli — Incorrect. Cholesterol emboli often occur abruptly and are seen in close association with arterial catheterization, prolonged anticoagulation, or acute thrombolytic therapy. Clinical features may include ulceration; however, livedo reticularis and cyanosis are more commonly observed. Histopathologic examination reveals cholesterol clefts limited to the intravascular space, in contrast to those observed in NXG.<sup>1</sup>

**C.** Necrobiosis lipoidica (NL) — Incorrect. Although NL and NXG may mimic each other clinically, the histopathologic findings of NL differ from those of NXG. Microscopic examination reveals layers of palisading granulomatous dermatitis alternating with degenerated collagen. The condition is thought to be associated with diabetes mellitus and abnormal glucose tolerance.<sup>2</sup>

**D.** Pyoderma gangrenosum (PG) — Incorrect. PG is a neutrophilic ulcerating condition associated with inflammatory bowel disease and hematologic disorders. Histopathologic examination reveals a sterile neutrophilic infiltrate. PG is a diagnosis of exclusion, and thus infection and other entities must be ruled out.<sup>3</sup>

**E.** Plane xanthoma — Incorrect. Plane xanthomas present as yellow to orange papules and plaques in various anatomic locations and typically do not ulcerate. They are associated with disorders of lipoprotein metabolism, and the anatomic distribution can be indicative of the underlying subtype.

The histopathologic findings vary, but the presence of foam cells is characteristic.<sup>1</sup>

**Question 2: Which of the following is the correct diagnosis most strongly associated with?**

- A. IgA monoclonal gammopathy
- B. IgG kappa monoclonal gammopathy
- C. Glucose intolerance
- D. Hyperlipoproteinemia
- E. Non-Hodgkin lymphoma

**Answers:**

**A.** IgA monoclonal gammopathy — Incorrect. PG has been found to be associated with hematologic disorders, including IgA monoclonal gammopathy, polycythemia vera, myelodysplastic syndrome, acute myeloid leukemia, chronic myeloid leukemia, and hairy cell leukemia.<sup>4</sup>

**B.** IgG kappa monoclonal gammopathy — Correct. NXG is associated with paraproteinemia, most commonly IgG monoclonal gammopathy (65%). There have been fewer associations with monoclonal gammopathy of the subtype IgG lambda (35%). Other hematologic, lymphoproliferative, and depositional disorders that have been associated include myelodysplastic syndrome, Waldenstrom macroglobulinemia, non-Hodgkin lymphoma, and amyloidosis.<sup>5</sup>

**C.** Glucose intolerance — Incorrect. Diabetes is present as comorbidity in 11% to 65% of patients affected by NL, hence the previous terminology, NL diabetorum.<sup>2</sup> Despite the association, control of blood glucose levels does not seem to affect the disease course.

**D.** Hyperlipoproteinemia — Incorrect. In addition to other subtypes, plane xanthomas may be associated with abnormal lipoprotein synthesis and metabolism. It is important to note that plane xanthomas may also occur in the setting of normal lipoprotein levels and may be associated with lymphoproliferative disorders, including IgG monoclonal gammopathy.<sup>1</sup>

**E.** Non-Hodgkin lymphoma — Incorrect. NXG may be associated with IgG lambda monoclonal gammopathy, non-Hodgkin lymphoma, Waldenstrom macroglobulinemia, amyloidosis, and myelodysplastic syndrome; however, IgG kappa monoclonal gammopathy is seen in a higher proportion of cases.<sup>5</sup>

**Question 3: Which is the most common site of involvement for the correct diagnosis?**

- A. Distal extremities
- B. Anterior shins
- C. Periorbital region
- D. Intertriginous areas
- E. Palmar creases

**Answers:**

**A.** Distal extremities — Incorrect. Cholesterol emboli typically occur in the setting of catheterization procedures or administration of thrombolytics. The condition classically presents as cyanosis, livedo reticularis, ulcers, or gangrene of the distal extremities and digits in the aforementioned clinical settings.<sup>1</sup>

**B.** Anterior shins — Incorrect. NL is typically characterized by atrophic and sometimes ulcerated yellow to brown plaques occurring in a pretibial distribution. In rare cases, lesions may occur on the scalp, face, or upper extremities.<sup>2</sup> NL was high on the clinical differential in this case, given the distribution of lesions. However, careful sampling and examination of the histopathology revealed findings consistent with NXG.

**C.** Periorbital region — Correct. NXG typically occurs in the periorbital region and presents as yellow papules and plaques. Other less frequent sites of involvement include the proximal extremities, trunk, and other facial areas. The anterior shins are an uncommon location for this entity, and thus,

clinicopathologic correlation was critical in coming to the correct diagnosis.

**D.** Intertriginous areas — Incorrect. Plane xanthomas can present in multiple different locations; however, those that are present within intertriginous areas and web spaces of the fingers are strongly associated with homozygous familial hypercholesterolemia.<sup>1</sup>

**E.** Palmar creases — Incorrect. Plane xanthomas occurring in the palmar creases are also known as xanthoma striatum palmare. This finding is considered nearly diagnostic of dysbetalipoproteinemia.<sup>1</sup>

**Abbreviations used:**

NL: necrobiosis lipoidica

NXG: necrobiotic xanthogranuloma

PG: pyoderma gangrenosum

**Conflicts of interest**

None disclosed.

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