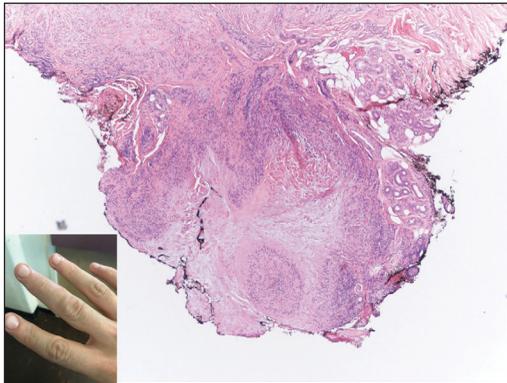


Multiple Nontender Subcutaneous Nodules on the Finger

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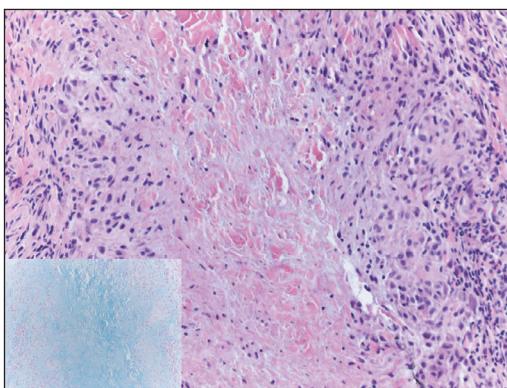
H&E, original magnification $\times 40$ (clinical presentation [inset]).

A 27-year-old man with a history of atopic dermatitis presented with asymptomatic bumps on the right third finger of several years' duration. He noted occasional trauma to the hands, including an incident to the affected finger requiring surgical repair. Physical examination revealed 15 to 20 firm, nontender, subcutaneous papulonodules on the right third digit, mostly on the dorsal and lateral aspects, without any apparent epidermal change. A 4-mm punch biopsy of a representative nodule was performed.

THE BEST DIAGNOSIS IS:

- epithelioid sarcoma
- necrobiosis lipoidica
- rheumatoid nodule
- subcutaneous granuloma annulare
- tophaceous gout

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H&E, original magnification $\times 100$ (Alcian blue pH 2.5, original magnification $\times 100$ [inset]).

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The authors report no conflict of interest.

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THE DIAGNOSIS:

Subcutaneous Granuloma Annulare

Subcutaneous granuloma annulare (SGA), also known as deep GA, is a rare variant of GA that usually occurs in children and young adults. It presents as single or multiple, nontender, deep dermal and/or subcutaneous nodules with normal-appearing skin usually on the anterior lower legs, dorsal aspects of the hands and fingers, scalp, or buttocks.¹⁻³ The pathogenesis of SGA as well as GA is not fully understood, and proposed inciting factors include trauma, insect bite reactions, tuberculin skin testing, vaccines, UV exposure, medications, and viral infections.³⁻⁶ A cell-mediated, delayed-type hypersensitivity reaction to an unknown antigen also has been postulated as a possible mechanism.⁷ Treatment usually is not necessary, as the nature of the condition is benign and the course often is self-limited. Spontaneous resolution occurs within 2 years in 50% of patients with localized GA.^{4,8} Surgery usually is not recommended due to the high recurrence rate (40%–75%).^{4,9}

Absence of epidermal change in this entity obfuscates clinical recognition, and accurate diagnosis often depends on punch or excisional biopsies revealing characteristic histopathology. The histology of SGA consists of palisaded granulomas with central areas of necrobiosis composed of degenerated collagen, mucin deposition, and nuclear dust from neutrophils that extend into the deep dermis and subcutis.² The periphery of the granulomas is lined by palisading epithelioid histiocytes with occasional multinucleated giant cells.^{10,11} Eosinophils often are present.¹² Colloidal iron and Alcian blue stains can be used to highlight the abundant connective tissue mucin of the granulomas.⁴

The histologic differential diagnosis of SGA includes rheumatoid nodule, necrobiosis lipoidica, epithelioid sarcoma, and tophaceous gout.² Rheumatoid nodules are the most common dermatologic presentation of rheumatoid arthritis and are found in up to 30% to 40% of patients with the disease.¹³⁻¹⁵ They present as firm, painless, subcutaneous papulonodules on the extensor surfaces and at sites of trauma or pressure. Histologically, rheumatoid nodules exhibit a homogenous and eosinophilic central area of necrobiosis with fibrin deposition and absent mucin deep within the dermis and subcutaneous tissue (Figure 1). In contrast, granulomas in SGA usually are pale and basophilic with abundant mucin.²

Necrobiosis lipoidica is a rare chronic granulomatous disease of the skin that most commonly occurs in young to middle-aged adults and is strongly associated with diabetes mellitus.¹⁶ It clinically presents as yellow to red-brown papules and plaques with a peripheral erythematous to violaceous rim usually on the pretibial area. Over time, lesions become yellowish atrophic patches and plaques that sometimes can ulcerate. Histopathology

reveals areas of horizontally arranged, palisaded, and interstitial granulomatous dermatitis intermixed with areas of degenerated collagen and widespread fibrosis extending from the superficial dermis into the subcutis (Figure 2).² These areas lack mucin and have an increased number of plasma cells. Eosinophils and/or lymphoid nodules occasionally can be seen.^{17,18}

Epithelioid sarcoma is a rare malignant soft tissue sarcoma that tends to occur on the distal extremities in younger patients, typically aged 20 to 40 years, often with preceding trauma to the area. It usually presents as a solitary, poorly defined, hard, subcutaneous nodule.

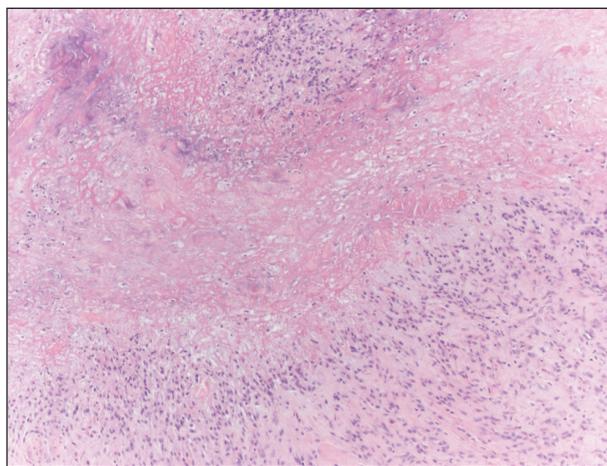


FIGURE 1. Rheumatoid nodule. Large areas of acellular collagen with pink fibrin centrally and basophilic cellular debris with a thin rim of histiocytes peripherally (H&E, original magnification $\times 100$).

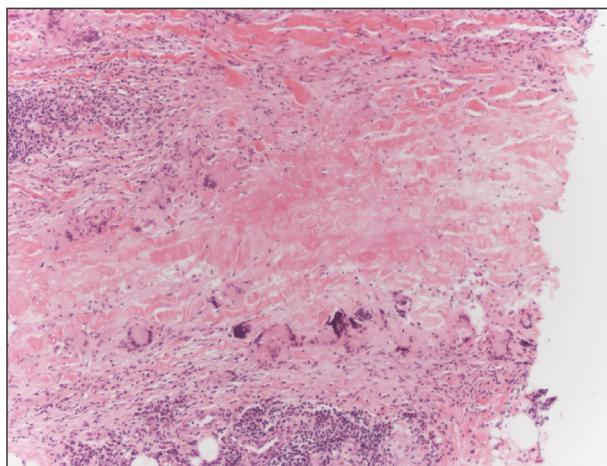


FIGURE 2. Necrobiosis lipoidica. Areas of acellular collagen surrounded by multinucleated histiocytes and plasma cells (H&E, original magnification $\times 100$).

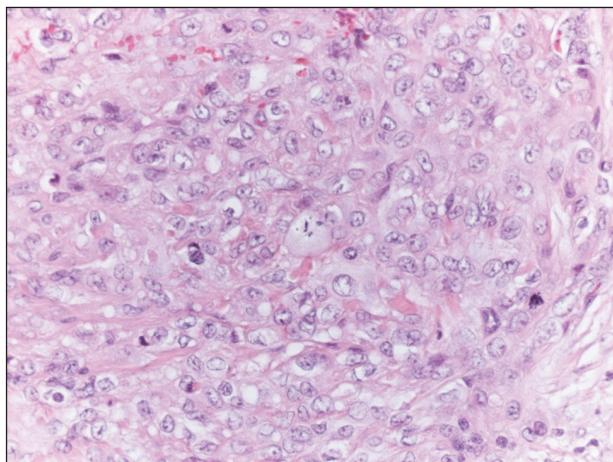


FIGURE 3. Epithelioid sarcoma. Epithelioid cells with hyperchromatic and pleomorphic nuclei as well as mitoses and slightly eosinophilic cytoplasm that resemble granulomatous inflammation (H&E, original magnification $\times 400$).

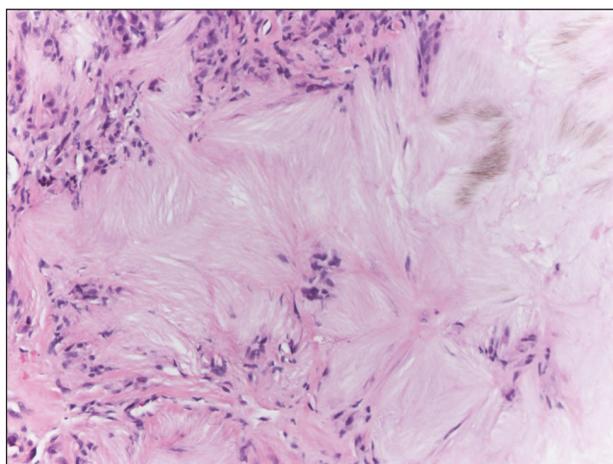


FIGURE 4. Tophaceous gout. Amorphous material with cleftlike spaces surrounded by histiocytes (H&E, original magnification $\times 200$).

Histologic analysis shows central areas of necrosis and degenerated collagen surrounded by epithelioid and spindle cells with hyperchromatic and pleomorphic nuclei and mitoses (Figure 3).² These tumor cells express positivity for keratins, vimentin, epithelial membrane antigen, and CD34, while they usually are negative for desmin, S-100, and FLI-1 nuclear transcription factor.^{2,4,19}

Tophaceous gout results from the accumulation of monosodium urate crystals in the skin. It clinically presents as firm, white-yellow, dermal and subcutaneous

papulonodules on the helix of the ear and the skin overlying joints. Histopathology reveals palisaded granulomas surrounding an amorphous feathery material that corresponds to the urate crystals that were destroyed with formalin fixation (Figure 4). When the tissue is fixed with ethanol or is incompletely fixed in formalin, birefringent urate crystals are evident with polarization.²⁰

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