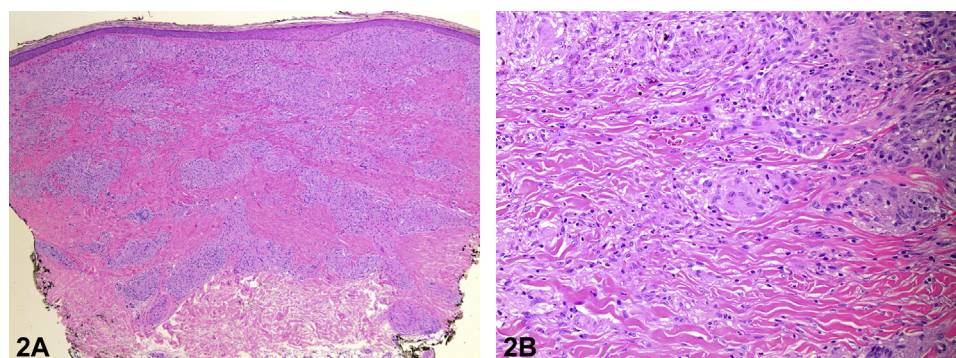


Papules developing in an old tattoo



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A 42-year-old woman presented with a 4-year history of mildly pruritic papules confined to the red ink of a tattoo that had been placed 20 years earlier on the lateral aspect of her right leg (Fig 1). Her medical history was significant for pulmonary sarcoidosis diagnosed about the time the papules appeared and glaucoma. Oral azathioprine 150 mg daily was being used to treat the pulmonary sarcoidosis. The physical examination revealed several 2- to 3-mm dermal papules confined to the red ink of a tattoo without confluent involvement. A 4-mm punch biopsy specimen was obtained from one of the papules (Fig 2, A and B).

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Question 1: What is the most likely diagnosis?

- A. Atypical acid-fast bacilli
- B. Red ink tattoo reaction (cinnabar)
- C. Cutaneous sarcoidosis
- D. Pseudolymphoma
- E. Squamous cell carcinoma

Answers:

A. Atypical acid-fast bacilli — Incorrect. The patient had no history of swimming or handling contaminated water that would be suggestive of swimming pool/fish tank granuloma. The tattoo was placed 20 years before the appearance of the papules, arguing against atypical acid-fast bacilli-contaminated ink.¹ Acid-fast bacilli staining was negative.

B. Red ink tattoo reaction (cinnabar) — Incorrect. Although granulomatous foreign body reactions to cinnabar are well reported, the papules in our patient appeared at about the same time as pulmonary sarcoidosis appeared, suggesting a unified cause. In addition, if this were an allergic hypersensitivity reaction to cinnabar, we would expect to see confluent inflammation throughout the entire area of red ink, not discrete papules as seen in our patient.

C. Cutaneous sarcoidosis — Correct. Cutaneous sarcoidosis arising in well-healed scars or old tattoos with the onset of pulmonary sarcoidosis is well described.^{2,3} The biopsy specimen revealed islands of naked epithelioid granulomas with a slight admixture of lymphocytes throughout the dermis that is typical of cutaneous sarcoidosis. Although cutaneous sarcoidosis in a tattoo most commonly involves several or all colors of ink, the restriction to 1 color in a tattoo cannot rule out the diagnosis of sarcoidosis.

D. Pseudolymphoma — Incorrect. Discrete dermal papules confined to red ink would be unusual in pseudolymphoma. Rather, plaque-like involvement of the entire red inked area would be expected. In addition, the dense infiltrate including eosinophils typical of pseudolymphoma was not seen in this case.

E. Squamous cell carcinoma — Incorrect. Our patient's Fitzpatrick skin type (V) and lack of sun damage argue against the diagnosis of a nonmelanoma skin cancer. In addition, there were no nests of atypical, glassy, squamous epithelial cells seen

extending from the epidermis into the dermis to suggest squamous cell carcinoma.

Question 2: What is the pathophysiologic explanation for this phenomenon?

- A. Immunologic reaction
- B. Infection/inoculation
- C. Malignant degeneration
- D. Trauma
- E. Delayed type IV hypersensitivity

Answers:

A. Immunologic reaction — Correct. Sarcoidosis is an exaggerated immune response to exogenous or autoantigenic stimuli. Although the pathophysiologic mechanism of sarcoidosis arising in tattoos is not fully understood, one proposed explanation is that a specific antigen in the tattoo pigment may drive a cell-mediated immune response characteristic of granuloma formation in predisposed individuals.^{3,4} Arguing against this explanation is the lack of confluent involvement in the red portion of the tattoo. The red area of the tattoo in which the papules appeared could also represent an immunocompromised district.⁴ The same mechanism that causes cutaneous sarcoidosis to appear in well-healed scars could be potentiated in the area of cinnabar tattoo ink. An unknown immunologic trigger is likely because both pulmonary sarcoidosis and localized cutaneous sarcoidosis occurred at the same time. Immunologic triggers described in other patients include vaccination, hepatitis C, interferon therapy, and sun exposure.⁵

B. Infection/inoculation — Incorrect. This would be the pathophysiologic explanation for atypical acid-fast bacilli infection of tattoos. Infection occurs when water containing the organism enters through a break in the skin, including inoculation by a tattoo artist from contaminated ink. This did not occur here.

C. Malignant degeneration — Incorrect. This would be the pathophysiologic explanation for squamous cell carcinoma, which is not seen in this case.

D. Trauma — Incorrect. There was no history of trauma to this site before the appearance of the papules within the tattoo, which had been placed decades before.

E. Delayed type IV hypersensitivity — Incorrect. Delayed type hypersensitivity reactions mediated by a T cell response are likely responsible for the majority of tattoo reactions. This type of response can lead to granulomatous or lichenoid inflammation or pseudolymphoma.

Two months later, this patient suddenly developed a low-grade fever and 2- to 4-cm tender, erythematous swollen areas on the shins. There was no scarring or atrophy.

Question 3: What is the most likely diagnosis?

- A.** Erythema nodosum
- B.** Necrobiosis lipoidica
- C.** Nodular vasculitis
- D.** Pretibial myxedema
- E.** Factitial disease

Answers:

A. Erythema nodosum — Correct. Of the nonspecific manifestations of sarcoidosis, erythema nodosum is the most common. It is a hypersensitivity reaction in fat septae, but the pathophysiologic basis of this condition in sarcoidosis is unknown. It manifests as tender, erythematous subcutaneous nodules, most often on the anterior tibia. It can be accompanied by fever, malaise, and polyarthralgia.

B. Necrobiosis lipoidica — Incorrect. This condition is associated with diabetes mellitus and presents with atrophy, which was not seen in this patient.

C. Nodular vasculitis — Incorrect. Nodular vasculitis involves medium-sized arteries in the reticular dermis and can appear much like the nodular swellings of erythema nodosum. It is not associated with sarcoidosis.

D. Pretibial myxedema — Incorrect. Pretibial myxedema is the result of the accumulation of glycosaminoglycans in the dermis. It is most commonly associated with Graves disease. It is typically asymptomatic and is characterized by swelling and induration of the lower legs. It is not associated with sarcoidosis.

E. Factitial disease — Incorrect. This would be a consideration if the nodules in the tattoo were thought to be of factitial origin. Histopathology for factitial disease would be nonspecific with acute inflammation and scattered erythrocytes.

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