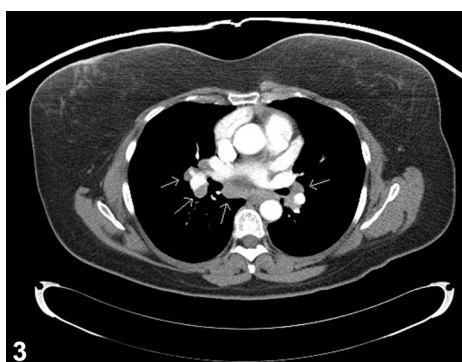
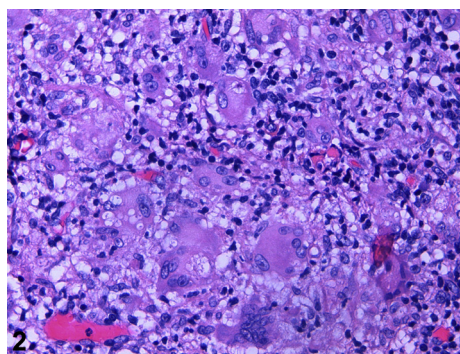
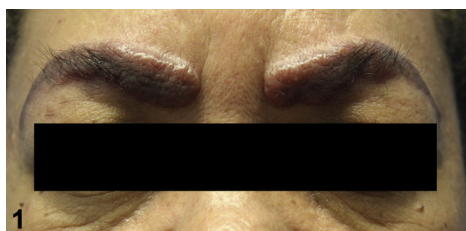


## Three-dimensional eyebrows



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A 53-year-old woman presented with a 3-month history of progressive thickening and pruritus in both eyebrows, which she had tattooed 11 years ago, with no systemic symptoms. Cutaneous examination found bilateral indurated erythematous-violaceous plaques (Fig 1). Skin biopsy found non-necrotizing epithelioid cell granulomas, without microorganisms (Fig 2). Image and laboratory tests found the following results: elevated angiotensin converting enzyme level of 76.3 IU/L (normal, 12–50 IU/L), a widened mediastinum with bilateral hilar enlargement in a chest radiograph that corresponded to adenopathies in the computed tomography, showing also bilateral pulmonary nodules (Fig 3). The following tests were negative or normal: pulmonary function tests, ophthalmologic examination, tuberculin skin test, and electrocardiogram.

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**Question 1: Which is the most likely diagnosis?**

- A. Tuberculosis
- B. Sarcoidosis
- C. Foreign body reaction
- D. Tuberculoid leprosy
- E. Atypical mycobacterial infections

**Answers:**

- A. Tuberculosis – Incorrect. Skin biopsy did not show the presence of necrotizing epithelioid cell granulomas and neither of microorganisms.<sup>1</sup>
- B. Sarcoidosis – Correct. Clinical, histologic, and imaging outcomes suggest sarcoidosis.<sup>1</sup>
- C. Foreign body reaction – Incorrect. It does not explain the systemic manifestations.<sup>1</sup>
- D. Tuberculoid leprosy – Incorrect. Skin biopsy did not show the presence of necrotizing epithelioid cell granulomas located along the course of nerves and neither of microorganisms.<sup>1</sup>
- E. Atypical mycobacterial infections – Incorrect. Skin biopsy did not show the presence of necrotizing epithelioid cell granulomas and neither of the microorganisms.<sup>1</sup>

The presence of granulomas in tattoos may suggest the following differential diagnoses: sarcoidosis, foreign body reaction, tuberculosis, and tuberculoid leprosy. Other dermatoses should also be considered such as deep fungal and atypical mycobacterial infections, although these are less common. Unlike mycobacterial infections, sarcoidal granulomas are often noncaseating, and up to nearly 90% do not show lymphocytic infiltrate at the periphery, named thereafter *naked granulomas*. Microbial stains and fresh tissue cultures may be useful to rule out an infectious origin, which were both negative in our patient that along with the histopathologic findings suggested sarcoidosis. Although foreign body reactions may have similar histopathologic features to sarcoidosis, systemic manifestations would not be explained by the first diagnosis.<sup>1</sup>

**Question 2: Select the correct answer in relation to granulomatous reactions in tattoos:**

- A. The presence of nonnecrotizing epithelioid cell granulomas confined to the tattoo supports the foreign body reaction diagnosis, so no other tests are required.

B. The presence of pigment inside epithelioid cells supports the foreign body reaction diagnosis, so no other tests are required.

C. There are no clear data regarding whether scar sarcoidosis (including tattoos) is associated with systemic disease or rather has a favorable prognosis.

D. Elevated ACE levels are specific enough for use as a diagnostic test for sarcoidosis.

E. In contrast to sarcoidal granulomas, tuberculoid granulomas may not appear in foreign body reactions.

**Answers:**

A. The presence of nonnecrotizing epithelioid cell granulomas confined to the tattoo supports the foreign body reaction diagnosis, so no other tests are required – Incorrect. The presence of nonnecrotizing epithelioid cell granulomas confined to the tattoo does not rule out sarcoidosis so other tests are required.<sup>2</sup>

B. The presence of pigment inside epithelioid cells supports the foreign body reaction diagnosis, so no other tests are required – Incorrect. The presence of pigment inside epithelioid cells does not rule out sarcoidosis, so other tests are required.<sup>2</sup>

C. There are no clear data regarding whether scar sarcoidosis (including tattoos) is associated with systemic disease or rather has a favorable prognosis – Correct. There is no clear evidence about the prognosis of scar sarcoidosis.<sup>3</sup>

D. Elevated ACE levels are specific enough for use as a diagnostic test for sarcoidosis – Incorrect. ACE levels are not specific enough for use as a diagnostic test for sarcoidosis.<sup>4</sup>

E. In contrast to sarcoidal granulomas, tuberculoid granulomas may not appear in foreign body reactions – Incorrect. Tuberculoid granulomas have been reported in tattoos.<sup>2</sup>

The presence of nonnecrotizing epithelioid cell granulomas confined to the tattoo or pigment inside epithelioid cells does not rule out sarcoidosis. Therefore, nonnecrotizing granulomatous reaction in tattoos should be further investigated to assess the possibility of a systemic involvement.<sup>2</sup> The recommended initial screening in suspected diagnosis of sarcoidosis includes chest radiograph, pulmonary function tests, electrocardiogram and echocardiogram, laboratory tests (including calcium, creatinine, urea nitrogen, ACE levels, liver function enzymes,

and blood cell count), urine analysis, ophthalmologic examination, and tuberculin skin test. ACE is produced by epithelioid cell granulomas, and 60% of patients with sarcoidosis have increased levels. Elevations higher than 50% the upper limit of normal are highly suggestive of sarcoidosis, but ACE levels are not specific enough for use as a diagnostic test.<sup>4</sup> There are no clear data in relation to the prognosis of scar sarcoidosis (which includes tattoo sarcoidosis), as several investigators have reported a higher incidence of organ involvement, whereas others claim a better outcome. Other cutaneous sarcoidosis variants, such as erythema nodosum, have a favorable prognosis and spontaneous resolution of skin lesions. However, lupus pernio is associated with chronic disease and sarcoidal organ involvement.<sup>3,5</sup> Finally, tuberculoid granulomas could be found in permanent tattoos, as some pigments induce this kind of chronic reaction.<sup>2</sup>

**Question 3. Which is the first-line of treatment in this case?**

- A. Topical glucocorticoids
- B. Systemic glucocorticoids
- C. Methotrexate
- D. Antimalarial agents
- E. Tetracyclines

**Answers:**

- A. Topical glucocorticoids — Correct. Because of normal pulmonary function tests, only topical glucocorticoids were initiated as a symptomatic treatment for eyebrow pruritus.<sup>3,6</sup>
- B. Systemic glucocorticoids — Incorrect. No systemic glucocorticoids were needed at the time of diagnosis or in the follow-up, as pulmonary function test results were normal and imaging findings in lungs resolved spontaneously.<sup>3,6</sup>

C. Methotrexate — Incorrect. Same explanation as answer B.<sup>3,6</sup>

D. Antimalarial agents — Incorrect. Same explanation as answer B.<sup>3,6</sup>

E. Tetracyclines — Incorrect. Same explanation as answer B.<sup>3,6</sup>

Treatment is not mandatory in all patients, because it can remain stable or even remit spontaneously. Treatment is recommended when there is organ involvement that may adversely affect quality of life.<sup>3,6</sup> In cutaneous sarcoidosis, treatment is usually necessary in patients with cosmetically disfiguring or symptomatic skin lesions.<sup>6</sup> Topical or intralesional corticosteroids are the first-line treatments. Systemic corticosteroids are preferred in rapidly disfiguring skin disease or in generalized distribution of skin lesions. Second-line treatments are used in nonresponsive patients or as corticosteroid-sparing agents, and these options include antimalarial agents, methotrexate, tetracyclines, thalidomide, and biologic anti-tumor necrosis factor agents such as adalimumab or infliximab.<sup>3,6</sup>

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