Pruritic papules in a longstanding tattoo

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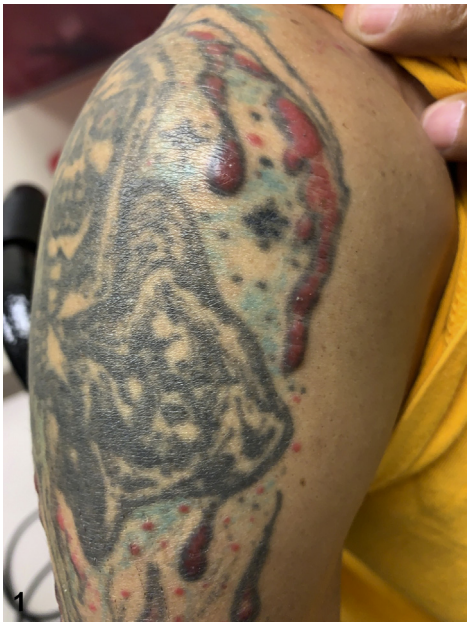

A 51-year-old man presented to clinic with extremely pruritic dermal papules within the red-inked areas of a tattoo on his right shoulder placed thirty years previously. He had a history of metastatic renal cell carcinoma treated with 4 cycles of ipilimumab and nivolumab, followed by single-agent nivolumab, which he was receiving on presentation. On examination, the patient had erythematous papules localized within the red-inked areas of the tattoo on his right shoulder (Fig 1), as well as pink dermal papules on his left eyebrow. Computed tomography of the chest/abdomen showed multiple enlarged lymph nodes. Skin biopsies demonstrated granulomatous dermatitis.

Question 1: What is the most likely cause of this patient's presentation?

A. *Mycobacterium fortuitum* infection

B. Mercuric sulfide hypersensitivity

C. Immunotherapy-associated reaction

D. Metastatic renal cell carcinoma

E. Hypertrophic scarring

Answers:

A. *Mycobacterium fortuitum* infection — Incorrect. *M. fortuitum* infection occurs weeks to months after tattoo administration and would demonstrate signs of infection such as redness, swelling, pain, and pustules. Acid-fast stain would be positive, and

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presence of *M. fortuitum* can be demonstrated by tissue culture. While it is reasonable to send for cultures, infection is likely not the primary cause of this patient's lesions arising decades later.

B. Mercuric sulfide hypersensitivity — Incorrect. Delayed-type hypersensitivity reactions to mercuric sulfide in red tattoo ink occur days to months after tattoo placement and likely would not demonstrate 30 years later. Histology would show pigment containing histiocytic macrophages, exogenous red pigment deposition, and foreign body granulomas. Red tattoo ink granuloma has been reported independently and in association with systemic sarcoidosis.[1,2] This patient had nontattoo areas of involvement and lymphadenopathy that favor systemic sarcoidosis.

C. Immunotherapy-associated reaction — Correct. Sarcoidosis is a rare immune-related adverse event secondary to immune checkpoint inhibitors such as anti-CTLA-4 and anti-PD-1 therapies.[3] This patient has sarcoidosis with secondary involvement in his tattoo 30 years after placement likely provoked by nivolumab, an anti-PD-1 immunotherapy. Histology would show well-formed, noncaseating granulomas with negative tissue cultures.

D. Metastatic renal cell carcinoma — Incorrect. Clinical examination was inconsistent with cutaneous metastases, and the patients have no other cutaneous areas of involvement. Histology would demonstrate dermal lobules of large clear cells with vascular stroma.

E. Hypertrophic scarring — Incorrect. Hypertrophic scars typically occur weeks to months after the initial injury, and histology would reveal increased collagen and fibroblasts.

Question 2: What workup is required for this patient?

A. No further workup is needed, proceed with intralesional triamcinolone

B. Culture and empirically treat for mycobacterial infection

C. Perform a workup for sarcoidosis

D. Obtain flow cytometry and positron emission tomography scan

E. Restaging of renal cell carcinoma

Answers:

A. No further workup is needed, proceed with intralesional triamcinolone — Incorrect. Red ink tattoo granuloma can represent skin involvement of sarcoidosis or delayed hypersensitivity granulomatous reaction. This patient requires workup for systemic sarcoidosis given the nontattoo areas of cutaneous involvement and history of immunotherapy. Hypertrophic scars can be treated with intralesional triamcinolone without further workup; however, this would demonstrate increased collagen bundles on histology.

B. Culture and empirically treat for mycobacterial infection — Incorrect. Mycobacterial infection would occur soon after tattoo administration. While it is reasonable to perform tissue cultures at the time of presentation, empiric treatment for infection is not warranted.

C. Perform a workup for sarcoidosis — Correct. Sarcoidosis is a systemic disease that can involve any organ, and evaluation of organ involvement is important for diagnosis and treatment. This patient's presentation correlated with his immunotherapy course and was recognized as an immune-related adverse event. A review of his imaging and evaluation for systemic sarcoidosis would be appropriate upon its discovery in the skin.

D. Obtain flow cytometry and positron emission tomography scan — Incorrect. Cutaneous lymphoma would require flow cytometry and positron emission tomography/computed tomography for staging and to enable distinction between primary and secondary cutaneous lymphoma. The histologic presentation lacked features of cutaneous lymphoma, such as epidermotropism, atypical lymphocytes, or monoclonality.

E. Restaging of renal cell carcinoma — Incorrect. Clinical examination and histology were not consistent with cutaneous metastases, and there was no evidence of metastatic progression to warrant preemptive restaging.

Question 3: A review of a recent bone metastasis surgical resection reveals incidental findings with similar histology. He also had suspected lymph node involvement but was asymptomatic without other visceral organ involvement. He had a good response to immunotherapy. What would be the next best course of action?

A. Recommend holding immunotherapy

B. Start hydroxychloroquine and monitor on immunotherapy

C. Start triple antibiotic therapy for mycobacterial infection

D. Laser ablation of tattoo

E. Systemic steroids

Answers:

A. Recommend holding immunotherapy — Incorrect. In advanced immune-related adverse events, this is appropriate; however, the patient was asymptomatic and his immunotherapy was effectively treating his malignancy. Holding immunotherapy would be preemptive at this time.

B. Start hydroxychloroquine and monitor on immunotherapy — Correct. The patient had an immune-related adverse event that required treatment but did not mandate interruption of immunotherapy. Interdisciplinary discussion would be important, as metastatic disease assessment can be challenging in the setting of sarcoidosis and may complicate restaging. In this case, the patient responded well to intralesional triamcinolone for the tattoo granuloma and hydroxychloroquine 200 mg daily. He has remained on immunotherapy without increasing toxicity and a continued response of his renal cell carcinoma.

C. Start triple antibiotic therapy for mycobacterial infection — Incorrect. Mycobacterial infection would have occurred weeks to months after initial tattoo administration, and this patient did not have evidence of mycobacterial infection on biopsy or tissue culture.

D. Laser ablation of tattoo — Incorrect. The patient did not have an extensive hypersensitivity reaction to the red tattoo ink that required tattoo removal, but rather had sarcoidal involvement of the tattoo ink. Tattoo ink removal would not resolve the patient's sarcoidosis.

E. Systemic steroids — Incorrect. Systemic steroids should be reserved for symptomatic or progressive sarcoidosis, as corticosteroids reduce the immunotherapy response rate and worsen progression-free and overall survival.[4] Given the limited skin and lymph node involvement without systemic organ disease, hydroxychloroquine and serial intralesional triamcinolone along with clinical monitoring would be most appropriate.

Conflicts of interest

None disclosed.

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