

Cutaneous Sarcoidal Granulomas: A Case Report of Pembrolizumab-Associated Dermatological Manifestations

Fatima Khan B.S.¹, Kristina Collins M.D.², Brett Keeling M.D.³

¹ Dell Medical School, Austin, TX

² Austin Skin, Austin, TX

³ Department of Internal Medicine, Division of Dermatology, Dell Medical School, Austin, TX

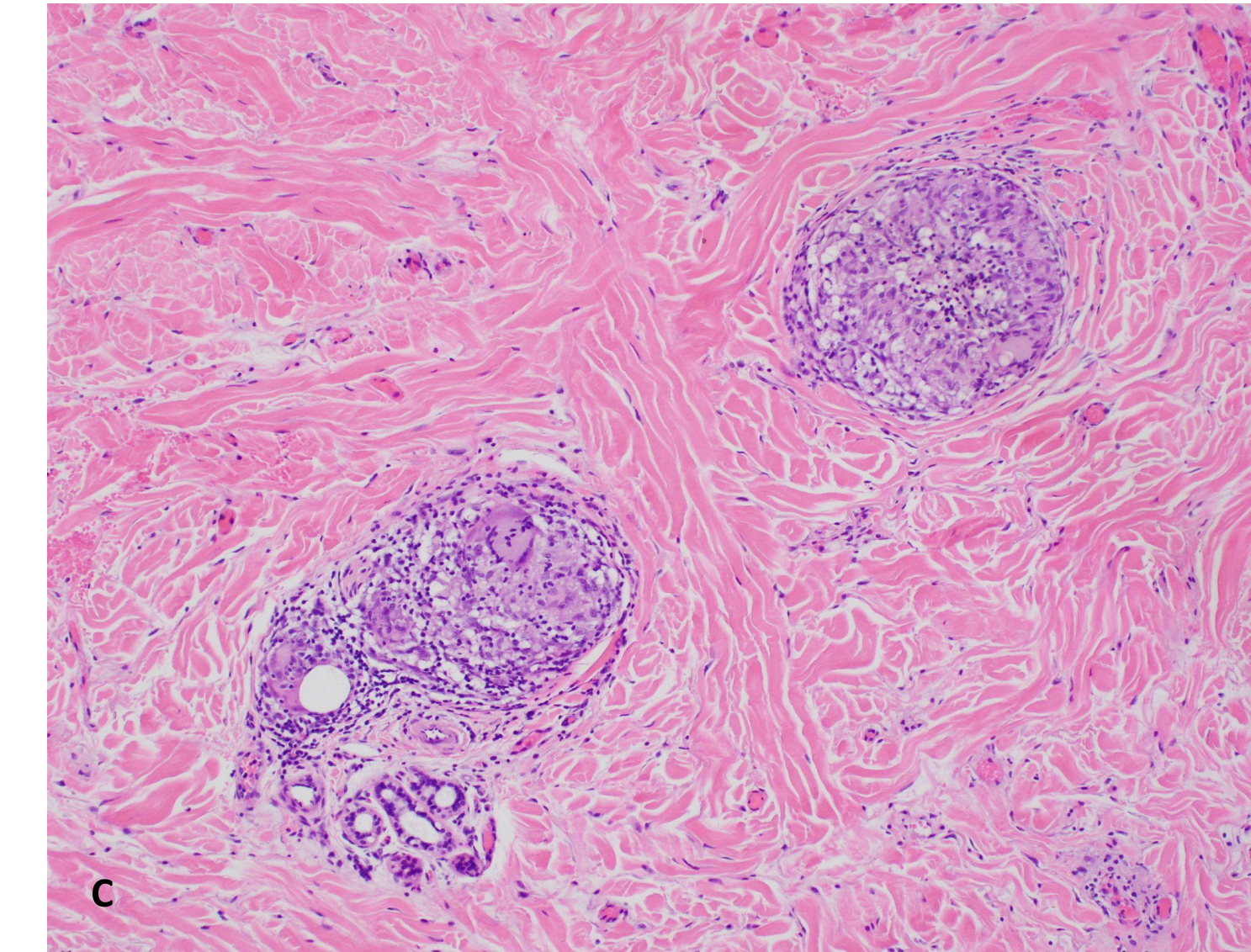
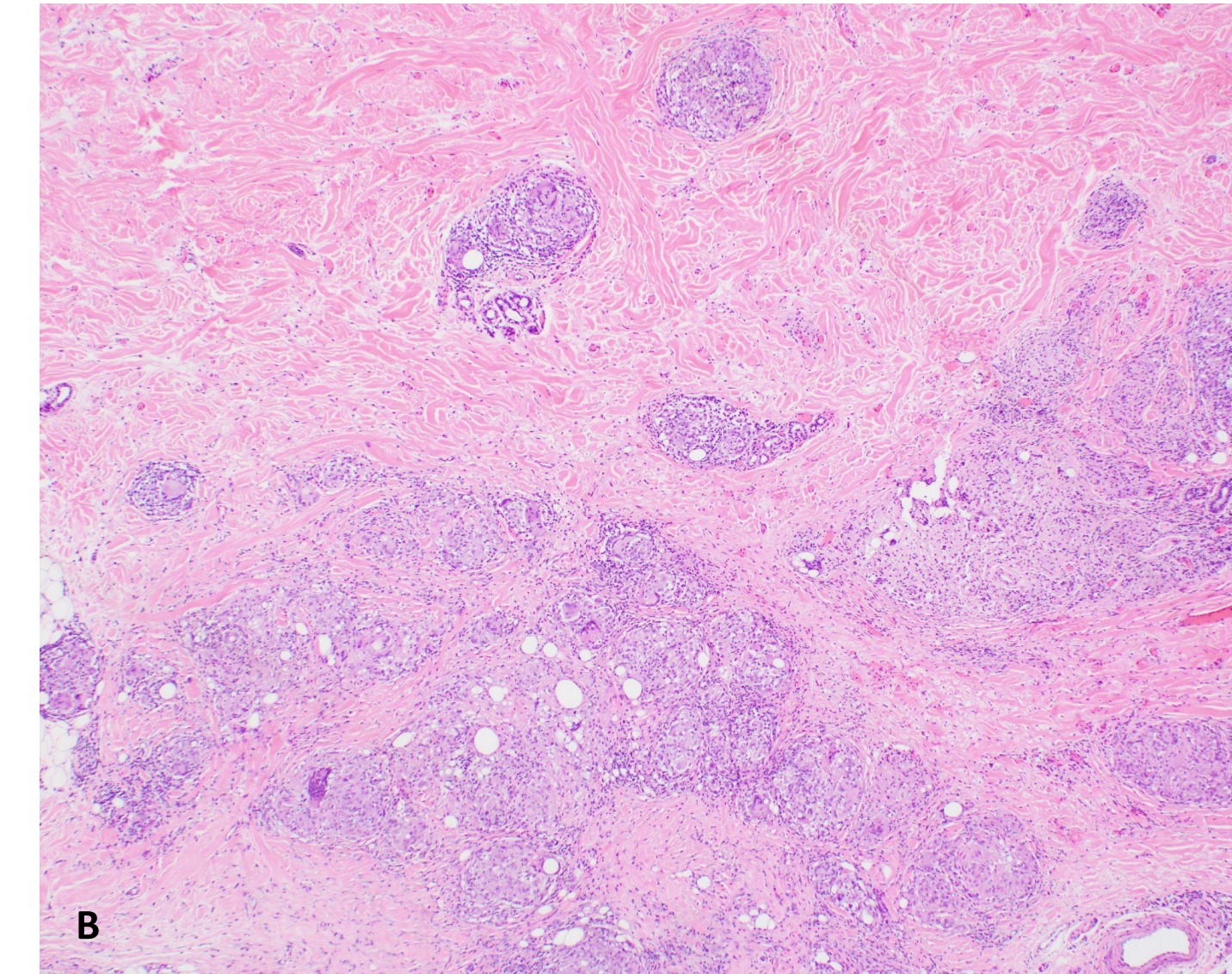
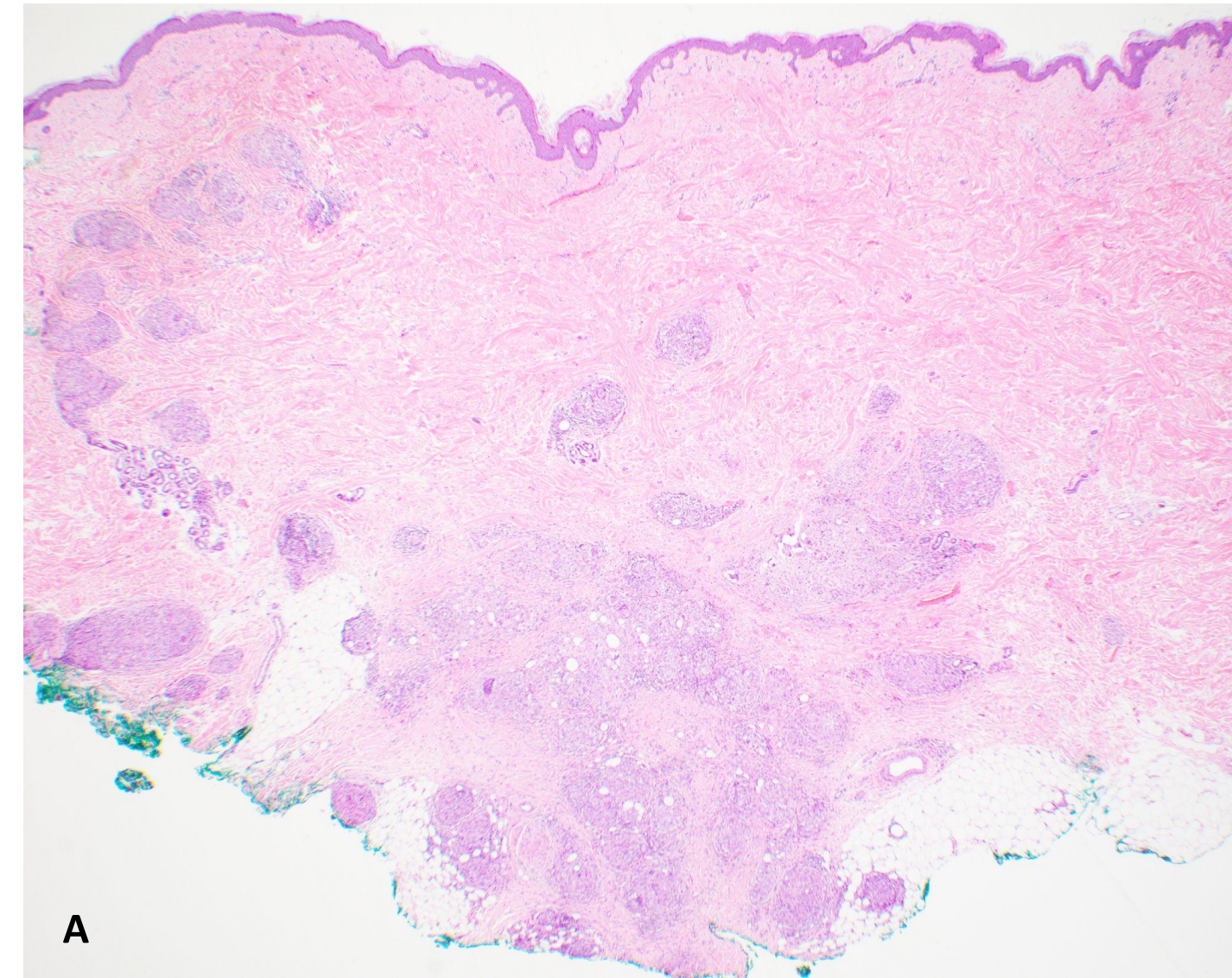


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Introduction

- Pembrolizumab, a PD-1 inhibitor, is a humanized monoclonal antibody that targets programmed-cell death protein-1, an important checkpoint in the cell cycle.
- Immune checkpoint inhibitors (ICI), such as Pembrolizumab are vital in cancer treatment and maintenance.
- These therapies can lead to various dermatologic adverse events, with recent reports of cutaneous sarcoidal granulomas linked to the setting of their use. Common ICI-associated sarcoidosis-like reactions include ipilimumab, nivolumab, pembrolizumab, and anti-PD-L1 therapy.¹
- As new ICIs emerge in oncology, understanding their clinical and histopathologic features in relation to their dermatologic manifestations is crucial for effective patient care.

Histopathology Images



Images A-C: A (2x magnification), B (4x magnification), C (10x magnification). Sections demonstrate diffuse involvement of dermal and subcutaneous tissue by well circumscribed, noncaseating epithelioid granulomas containing multinucleated histiocytes.

Case Presentation

- Patient is a 72-year-old female with stage 4 uterine cancer in remission, status post-hysterectomy, referred by her oncologist for evaluation of pruritic nodules located on her abdomen and lower back.
- At the time of dermatology evaluation, the patient was status-post 11 cycles of Pembrolizumab/Carboplatin/Paclitaxel
- A previous PET scan demonstrated metabolically active lymphadenopathy of the mediastinum, bilateral hilar, and supraclavicular fossa. Nonspecific cutaneous uptake in the skin of the torso and posterior right thigh was also present.
- Physical examination demonstrated firm nodules with little epidermal change.
- A punch biopsy and excisional biopsy were submitted for routine light microscopy while a second punch biopsy was submitted for tissue culture.
- Histologic exam revealed sarcoidal granulomas throughout the dermis and extending into the subcutis. Special stains for bacteria, mycobacteria, and fungi were negative. The separate tissue culture was also negative for infectious organisms.

Discussion

- Immunomodulators including CTLA-4 inhibitors, PD-1 inhibitors, and PD-L1 inhibitors have been identified to have various inflammatory dermatologic toxicities, including sarcoidal granulomatous dermatitis in the treatment of patients with various malignancies including uterine leiomyosarcoma and Hodgkins lymphoma.^{1,2}
- Specifically, in the case of this patient, PD-1 inhibitors, such as pembrolizumab, have been described to have the inflammatory manifestation of sarcoidal granulomatous dermatitis.²
- The onset of cutaneous or systemic lesions typically occur 4-14 weeks after treatment initiation.^{1,3} Cutaneous lesions can often be concerning for recurrence of malignancy, so prompt diagnosis is imperative.
- Drug-induced sarcoid like reactions frequently involve the skin, lungs, and mediastinal lymph nodes.³ Notably, the patient's PET scan showed activity in these areas as well.
- The ddx includes infections and this must be systematically ruled out as a potential cause of granulomatous inflammation
- Because sarcoidal granulomas can be due to various etiologies, the clinician must consider drug-induced sarcoidal granulomas in the setting of immunomodulator use.

Conclusion

- While cutaneous sarcoidal granulomas may be self-resolving, prompt diagnosis with biopsy is important to rule out malignancy.³
- Treatment options include corticosteroids, discontinuation of the immunomodulator, or close observation without interruption of therapy.¹
- The clinician must weigh the beneficial effects of the medication against the severity of the eruption in the decision to continue ICI therapy.¹
- ICI-induced sarcoidal reactions do not require treatment unless there is evidence of organ dysfunction.¹
- As ICIs are rapidly become a mainstay of cancer treatment, further research is needed to understand the genesis and best therapeutic approach of ICI-induced sarcoidal reactions.

Sources

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3. Mazumder, A., Mehrmal, S., & Chaudhry, S. (2023). Immunotherapy-induced exclusively cutaneous sarcoid-like reaction. *BMJ case reports*, 16(7), e252766. <https://doi.org/10.1136/bcr-2022-252766>