An ulcerated violaceous nodule on the thigh

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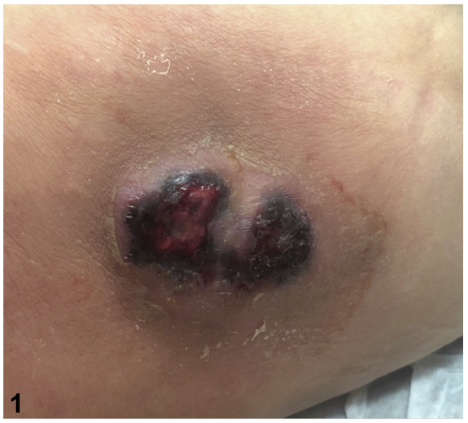

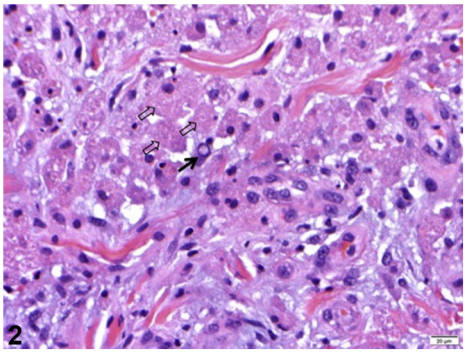

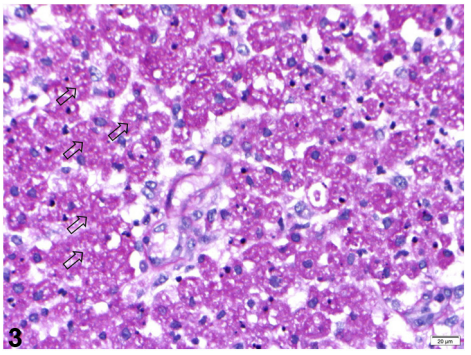

A 42-year-old woman presented with a plaque on the medial aspect of her thigh lasting for one month. She reported bloody and purulent discharge, fevers, and debilitating local pain. She had a history of renal transplant for chronic idiopathic glomerulonephritis, for which she received prednisone, mycophenolate mofetil, and tacrolimus, and also a history of antiphospholipid antibody syndrome, for which she received warfarin treatment. Examination revealed a 7-cm ulcerated violaceous nodule (Fig 1). An incisional biopsy was obtained for diagnostic clarification (Figs 2 and 3). Tissue culture grew 3+ *Escherichia coli*, 3+ *Pseudomonas aeruginosa*, *and* 1+ *Bacteroides fragilis*.

Question 1: What is the most likely diagnosis?

A. Calciphylaxis

B. Malakoplakia

C. Chancroid

D. Angiosarcoma

E. Pyoderma gangrenosum

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Answers:

A. Calciphylaxis — Incorrect. Calciphylaxis presents as painful retiform purpuric or necrotic plaques and may be due to diffuse deposition of calcium salts in cutaneous blood vessels with associated thrombosis. It is most commonly associated with chronic renal failure, although there are many other reported associations, such as warfarin use. Pathology would typically reveal calcification within blood vessels and in fat, and tissue cultures would be negative.[1]

B. Malakoplakia — Correct. Malakoplakia is a rare granulomatous inflammatory reaction to infection by gram-negative bacteria, primarily *Escherichia coli*.[2] The pathogenesis likely reflects impaired macrophage phagolysosome digestion of bacteria, accounting for its prevalence in immunocompromised patients, including the transplant patient population.[3] Although the presenting morphology is heterogeneous, nodules with ulceration and purulent discharge are often observed.[4]

C. Chancroid — Incorrect. While both chancroid and malakoplakia can present as painful ulcers, chancroid classically presents as locally destructive genital ulcers caused by the gram-negative bacterium, *Haemophilus ducreyi*, which did not grow from this patient's tissue culture.[1]

D. Angiosarcoma — Incorrect. While both cutaneous angiosarcoma and malakoplakia can present as violaceous edematous nodules with ulceration, angiosarcoma typically presents on the head and neck of elderly men, or in areas of prior radiation or chronic lymphedema.

E. Pyoderma gangrenosum — Incorrect. Pyoderma gangrenosum often presents as a single painful nodule or pustule that progresses to an ulcer with undermined and violaceous borders. Exclusion of infection is considered a diagnostic criterion.[5]

Question 2: What are the classic histopathologic findings for this diagnosis?

A. Von Hansemann cells with Michaelis-Gutmann bodies

B. Vascular calcification

C. Donovan bodies

D. Dermal neutrophilic infiltrate

E. Infiltrative sinusoidal pleomorphic endothelial cells and blood

Answers:

A. Von Hansemann cells with Michaelis-Gutmann bodies — Correct. An early histopathologic feature of malakoplakia, as seen in Fig 2, includes von Hansemann cells, or histiocytes with lightly-staining vacuolated cytoplasm.[3] The intracytoplasmic vacuoles are periodic acid-Schiff—positive (Fig 3), diastase-resistant, and are thought to result from abnormal phagocytosis of bacteria. Calcified spherical inclusions arising from these vacuoles, Michaelis-Gutmann bodies, are pathognomonic for malakoplakia.[2,3] Von Kossa and Perls' Prussian blue stain for iron can highlight the mineralization within these bodies and assist with diagnosis.[4]

B. Vascular calcification — Incorrect. Calcification of small-to-medium blood vessels is characteristic of calciphylaxis, not malakoplakia. The necrosis in calciphylaxis is secondary to reactive intimal proliferation, thrombosis, and ischemia.[1]

C. Donovan bodies — Incorrect. Donovan bodies are rod/oval-shaped organisms associated with granuloma inguinale, which is a rare sexually transmitted infection due to *Klebsiella granulomatis*. They can be identified intracellularly within the cytoplasm of histiocytes, but are not found in malakoplakia.[1]

D. Dermal neutrophilic infiltrate — Incorrect. While early lesions of pyoderma gangrenosum can present on histopathology with sterile perifollicular inflammation, later lesions show an ulcerated epidermis and superficial dermis overlying a dense neutrophilic-predominant dermal infiltrate.[1]

E. Infiltrative sinusoidal pleomorphic endothelial cells and blood — Incorrect. Infiltrative interwoven networks of sinusoidal vessels describe the histopathology findings of angiosarcoma, which can vary in cellular atypia, depending on the degree of differentiation. In poorly differentiated angiosarcoma, the endothelial lumen may not be visible, and cells can be highly mitotically active.

Question 3: What is the most appropriate initial treatment?

A. Increasing the dose of prednisone

B. Intravenous sodium thiosulfate

C. Switching warfarin to apixaban

D. Ciprofloxacin

E. Wide local excision

Answers:

A. Increasing the dose of prednisone — Incorrect. Systemic steroids would be appropriate for a primary inflammatory process such as pyoderma gangrenosum, but would fail to address the infectious etiology of malakoplakia and could cause harm by resulting in further immunosuppression. The opposite situation, a reduction in immunosuppression, could be beneficial in patients with malakoplakia, in addition to treatment with antibiotics.[2,3]

B. Intravenous sodium thiosulfate — Incorrect. Intravenous sodium thiosulfate is often used to treat calciphylaxis, with a possible mechanism of action of calcium chelation and solubilization. Calcium deposition is not a driving factor in malakoplakia pathophysiology and does not address its infectious etiology.[1]

C. Switching warfarin to apixaban — Incorrect. Anticoagulation is indicated for patients who meet the diagnostic criteria for antiphospholipid antibody syndrome and may also be beneficial in patients with other forms of vasculopathy. However, anticoagulation is not considered a therapeutic option for malakoplakia.[4]

D. Ciprofloxacin — Correct. Standard of care in the treatment of malakoplakia is a prolonged course of antibiotics to address the underlying infection, as well as consideration of surgical excision and immunosuppression reduction when appropriate. Antibiotic choice should be guided by susceptibility results, with preference given to those antibiotics with intracellular efficacy, such as fluoroquinolones and trimethoprim-sulfamethoxazole.[2,3]

E. Wide local excision — Incorrect. While surgical intervention can augment the efficacy of antibiotic treatment substantially, wide local excision alone is not the standard of care for malakoplakia.[4]

Conflicts of interest

None disclosed.

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