

Necrotizing *Escherichia coli* skin and soft tissue infection with malakoplakia-like features mimicking pyoderma gangrenosum



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Key words: malakoplakia; pyoderma gangrenosum.

INTRODUCTION

Malakoplakia is an uncommon, chronic, granulomatous disease that most commonly involves the genitourinary system of adult patients.¹ The pathogenesis of malakoplakia is thought to be associated with macrophage dysfunction. In immunocompromised patients or in the setting of autoimmune disease, macrophages are unable to phagocytose and kill bacteria successfully.¹

Herein, we present a case of necrotizing skin and soft tissue infection caused by *Escherichia coli*, with malakoplakia-like features mimicking pyoderma gangrenosum (PG) in a pediatric patient with acute lymphoblastic leukemia.

CASE REPORT

A 17-year-old female presented with pancytopenia secondary to acute lymphoblastic leukemia and was undergoing induction chemotherapy with cytarabine, vincristine, daunorubicin, pegaspargase, prednisone, and intrathecal methotrexate for the 27th day. The patient was evaluated for a patch on the left side of the lower back (Fig 1, A). The exquisitely painful lesion was located at the site of a bone marrow biopsy that was performed 30 days prior to the presentation. The clinical presentation, white blood cell count of 2200/mm³, and severe neutropenia raised concern for an angioinvasive infection. Two punch biopsies were obtained for hematoxylin and eosin staining and tissue culture. Epidermal and dermal necrosis with minimal perivascular lymphocytic inflammation was noted on the initial biopsy. No evidence of vasculopathy was observed. Grocott

Abbreviation used:

PG: pyoderma gangrenosum

methenamine silver staining showed negative results. The tissue culture showed a growth of *E coli* susceptible to meropenem. The patient was considered to have *E coli* cellulitis and was treated accordingly. The therapy included vancomycin, voriconazole, and acyclovir for broad-spectrum coverage and was continued for 14 days. Over the course of the treatment, the lesion progressed into ulceration with violaceous-gray borders and undermined tissue edges (Fig 1, B). Based on this progression, the positive wound culture was considered contamination rather than pathogen. Based on the presentation, history of malignancy, possible pathergy, and tentative exclusion of infectious etiologies, a presumptive diagnosis of ulcerative PG was made. Treatment included high-dose prednisone with mercaptopurine and methotrexate as a part of the chemotherapy regimen.

Over 5 weeks, the ulcer worsened and grew to 9 cm × 6 cm × 3 cm with extension to the muscle (Fig 2). Repeat biopsy and histology revealed a suppurative granuloma with collections of foamy histiocytes with granular eosinophilic cytoplasm, consistent with von Hansemann cells (Fig 3, A). Gram stain revealed Gram-negative cocci and rods (Fig 3, B). Tissue culture again showed the growth of *E coli*. Concern arose for necrotizing malakoplakia-like *E coli* infection, based on the histopathologic finding

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Funding sources: None.

IRB approval status: Not applicable.

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JAAD Case Reports 2021;12:■-■.
2352-5126

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<https://doi.org/10.1016/j.jidcr.2021.03.047>

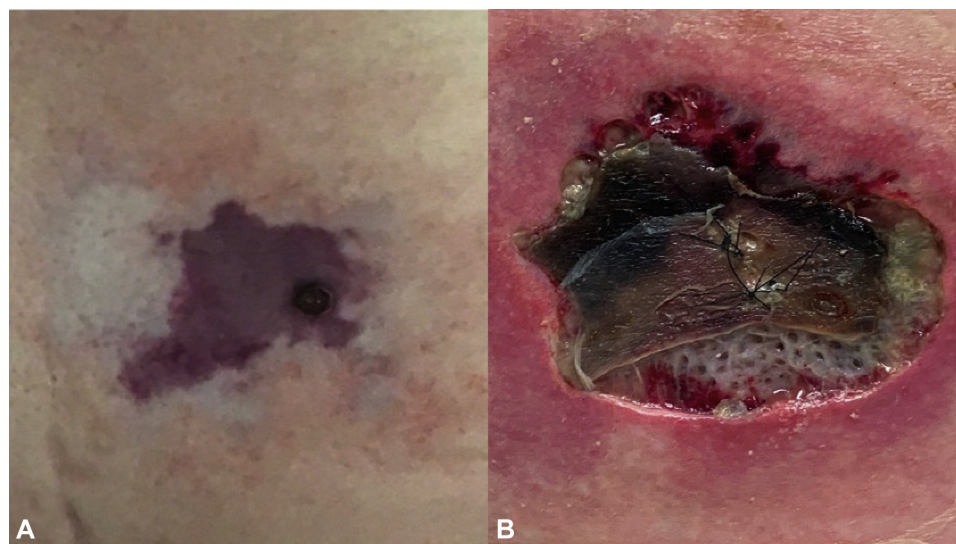


Fig 1. **A**, Initial examination revealed a well-demarcated, stellate purpuric patch involving the left side of the lower back. **B**, After the treatment for *E coli* cellulitis, the wound progressed to a 6 cm × 5 cm × 1 cm cribriform ulceration with a violaceous-gray border.



Fig 2. Follow-up examination showed a 9 cm × 6 cm × 3 cm ulceration with violaceous-gray borders and undermined tissue edges with extension to muscle.

of von Hansemann cells and Gram-negative rods as well as the persistently positive tissue culture.

Prednisone was discontinued. The patient was started on intravenous cefepime every 8 hours for 17 days and topical gentamicin 3 times daily for several months. The intravenous and topical medications provided coverage for the *E coli* isolate as the tissue culture revealed sensitivity to both agents. No bacteria were identified on the examination of biopsies performed 2 weeks later. Over the course of 2 months, the ulceration completely healed with a residual stellate, atrophic scar (Fig 4).

DISCUSSION

Malakoplakia is a rare, granulomatous condition associated with an underlying bacterial infection in the setting of macrophage dysfunction.¹ In this condition, macrophages are unable to phagocytose and effectively kill bacteria.¹ *E coli* is the most common underlying infection. Additional infectious pathogens have been identified, including *Mycobacterium tuberculosis*, *Staphylococcus aureus*, and *Proteus*.¹ Immunosuppression contributes to this immune dysfunction, with a study reporting reversal of the macrophage defect with cessation of immunosuppression.² Malakoplakia typically affects adult patients, with an average age of 50 years at presentation.³ Of the more than 500 described cases of malakoplakia, fewer than 15 have been reported in pediatric patients.³

Our patient presented with *E coli*-associated skin and soft tissue infection, with clinical progression despite appropriate antimicrobial treatment, probably due to severe neutropenia. With additional immunosuppression to treat suspected ulcerative PG, histopathologic malakoplakia-like features developed. Histopathologic findings in malakoplakia include von Hansemann cells, which are large histiocytes with granular eosinophilic cytoplasm. Due to an impaired bactericidal activity within von Hansemann cells, secondary lysosomes containing partially digested organisms are fused and calcified to form Michaelis–Gutmann bodies.⁴ Michaelis–Gutmann bodies, also considered pathognomonic for malakoplakia, have a laminated or targetoid appearance. These may be absent if the

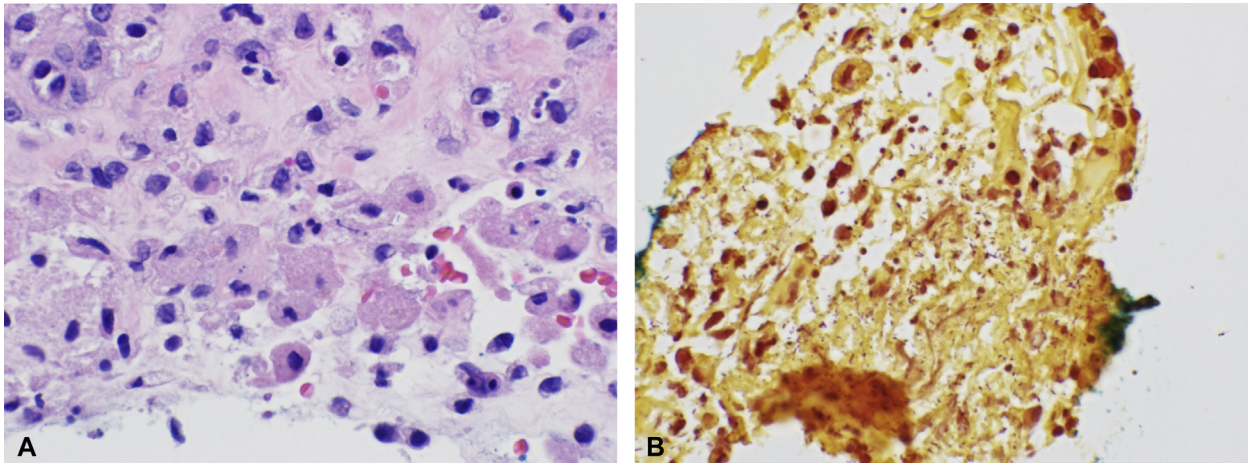


Fig 3. **A**, Punch biopsy showed a suppurative granuloma with collections of foamy histiocytes with granular eosinophilic cytoplasm, consistent with von Hansemann cells. **B**, Gram stain revealed Gram-negative cocci and rods.



Fig 4. The ulceration healed with a residual stellate, atrophic scar.

plane of the section does not pass through the central core.⁴ Michaelis–Gutmann bodies stain with periodic acid-Schiff stain and von Kossa stain and occasionally with Perls Prussian blue stain.⁴ When considering malakoplakia, all 3 stains should be utilized. In our patient, von Hansemann cells and Gram-negative rods were demonstrated on the repeat histopathologic evaluation of the lesion following additional immunosuppression.

Usually, the genitourinary system is the primary site of malakoplakia development.¹ Primary cutaneous malakoplakia is very unusual, with fewer than 60 cases reported in the literature. This condition most often affects the genital and perianal skin. The clinical presentation of cutaneous malakoplakia varies, with suppurative nodules, plaques, and ulcerations seen most

frequently.⁵ In the case of our patient, an ulcer was present with violaceous-gray borders and undermined tissue edges. The clinical features and context suggested ulcerative PG. The history of malignancy, possible pathergy in the setting of recent bone marrow biopsy, and tentative exclusion of infectious etiologies supported this diagnosis.

However, in this patient, the ulceration continued to progress despite high-dose prednisone and additional immunosuppressive medications within the chemotherapy regimen, prompting reconsideration of the diagnosis. Recently published consensus guidelines have suggested diagnostic criteria of ulcerative PG, including a major criterion of biopsy histology consistent with PG and 4 of the 8 minor criteria. The described patient met 4 of the minor criteria at the time of PG diagnosis, including pathergy, development of ulceration within 4 days, peripheral erythema, and undermined border and tenderness at ulceration site. However, the patient's biopsy was not consistent with PG, and thus, the patient did not meet all the suggested diagnostic criteria. Therefore, these guidelines may provide additional direction for diagnosis reconsideration when only a few clinical criteria are met, as in our case.⁶

This case highlights the importance of reconsidering the PG diagnosis when ulceration does not improve with treatment or the diagnostic criteria are not met. Infectious etiologies should be promptly reconsidered in these cases.

Conflicts of interest

None disclosed.

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