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Methicillin-resistant *Staphylococcus aureus* (MRSA) panniculitis in a patient undergoing stem cell mobilisation

Ada Pei Yu Ng,¹ Yen-Lin Chee,² SB Justin Wong,³ Wei-Ying Jen²

¹Department of Internal Medicine, National University Health System, Singapore

²Department of Haematology, National University Cancer Institute Singapore, National University Health System, Singapore

³Department of Pathology, National University Health System, Singapore

Correspondence to

Dr Ada Pei Yu Ng;
ada_ng@nuhs.edu.sg

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SUMMARY

Methicillin-resistant *Staphylococcus aureus* (MRSA) can cause a wide range of skin infections, however MRSA panniculitis without bacteremia is a rare manifestation. Here, we report a woman in her 20s with relapsed Hodgkin lymphoma undergoing stem cell mobilisation who presented with bilateral subcutaneous nodules over her shins. Ultrasound scan of one nodule showed non-specific inflammatory changes. Punch biopsy of a nodule showed lobular panniculitis with Gram-positive cocci. Blood cultures were negative but a culture from the biopsy grew MRSA. She was started on doxycycline with improvement in her symptoms. This case serves as a reminder to consider infections as a cause of panniculitis in immunocompromised patients.

BACKGROUND

Panniculitis usually presents as painful erythematous nodules or plaques and is characterised by inflammation of subcutaneous adipose tissue. Recognition, diagnosis and evaluation is challenging because of its rarity and myriad causes, including infection, malignancy, drugs and inflammatory conditions. Infectious panniculitis can occur primarily after direct inoculation or secondarily from hematogenous spread.¹ We report a case of methicillin-resistant *Staphylococcus aureus* (MRSA) panniculitis.

CASE PRESENTATION

A female in her 20s with relapsed Hodgkin lymphoma (HL) was referred to our centre for autologous stem cell transplantation. She was diagnosed with stage 2 HL in 2016 and underwent chemoradiotherapy, attaining complete remission. She relapsed in 2019 with a recurrent mediastinal mass and widespread lymphadenopathy. She underwent salvage chemotherapy with bendamustine and brentuximab (BB), which was uneventful except for a grade 1 cutaneous adverse drug reaction (CADR) to BB affecting 5% of her body surface area. This resolved with topical steroids and antihistamines. She had no other significant medical or surgical history. Medication on admission for stem cell harvesting included chlorpheniramine 4 mg two times per day, mometasone 0.1% lotion two times per day for her previous CADR and acyclovir 400 mg two times per day for prophylaxis against herpes zoster.

The patient went on to receive mobilisation chemotherapy with ifosfamide, carboplatin and

etoposide. Pegfilgrastim was administered on days 5 and 11. On day 11, she was admitted with a fever of 38.3°C and pain in her legs. Examination revealed bilateral scattered tender, indurated subcutaneous nodules over her shins with mild overlying erythema, approximately 3–5 cm in diameter (figure 1). There was a residual dry scaly excoriated hyperpigmented rash from the previous CADR.

INVESTIGATIONS

Investigations on admission showed a white cell count of $0.79 \times 10^9/L$, with neutrophils $0.56 \times 10^9/L$. Following admission, she was started on daily filgrastim due to her neutropaenia and low CD34+ count, which precluded successful mobilisation. C-reactive protein (CRP) was elevated at 74, and procalcitonin was 0.18. Blood cultures and a blood fungal culture were negative. An ultrasound scan of the leg nodule showed vague increased echogenicity and increased vascularity in the subcutaneous tissue with no evidence of abscess formation. A punch biopsy of the nodule confirmed lobular panniculitis with an inflammatory cell infiltrate composed of numerous neutrophils, mixed with lymphocytes,



Figure 1 Photo of subcutaneous nodule on the lower limb.



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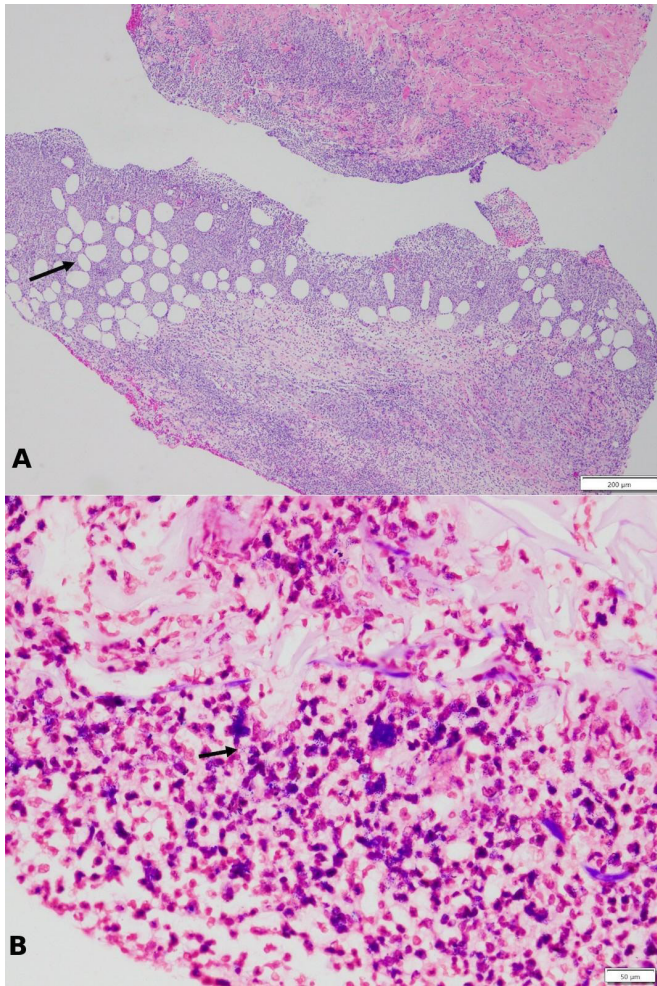


Figure 2 (A) Histology slide showing lobular panniculitis with an inflammatory cell infiltrate composed of numerous neutrophils, mixed with lymphocytes, eosinophils, histiocytes and occasional multinucleated giant cells. (B) Histology slide showing Gram-positive cocci.

eosinophils, histiocytes and occasional multinucleated giant cells (figure 2A). Granulomas were not observed. No features of vasculitis were identified. Gram-positive cocci were present in the dermis and subcutis (figure 2B). No fungal organisms or acid-fast bacilli were seen on Grocott's methenamine silver or Ziehl-Neelsen stains. Culture from the punch biopsy grew MRSA. Her antinuclear antibody titre was negative at <1:80. A tuberculosis quantiferon test was negative, and a chest radiograph was normal.

TREATMENT

A diagnosis of infective panniculitis secondary to MRSA was made. She was started on doxycycline with resolution of her fever and nodules. Her filgrastim injections were continued till neutrophil recovery.

OUTCOME AND FOLLOW-UP

The patient unfortunately failed to mobilise peripheral blood stem cells but went on to have a successful bone marrow harvest with no evidence of microbial contamination of her cryopreserved stem cells. Her lower limb subcutaneous nodules also resolved completely without scarring nor atrophy following treatment with doxycycline.

DISCUSSION

Panniculitis can be classified as septal or lobular, with or without vasculitis. Histologically, infectious panniculitis presents as a neutrophilic predominant mixed inflammatory infiltrate with a lobular pattern of inflammation.² Infective panniculitis can be caused by bacterial, mycobacterial, fungal, protozoal or viral infections. *S. aureus* is a skin commensal commonly responsible for primary cutaneous lesions such as folliculitis, carbuncles or cellulitis. Deeper pathology such as abscesses or rarely, panniculitis may result from haematogenous spread in bacteraemic patients,³ or following inoculation from primary superficial lesions. In our patient, repeated blood cultures were negative for *S. aureus*. Given this, we hypothesise that her prior CADR to BB chemotherapy resulted in weakened skin integrity, superficial inoculation and subsequent deep tissue infection which flared opportunistically when she was neutropaenic. To our knowledge, MRSA-induced panniculitis without bacteraemia is rare. However, there have been a few reports of this phenomenon with *Pseudomonas aeruginosa*.^{4,5}

We initially considered filgrastim-induced panniculitis as a differential. Filgrastim has been associated with several cutaneous reactions such as Sweet's syndrome, pyoderma gangrenosum and vasculitis. A few cases have been reported in association with pegfilgrastim.⁶ Possible hypotheses include secondary cytokine production after filgrastim administration and neutrophil activation.⁷ In our patient, the temporal relationship between administration of pegfilgrastim and her symptoms initially led us to suspect pegfilgrastim as the cause of her panniculitis. However given her positive biopsy culture for MRSA, the presence of Gram-positive cocci in her dermis and subdermal layer, and clinical response to doxycycline despite being continued on filgrastim, we deemed this unlikely.

The site of the lesions, clinical context of HL and neutrophil-rich inflammatory infiltrate also raise the possibility of erythema nodosum. Erythema nodosum is usually idiopathic, but has also been associated with infection, drug, inflammatory condition or malignancy.⁸ Although this is classically a septal panniculitis,⁹ there can be histological overlap in some cases.¹⁰ Our patient's biopsy was in keeping with that of a lobular panniculitis. Her culture was positive for MRSA which is not a typical infection associated with erythema nodosum. In view of this and her quick response to doxycycline, we concluded erythema nodosum to be less probable.

The possibility of bacterial contamination during the biopsy procedure was also considered. MRSA is endemic in health-care facilities,¹¹ and patients who are colonised with MRSA may contaminate surrounding environmental surfaces.¹² Our institution carries out active surveillance to identify MRSA-colonised patients. Our patient's MRSA swabs (nasal, axilla and groin) were persistently negative. In addition, the procedure was done under aseptic technique, MRSA was cultured and demonstrated in histology specimens, and she improved following the

Learning points

- ▶ Infectious panniculitis due to *Staphylococcus aureus* in the absence of bacteraemia is extremely rare.
- ▶ Careful workup including biopsy and culture is important to allow correct identification of aetiology and appropriate management.
- ▶ Appropriate diagnosis allowed continued filgrastim injections so that her time-sensitive stem cell harvest could proceed.

institution of antimicrobial therapy. In light of this, bacterial contamination was considered unlikely.

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