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Case Report

Ecthyma gangrenosum secondary to methicillin-sensitive *Staphylococcus aureus*

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ABSTRACT

Ecthyma gangrenosum (EG) is a well-described skin manifestation of *Pseudomonas aeruginosa* septicemia in immunocompromised patients. However, it can be seen in association with other bacteria, viruses, and fungi. We report a case of a 54-year-old African American female with metastatic gastric adenocarcinoma and recent chemotherapy and neutropenia who developed EG-like lesions due to methicillin-susceptible *Staphylococcus aureus*. We also review the literature to evaluate all reported cases of *S aureus*-associated EG and their clinical presentation, diagnosis, and treatment.

Introduction

Ecthyma gangrenosum (EG) is a well-described skin manifestation of *Pseudomonas aeruginosa* septicemia in immunocompromised patients. EG is most commonly seen in *Pseudomonas* septicemia. However, it may be seen in association with infections caused by other gram-negative bacteria and fungi and can rarely be caused by gram-positive organisms such as *Staphylococcus* and *Streptococcus* species. We report a case of a 54-year-old African American female with neutropenia in the setting of metastatic gastric adenocarcinoma and recent chemotherapy who developed EG-like lesions due to methicillin susceptible *Staphylococcus aureus*. In addition, we also review the literature and discuss all reported cases of *S aureus*-associated EG manifestation, diagnosis, and treatment.

Case report

A 54-year-old African American female with a medical history significant for systemic lupus erythematosus on chronic therapy with systemic steroids and hydroxychloroquine was recently diagnosed with gastric adenocarcinoma with metastatic liver lesions. She presented to our hospital with fever and painful skin lesions. The patient had received a first round of chemotherapy with 5-fluorouracil, cisplatin, and trastuzumab. Seven to ten days after the last dose of chemotherapy she noted multiple painful skin lesions.

On admission, the patient's blood pressure was 86/52 mmHg, heart rate 122 bpm, and temperature 103.7 °F. The patient was alert, oriented, and not in any acute distress. Skin examination revealed three 3-12–mm, tender, indurated, and erythematous papules and plaques with violaceous-gray centers located on the left popliteal fossa, right anterolateral knee, and right external ear canal. Additionally, there were 4-5–mm vesicles at the right mandibular angle and right arm, and pustules scattered on the mid chest (see Figs. 1 and 2).

Admission laboratory studies revealed pancytopenia and elevated erythrocyte sedimentation rate and C-reactive protein. Additional results are shown in Table 1.

Three sets of blood cultures obtained prior to administration of antibiotic therapy showed no growth. Fungal blood cultures were negative. Chest imaging did not reveal any pathology. Transthoracic and transesophageal echocardiograms showed normal valvular function without vegetations.

The patient's initial therapy with intravenous cefepime, vancomycin, and metronidazole was changed to intravenous acyclovir, vancomycin, and double pseudomonas coverage with meropenem and amikacin after evaluation by the infectious disease and dermatology teams.

Cutaneous punch biopsies were obtained from the violaceous-gray lesion on the left popliteal fossa and a pustule from the chest. Histopathology of the violaceous-gray lesion revealed prominent edema and numerous gram-positive cocci in the superficial dermis (see Figs. 3 and 4). Additionally, there was a perivascular inflammatory cell infiltrate in the superficial and deep dermis composed of lymphocytes, histiocytes, and neutrophils, as well as dilated blood vessels with extravasated erythrocytes. Special stains for acid fast bacilli and fungal organisms were negative. The chest pustule histologically

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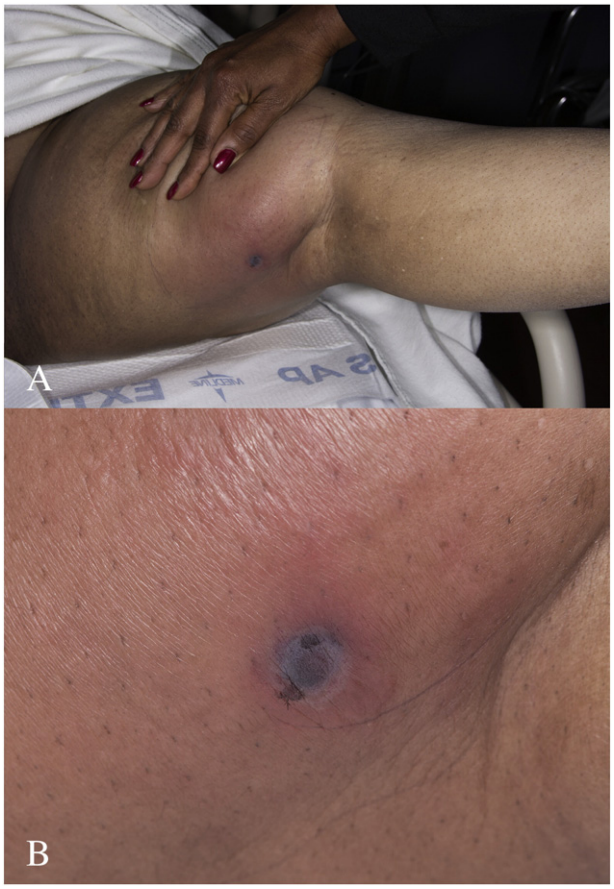

Fig. 1. Indurated, erythematous papule with violaceous-grey center.

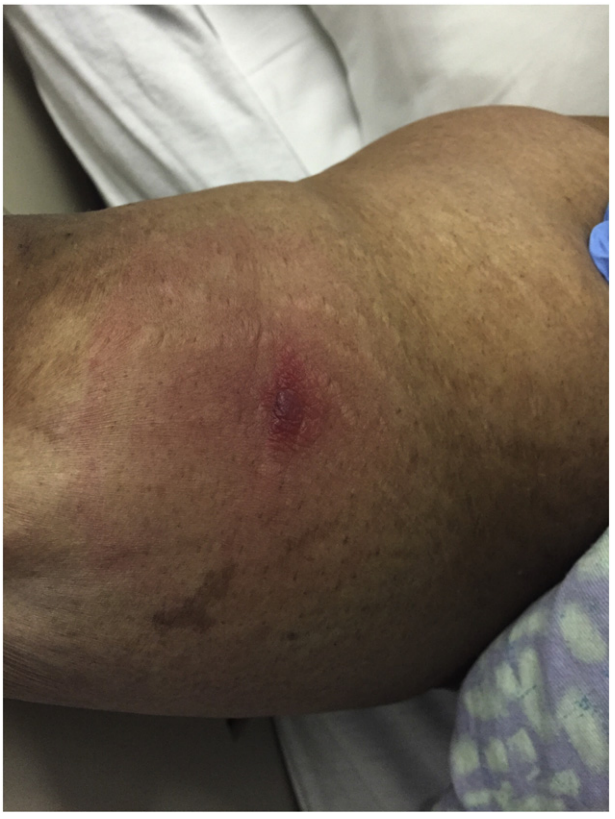

Fig. 2. Indurated, erythematous plaque with central edema.

demonstrated an intraepidermal pustular dermatitis with gram-positive cocci. Tissue cultures from both specimens grew methicillin-susceptible *Staphylococcus aureus*, with an oxacillin minimum inhibitory concentration of 0.5 mcg/ml.

Acyclovir, meropenem, and vancomycin were discontinued. All blood cultures remained negative throughout hospitalization, and the patient was discharged home to complete 2 weeks of intravenous oxacillin.

Discussion

Ecthyma gangrenosum (EG) is a well-described skin manifestation of *P aeruginosa* septicemia in immunocompromised patients. EG lesions usually are round, indurated, ulcerated papules progressing into plagues with a central gray-black eschar and surrounding erythema. Lesions may evolve from initial vesiculobullous lesions and rapidly become hemorrhagic.

The clinical differential diagnosis in our case included EG associated with invasive pathogens: *Pseudomonas*, *Staphylococcus* sp., fungal infection such as *Aspergillus* sp., *Fusarium* sp., disseminated varicella zoster virus, and herpes simplex virus; noninfectious entities such as vasculitis were also considered. Ecthyma ("deep impetigo") was not considered in our differential diagnosis, as clinically the skin lesions in our patient did not start as superficial epidermal erosions and crusting that progressed deeper into the dermis to create crusted ulcers.

EG is most commonly seen in *Pseudomonas* septicemia; however, it may be seen in association with infections caused by other gram-negative bacteria, such as *Aeromonas hydrophilia, Klebsiella pneumonia, Escherichia coli, Neisseria gonorrhea, Citrobacter freundii, Serratia marcescens*, and fungi including *Candida albicans*, *Aspergillus fumigatus, Fusarium solani, Pseudallescheria boydii* and *Curvularia* sp. The viral pathogens herpes simplex viruses 1 and 2 and varicella-zoster virus can be associated with EG as well. Rarely, EG can be caused by gram-positive organisms such as *Staphylococcus* and *Streptococcus* species (Kao et al. 2001; Reich et al. 2004).

A review of English literature in PubMed between January 1, 1990, to January 31, 2016, was performed using the following keywords: non-pseudomonal ecthyma gangrenosum, methicillin-resistant *Staphylococcus aureus,* and methicillin-susceptible *Staphylococcus aureus*. This search revealed 5 other reported cases of EG associated with *S aureus* infection. EG usually occurs in the patients with underlying immunodeficiency. Predisposing factors include neutropenia,

Table 1
Blood Test Performed on Admission.

Blood test	Patient's results	Normal reference range
White blood cell count	0.8×10^3/uL	3.6-11.0 $\times 10^3$/uL
Absolute neutrophil count	0.4×10^3/uL	1.4-6.3 $\times 10^3$/uL
Platelet count	78×10^3/uL	150-440 $\times 10^3$/uL
Hemoglobin	7.7 g/dL	12.0-16.0 g/dL
Erythrocyte sedimentation rate	150 mm/h	0-20 mm/h
C- reactive protein	132.9 mg/L	<1.0 mg/L
Creatinine	0.9 mg/dL	0.6-1.2 mg/dL
Blood urea nitrogen	10 mg/dL	8-24 mg/dL
Beta-D glucan	31 pg/mL	<31 pg/mL is negative, >80 pg/mL positive
Aspergillus Galactomannan index by EIA	0.08	index equal to or greater than 0.5 positive