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Suspected Ecthyma Gangrenosum Associated with Methicillin-Sensitive Staphylococcus Aureus Bacteremia

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Abstract Ecthyma gangrenosum (EG) is a well-recognized but rare skin infection most commonly occurring in the setting of immunocompromised individuals with bacteremia. Currently, there are very few reports of EG caused by methicillin-resistant Staphylococcus aureus (MRSA) and even fewer cases caused by methicillin-sensitive Staphylococcus aureus (MSSA). We present only the second case of bacteremic EG associated with MSSA bacteremia and aim to review the literature as well as examine common findings amongst patients with EG associated with Staphylococcus aureus.

Keywords: *Ecthyma gangrenosum, Staphylococcus aureus, MRSA, MSSA, bacteremia*

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1. Introduction

Ecthyma gangrenosum (EG) is a well-recognized but rare skin infection most commonly occurring in the setting of immunocompromised individuals. Pseudomonas aeruginosa is the most frequent organism identified in EG. In rare cases, it may be caused by other bacteria, viruses, and even fungi. [1] Currently, there are very few reports of EG caused by methicillin-resistant Staphylococcus aureus (MRSA), and even fewer cases caused by methicillin-sensitive Staphylococcus aureus (MSSA). [2] We present only the second case of bacteremic EG associated with MSSA bacteremia and aim to review the literature as well as examine common findings amongst patients with EG associated with Staphylococcus aureus.

2. Case Report

A 71-year-old male with a past medical history of stage IV small cell lung cancer with metastasis to the brain on chemotherapy presented to the emergency department with complaints of fever, diarrhea, and painful skin lesions on upper and lower lips as well as neck and right elbow. Carboplatin, etoposide, and atezolizumab were started approximately one week prior. His temperature on arrival at the hospital was 100.4°F, with labs revealing a white blood cell count of 0.6 × 10^9/L, an absolute neutrophil count of 0.2 x 10^9/L, and a platelet count of 30,000 x 10^9/L.

A physical exam revealed four tender papules and plaques with surrounding induration and erythema around a necrotic center on the patient's upper and lower lips as well as on his right posterior elbow, left proximal palmar hand, and at the base of the second phalange on his left dorsal hand (Figure 1). Blood cultures were positive for methicillin-sensitive staphylococcus aureus (MSSA) in 2/2 sets. The patient was initially started on IV vancomycin and cefepime for suspected febrile neutropenia and bacteremia. Given the bacteremia and associated neutropenia, the patient's skin findings were suspected to be EG secondary to methicillin-sensitive Staphylococcus aureus bacteremia. Throughout the patient's hospital course, the patient's neutropenia and skin lesion began to improve, and thus, a skin biopsy was forgone. The patient was ultimately de-escalated to IV cefazolin and discharged home.

Given this patient's neutropenia, typical skin lesions, and MSSA bacteremia, MSSA bacteremia EG was the most likely diagnosis. However, other EG-associated pathogens were also considered in the differential diagnosis. Noninfectious causes such as autoimmune vasculitis, pyoderma gangrenosum, septic emboli, calciphylaxis, and disseminated intravascular coagulation were also considered.

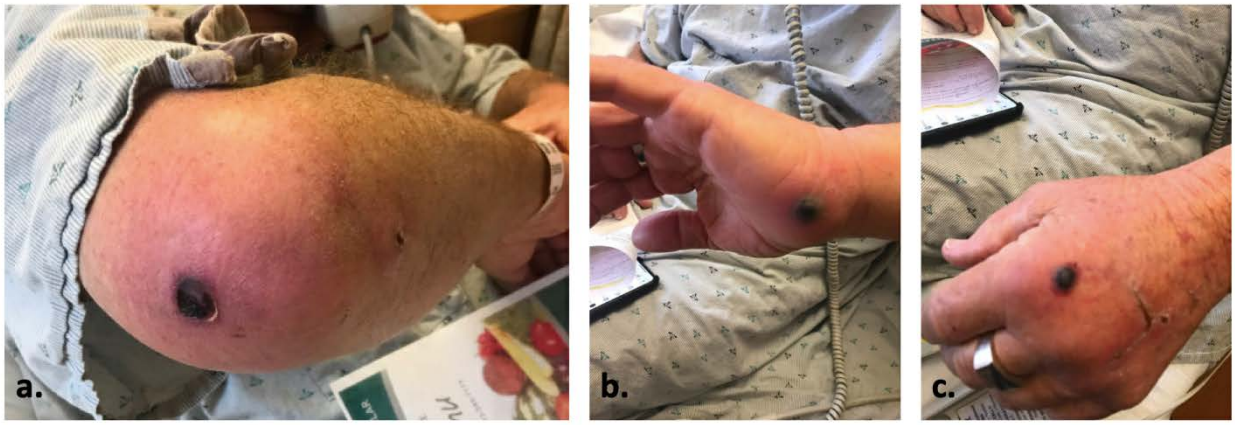

Figure 1. The initial presentation revealed papules with surrounding induration and erythema around a grey-black necrotic center on the right posterior elbow **(a)**, left proximal plantar hand **(b)**, and at the base of the second phalange on his left dorsal hand **(c)**

3. Discussion

EG is a rare cutaneous infection most commonly associated with *P. aeruginosa*. Although *P. aeruginosa* has been identified in up to 75% of EG cases, other organisms have been reported, such as MRSA, *streptococcus pyogenes, Escherichia coli, Klebsiella pneumoniae,* fungi, and viruses. [1] Our patient presented with MSSA-associated EG, an organism not often thought of when a patient presents with EG. We completed a PubMed review between 1966 and 2022, using keywords of ecthyma gangrenosum, Staphylococcus aureus, methicillin-sensitive, and methicillin-resistant (Table 1). [2-12] We found only eleven cases of Staphylococcus aureus-associated EG, with only four reported cases of MSSA. The median age of patients was 40 years old, and 45% of these cases were seen in women (5 cases).

EG lesions begin as painless, round erythematous macules and patches that evolve to become tender with a central gangrenous ulcer and gray-black eschar surrounded by erythema. Skin findings can progress rapidly from vesiculobullous to hemorrhagic lesions. [10] While EG can occur anywhere on the body, the most common locations are the gluteal/perineal area (57%), followed by the extremities (30%), the trunk (6%), and the face (6%). [1] Staphylococcus aureus-associated EG presents in similar locations, with 7 cases affecting the lower extremities, 5 affecting the trunk, 3 affecting upper extremities, 3 affecting the head/face, and 2 affecting the gluteal/perineal area.

In our case, the organism was found through blood cultures; however, a skin biopsy or culture was not obtained due to the significant clinical improvement following empiric antibiotic therapy. Of the eleven reported cases of EG associated with Staphylococcus Aureus, only two cases with positive blood cultures were noted, ten cases reported culture lesions positive for Staphylococcus Aureus, and five cases reported gram-positive cocci on skin biopsy. The diagnosis of EG is made clinically based on the characteristic appearance and a high degree of clinical suspicion with blood cultures, tissue cultures, and a biopsy supporting the diagnosis. [13] Thus, given the risk factors found in this patient, MSSA bacteremia, and characteristic skin findings, he was diagnosed clinically with EG. However, it can not be ruled out that this patient's EG was unrelated to the MSSA bacteremia and that another non-bacteremic pathogen caused the EG.

Immunocompromised individuals are particularly susceptible to EG, with up to 62% to 75% of affected individuals having an underlying immunodeficiency. [13] Predisposing conditions include neutropenia, malignancy, diabetes mellitus, malnutrition, and burn wounds. [13] This patient fits the typical predisposing factors given his history of small cell lung malignancy, chemotherapy, and neutropenia. Predisposing factors we found common amongst Staphylococcus aureus-EG include other forms of malignancy (2 cases), history of chemotherapy (2 cases), and CKD (2 cases). Interestingly, three patients had past medical histories that would not support the clinical picture for EG, which included COPD and chronic alcohol use, with one patient having no significant past medical history. Common lab findings amongst Staphylococcus aureus-EG include neutropenia (3 cases), leukocytosis (3 cases), and leukopenia (2 cases).

EG is separated into two groups based on pathogenesis, bacteremic and non-bacteremic, with the bacteremic form being more common. In bacteremic EG, skin findings are the result of the hematogenous spread of a causative organism to the skin, subsequently leading to perivascular invasion causing ischemic necrosis of the surrounding skin. [13] In the non-bacteremic form, localized infections by organisms release toxins and enzymes, causing localized skin and vascular destruction. [13] While bacteremic EG is considered to be more common, we found only two other cases of bacteremic Staphylococcus aureus-EG, one case being MRSA associated and the other MSSA, which may seem counterintuitive given that Staphylococcus aureus is known to often spread hematogenously and is the most common cause of gram-positive bacteremia. [12,14,15] Thus, this case represents only the second MSSA bacteremia EG. While our patient was discharged home, the two other cases of bacteremic Staphylococcus aureus-EG died from sepsis and multiple organ failure. Furthermore, all of the patients with non-bacteremic Staphylococcus aureus-EG were discharged home. Thus, bacteremic-associated Staphylococcus aureus-EG may carry a higher risk of death, and our patient appears to be the only person to have survived this.

Table 1. Characteristics of patients diagnosed with Staphylococcus Aureus-associated EG. (a. Two rounds of hyper-CVAD (cyclophosphamide, vincristine sulfate, doxorubicin hydrochloride (Adriamycin), and dexamethasone). b. 5-fluorouracil, cisplatin, and trastuzumab. c. Carboplatin, etoposide, and atezolizumab)

Author	Age & Gender	PMH	Medications	Location of EG	Bacteremic/ Non-bacteremic	ANC	WBC	Blood Culture	Tissue Culture	Biopsy	Antibiotics	Outcome
Şen et al. (2009)	69-year-old male	COPD	NR	Upper, lower extremity	Bacteremic	NR	6.2 x 10^9/L	MRSA	MRSA	No biopsy	IV ampicillin/sulbactam + meropenem + teicoplanin	Died of septic shock
Pechter et al. (2012)	8-month-old female	None	NR	Face, neck, back, genitalia	Non-bacteremic	0	NR	(-)	MRSA	GPC in dermis Vasculitis Dermal necrosis Epidermal necrosis	Ceftriaxone->IV vancomycin + cefepime + amikacin- > vancomycin	DC
Chang et al. (2012)	35-year-old female	T-cell ALL	Chemotherapy[a] (7-days prior), MTX	Buttocks, B upper thighs, abdomen.	Non-bacteremic	0.8 x 10^9/L	0.4 x 10^9/L	(-)	MRSA	GPC in dermis. Epidermal necrosis	IV vancomycin	DC
Jaque et al. (2013)	71-year-old female	DM-2, HTN, stage-V-CKD, amputation of first toe (1-month prior)	NR	Scalp, face, upper limbs	Non-bacteremic	NR	27 x 10^9/L	(-)	MRSA	GPC in dermis Necrotizing dermal inflammation Neutrophilic vasculitis	IV ceftriaxone and IV clindamycin-> piperacillin/tazobatam +vancomycin	DC
Barry et al (2021)	19-year-old male	CKD, type-II RTA	NR	Abdomen, R thigh	Non-bacteremic	NR	22 × 10^9/L	(-)	MRSA	GPC Ulceration with neutrophils of epidermis and dermis with granulation tissue	IV cefepime->IV cefuroxime +linezolid	DC
R.G. et al. (2017)	47-year-old male	Chronic alcohol abuse	NR	B thighs	Non-bacteremic	NR	12 x 10^9/L	(-)	MRSA	Epidermal necrosis Dermal infilitrate (neutrophils, lymphocytes and histiocytes) Gram stain not perfromed	IV ceftriaxone-> imipenam and amikacin	DC
Song et al. (2015)	15-month-old female	None	NR	Trunk, axillary region	Non-bacteremic	11.27 x 10^9/L	16 x 10^9/L	(-)	MSSA	Dermal infitrate (neutrophils and lymphocytes) Neutrophilic vasculitis	Ceftriaxone-> cefepime and clindamycin + doxycycline-> PO cephalexin	DC
Ivanaviciene et al. (2015)	54-year-old female	SLE, metastatic gastric cancer	HCQ, SST, Chemotherapy[b]	L popliteal fossa, R anterolateral knee, R external ear canal.	Non-bacteremic	0.4 × 10^9/L	0.8 × 10^9/L	(-)	MSSA	GPC in dermis. Perivascular dermal infilitrate (lymphocytes, histiocytes, and neutrophils)	IV vancomycin + nafcillin	DC
Ungprase et al. (2013) t	40-year-old male	AIDS, MRSA Skin abscess (2-weeks prior)	NR	Trunk, lower extremity	Non-bacteremic	NR	4.1 x 10^9/L	(-)	(-)	No biopsy	IV vancomycin -> PO linezolid	DC
Shah et al. (2021)	62-year-old male	HTN, HLD, R. toe crush injury (1-week prior)	NR	R lower extremity	Bacteremic	NR	NR	MSSA	MSSA	GPC in dermis Necrobiosis Suppurative dermatitis	IV vancomycin + cefepime then- > nafcillin	Died of multiple organ failure

Author	Age & Gender	PMH	Medications	Location of EG	Bacteremic/ Non-bacteremic	ANC	WBC	Blood Culture	Tissue Culture	Biopsy	Antibiotics	Outcome
Fang et al. (2022)	1-year-old male	AD transient neutropenia	NR	L arm, chest, abdomen, R thigh	Non-bacteremic	0.855 x 10^9/L	NR	(-)	MSSA	GPC in dermis Necrotitic vasculitis	IV cefepime + amikacin + teicoplanin- > cefepime	DC
Presenting case	71-year-old male	Stage IV small cell lung cancer	Chemotherapy[c] (7-days prior)	Upper and lower lips, neck, R elbow, L hand	Bacteremic	0.6 x 10^9/L	0.4 x 10^9/L	MSSA	NC	NC	IV vancomycin + cefepime -> cefazolin	DC

PMH: Past medical history; **EG:** Ecthyma gangrenosum; **ANC:** Absolute neutrophil count; **WBC:** White blood cell count; **COPD:** Chronic obstructive pulmonary disease; **ALL:** Acute lymphocytic leukemia; **DM-2**: Type 2 diabetes; **HTN:** Hypertension; **CKD:** Chronic kidney disease; **RTA:** Renal tubular acidosis; **SLE:** Systemic lupus erythematous; **AIDS:** Acquired immunodeficiency syndrome; **HLD:** Hyperlipidemia; **AD**: Atopic dermatitis; **NR:** Not reported; **MTX:** Methotrexate; **HCQ:** Hydroxychloroquine; **SST:** Systemic steroid therapy; **B:** Bilateral; **R:** Right; **L:** Left; **MRSA:** Methicillin-resistant *Staphylococcus aureus;* **MSSA:** Methicillin-sensitive *Staphylococcus aureus;* **(-):** Negative; **GPC:** Gram-positive cocci; **IV:** Intravenous; **DC:** Discharged.

Broad-spectrum antibiotics should be initiated following cultures in patients with suspected EG with narrowing of antibiotics following identification of antimicrobial susceptibilities. [13,16] This patient was successfully treated with IV vancomycin and cefepime and was later de-escalated to IV cefazolin. Of the eleven cases we found from the literature review, six were treated with vancomycin, and four were treated with cefepime. Other antibiotics we found commonly used were amikacin (3 cases), linezolid (2 cases), nafcillin (2 cases), and teicoplanin (2 cases).

4. Conclusion

While *P. aeruginosa* is the most common etiology of EG, although rare, other infectious pathogens should be considered in the differential, such as *Staphylococcus aureus*. This case is unique as it represents only the second case of EG due to MSSA bacteremia and the only case to have survived bacteremic-associated Staphylococcus aureus-EG. Thus, a history of immunosuppression, early culturing, and a high degree of clinical suspicion is necessary when considering rare etiologies of EG.

References

[1] Vaiman M, Lazarovitch T, Heller L, Lotan G. Ecthyma gangrenosum and ecthyma-like lesions: review article. *Eur J Clin Microbiol Infect Dis*. 2015; 34(4): 633-639.

[2] Fang KC, Lin FJ, Chen CH, et al. Ecthyma Gangrenosum Secondary to Methicillin-Sensitive Staphylococcus aureus in an Atopic Child with Transient Neutropenia: A Case Report and Review of the Literature. *Diagnostics*. 2022; 12(7): 1683.

[3] Şen H, İnangil G, Şahin L, Dere K, Özkan S, Dağli G. Ecthyma-gangrenosum-like lesions associated with methicillin-resistant Staphylococcus aureus infection. *Int J Infect Dis*. 2009; 13(4): e173-e175.

[4] Pechter PM, Marchione R, Milikowski C, Berman B. Ecthyma gangrenosum secondary to Staphylococcus aureus in an infant with transient neutropenia. *Pediatr Dermatol*. 2012; 29(3): 320-323.

[5] Chang AY, Carlos CA, Schuster M, Xu X, Rosenbach M. Nonpseudomonal ecthyma gangrenosum associated with methicillin-resistant staphylococcus aureus infection: a case report and review of the literature. *Cutis*. 2012; 90(2): 67-69.

[6] Jaque A, Moll-Manzur C, Dossi MT, Berroeta-Mauriziano D, Araos-Baeriswyl E, Monsalve X. [Ecthyma gangrenosum caused by Staphylococcus aureus]. *Rev Chilena Infectol*. 2016; 33(3): 336-339.

[7] Barry M, Alhijji A, Alsubaie A. Ecthyma gangrenosum secondary to MRSA in a young patient with chronic kidney disease. *IDCases*. 2021; 23: e01026.

[8] R G S, Muralidhar V. Non-pseudomonal ecthyma gangrenosum caused by methicillin-resistant Staphylococcus aureus (MRSA) in a chronic alcoholic patient. *BMJ Case Rep*. 2017; 2017.

[9] Song SS, Matiz C, Tom WL, Calame A, Krakowski AC, Friedlander SF. Ecthyma Gangrenosum-Like Lesions Secondary to Methicillin-Sensitive Staphylococcus aureus in an Immunocompetent Child. *Pediatr Dermatol*. 2015; 32(6): e259-e262.

[10] Ivanaviciene J, Chirch L, Grant-Kels JM, Kerr PE, Finch J. Ecthyma gangrenosum secondary to methicillin-sensitive Staphylococcus aureus. *Int J Womens Dermatol*. 2016; 2(3): 89-92.

[11] Ungprasert P, Permpalung N, Kue-A-Pai P, Ammannagari N, Chongnarungsin D. A rare case of ecthyma gangrenosum associated with methicillin-resistant Staphylococcus aureus infection. *J Infect Chemother*. 2013; 19(4): 761-763.

[12] Shah DJ, Leibowitz R, Salonia J. Ecthyma gangrenosum: A rare manifestation of staphylococcus aureus infection. *Journal of Scientific Innovation in Medicine*. 2021; 4(2).

[13] Shah M, Crane JS. Ecthyma Gangrenosum. In: *StatPearls*. StatPearls Publishing; 2022.

[14] Huminer D, Siegman-Igra Y, Morduchowicz G, Pitlik SD. Ecthyma Gangrenosum Without Bacteremia: Report of Six Cases and Review of the Literature. *Arch Intern Med*. 1987; 147(2): 299-301.

[15] Zhu Q, Yue Y, Zhu L, et al. Epidemiology and microbiology of Gram-positive bloodstream infections in a tertiary-care hospital in Beijing, China: a 6-year retrospective study. *Antimicrob Resist Infect Control*. 2018; 7: 107.

[16] Leekha S, Terrell CL, Edson RS. General principles of antimicrobial therapy. *Mayo Clin Proc*. 2011; 86(2): 156-167.