



## Ecthyma Gangrenosum Complicated by Fungal Pansinusitis

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### TEACHING POINTS

1. Providers should be aware of the characteristic morphology of Ecthyma Gangrenosum and the need for closer evaluation and examination of the skin on physical exam of immunocompromised patients.
2. Antipseudomonal antibiotics are recommended as empiric treatment for Ecthyma Gangrenosum due to the high prevalence of *Pseudomonas aeruginosa* as the causative pathogen in Ecthyma Gangrenosum.
3. Prompt and extensive workup for Ecthyma Gangrenosum should include coordinated care with specialist secondary to the high case fatality rate.

A 69-year-old Caucasian female initially presented to her outpatient oncology clinic with a fever and headache chief complaint. Her past medical history was significant for sinusitis, chronic kidney disease stage 4, thrombocytopenia, obstructive sleep apnea (OSA) on continuous positive airway pressure (CPAP), chronic anemia, non-insulin-dependent (type II) diabetes mellitus (NIDDM), metastatic multiple myeloma s/p bone marrow transplant undergoing chemotherapy with Lenalidomide (Revlimed), and myelodysplastic syndrome. The symptomology's onset and duration was one day prior to clinic presentation, with progressively worsening facial pain, symptoms of sinusitis, and right temple scalp pain (without tenderness to palpation). The development of a dark lesion (round necrotic macule) on the right temple was noted during the physical exam. These findings prompted concern from outpatient oncologists and subsequent transfer of the patient to the ER for work-up labs and admission.

On admission, the patient was febrile at 100.7 F. Initial labs revealed pancytopenia with leukopenia (leukocytes 0.7 x10<sup>3</sup>L), severe neutropenia (absolute neutrophil count 121 cells/microL), anemia (hemoglobin 9.7 g/dL), and thrombocytopenia (platelets 50x10<sup>3</sup>/mL). The patient was admitted to the medical ward with concern for neutropenic fever, ecthyma gangrenosum (EG), and sinusitis. Blood cultures were ordered, and she was initiated on broad empiric

coverage with IV Vancomycin, Piperacillin / Tazobactam, and Metronidazole. The oncology team was consulted, and they recommended holding Lenalidomide to mitigate the risk of possibly increasing the patient's susceptibility to infections. Infectious Disease (ID) service was consulted, and they ordered further workup due to concern for fungal sinusitis per worsening sinus tenderness. A CT of the brain w/o contrast showed findings consistent with sinusitis, and labs showed elevated inflammatory markers with ESR of 74 mm/hr.

On hospital day #2, the patient complained of new-onset diplopia developing in her right eye accompanied by right-sided progressive headaches. On physical exam, there was no temple tenderness to palpation; thus, significantly lowering the likelihood of the etiology of temporal arteritis on our differential. In the context of the earlier noted necrotic skin lesion, EG remained high on our differential. The patient began developing ecchymosis of the left eye upon subsequent hospital days. An MRI of the brain and orbit was ordered due to increasing concern for an invasive fungal or gram-negative rod infection, especially in the context of her immunocompromised state from chemotherapy and history of diabetes.

On hospital day #3, MRI results were notable for progressing pansinusitis. Per ID team recommendations, IV Vancomycin was discontinued, and the patient was started on IV Amphotericin 300 mg q daily for fungal sinusitis. Blood cultures revealed that 1 out of 4 samples to be significant for gram-negative rods. Antibiotic sensitivities identified Cefepime sensitive *Pseudomonas aeruginosa* (*P. aeruginosa*), which was essential to establish *P. aeruginosa* bacteremia diagnosis in the context of clinical presentation. IV Piperacillin / Tazobactam was discontinued in-lieu of Cefepime and Metronidazole – the patient was treated for an additional nine days. The patient responded adversely to Amphotericin; she developed an electrolyte imbalance, diarrhea, and type 4 tubular acidosis. She was managed with fluid repletion, Diphenoxylate / Atropine, and Sodium bicarbonate 325 mg PO BID.



Throughout her hospital course, the patient's symptomology of headaches, double vision, and sinus tenderness incrementally resolved. EG lesion on the right scalp progressively resolved and reduced in size relative to the initial presentation (see Figure #1). Repeat blood cultures were negative for *P aeruginosa*. One day before discharge, IV Metronidazole was discontinued, and the patient was transitioned from IV to oral antibiotics—IV Cefepime was transitioned to Augmentin 875/125 mg PO Q12 for seven days. Amphotericin transitioned to Voriconazole 200 mg PO Q12Hrs for five weeks, per ID team recommendations.

On hospital day #14, pancytopenia resolved with CBC resulting a WBC of  $1.46 \times 10^3$ , neutrophils at 28.7%, equating to an absolute neutrophil count (ANC) 419 cells/microL. She was deemed stable for discharge per ID and Oncology teams and stable enough to restart her chemotherapy for underlying Multiple Myeloma, per oncology. She was discharged to home with a scheduled follow-up with outpatient oncology for future management and outpatient Otolaryngology (ENT) to evaluate further and monitor for successful clearance of pansinusitis.

**Figure 1. Right Scalp EG Lesion Photograph:** It was taken on the day of discharge (Hospital day #14), evidence of a reduction in lesion diameter per initial presenting size (light brown region diameter- blue arrow). It is characterized by a flat, round, black eschar with surrounding erythema (green arrow).

## DISCUSSION

Ecthyma Gangrenosum (EG) is a rare and rapidly progressive skin infection with resulting ulcerative lesions that extend deep into the dermis with a propensity for sepsis. EG is commonly due to bacteremia from *P aeruginosa* occurring in immunocompromised or critically ill patients (leukemia, lymphoma, post-chemotherapy, severe burns, severe malnutrition, etc.) carrying a high mortality rate, especially with delayed diagnosis and the absence of appropriate therapy.<sup>1,2</sup> Generally, an immunocompromised status with hematological malignancies and neutropenia are the major risk factors for the development of EG. While *P aeruginosa* is the most common pathogen, other bacteria, viruses, and fungi have also been reported as causative agents to the pathogenesis. EG is typically a clinical diagnosis, and the characteristic EG lesions are frequently present on the physical exam. Scrutiny and examination of the skin are necessary if clinical suspicion warrants EG among the differential, especially in immunocompromised states. Additionally, to complicate diagnosis, EG may present at any anatomic location, in various stages of development, and maybe single or multiple lesions. This is evident per this case in which the lesion was obscured by the patient's hair and well developed upon discovery. Lesions can initially be characterized as painless erythematous macules that develop into pustules, bullae, or crusted ulcers with surrounding

raised, erythematous margins that develop into gangrenous ulcers within 12 to 18 hours. These rapidly progressing lesions can involve the skin or mucous membranes - the presence of such morphological lesions warrants immediate work-up.<sup>3</sup>

EG bacteremia's mortality rate ranges from 38% -77%; therefore, it is essential for providers to be able to identify the hallmark features quickly and to make the diagnosis and initiate appropriate treatment.<sup>4</sup> Prognosis of EG is highly associated with the early implementation of optimal antibiotics coverage, with an overall cure rate of 67% for patients receiving appropriate antibiotics, but only 14% for those not receiving proper antibiotic coverage. Antipseudomonal antibiotics are recommended as an empiric treatment to reduce morbidity and mortality due to the high prevalence and likelihood that most EG cases are due to *P aeruginosa*.<sup>5</sup> Blood cultures are imperative for identifying the causative pathogen and appropriate treatment. Lastly, although infrequent and unlikely, the possibility of Fungal Ecthyma Gangrenosum cannot be excluded from the working differential. It is important to note that negative blood cultures do not necessarily exclude EG as suspected lesions' etiology. Surgical debridement may be warranted for invasive necrotic ulcerations, while tissue samples are ultimately necessary for a definitive diagnosis of EG in some cases.<sup>6</sup>

Although direct seeding of *P aeruginosa* upon the dermis is the most likely mechanism, this patient's presentation may have resulted from multifactorial contributory agents. Perhaps the EG anatomical lesion location signifies a longstanding progressive mechanical breakdown from the CPAP's occluding straps on a nightly basis for managing her OSA. The propensity of such long-term mechanical pressure to induce breakdown in the dermal barrier results in prolonged healing and increased susceptibility for infections, especially in patients with diabetes. Such context is evident in our patient and more evident by the severe neutropenia exacerbated by the patient's ongoing chemotherapy and multiple metastatic myelomas creating the context of a highly susceptible immunocompromised state conducive to the development of EG.

The presented case is unique for various reasons; however, it highlights the criticality of a stepwise and coordinated diagnostic approach for successfully managing a rare presentation of Ecthyma Gangrenosum secondary to septicemia of *P aeruginosa*, further complicated by pansinusitis. The diagnosis of EG was chiefly ascribed based on the pertinent positives and negatives of the physical exam, characteristic morphology of the patient's lesion, and contextual information of the patient's immunocompromised status. Prompt identification and treatment with empiric antimicrobial therapy were essential for EG management, ensuring the covering of *P aeruginosa*; efficient collaborative coordination of care and consultations were imperative for timely diagnosis, management, and treatment.

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