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Case and Review

Ecthyma Gangrenosum of Fungal Origin: A Case Report

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Keywords
Ecthyma gangrenosum · Fungal infection · *Candida* · Steroids

Abstract
Introduction: Ecthyma gangrenosum (EG) is usually a dermatologic manifestation of a *Pseudomonas aeruginosa* infection in an immunocompromised individual but may sometimes be caused by other bacteria or fungi in an immunocompromised or non-immunocompromised individual. ***Case Presentation:*** A 75-year-old woman with a history of high blood pressure and sequels of ischemic cerebral infarction presented with a 5-day history of general malaise, cough with yellow sputum, and respiratory distress. The patient had pale mucous membranes, temperature of 38.5°C, tachycardia, normal blood pressure, SaO_2 of 85%, intercostal retractions, and severe bronchospasm upon hospital admission. No skin lesions were seen. The patient was admitted to the intensive care unit (ICU) because of her critical condition and was supported with invasive mechanical ventilation. Her blood count showed 8,100 leukocytes/mm^3, neutrophils 79%, hemoglobin 10.1 g/dL, creatinine 1.1 mg/dL, and C-reactive protein 328 mg/dL. Arterial blood gases showed metabolic acidosis and moderate hypoxemia. The initial report of blood and urine cultures was negative for bacteria, and positive for influenza A H1N1. The patient was treated with oseltamivir and intravenous methylprednisolone for acute respiratory distress syndrome associated with the viral infection that occurred. Subsequently, violaceus macular and papular lesions appeared, which evolved into ulcerated lesions with erythematous border and necrotic center were seen in the anterior region of the chest and abdomen, from where *Candida metapsilosis* was

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isolated. EG was reported in this patient, who was also immunocompromised because of steroid use, had a prolonged stay in the ICU and received broad-spectrum antibiotics. Fungemia and urinary infection due to different fungi were also found. ***Conclusion:*** It is worth mentioning that EG can be caused by germs other than *P. aeruginosa* and fungal infections should not be ruled out.

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Introduction

Ecthyma gangrenosum (EG) is an infectious disease that is frequently related to bacteria, particularly *Pseudomonas aeruginosa,* and is observed mainly in immunosuppressed individuals. However, several reports described etiologies related to filamentous fungi and yeasts [1]. Regarding the pathogenesis of this rare disease, the invasion of the infectious agent through the blood vessels' walls, causing thrombosis in arteries and veins, has initially been documented, which ultimately leads to necrosis of the epidermis and subdermal tissues.

The most common clinical manifestation of EG is the presence of macules with hemorrhage, which become ulcers with a necrotic surface and are always associated with an erythematous halo, which is the characteristic on which the initial diagnosis is based on. These findings should be accompanied by microbiological tests to establish the specific pathogenic agent and thus determine the most appropriate treatment [2]. EG is more common in pediatric, diabetic, or immunocompromised patients and is frequently located in the arms and legs [3, 4]. In this report, the patient had not been diagnosed with diabetes or any other immunosuppressive disease, and the lesions were located on the abdomen and chest.

Based on the above, this case report describes a diagnosis of EG associated with systemic fungal infection made in a patient with a long stay in the intensive care unit (ICU) and subjected to steroid use. Healthcare staffs need to be alert to the presence of similar dermatological symptoms since they are generally the manifestation of sepsis, which is not always associated with bacterial involvement. Below, we describe the case of an elderly patient with a prolonged stay in the ICU due to a viral lung infection, who finally presented multiple fungal infections. This compromised the skin through classic EG lesions, indicating marked systemic compromise caused by fungi. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000542105).

Case Presentation

This is a 75-year-old woman with a history of stroke, chronic obstructive pulmonary disease, chronic kidney failure, high blood pressure, and osteoarthritis, without a history of allergies. She presented clinical symptoms for 5 days with general malaise, cough, and yellow expectoration. The patient was admitted to the emergency room of a tertiary clinic with signs of respiratory failure, so she was transferred to the ICU. Her blood count showed no leukocytosis, creatinine levels were 1.1 mg/dL, and arterial blood gases with severe hypoxemia. Her chest X-ray showed bibasal alveolus-interstitial infiltrates (Fig. 1).

Support was provided with invasive mechanical ventilation. Influenza A H1N1 was positive in the bronchial secretion sample, so treatment with oseltamivir was started every 12 h. Acute respiratory distress syndrome was diagnosed based on radiological worsening, a

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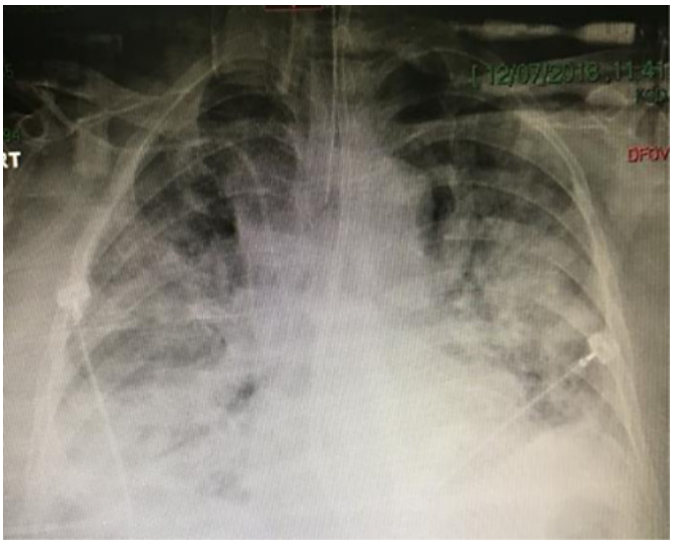

Fig. 1. Chest X-ray. Predominantly basal alveolar interstitial infiltrates that are associated with viral infection.

decrease in the blood pressure index of 0_2/inspired fraction of 0_2 (P/F ratio), and the need for PEEP ≥10 cm H_2O. Therefore, intravenous methylprednisolone was started at 2 mg/kg/day.

The initial skin lesions were macules and violaceus papules, rounded, that subsequently evolved with necrotic areas in the center and slight bleeding at the edges, indurated, and with surrounding erythema appeared in the following days, located in the left anterior region of the chest and in the left upper abdominal region (Fig. 2a, b). No similar injuries were reported in the clinical history prior to hospitalization to the ICU.

Furthermore, sputum culture with abundant yeast and growth of blastoconidia was reported, as well as blood cultures with growth of budding yeast and urine culture with growth of blastoconidia. The initial culture of the skin lesions was negative, no Gram stain or KOH smear was performed, showing clinical worsening with respiratory deterioration, acute kidney injury, multiple organ failure, and worsening of the abdominal lesions. *C. metapsilosis* was subsequently reported in the biopsy and culture of these lesions (Fig. 3); *Cryptococcus neoformans*, Grubii variety, in blood cultures and *Candida albicans* in urine culture. Considering the lack of improvement with the use of caspofungin, the infectious disease unit began treatment with liposomal amphotericin and 400 mg fluconazole intravenously/day.

Finally, the patient presented with nosocomial pneumonia with isolation of *Stenotrophomonas maltophilia*, with subsequent clinical worsening, requirement for renal replacement therapy, and increase in lung infiltrates. During her stay in the ICU service, the patient died 8 days after the last antifungal treatment regimen was administered. Figure 4 summarizes the main facts of the case.

Discussion

EG is a classically described dermatological infectious disease, caused mainly by *P. aeruginosa*. However, it can also be caused by another series of pathogens, such as *Aeromonas hydrophila*, *Staphylococcus aureus, Serratia marcescens, Escherichia coli, Neisseria meningitidis, Vibrio vulnificus,* and *Burkholderia cepacia* and by the fungi *Fusarium sp*, *Candida sp*, *Mucor sp*, and *Aspergillus sp* [5–7]. Although much less frequently, fungi can also cause EG, as occurred in this case.

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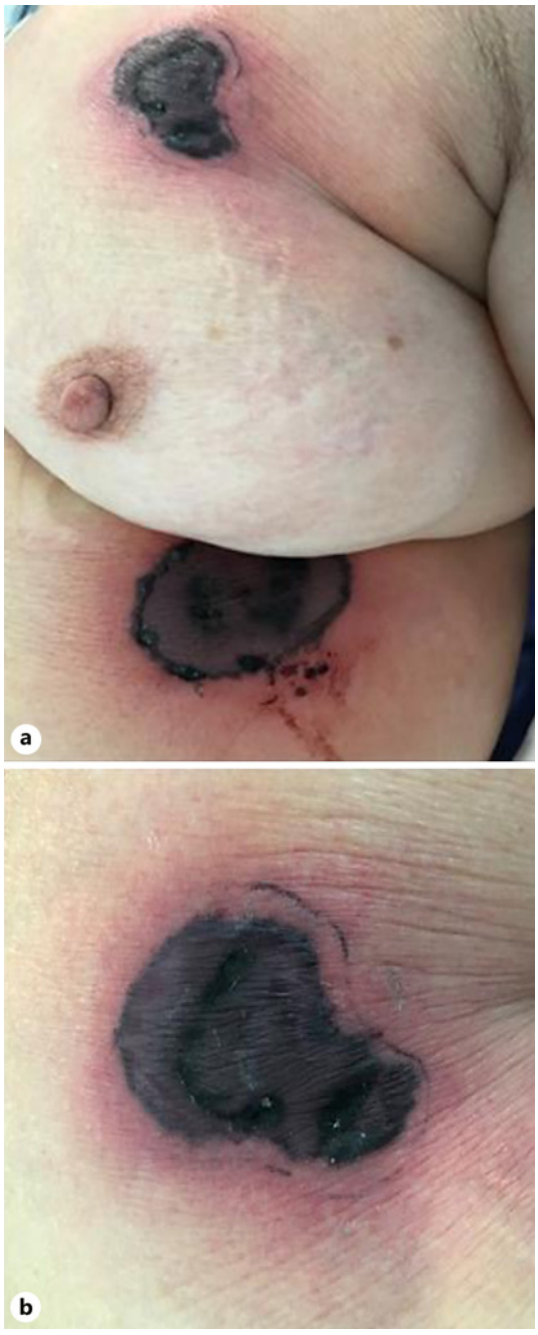

Fig. 2. a EG in the chest and abdomen. **b** Clinical appearance of the injury. An ulcer with a gray-blackish eschar surrounded by a peripheral erythematous halo is seen, located in the left anterosuperior region of the abdomen.

There are predisposing factors for the development of EG, such as local humidity, diabetes mellitus, obesity, peripheral vascular disease, neutropenia, infection by the human immunodeficiency virus, and factors that involve disruption of the epidermal barrier [8]. It must be mentioned that our study patient had some predisposing factors for developing this condition, such as being an elderly patient, obesity, consequences of a stroke, prolonged invasive ventilatory support, use of steroids, and prolonged hospital stay.

Although bacteria, and to a lesser extent fungi, are the cause of this pathology, viruses and parasites have also been implicated [9]. Other studies have shown that necrotic lesions can also occur in immunocompetent people [3], although evidence clearly shows that patients suffering from EG are individuals with immunosuppressive complications [4]. In this study,

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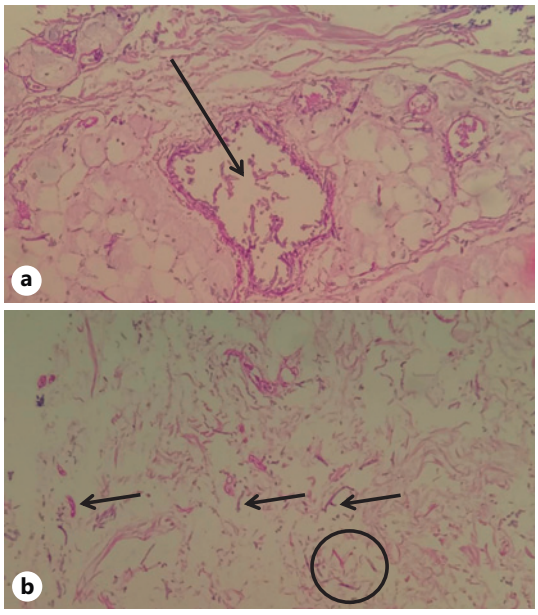

Fig. 3. a Mycotic abscess in biopsy of EG from abdominal lesion. **b** The arrows and the circle indicate fragments of *Candida* hyphae isolated in the culture.

where Vaiman et al. [3] reviewed 167 cases of patients diagnosed with EG, it was determined that necrotic lesions also occur in immunocompetent and healthy individuals. In this report, the patient was treated with several antibiotics for viral pneumonia complicated by nosocomial bacterial infection during her hospitalization. She also received both inhaled and intravenous steroids, used for the management of chronic obstructive pulmonary disease and acute respiratory distress syndrome, which potentiated her immunosuppression. Furthermore, fungal etiology has been reported in up to 9% of cases [3], as occurred in this case, in which fungal infections were also manifested in different sites due to different fungi. Thus, the presence of fungal EG in immunosuppressed individuals could suggest the presence of other fungi in different systems.

Epidemiologically, cryptococcosis is another opportunistic infection that should not be ruled out in markedly immunocompromised patients. In fact, 6–50% of AIDS patients suffer from it, which is why it is considered a major cause of infection in this type of patient [10]. Our study patient's immunocompromise was considerable since sepsis due to *C. neoformans* Grubii variety was determined without having human immunodeficiency virus infection or any advanced neoplastic disease. Disseminated candidiasis can cause EG in immunocompromised patients, where *Candida tropicalis*, *Candida Krusey*, and *C. albicans* are the most common [11]. The lesions usually present as centrally located erythematous papules and nodules. The presence of fever, papular erythematous skin lesions, and diffuse muscle pain point toward the suspected diagnosis of disseminated candidiasis [12].

EG is a rare condition, where the importance of an adequate microbiological study is emphasized to achieve a diagnosis of the causative agent [13]. In this report, various microbiological tests were performed on the patient, such as blood cultures from the central venous catheter and cultures of the dermatological lesions, in order to detect the causative agent of EG. Fungal infection was found after several attempts, where abundant budding yeasts were isolated with the diagnostic tests used, which preceded the identification of other fungal infectious agents, such as *C. neoformans,* in the blood culture of the central venous catheter and *C. albicans* in urine culture. This was documented after the report of *C. metapsilosis* in cultures of tissue biopsied from skin lesions in the region of the left hypochondrium.

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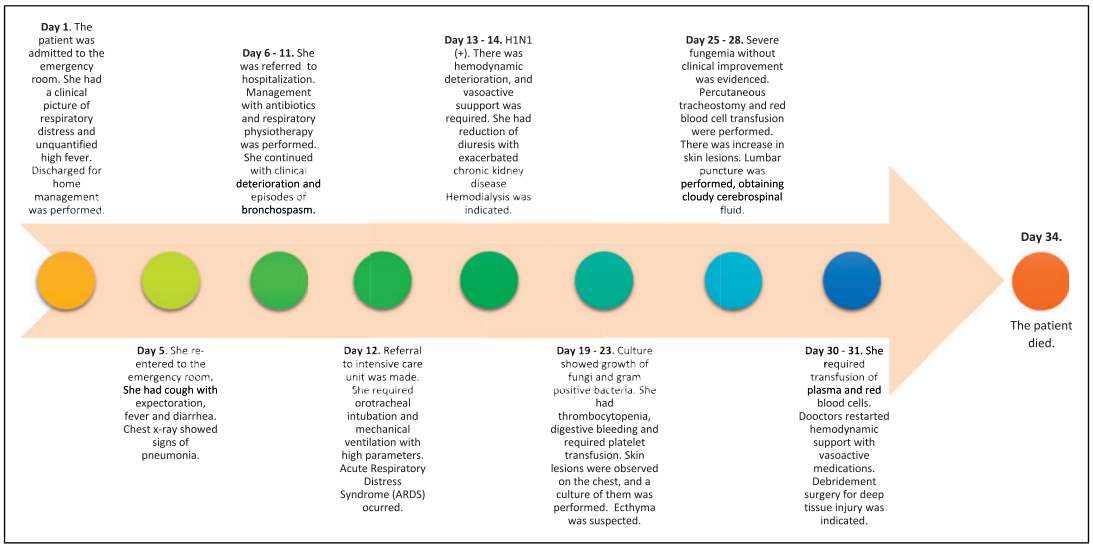

Fig. 4. Timeline of the main events of the case.

Necrotic eschars with a greenish center were especially noted in extremely weakened patients in a study conducted by Flores et al. [2] on the clinical manifestations of skin infections in adults. These lesions generally present as painless macules that become hemorrhagic vesicles, and eventually evolve into necrotic ulcers with black eschar and surrounding erythema [14]. In this report, the patient's lesions had violaceous, rounded, deep characteristics, with necrotic areas in the center and bleeding at the edges, indurated, and with erythema surrounding the lesion.

The sites most frequently affected by EG include the arms and legs, although it can affect almost the entire skin surface [14]. Unlike what was described in the bibliographic evidence, the patient presented injuries in the left anterior region of the chest and in the left upper abdominal region, and similar injuries were not reported prior to hospitalization to the ICU.

To ensure adequate treatment, the necessary diagnostic tests must be performed in EG in order to determine its etiology [15]. Dermatological clinical presentation is essential to aid in the diagnosis, as occurred in this case, where the patient was found with blackish lesions located on the skin of the left hypochondrium region. This diagnosis was suspected and confirmed by the multidisciplinary teams who were in charge of the ICU. EG-type lesions caused by fungi such as *Candida* must be ruled out in immunocompromised patients, where a definitive diagnosis supported by blood cultures and skin biopsy with cultures is necessary, as was performed in this case [16]. It should be considered that series of cases have been reported with a percentage of sepsis associated with EG of up to 38% [1], demonstrating how septic or immunocompromised individuals died more frequently than those who were immunocompetent or non-septic, thus suggesting a poor prognosis [14]. Early detection of EG and early termination of its etiologies are essential for adequate therapeutic management.

Conclusion

EG should be suspected in patients who have characteristic skin lesions together with a state of immunosuppression such as diabetes mellitus or steroid use, although it can also occur in immunocompetent individuals. Early detection of EG lesions guarantees a timely therapeutic approach. Several microbiological etiologies have been reported, where *P.*

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aeruginosa accounts for more than 2/3. However, it must be kept in mind that fungal infections can involve the skin, thus indicating the severe immunological compromise of the affected individual. Likewise, we do not recommend dividing cases into those without *Pseudomonas* and those with *Pseudomonas*, as was done previously. This case report shows how immunosuppression led a patient treated in the ICU to present infections caused by several fungi in different sites of the body such as skin, orotracheal secretion, blood, and urine.

Statement of Ethics

The study complied with the Declaration of Helsinki [17]. Written informed consent was obtained from the patient's next of kin for publication of the details of their medical case and any accompanying images. This investigation was approved by the Ethics Review Board of Clínica Palma Real and its Scientific Committee (Act 01/2023).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Germán Andrés León-Sánchez, Heiler Lozada-Ramos, and Andrés Darío Restrepo Becerra: data collection, literature review, and manuscript writing. Jorge Enrique Daza-Arana, and Ruben Varela-Miranda: data analysis and manuscript editing.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online version. Supplementary material files or other queries may be directed to the corresponding author upon reasonable request.

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