Case Report

Multidisciplinary management of a patient with eyelid ecthyma gangrenosum due to *Pseudomonas aeruginosa* infection

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ABSTRACT

Pseudomonas aeruginosa is a Gram-negative bacillus, responsible for frequently serious infections that cause high morbidity and mortality, especially in immunosuppressed hosts or with underlying malignant processes. Ecthyma gangrenosum is a highly suggestive, though not pathognomonic, manifestation of disseminated *P. aeruginosa* infection. The palpebral presentation of the latter is estimated to be <6%, so initial clinical suspicion and early multidisciplinary management are of great importance. This article aims to show the diagnostic and therapeutic challenge of a patient who abruptly presents septicemia by *Pseudomonas*, accompanied by severe periocular skin symptoms in a tertiary hospital.

Key words: Cellulitis, Ecthyma gangrenosum, Necrosis, Neutropenia, Oculoplastic, *Pseudomonas*

Pseudomonas are Gram-negative bacteria that are commonly found in the environment, and capable of inhabiting soil, water, plants, and animals. Of all the species, *Pseudomonas aeruginosa* is by far the most relevant as a human pathogen. *P. aeruginosa* is currently considered a highly worrisome pathogen [1]. L. Barker first described ecthyma gangrenosum (EG) in 1987; its appearance is postulated as a pathognomonic sign of *P. aeruginosa* septicemia, mainly in immunocompromised patients. However, a minority of cases are described in healthy patients with no known immune alteration. Lesions occur more frequently in the gluteal or perineal regions (57%) followed by the extremities (30%), and only 6% affect facial areas, being palpebral presentation exceptional [2]. A high clinical suspicion and an early diagnosis of the causative agent are essential; thus, the rates of treatment success, morbidity, and mortality are directly related to the coexistence of a septic state, the degree of neutropenia, and the extent of the lesions.

Our objective is to present the diagnostic and therapeutic challenge of this specific case, as well as the importance of early multidisciplinary management.

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CASE REPORT

A 71-year-old woman whose personal history of interest includes arterial hypertension and type 2 diabetes diagnosed in 2013. In 2014, she was diagnosed with agranulocytosis (febrile neutropenia episode with admission to hematology without evidence of secondary cause) and has chronic anemia since 2011 with low ferritin and Vitamin B12 levels for which, she received iron treatment on numerous occasions. She has no known drug allergies. She does not report an ophthalmological history of interest.

Her first contact with our ophthalmology service was through the hospital emergency department, referred by a general practitioner after clinical worsening and an increase in the right periocular inflammatory signs associated with the impossibility of spontaneous eyelid opening in the context of a 10-day history of upper respiratory catarrhal symptoms.

On initial examination, she presented with extensive phlogistic signs and skin induration that prevented correct evaluation of the eyeball (Fig. 1). The patient has a poor general appearance and there was significant dryness of mucous membranes. Blood pressure was 135/60 mmHg; heart rate was 116 bpm; respiratory rate was 26 rpm; basal oxygen saturation (SaO_2) was at 97%; and body temperature was at 38.2°C. Considering the presence of rapid deterioration in her overall status, vital signs, complete

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laboratory tests, and orbital computed tomography were requested.

In the blood test results, it was worth noting severe neutropenia with lymphopenia, and alterations in coagulation times. In the white series: Leukocytes (count) 0.47 × 10^3 (normal range: 3.60–10.50), neutrophils (count) 0.29 × 10^3 (normal range: 1.50–7.70), and lymphocytes (count) 0.16 × 10^3 (normal range: 1.10–5.0). Hemostasis values showed:

Prothrombin time (ratio) was 1.46 ratio (normal range: 0.8–1.2), prothrombin time (seconds) was 16.3 s (normal range: 9–13.4), and prothrombin time (%) was 58% (normal range: 75–140). Elevation in acute phase reactants with a C-reactive protein at 437.4 mg/L, as well as procalcitonin levels at 14.18 ng/mL (normal range <0.1). The imaging test (Fig. 2) showed right pre-septal periorbital cellulitis with ocular proptosis, although without data of post-septal involvement. After contrast administration, uptake was observed preceding the anterior chamber, 3 mm thick, suggestive of a collection/abscess.

Given the clinical suspicion of infectious orbital cellulitis of unknown etiology and severe sepsis, the patient was admitted to the intensive care unit (ICU) for monitoring and treatment. Empirical treatment was started with meropenem 2 g intravenous (IV) infusion every 8 h, amphotericin B 200 mg IV every 24 h, filgrastim 30 units IV every 24 h, and saline 500 cc + 150 mg dexketoprofen infusion 21 mL/h. In ICU, the patient remained stable without developing organic failure, although significant cellulitis symptoms persisted with necrotic and even ulcerated lesions on the upper eyelid. In the initial drainage of the ophthalmic discharge, *P. aeruginosa* grew with sensitivity to meropenem (MIC = 1 µg/mL). The same bacteria with the same susceptibility pattern grew in the initial blood cultures. Cultures of blood and pus from the lesion for fungi and serum galactomannan antigen were negative, so amphotericin B was discontinued after 6 days of treatment. The initial suspicion of mucormycosis is, therefore, ruled out. Given that the patient had severe neutropenia since admission and that several years before she had another episode of this same cytopenia, a consultation was made with the hematology unit, which considered that the patient suffered from cyclic neutropenia and recommended treatment with granulocyte colony-stimulating factor.

The ophthalmology department performed an extensive curettage of the necrotic lesion under aseptic conditions and local anesthesia (Fig. 3). Debridement of the right malar and upper palpebral areas was performed, as well as deeper planes of the internal canthus. Subsequently, a wide defect of continuity solution, loss of the internal palpebral fissure with separation of the edges, extensive purulent material, and mucosal granulation tissue were revealed. Treatment was prescribed twice a day with chloramphenicol antibiotic ointment and occlusion with castor oil patches (linitul).

One month after the acute symptoms and after verifying the sterilization of the orbit by taking new skin cultures, surgical repair under general anesthesia was carried out jointly by ophthalmology and plastic surgery (Fig. 4). During the

Figure 1: Photographs of the macroscopic evolution of the right palpebral lesion. The first image was taken on admission to intensive care and the second 5 days after transfer to the ward

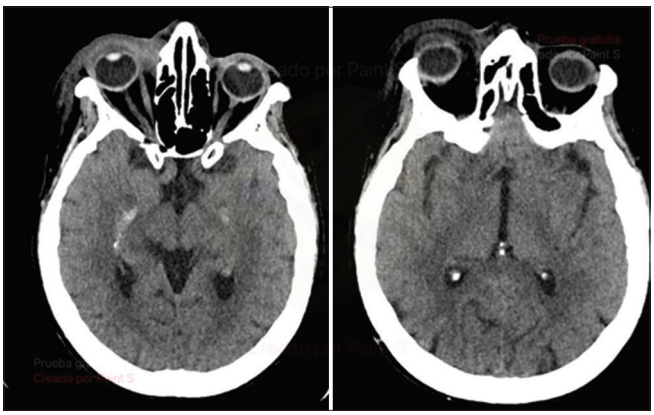

Figure 2: Computed tomography image of the orbit in the axial section upon arrival at the emergency room showing slight right proptosis, increase and inflammation of soft tissues, and collection between the anterior chamber of the right eye and the palpebral tarsal conjunctiva

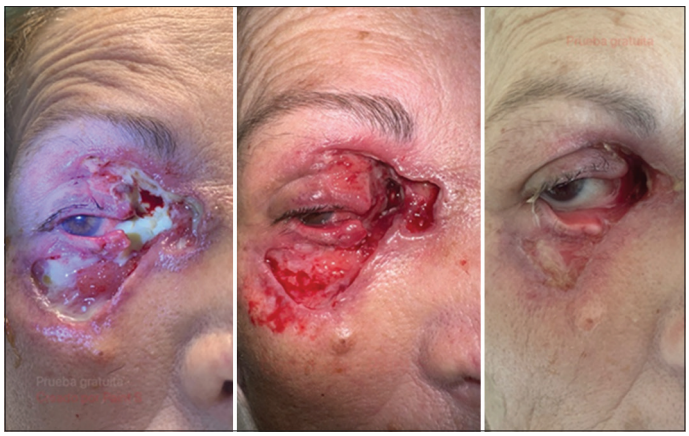

Figure 3: Photographic images of the curettage process of the right palpebral and malar necrotic eschar. The last image shows severe residual scarring ectropion 7 days after curettage

intervention, the disappearance of the medial palpebral ligament and the entire lacrimal apparatus (sac and upper and lower lacrimal ducts) was observed. We also found that a quarter of the lower internal eyelid had intense fibrosis. Necrotic debris in the orbit was cleaned, followed by suturing the eyeball to the nasal wall and tenzel flap to recompose the palpebral anatomy. With the help of the plastic surgeon, a free preauricular skin graft was

performed on the lower eyelid, covering its surface with sterile gauze to facilitate proper adhesion. We finished the intervention by making a glabellar flap in the inner canthus and upper eyelid, closing with 6/0 vicryl suture, and 6/0 and 4/0 silk.

During her admission, the patient suffered from hypokalemia secondary to the infusion of amphotericin B. Follow-up after surgery showed satisfactory results, and given the absence of complications, the antibiotic regimen was simplified to ciprofloxacin 750 mg/12 h orally. From discharge, close follow-up was carried out by infectious diseases, ophthalmology, and hematology. In post-operative check-ups, the scar appeared very well, with no new symptoms or local infectious signs (Fig. 5).

DISCUSSION

In patients with some degree of immune compromise, periorbital infections are serious, although infrequent. There are many microbial agents involved, among which we should highlight: Streptococci, Staphylococci, *Toxoplasma gondii*, *Propionibacterium acnes*, and *Pseudomonas*, without forgetting fungal elements such as *Aspergillus* genus that could be associated [3].

P. aeruginosa is found as a nosocomial pathogen that enters the bloodstream through skin microcracks in patients with mechanical ventilation, major burns, vascular catheters, or urinary foci. Its virulence and infectivity come from the production of toxins that inhibit the migration and leukotaxis of the immune system. Due to cellular mechanisms and elastase production, it achieves the destruction of the vascular wall, penetrating the subcutaneous tissue, triggering an ulcerative reaction and skin necrosis. In the present case, the frank neutropenia was observed in the emergency laboratory tests on admission is striking, in a presumably "healthy" patient with values within normality in the analytical tests 2 months before, the only trigger being a concomitant viral infection. The latter is not excessively new, since several studies defend that *Pseudomonas* infection can occur in the absence of immunosuppression or in patients who present a transient immune weakening secondary to a viral picture [4].

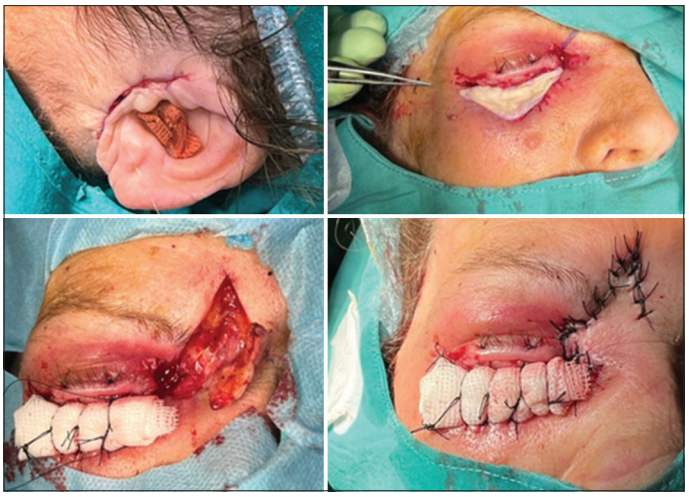

Figure 4: Oculoplastic and repair surgery intervention of the right palpebral and malar defect

Regarding the characteristic skin manifestation of *Pseudomonas* bacteremia called EG, its evolutionary stages develop in a period between 2 and 5 days. Initially, it manifests as an erythematous macule, then vesicles and bullae secrete pus or serosanguinous fluid. In its late stage, ulcerated lesions rapidly evolve into a necrotic eschar with a red peripheric halo [2,5,6]. Kim *et al*. [2] conjecture the possibility of a predisposition to the medial canthal region of yet unknown etiopathogenesis.

The diagnosis is both clinical and microbiological, through the isolation of *P. aeruginosa* in skin samples or blood cultures. The anatomopathological results show non-specific acute changes, without added diagnostic value. There are a series of clinical criteria to facilitate the therapeutic management of orbital infectious cellulitis described by Oxford and McClay. Among the latter, conservative medical management is recommended in patients with normal visual acuity and pupillary reflexes, preserved intraocular pressures, proptosis <5 mm, and abscesses <4 mm on imaging tests [7]. From the ophthalmological point of view, the impossibility of examining the eyeball anatomically and functionally due to the surrounding necrotic eschar was an added challenge in the management of our patient, doubly justifying the debridement performed during admission. Maccheron *et al*. [8] describe a case of a patient with myelodysplastic syndrome who simultaneously developed eyelid EG with orbital cellulitis and panophthalmitis, requiring enucleation due to the unfavorable evolution of the clinical picture. In contrast, Homer *et al*. [9] reported a case of GD in a patient treated for a dendritic cell neoplasm who, after taking oral ciprofloxacin and local debridement, presented a spontaneous resolution of the palpebral necrosis. Lee and Lai [10] in addition to presenting a case of necrotizing fasciitis caused by *Pseudomonas*, they carried out a bibliographic summary of 16 studies that deal with periorbital infections caused by this agent. In this review, they highlighted the involvement of the eyelid, the conjunctiva, and the medial canthus and underlined the secondary sequelae of necrosis of the lacrimal apparatus such as lagophthalmos and epiphora, the latter mostly requiring reconstructive surgery in a second stage.

The singularity of our clinical case lies in the integrity with which all the structures of the eyeball, both anterior and posterior,

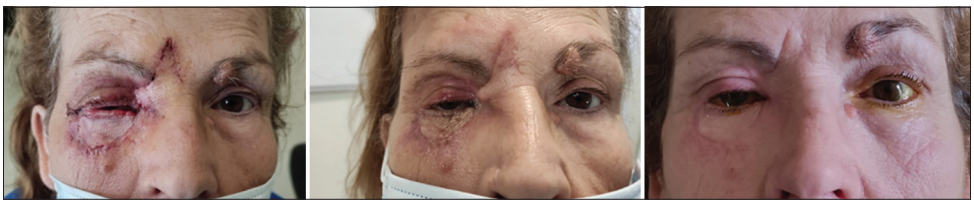

Figure 5: Follow-up of oculoplastic surgery at 1 week, 1 month, and 6 months

are respected. There was no infectious penetration into deep planes, thus preserving monocular vision, despite the extensive infection observed on clinical examination. During the acute episode, clinical signs of inflammation appear that mimic entities that present in a similar way, which is why the differential diagnosis in this profile of patients adds complexity. It is mandatory to exclude invasive fungal disease in diabetic patients with evidence of orbital skin necrosis and rapid progression as observed in our case.

In this type of potentially very serious infection, the initiation of early empirical antibiotic treatment is extremely important. From a medical point of view, the most frequently prescribed antimicrobials empirically in cases of pre-septal cellulitis are amoxicillin/clavulanic acid 875/125 mg or cefuroxime axetil 500 mg/12 h, using ceftriaxone 1 g/12 h IV in the more serious forms. In post-septal or orbital cellulitis, ceftriaxone 1 g/12 h or cefotaxime 2 g/6 h IV plus linezolid 600 mg/12 h IV or daptomycin 8–10 mg/kg/day IV is recommended if there is suspicion of infection by *Staphylococcus aureus* methicillin-resistant. Add 500 mg/8 h IV if there is an odontogenic focus or chronic sinusitis and liposomal amphotericin b 5–10 mg/kg/24 h IV if the existence of fungi is suspected. The most recent bibliography indicates that there is no evidence of the clinical advantage of combining two antibiotics in cases of sepsis caused by *Pseudomonas*, being preferable once the agent and its sensitivity are known, to use a single drug [6]. Adequate and early sampling for gram and culture is essential to know the pathogen and its sensitivity to antimicrobials. Other measures to be taken in addition to antimicrobial treatment are as follows: (1) Conservative debridement, (2) normalization of the neutrophil immune cell count in patients with neutropenia, and (3) some authors recommend hyperbaric therapy to promote tissue restoration [4,5]. Local skin care with chlorhexidine and polymyxin B and covering with paraffin dressings will also be indicated.

Finally, although our patient had a successful recovery with a favorable evolution during admission and after hospital discharge, we must consider that the prognosis of patients with sepsis or *Pseudomonas* bacteremia is serious, with very high mortality rates, in some series, it reaches 95% [2].

CONCLUSION

EG is a rare dermatological condition often linked to severe *P. aeruginosa* infections, particularly in immunocompromised patients such as those with neutropenia. Due to the limited number of cases, the risk factors for GE are not fully understood. The presence of these lesions indicates a severe infection, necessitating early detection and prompt systemic treatment to avoid poor outcomes. Collaboration among specialists enhances diagnosis and treatment. Further research is needed to better understand the epidemiology, pathophysiology, and optimal management of GE.

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