B-ENT, 2017, **13**, 315-319

Sinonasal ecthyma gangrenosum

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Key-words. Ecthyma gangrenosum, invasive fungal disease, *P aeruginosa*, functional endoscopic sinus surgery, immunocompromised

Abstract. *Sinonasal ecthyma gangrenosum. Problems/objectives:* Ecthyma gangrenosum, formerly known as pyogenic gangrenosum, is a rare skin infection caused by *Pseudomonas aeruginosa*. The infection mostly affects patients that are immunocompromised. Few previous studies have described ecthyma gangrenosum in the sinonasal tract.
Methodology: A 56-year-old woman that was immunodepressed was admitted to the Hospital Clinic of Barcelona with acute rhinosinusitis symptoms. Imaging showed signs of invasive infection at the level of the left maxillary sinus. Functional endoscopic sinus surgery was performed to debride the lesion until viable tissue was visible in the pterygopalatine and infratemporal fossa.
Results: Microbiological analysis revealed the presence of multiresistant *P. aeruginosa*. Pathological anatomy studies pointed to extensive tissue necrosis and ruled out the presence of mycotic structures. The patient was treated with topical and intravenous colistin and meropenem, based on the antibiogram, with rapid improvement.
Conclusions: It is important to consider ecthyma gangrenosum in the differential diagnosis of sinonasal necrotizing lesions.

Introduction

Ecthyma gangrenosum is a rare skin infection caused by gram-negative bacteria. The most frequent pathogen is *Pseudomonas aeruginosa*.[1] In subjects that are immunocompromised, *P. aeruginosa* is considered an opportunistic pathogen. Typically, the skin infection manifests as erythematous macules that evolve to hemorrhagic-vesicle blisters, with subsequent ulceration, and rapid progression to necrotic lesions.

Few cases of sinonasal gangrenous ecthyma have been described previously. After carefully reviewing these cases, we found only one case that originated in the sinonasal tract.[2] That case report described a patient that was immunocompromised and had a recent diagnosis of acute lymphocytic leukemia. The patient had experienced several days of fever, confusion, a right frontal headache, and right-sided facial pressure. The computed tomography (CT) scan revealed opacification in the right frontal sinus and a fronto-ethmoidal recess. The patient was diagnosed with acute invasive fungal sinusitis. Consequently, the patient was treated with endoscopic debridement. However, the pathology report and cultures showed the presence of *P. aeruginosa*, rather than a fungal species.

Case report

We describe a 56-year-old woman with history of renal transplantation 18 months prior, due to diabetic nephropathy. Consequently, she was currently under immunosuppressive treatment with tacrolimus, sirolimus, and prednisone. She presented at the emergency department with headache, maxillary pain, bloody rhinorrhea, intermittent blurred vision, and hypoesthesia on the left cheek, which had continued for the past 2 weeks. Her medical history was extensive; it included longstanding type-2 diabetes, treated with metformin and insulin, diabetic retinopathy, and arterial hypertension. A physical examination showed an afebrile condition without signs of meningeal irritation, functional cranial nerves, and normal consciousness. The blood analysis revealed normal renal function, 30% hematocrit, 2.2×10^9/L leukocytes, 0.4×10^9/L lymphocytes, 1.3×10^9/L neutrophils, and C-reactive protein (CRP) 8 mg/dL. Nasal endoscopy showed necrotic mucosa and a purulent secretion that occupied the left nasal fossa.

A CT image of the paranasal sinuses demonstrated extensive left-sided pansinonasal occupation with homogeneous density, bone erosion that affected the cranial portion of the medial wall of the maxilla,

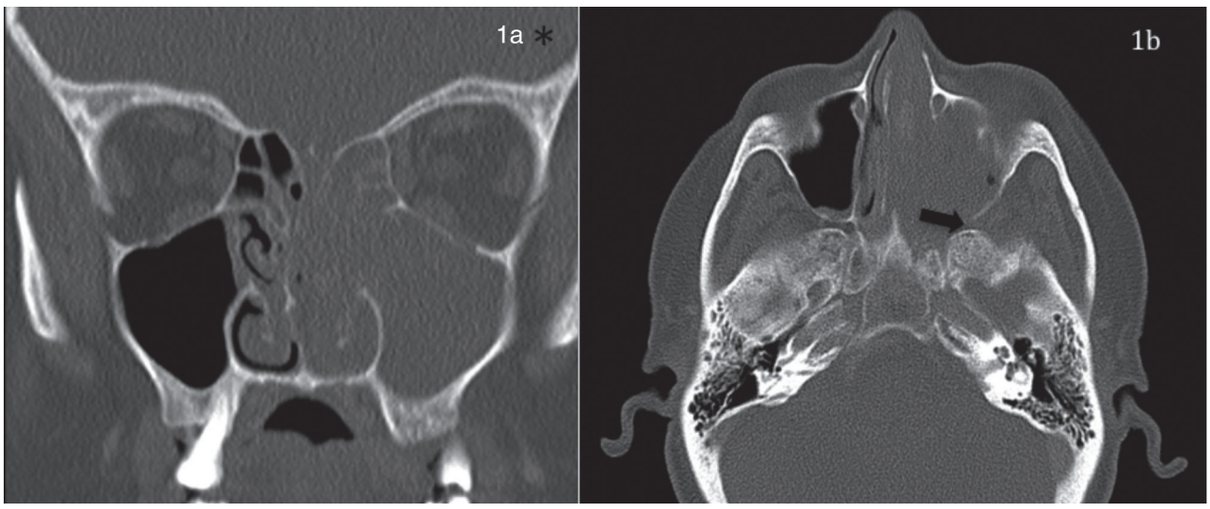

Figure 1

Preoperative CT of a patient with ecthyma gangrenosum in the sinonasal tract. 1a: Coronal section demonstrates left-sided pansinonasal occupation with homogeneous density. 1b: Axial section shows bony erosion of the medial wall of the maxillary sinus (asterisk) and infiltration of the left pterygopalatine fossa (arrow).

and infiltration of the left pterygopalatine fossa. The orbit and anterior cranial fossa showed no significant alterations (Figure 1).

A differential diagnosis was performed at the time of presentation. Given her comorbidity, the most probable diagnosis was invasive mucormycosis.

Functional endoscopic sinus surgery was performed for extensive surgical debridement of non-vital tissue and bone. Under endoscopic vision, extensive necrosis was observed in the inferior and middle turbinate, the middle meatus, the septal mucosa, and the roof of the nasal fossa. No necrotic tissue was observed on the contralateral side, but the nasal septum visibly bulged into the nasal fossa. A left inferior turbinectomy was performed, followed by a medial maxillectomy, and an anterior and posterior ethmoidectomy and sphenodotomy. The ascending palatine process was drilled out, and the posterior wall of the maxilla was dehiscent, with necrotic tissue expanding into the pterygopalatine fossa. All necrotic tissue was resected, until only vital tissue was visible in the infratemporal fossa. The internal maxillary artery was coagulated. Next, the lamina papyracea was partially resected, and infiltration was observed in the superior part of the periorbita. Finally, the vidian canal was drilled out, until vital tissue was visible. The posterior part of the septum was necrotic, thus it was also resected.

During surgery, fresh and fixed tissue samples were obtained for pathology and microbiology analyses. The anatomopathological report revealed extensive tissue necrosis without mycotic structures (Figure 2a). Microbiological studies showed the presence of multiresistant *P. aeruginosa* in the nasal samples. Initial blood cultures and cultures of cerebrospinal fluid (CSF) were negative.

The antibiogram showed resistance to amikacin, ceftazidime, ciprofloxacin, gentamicin, imipenem, piperacillin/tazobactam, and tobramycin; it also showed partial resistance to meropenem. The only adequate sensitivity to an antibiotic was observed with colisitin. Based on the antibiogram, the patient was treated with intravenous meropenem and colistin; topical (nebulized) colistin was also added to the treatment protocol. Although the microbiological studies did not show fungal growth, mucor prophylaxis (amphotericin and caspofungin) was added, because an invasive fungal infection is considered to be a life-threatening condition in a patient that is immunocompromised. The nephrologist closely monitored renal function.

Initially, we observed clinical and biochemical improvement. However, after 10 days, the patient developed a fever that rose to 39 °C, became somnolent (the Glasgow Coma Scale (GCS) fell to 12), anisocoric, and developed dysarthria. Magnetic resonance imaging (MRI) with gadolinium showed leptomeningeal uptake, which suggested meningitis. A CSF culture confirmed the diagnosis of multiresistant *P. aeruginosa* meningitis.

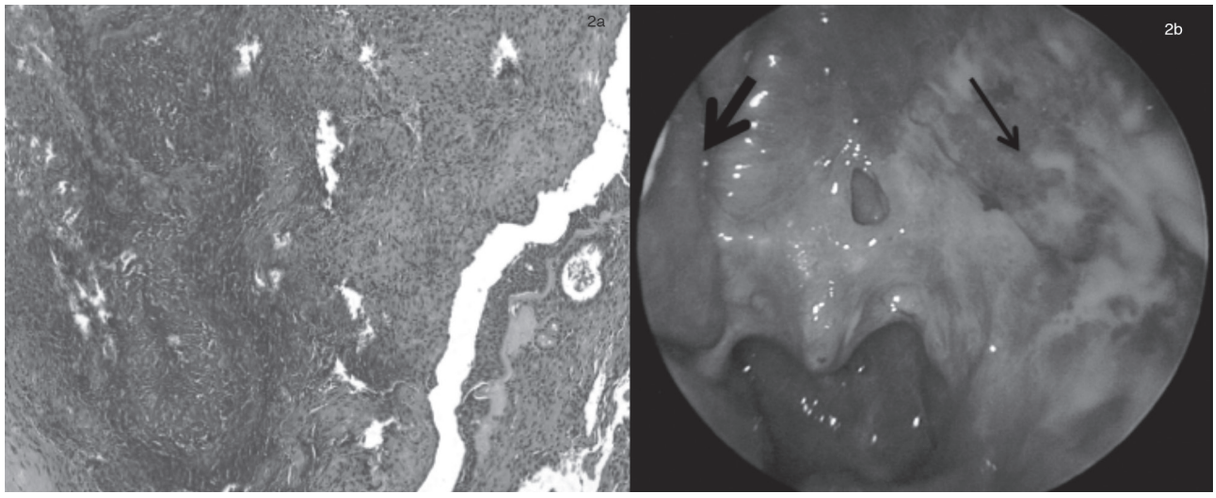

Figure 2

Evidence of sinonasal ecthyma gangrenosum. 2a: Hematoxylin-eosin (HE) staining (10 x magnification) of a biopsy from the lateral wall of the left-sided maxillary sinus shows evidence of extensive tissue necrosis without mycotic structures. 2b: Endoscopic view after surgical debridement. The black thin arrow indicates the left lateral wall, the black thick arrow indicates the right lateral wall, the black circle indicates the sphenoid ostium, and the asterisk indicates the choana.

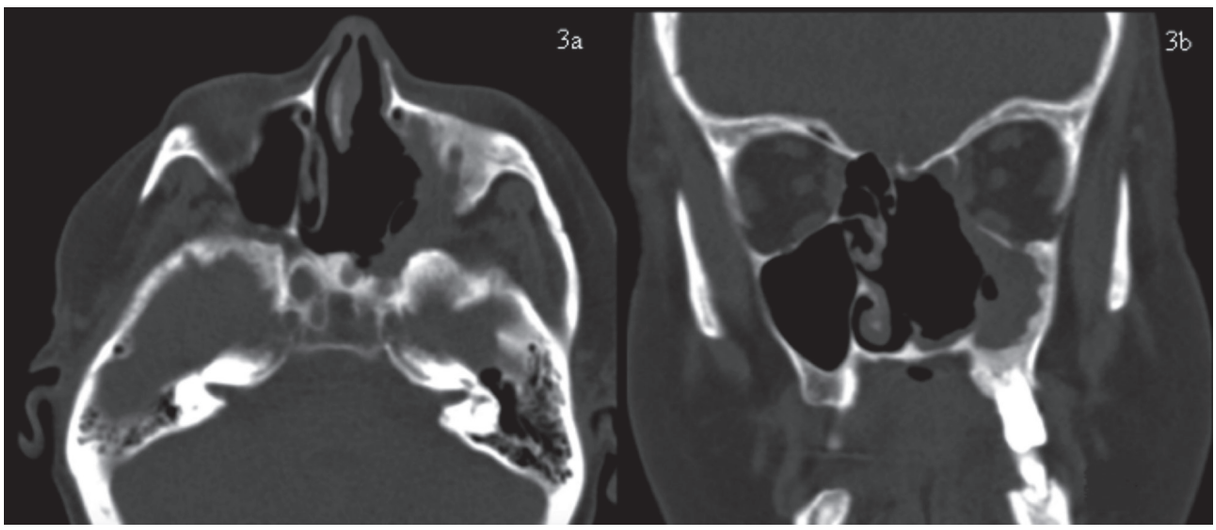

Figure 3

Postoperative CT of a patient with ecthyma gangrenosum in the sinonasal tract. 3a: Coronal section. 3b: Axial section. Postsurgical, left-sided changes show no residual sinonasal occupancy.

Linezolid, rifampicin, and ceftazidime/avibactam were added to the treatment. Fortunately, the patient progressed favorably, and achieved complete resolution at 1 month after the disease onset.

Follow-up endoscopic (Figure 2b) and radiological examinations, MRI in T2 with diffusion, and CT scans (Figure 3) were performed to rule out the presence of a cerebrospinal fluid fistula and cranial base defects. The results were negative. Currently, the patient follows ambulatory controls and she is asymptomatic.

Discussion

We here present a rare, well-documented case of sinonasal gangrenous ecthyma caused by *P. aeruginosa*. According to the literature, 12% of patients with a history of solid organ transplantation develop acute bacterial rhinosinusitis (ARS).[3] In patients that are immunocompromised, ARS can develop rapidly and disseminate systemically; the mortality rate is 40%.[4] ARS is most frequently caused by *Streptococcus pneumonia, Haemophilus*

influenzae, and *Moraxella catarrhalis*; however, in these patients, many opportunistic bacteria and fungi can cause sinusitis, including *Staphylococcus aureus, P aeruginosa, Streptococcus viridans, Staphylococcus epidermidis, Candida albicans, Aspergillus fumigatus*, and mucor species.[5]

In severe cases of invasive ARS, the infection can extend into intracranial and/or intraorbital spaces, resulting in changes in vision, reduced consciousness, or neurological deficits. When the spread is systemic, a high fever and hemodynamic instability are the most prominent signs of sepsis due to bacteremia.[6]

In addition to *P. aeruginosa*, similar clinical manifestations have been described with infections of *Escherichia coli, Stapholococcus aureus*, and mucor species.[1] Most patients with gangrenous ecthyma have bacteremia associated with Pseudomonas, but the bacteremia rarely evolves to include cutaneous involvement. In patients that are not immunocompromised, previous antibiotic use or a viral infection could predispose the patient to develop ecthyma gangrenosum, by altering the normal skin and/or mucosal flora and/or by altering the mucocutaneous barrier.[7] Some conditions can mimic ecthyma gangrenosum or start with cutaneous ecthyma and secondarily extend to the nasal cavity. Kelley *et al*.[8] described a case of ecthyma that initially affected the external part of the nasal wing with a secondary extension into sinonasal tissue. Levy *et al*.[9] described an ecthyma gangrenosum-like lesion that arose due to Exserohilum, in an 8-year-old child that was immunocompromised with chemotherapy for leukemia. Several authors have reported cases of orbital cellulitis caused by a Pseudomonas infection In those cases, the lamina papyracea and sinonasal cavity was objectively affected without major sinonasal involvement.[10,11]

Zomorrodi *et al*.[7] published a review of the different cases of ecthyma gangrenosum reported in literature between 1974 and 2014. They observed that the majority of cases involved the gluteal and perineal regions (57%), followed by the extremities (30%), and the trunk, head, and neck regions (12%).

Typically, ecthyma gangrenosum lesions start with purpuric macules that evolve to bullas and black-grey scars with an erythematous halo. These different stages evolve within 12 h, and patients can have different stage lesions at the same time.

When patients that are immunocompromised show symptoms of complicated acute rhinosinusitis, the initial evaluation should include nasal endoscopy, nasal culture, and endoscopy-guided biopsies. Radiological imaging is essential in the diagnosis. Imaging can reveal signs that indicate an acute invasive process, like bone erosion or changes in the signal intensity of the soft tissues beyond the paranasal sinuses.[12] The differential diagnosis should consist of invasive fungal infections, neoplastic processes (particularly natural killer/T-cell lymphomas), antineutrophilic cytoplasmic antibody-associated vasculitis, and intranasal drug abuse.[13]

Bodey *et al*.[14] showed that the infection resolution rate was highly dependent on early recognition, early antibiotic (AB) treatment (a short interval between the onset of symptoms and treatment), and culture-guided specific AB treatment. In cases of sinonasal involvement, extensive surgical debridement is mandatory.

Colistin (or Polymixin E) is a traditional polypeptide antibiotic for treating Gram-negative bacteria. Its mechanism of action is to alter the permeability of the bacterial cell membrane, which causes cell death. Currently, colistin has re-emerged as a valuable alternative for treating multiresistant *P. aeruginosa*, and it is one of few remaining therapeutic resources that can effectively fight these multiresistant bacterial strains. Colistin is available in intravenous, intramuscular, and nebulized forms. The most important side effects are nephrotoxicity and neurotoxicity, but both seem to be reversible. It is recommended that, preferably, colistin should not be used in monotherapy, due to the high risk of inducing bacterial resistance.[15]

Conclusion

Ecthyma gangrenosum caused by *P. aeruginosa* should be considered in the differential diagnosis of sinonasal necrotizing lesions in patients that are immunocompromised. A correct diagnosis at an early stage of the disease and appropriate medical and surgical treatments will reduce morbidity and mortality in these patients

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