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Facial cellulitis due to *Staphylococcus aureus* with metastatic infection and torpid course. A pediatric case report

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ABSTRACT

Bacteremia due to *Staphylococcus aureus* is defined as the isolation of this microorganism in at least one blood culture. A metastatic infection is caused by the hematogenous dissemination and subsequent location of the microorganism in a site other than the one where the infection started. The prevalence of these secondary sources of infection is low in the pediatric population, which is a diagnostic challenge.

Here we describe the case of a pediatric patient with facial cellulitis due to *Staphylococcus aureus*, with metastatic infection and torpid course.

Keywords: Staphylococcus aureus*, bacteremia, complications, pediatrics.*

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INTRODUCTION

Staphylococcus aureus (SA) infections are prevalent in Argentina. It has been estimated that almost 80% of them are caused by community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) and may have a severe course. Patients older than 8 years of age with pneumonia, meningitis, or sepsis account for a higher morbidity and mortality. In recent years, the rate of hospitalization for CA-MRSA has increased.[1,2]

Bacteremia due to *Staphylococcus aureus* is defined as the isolation of this microorganism in at least one blood culture. A metastatic infection is caused by the hematogenous dissemination and subsequent location of the microorganism in a site other than the one where the infection started.[3] The prevalence of these secondary sources of infection is low in the pediatric population, with SA as their most common cause, so it poses a diagnostic challenge.[4,5]

Here we describe the case of a pediatric patient with facial cellulitis due to *Staphylococcus aureus*, with metastatic infection and torpid course.

CASE REPORT

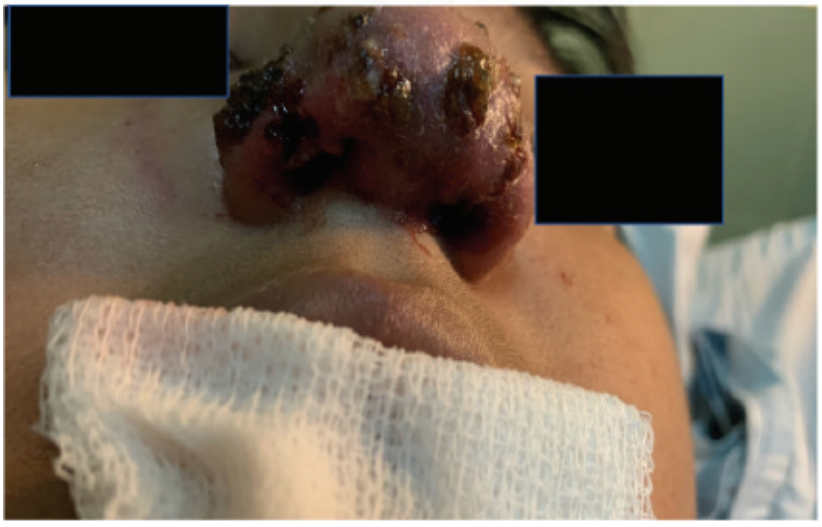
This was a male, 10-year-old, obese patient who weighed 105 kg (body mass index: 40 kg/m^2), with no health checkups in the past year. He had a personal and family history of furunculosis. He consulted due to an inflammatory lesion in the nasal region accompanied by edema and perinasal and periorbital erythema (*Figure 1*). The patient received antibiotic therapy for his lesion, which consisted in trimethoprim-sulfamethoxazole orally for 48 hours at an optimal dose (320 mg/day), prior to the consultation, but without improvement.

At the time of admission to the pediatric hospitalization ward, the patient had a fever and was in a fair general condition. His lab tests results showed a clear leukocytosis with neutrophilia (20 300 WBCs/mm^3, 77% neutrophils, 10% lymphocytes, 12% monocytes) and high C-reactive protein (13.6 mg/dL). Kidney and liver function tests were within normal ranges.

A computed tomography of the face and skull showed thickening of the facial integuments, mainly at the periorbital and nasal level. With an initial diagnosis of nasal bridge cellulitis, on the first day of hospitalization, the patient received empirical intravenous antibiotic therapy with vancomycin and piperacillin-tazobactam, after collecting 2 samples for peripheral blood culture. Two positive blood cultures were observed, at 12 and 15 hours, according to a qualitative method for methicillin-resistant *Staphylococcus aureus* (sensitive to vancomycin, trimethoprim-sulfamethoxazole, linezolid, clindamycin, minocycline, tigecycline, ceftaroline, ciprofloxacin, erythromycin; resistant to oxacillin).

A search for metastatic infection was performed. A whole-body bone scan with radiolabeled-ciprofloxacin showed uptake in the right humeral head, the upper jaw at the level

Figure 1. Maculopapular erythematous lesion with honey-colored crusts in the nasal region accompanied by edema and perinasal and periorbital erythema

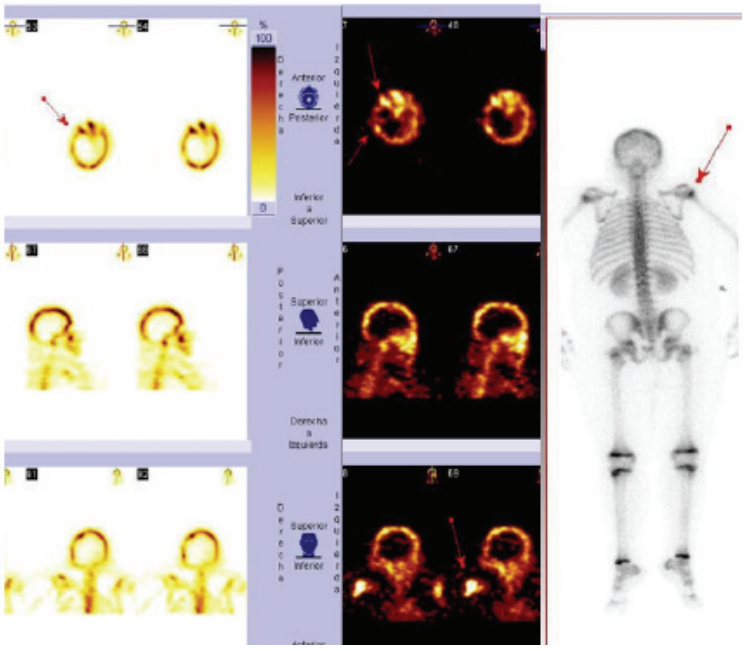


of the nasal notch, the frontal bone and the right zygomatic bone (*Figure 2*). The computed tomography of the chest showed nodules in both lung fields, with small left apical cystic image (*Figure 3*).

The chest X-ray, the fundus oculi, the echocardiogram, and the magnetic resonance imaging of the brain were within normal ranges. The patient had invasive CA-MRSA disease with a torpid clinical course, and the skin was the original source of infection.

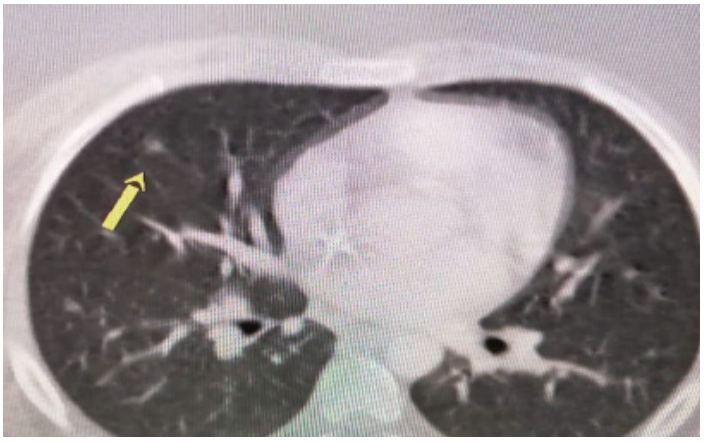
Control blood cultures were performed every 48 hours. They were negative 96 hours after starting the intravenous antibiotic therapy. Given the persistence of fever (without clinical respiratory involvement or hemodynamic instability) and the presence of metastatic infections at the bone and pulmonary levels, the antibiotic regimen

Figura 2. Whole-body bone scan with a 15-mCi (740-MBq) dose of 99mTC-MDP. 99mTc-ciprofloxacin (INFECTON), facial bones and skull



Increased uptake of labeled diphosphonates in the right humeral head, focal hyper-uptake in the upper jaw at the level of the right nasal notch, the prolongation of this bone towards the frontal bone, and at the level of the right zygomatic bone.

Figure 3. Computed tomography of the chest



Nodules in both lungs.

was changed to vancomycin and linezolid, on the tenth day of hospitalization, according to the antibiogram.

After receiving vancomycin for 20 full days and vancomycin and linezolid for 10 full days, the patient developed generalized erythema with pruritus, facial edema, mucous membrane involvement, angular cheilitis, odynophagia, and petechiae on the palate, associated with eosinophilia (1320 eosinophils/mm^3) and a mild increase in transaminases. His condition was interpreted as a drug reaction with eosinophilia and systemic symptoms (DRESS) (*Figure 4*) and therefore, antibiotics were fully discontinued; corticosteroids were prescribed and the patient was transferred to an intermediate care unit.

The skin and mucous membrane involvement improved and eosinophils decreased to 704 eosinophils/mm^3. The patient completed treatment for invasive MRSA infection with clindamycin and was restarted on antibiotic therapy after 24 hours of control in the intermediate care unit. The patient had a favorable clinical course, and received a total of 6 weeks of antibiotic therapy; antibiotics were administered orally for the last 2 weeks.

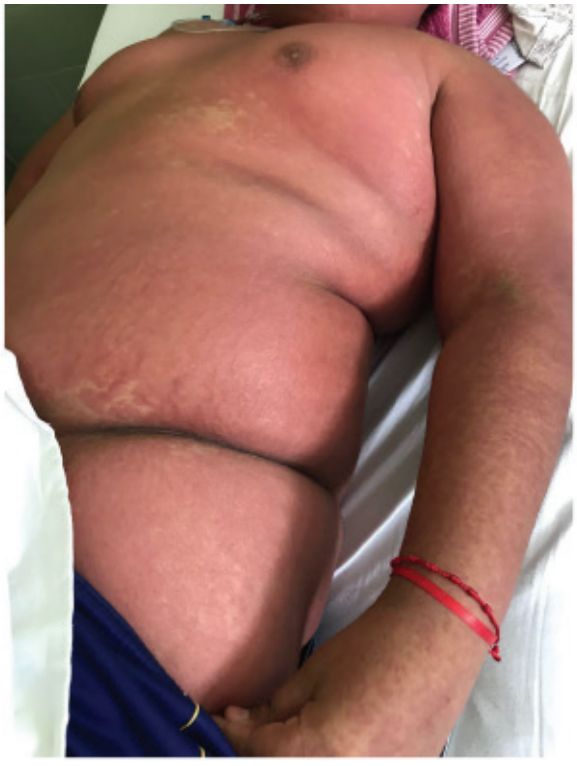
The patient was assessed by an interdisciplinary team from the Departments of Infectious Diseases, Diagnostic Imaging, Bacteriology, and Endocrinology.

DISCUSSION

The prevalence of metastatic infections as complications secondary to *Staphylococcus aureus* bacteremia is low in pediatrics. The prevalence of these metastatic infections in adults is approximately 50%, while it is less than 20% in pediatric patients;[4,5] it is higher in patients with predisposing underlying diseases, such as nutritional disease, immunosuppression, blood disease, cancer, or congenital heart disease, among others.[6,7]

Various studies carried out in Argentina[3,7] have described a different distribution in order of frequency of secondary sources of infection compared to adults. Metastatic infections in order of frequency in the pediatric population are pulmonary, osteoarticular, and skin and soft tissue; cardiovascular, abdominal, and ocular involvement is less common. In the

Figura 4. Confluent, intense, pruritic micromaculopapular erythematous rash, compatible with drug-induced skin reaction



case described here, the metastatic infections were related to osteoarticular and pulmonary involvement. As in the bibliography, in this case, the primary source of infection was the skin. It should be noted that, in most of the case series described, in 90% of events, a primary site of infection was detected at onset.[3]

The persistence of positive blood cultures 48 hours after the first positive blood culture was directly related to a greater risk for metastatic infection due to MRSA.[1,3,8] According to other studies, persistent bacteremia after the fifth day and sepsis on admission are associated with an increased risk for morbidity and mortality.[9]

In the clinical case described here, the early search for metastatic infections led to a timely treatment, considering the persistence of positive blood cultures and the patient's age as factors associated with a greater morbidity.[1] Regarding the search for deep sites of infection or metastatic infections, although ancillary tests –such as an echocardiogram and fundus oculi– were requested, it is important to note the higher frequency of pulmonary involvement in pediatric patients; therefore, it was relevant to search for this source of infection with an X-ray and computed tomography of the chest. Regarding osteoarticular involvement, a ^{99m}Tc-ciprofloxacin bone scan was useful for the diagnosis of bone source of infection. This type of scan has been extensively assessed with good results in the diagnosis of active osteoarticular bacterial infections.[10]

According to the annual report (2020) on antibiotic resistance by the hospital's Department of Clinical Microbiology, resistance to clindamycin in community-acquired skin and soft tissue *Staphylococcus aureus* infections was 13.8% (95% confidence interval [CI]: 4.5-32.6) and to vancomycin, 0% (95% CI: 0-14.6). In the case of hospital-acquired methicillin-resistant *Staphylococcus aureus* infections, the reported resistance to clindamycin was 27.9% (95% CI: 15.8-43.9) and to vancomycin, 0% (95% CI: 0-10.2).[11]

The initial empirical antibiotic therapy was selected following clinical practice guidelines[12] and considering that, for hospitalized patients with complicated skin and soft tissue infections, one of the options includes intravenous vancomycin (evidence A-I). For children with acute hematogenous osteomyelitis due to MRSA, vancomycin is recommended (evidence A-II). In our case, an obese patient with severe facial infection, the initial empirical antibiotic therapy was extended to include piperacillin-tazobactam so that Gram-negative and anaerobic microorganisms would also be covered. According to different studies, a lower percentage of persistent positive blood cultures on the fifth day of treatment was observed for patients receiving combination therapy with vancomycin plus beta-lactam (piperacillin-tazobactam), than for those receiving vancomycin alone.[13] In a stable patient without ongoing bacteremia or intravascular infection, clindamycin may be used as empirical therapy if the rate of clindamycin resistance is low (e.g., <10%) with transition to oral therapy if the strain is susceptible (evidence A-II). The exact duration of treatment should be customized, but a minimum cycle of 4 to 6 weeks is usually recommended for osteomyelitis. Alternatives to vancomycin and clindamycin include daptomycin or linezolid (evidence C-III).[14]

In SA infectious conditions in pediatrics, it is relevant to suspect and search for metastatic sources of infection, based on their order of frequency, for a timely diagnostic and therapeutic approach. ■

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