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Cent. Eur. J. Med. • 8(2) • 2013 • 220-224
DOI: 10.2478/s11536-012-0106-9

Central European Journal of **Medicine**

Complicated course of facial cellulitis caused by *Staphylococcus aureus* in a 13-year-old boy with neutropenia – an adverse event analysis

Case Report

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Received 25 July 2012; Accepted 21 September 2012

Abstract: Background: Facial cellulitis is a rare disease in children, associated with high risk of complications among immunocompromised patients. Objective: A report on complicated facial cellulitis in a neutropenic teenager with risk factor analysis. Case report: A 13-year-old boy with neutropenia was taken to hospital. He initially complained of severe pain and redness of the nose - treated as an allergy. The skin condition deteriorated, a dermatologist diagnosed erysipelas and recommended amoxicillin. Deformation, oedema, erythema, blistering and oozing erosions of the nose, high C-reactive protein and neutropenia were found upon admission. An ultrasound scan revealed abscesses in the subcutaneous tissue. Intravenous penicillin and clindamycin were administered. Methicillin-sensitive *Staphylococcus aureus* was isolated from the skin lesions. The boy required multiple surgeries and granulocyte-colony stimulating factor therapy. Conclusions: Facial cellulitis may be severe in immunodeficient patients. Delayed, inadequate empiric treatment and communication difficulties may increase the risk of complications.

Keywords: *Cellulitis • Neutropenia • Adverse event • Management • Staphylococci*

1. Introduction

Erysipelas and cellulitis are bacterial infections which are more common in infants, young children and the elderly [1-3]. The incidence is estimated at 2.49 cases per 1,000 patient-years [4]. It mainly affects the lower extremities and the face (in a butterfly-shaped distribution) [1-3,5,6]. It is usually caused by group A streptococci, but more rarely by other streptococci groups, staphylococci, *Haemophilus influenzae*, *Pseudomonas aeruginosa* or other gram-negative bacilli [2,3,6]. Specifically, in bullous erysipelas, *S. aureus* was reported in 50% of cases [7]. Unusual infectious agents particularly affect people with chronic diseases, especially immunocompromised patients [4-6,8-11]. Neutropenia is usually associated with mucosal or skin barrier disruption, and the indigenous colonizing pathogens are responsible for most infections. Frequent hospitalization, recurrent infections treated with broad-spectrum antibiotics and antimicrobial prophylaxis lead to the selection of resistant strains. In this group of patients, fungal infections also need to be considered [2,12-14].

So-called “simple cases”, usually caused by streptococci, should be treated with penicillin or a first-generation cephalosporin [2]. In patients with risk factors such as neutropenia, staphylococcal infections are more likely and high doses of broad-spectrum antibiotics should be used [2,12-14]. The majority of *S. aureus* strains are methicillin sensitive (MSSA), produce penicillinase and are resistant to natural penicillins. High risk patients require special care, often hospital admission and detailed investigation because of the disease’s severe course [2]. In order to detect those at risk, detailed anamnesis, good cooperation with the patient and their family and adequate, controlled therapy must be carried out.

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2. Case report

We present a case of a 13-year-old boy, with congenital neutropenia of unknown origin (genetic tests did not confirm cyclic neutropenia or Kostmann neutropenia) and a history of recurrent bacterial infections of the ears and skin. Because of recurrent fevers, he was treated with antibiotics every few weeks. The current disease started in the winter, one week after a common cold, with concomitant rhinitis. Initially, the patient was complaining of severe pain and redness of the nose. After 3 days, he consulted a general practitioner and laryngologist, who diagnosed an allergy and prescribed antihistamines. In the following days, the oedema and erythema worsened. The dermatologist diagnosed erysipelas and recommended treatment with oral amoxicillin (without clavulanate – 750 mg every 12h, 37 mg/kg - weight 41 kg). Because the skin condition deteriorated and a fever appeared over the following weekend, the patient's mother (on her own initiative) increased the drug dose to 750 mg every 8 hours (55 mg/kg). After two days, the boy visited the dermatologist again and he was referred to our Department of Paediatrics and Infectious Diseases.

Upon admission the patient's condition was moderately severe. He had a fever (39°C), tachycardia and complained of weakness. Deformation, substantial inflammatory infiltration, oedema and erythema of the nose were found in the patient. Blisters and weeping erosions partially covered with scabs were found on the skin of the bridge of the nose.

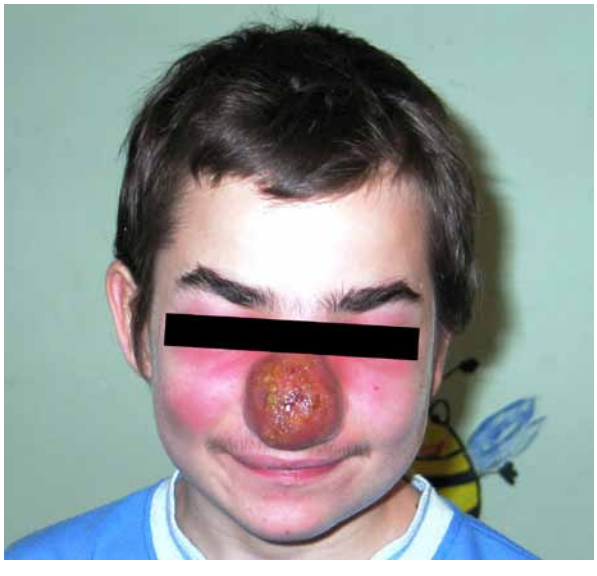

Figure 1. Facial cellulitis - inflammatory infiltration, blistering and oozing erosions.

The inflammatory infiltration included the cheeks. He had cervical lymphadenopathy and difficulty opening his mouth. Staphylococcus aureus raised inflammatory markers (C-reactive protein 187.8 mg/L, leukocytosis 26.36 K/μL), neutropenia (8% granulocytes, 72% monocytes), anemia (hemoglobin 10.5 g/dL) and decreased prothrombin index (61.6%). Intravenous administration of crystalline penicillin (6 mln units per day) and clindamycin (1200 mg per day) was used, which led to a rapid improvement. On the second day of treatment, his temperature returned to normal and the CRP decreased. *Staphylococcus aureus* MSSA (sensitive to clindamycin) was isolated from the skin lesions. An ultrasound scan revealed abscesses in the subcutaneous tissue and consequently surgical intervention was required. After transfer to the Department of Laryngology, a CT scan of the face was performed. It revealed symmetric thickening of the nasal soft tissues with some hypodense areas, suggestive of purulent inflammation, and tissue inflammation of the cheeks. There was no osteocartilaginous destruction. The abscesses were incised and the patient returned to our department.

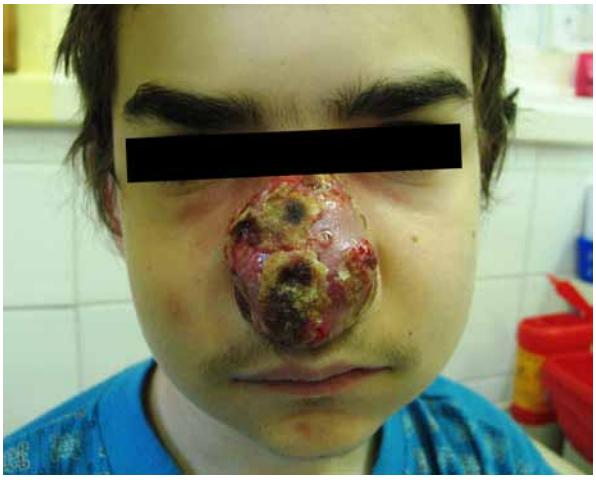

Figure 2. Facial cellulitis during antibiotic therapy and after abscess incision.

Because of a recurrence of the perinasal tissue abscesses and the development of necrosis, the boy required multiple surgeries, long-term antibiotic therapy and granulocyte growth factor treatment. These procedures greatly improved the patient's condition – the number of granulocytes increased and the wounds healed. The patient was referred for plastic reconstruction of the nose.

3. Discussion

The authors present a case of complicated facial cellulitis in a patient with neutropenia. The course of infection in patients with immunodeficiency, especially with granulocyte deficiency, may be more severe and more difficult to treat because of the body's inadequate or poor response to the treatment, and unusual pathogens inducing the disease and their resistance to conventional treatment. This should be taken into account in further diagnostic and therapeutic procedures.

The need to improve the patient's health security calls for a detailed analysis of treatment failures and therapeutic problems to find out the key elements in preventing the emergence of adverse events. This approach to the case analysis is a manifestation of the safety culture in health service provision [15].

The authors have analysed adverse events that took place and influenced the course of their patient's disease. The first key element was the wrong diagnosis at the beginning of the disease. The nasal pain and erythema was misinterpreted as an allergy by two doctors. Perhaps proper analysis of the patient's medical history (no allergy in the past, rhinitis one week previously, winter season, neutropenia and history of recurrent skin infections) would have helped to establish the correct diagnosis.

Another adverse event was the inappropriate treatment implemented by the dermatologist. Amoxicillin is an antibiotic very effective against *Streptococcus spp.*, but not *Staphylococcus*. Schito et al. [16] found that the resistance of *S. aureus* MSSA to amoxicillin in Europe was over 90%, caused by penicillinase production. In immunodeficient patients, antibiotics active against *S. aureus* should be used. The effectiveness of therapy must be checked 24-48 hours after initiation [2]. Lack of improvement or deterioration is an indication for further diagnostics and consequently a change in the treatment method. The drug dosage was also incorrect, because standard therapy assumes 750 mg 3 times a day.

Both events described above might be related to inadequate communication between doctor and patient. It is also very important to inform the patient or his parents about the possible unfavourable course of the disease, including severe potential complications, especially if there are risk factors of a poor outcome. In our case, the boy's parents were not aware of the danger, despite his history of recurrent bacterial infections. They were not informed that they had to observe their son and, if there was no improvement, to contact the doctor immediately. As they did not know how severe skin and soft tissue infections (SSTI) might be, and because of the upcoming weekend, they tried to modify the therapy on their own. They increased the drug dose to the optimal daily dose. As the wrong antibiotic was prescribed, such actions would not have provided any improvement. As the boy's condition deteriorated, he required hospitalisation.

Upon admission, after a preliminary examination, the patient was prescribed antibiotics efficient against streptococci and staphylococci – penicillin and clindamycin in combination [6]. As we know, the number of resistant bacterial strains is increasing, especially among methicillin resistant *S. aureus* (MRSA) [2,17].

Jones et al. [18] found that MSSA strains had 100% susceptibility to amoxicillin with clavulanate and cefotaxime, almost 100% to ceftriaxone, and a very high susceptibility to trimethoprim/sulphamethoxazole (>94.5%) and levofloxacin (>91.4%). MRSA was detected in 12.4-44.4% of *S. aureus* in SSTI cases. The MSSA and MRSA susceptibility to clindamycin is also high. In Sader et al. [19] MSSA resistance to clindamycin in children was only 3%. In Deotale et al. [20] 14.5% of isolates showed inducible clindamycin resistance and 3.6% constitutive resistance. Some studies show that 40-95% of MRSA strains are also susceptible to clindamycin [19-22]. Antibiotic resistance has to be taken into account in treatment strategies, especially in patients with chronic diseases and immunodeficiency. If there is no response to the antibiotic therapy, or if the response is very poor, it has to be changed immediately. In immunocompromised hosts with severe infections, or suspected gram-positive infections, empirical broad-spectrum antibiotics are recommended, such as vancomycin (all MSSA and MRSA strains in the Jones et al. study were sensitive to vancomycin), linezolid or daptomycin [2,13,14,23].

In case the therapy is ineffective, particularly among patients with immune disorders, hospital admission should be recommended for the performance of detailed investigation and to determine the appropriate targeted antibiotic therapy. The purpose of hospitalisation should also be the detection of complications. The most severe complications of SSTI are sepsis, meningitis, toxic shock syndrome, encephalitis, cavernous sinus thrombosis, necrotizing fasciitis and septic arthritis; the most common are recurrent infections, hemorrhagic, bullous, cutaneous abscesses and local necrotising lesions [4,5,9,11,24]. The detection of complications influences further management.

In our patient, the most important factor determining the course of the disease and further complications was the underlying disease – neutropenia. This condition predisposed to necrosis, large loss of the nasal skin and soft tissues and a big scar. It is essential to interview the patient thoroughly, paying special attention to details of chronic diseases, its clinical course, previous treatment and complications. In the case of a severe infection, the cooperation of many specialists is required – the dermatologist, infectious disease specialist, surgeon and haematologist.

4. Conclusions

Cellulitis of the face might be a severe and life-threatening disease in immunodeficient patients. Incomplete anamnesis, lack of co-operation with the patient (delayed feedback) or his parents, incomplete information about the patient's condition, and delayed and inadequate empiric therapy are the main causes of complications. In severe skin and soft tissue inflammation, the staphylococcal etiology and its sensitivity to antibiotics has to be taken into account.

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