CASE REPORT

When a Desquamating Rash Leads to a Challenging Diagnosis

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Abstract

A desquamating rash may pose a true clinical challenge. Therefore, the history and clinical course are crucial to making an accurate diagnosis. We present the clinical case of a 17-year-old boy submitted to a *pilonidalis sinus* excision, who presented to the emergency department with erythema and desquamation of lips, a scarlatiniform rash, an extensive desquamation of the hands and feet, and an infection of the surgical site. Given the suspicion of a staphylococcal scalded skin syndrome intravenous antibiotics were immediately started. During day six of admission, a sudden itching erythematous and desquamative rash appeared on the face and body, which worsened after the administration of cefuroxime. Therefore, that antibiotic was stopped and subsequently clinical improvement was observed. A skin biopsy revealed toxiderma. A positive oral provocation test for cefuroxime confirmed the cause of toxiderma. This case leads to discussion about the importance of the clinical course to make the correct diagnosis.

Keywords: Adolescent; Cefuroxime/adverse reactions; Exanthema/etiology; Drug Hypersensitivity; Staphylococcal Scalded Skin Syndrome/complications; Staphylococcal Scalded Skin Syndrome/diagnosis; Staphylococcal Scalded Skin Syndrome/drug therapy

Introduction

Fever and rash are often the presenting symptoms of several infectious and non-infectious conditions. Staphylococcal scalded skin syndrome and scarlet fever usually have a typical clinical course that allows clinicians to distinguish them but, in some cases, they may overlap making the diagnosis more challenging. Infectious and non-infectious conditions (such as a drug-induced reaction) may occur simultaneously or consecutively presenting with similar symptoms that increase the diagnostic challenge. A prompt recognition of a staphylococcal scalded skin syndrome is essential, having always in mind other diagnostic possibilities whose clinical course will be determinant in making the best clinical decision.

The staphylococcal scalded skin syndrome occurs predominantly in newborns and infants, but cases in older children and adults have also been described.[1,2] It is caused by exfoliative toxins A and B released by *Staphylococcus aureus*.[3] Clinical findings include an erythematous rash resembling scarlet fever, which poses an important differential diagnosis.[4,5] Desquamation with a scalded appearance especially in skin creases, palms, and soles, and intact bullae may be absent.[1,4,6,7] Fever, periorificial crusting, positive Nikolsky sign, and the absence of mucosal involvement are characteristics of this disease.[6] Immediate recognition and initiating treatment with antibiotics are essential to ensuring a good clinical course.

However, during treatment, several complications can emerge thereby making the physician question the original diagnosis and to then consider alternative ones. Despite being unusual, toxiderma, a drug-induced skin reaction, can occur and although it may have a heterogeneous clinical picture, it can lead to a symmetric erythematous rash with erythema on the palms and fingers and flexural dermatitis.[8,9] Withdrawal of the suspected drug is crucial to ensuring complete resolution.[9]

We describe a case of staphylococcal scalded skin syndrome that suffered severe exacerbation when an allergic reaction has developed. Since the desquamating rash has many differential diagnoses, a multidisciplinary approach was imperative in managing this clinical challenge.

Case Report

A 17-year-old Caucasian boy with a personal history of asthma and allergic rhinitis, with no history of drug

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allergy, and with all of his immunizations up to date, was submitted to a *pilonidal sinus* excision. Two days after the procedure, he experienced a high fever (maximum temperature of 39.5º C), odynophagia, tonsillitis with exudate, a conjunctival erythema without exudation, and a progressive erythematous maculopapular rash that was first noted on the trunk without desquamation or palmoplantar involvement.

On the same day, he was observed at the emergency department where he underwent blood tests showing a C-reactive protein (CRP) of 19 mg/dL and no leukocytosis. He was discharged after the administration of 1,200,000 UI of intramuscular penicillin for a scarlet fever. Eight days after the onset of the symptoms, he attended his surgery appointment complaining of fatigue and knee pain without arthritis or fever. A general examination revealed the erythema and desquamation of the lips, a scarlatiniform rash in the upper third of the trunk, an extensive desquamation with erythema, and edema of the hands (Fig. 1) and feet (Fig. 2) and marked infection signs at the surgical site with redness and purulent exudate. The blood tests that were conducted revealed leukocytosis of 24,600 cell/µL with neutrophilia of 15,060 cells/µL, CRP of 7.58 mg/dL and a negative pharyngeal rapid antigen test to detect group *A Streptococcus*. Given the hypothesis of a staphylococcal scalded skin syndrome, he was admitted for intravenous antibiotic therapy with flucloxacillin (130 mg/kg/day) and clindamycin (40 mg/kg/day) along with intravenous fluid therapy and surgical site cleaning and disinfection. In the following days, his clinical improvement was observed. Blood cultures were negative. Viral serologies and autoimmunity studies were all negative. Antistreptolysin O titer was also normal. An echocardiogram was performed showing no abnormalities. Cultures from the purulent exudate aspirate of the surgical site, after washing with sterile saline, were positive for a multidrug sensitive strain of *Escherichia coli* sensitive to cefuroxime, gentamicin, and piperacillin-tazobactam. As the patient still maintained an exuberant purulent exudate despite the instituted antibiotic therapy, and after having received the cultural results, flucloxacillin was replaced by cefuroxime (150 mg/kg/day) in association with clindamycin to target staphylococcal scalded skin syndrome and the surgical site infection.

On the following day, the fever restarted, and the CRP increased to 9 mg/dL. Flucloxacillin was reintroduced in addition to clindamycin and cefuroxime with clinical improvement. On day six of admission, a sudden itching erythematous, symmetrical, maculopapular, and desquamative rash appeared on the face with periorbital edema, body, inguinal region, thighs, hands (Fig. 3), and feet (Fig. 4) with worsening observed after the administration of cefuroxime. Consequently, cefuroxime was suspended and piperacillin-tazobactam (300 mg/kg/day) was initiated, with the total remission of the rash and associated itching. A cutaneous biopsy was performed and showed superficial and deep perivascular inflammatory infiltrate with numerous eosinophils, reveling toxiderma. He completed 10 days of flucloxacillin, but since the purulent exudate in the surgical site reappeared, amikacin (15 mg/kg/day) was added to the antibiotic therapy.

The patient was discharged 22 days after admission with the complete resolution of the rash having completed 10 days of flucloxacillin, 23 days of clindamycin, 14 days

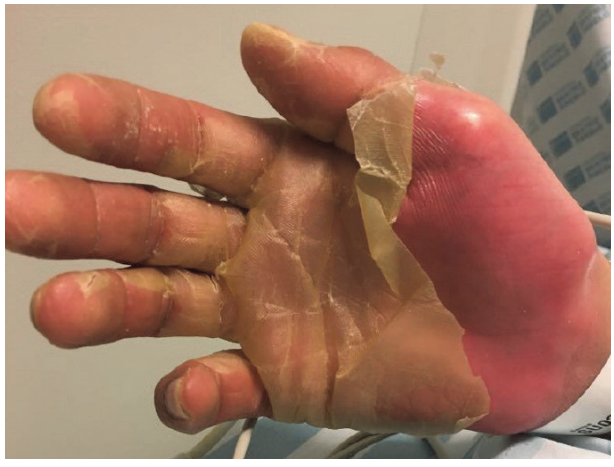

Figure 1. Lamellar desquamation with erythema and edema of hands on hospital day one.

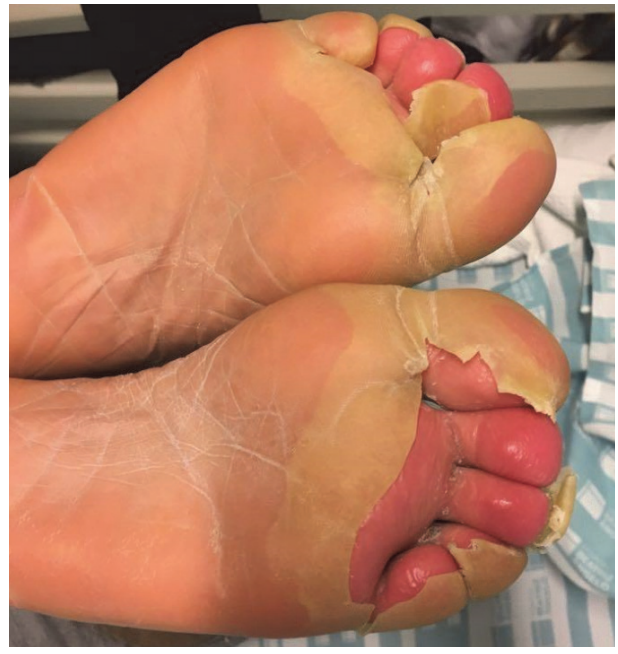

Figure 2. Lamellar desquamation with erythema and edema of the feet on hospital day one.

of piperacillin-tazobactam and 12 days of amikacin. At the six-month follow-up appointments in pediatrics and allergology, he presented as asymptomatic and fully recovered. A positive provocation test with an immediate reaction showing an erythematous urticariform rash after cefuroxime intake confirmed the causal link to toxiderma.

Discussion

This clinical case represents two consecutive and somewhat overlapping pathologies (staphylococcal scalded skin syndrome and severe allergic reaction to cefuroxime). The desquamating rash played the role of a disturbing factor introducing doubts regarding the initial diagnosis and considering other possible diagnoses. Desquamating rash by itself is a true clinical challenge when considering the numerous diagnostic possibilities. However, the clinical course in most cases is crucial for the correct diagnosis.

In the reported case, the first presentation with fever, odynophagia, and tonsillitis with exudate and an erythematous rash led to the consideration of scarlet fever as the most probable diagnosis. However, the clinical evolution revealed the desquamation of the lips, an extensive desquamation with erythema, and edema of the hands and feet and marked infection signs at the surgical site. Therefore, staphylococcal scalded skin syndrome was suspected, in which the surgical site was the most probable origin of *Staphylococcus aureus*. Staphylococcal scalded skin syndrome typically starts with a local infection, namely in a circumcision site.[6] In this case, the patient had just been submitted to a *pilonidalis sinus* surgery having a surgical wound as a potential entrance for skin pathogens. In staphylococcal scalded skin syndrome, blood cultures are generally negative,[10] but cultures of nasopharynx, conjunctiva, and umbilicus can confirm the diagnosis. However, in this case, the cultures were obtained after antibiotics having been started and the diagnosis was made based on the history and physical findings. An abrupt and tender erythroderma, sometimes resembling scarlet fever,[4-6] with accentuation in the flexural and periorificial area are characteristics of staphylococcal scalded skin syndrome and especially in the beginning of the condition, staphylococcal scalded skin syndrome and scarlet fever may overlap. In staphylococcal scalded skin syndrome, the affected skin typically desquamates leaving the skin with a scalded appearance, while in scarlet fever desquamation, it is thinner and superficial and occurs later in the clinical course (it may take two to six weeks).[6,7] Moreover, periorificial crusting with desquamation and mucosal sparing is also typical of staphylococcal scalded skin syndrome.[6,11]

Staphylococcal scalded skin syndrome usually has a good prognosis with the resolution of symptoms in two to three weeks with the correct treatment and proper supportive measures.[6,7] However, complications might emerge, such as sepsis, secondary infections, and dehydration.[7] Other complications may appear due to iatrogenic causes, and their manifestations may overlap with the initial diagnosis being difficult to distinguish them.[8]

In the course of our clinical case, the reappearance of a symmetrical erythematous rash associated with itching throughout the body with periorbital edema, and exacerbated in the inguinal region, thighs, hands, and feet, introduced some doubts to the initial diagnosis. Nonetheless, the worsening of the rash with the administration of cefuroxime corroborated the possibility of a drug-induced reaction, which was later confirmed by a skin biopsy and an oral provocation test. Toxiderma presents characteristically with erythema and scaling, and if there is a strong reaction, the rash can be confluent resulting in erythroderma.[9,12] Antibiotics, namely cephalosporins, are one of the drugs most frequently responsible for drug-induced skin reactions.[13] Similarly to our case, the diagnosis is often based upon clinical findings as well as a detailed history and evaluation of the chronology between the drug administration and skin reaction. Skin biopsies can be helpful in establishing the diagnosis, but a positive provocation test will confirm the drug sensibility. Prompt identification and discontinuation of the drug in question is essential.[14]

This case points out the need for strong clinical suspicion and the relevance of the clinical history and course to reach a correct diagnosis and to rapidly institute the most adequate treatment. Iatrogenic conditions must always be considered after any medical intervention, so that they can be recognized and treated accordingly, but most importantly to be prevented.

WHAT THIS CASE REPORT ADDS

- The differential diagnosis of a desquamating rash is a true clinical challenge, but the history and clinical course are crucial clues for establishing a correct diagnosis.
- Staphylococcal scalded skin syndrome is a cause of infection in early childhood, but it can also occur in adolescents and adults.
- The diagnosis is clinical in most cases and prompt initiation of antistaphylococcal antibiotics is essential for achieving a good clinical course.
- Complications can emerge from staphylococcal scalded skin syndrome, but other possibilities must be considered in case of the absence of clinical improvement, including drug-induced reactions.
- Identification and discontinuation of the suspected drug is important to resolve the symptoms when a drug-induced reaction is considered.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Confidentiality of data

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Awards and presentations

This case was presented at the 19th National Congress of Pediatrics, 2018, Estoril, Portugal.

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Quando uma Erupção Cutânea Descamativa Representa um Desafio Diagnóstico

Resumo

Uma erupção cutânea descamativa pode representar um verdadeiro desafio clínico. Por isso, a história e a evolução clínica são cruciais para um diagnóstico rigoroso. Apresentamos o caso clínico de um adolescente de 17 anos submetido a excisão de sinus pilonidal, que recorreu ao serviço de urgência por eritema e descamação dos lábios, erupção escarlatiniforme, extensa descamação das mãos e pés e infeção da ferida cirúrgica. Perante a suspeita de síndrome da pele escaldada estafilocócica, iniciou-se de imediato a administração de antibióticos por via intravenosa. Durante o sexto dia de internamento, surgiu uma erupção cutânea pruriginosa, eritematosa e descamativa na face e no corpo, que se agravou após a administração de cefuroxima. O tratamento antibiótico foi interrompido, com melhoria clínica. A biópsia de pele revelou toxicodermia. Um teste de provocação oral positivo para cefuroxima confirmou a causa da toxidermia. Este caso sublinha a importância da evolução clínica na formulação de um diagnóstico correto.

Palavras-Chave: Adolescente; Cefuroxima/efeitos adversos; Exantema/etiologia; Hipersensibilidade a Drogas; Síndrome da Pele Escaldada Estafilocócica/complicações; Síndrome da Pele Escaldada Estafilocócica/diagnóstico; Síndrome da Pele Escaldada Estafilocócica/tratamento farmacológico