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CASES FOR DIAGNOSIS

Facial Edema and Morbilliform Rash Associated with Fever and Liver Disease in a Patient on Treatment with ceftazidime

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Clinical History

The patient was a 50-year-old man who was admitted for reconstruction of a colostomy created 3 months earlier due to colorectal cancer (T3N0M0). During the admission, he presented an episode of fever of 37.8°C with positive blood cultures for *Staphylococcus aureus*, which was treated with an intravenous antibiotic (ceftazidime, 1g/8 h) and paracetamol (1g/8 h).

Two weeks after starting the antibiotic, the patient developed a further episode of fever of 38.5°C, associated with rigors, painful lateral cervical lymphadenopathies, and the appearance of skin lesions.

Physical Examination

The patient presented symmetrical facial edema that affected both external auditory meatus, causing conduction deafness (Figure 1). There was also a violaceous, pruritic, morbilliform rash that started on the trunk and upper limbs and progressively spread to the whole body, respecting the palms of the hands, soles of the feet, and the mucosas (Figure 2).

Additional Tests

Blood cultures were negative and blood tests revealed eosinophilia (2×10^5/L) and elevation of the liver enzymes (aspartate aminotransferase, 89; alanine aminotransferase, 102; gamma-glutamyltronsferase, 322). Atypical lymphocytes were seen in a peripheral blood smear.

Biopsy was performed and showed an intense infiltrate of atypical lymphocytes with a small number of eosinophils in an edematous superficial dermis (Figure 3).

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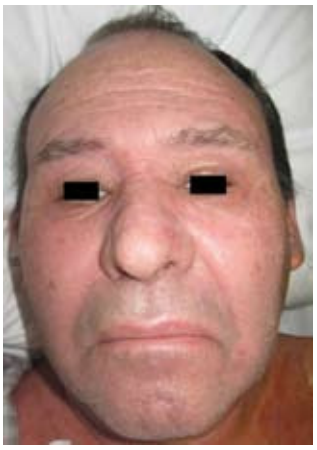

Figure 1.

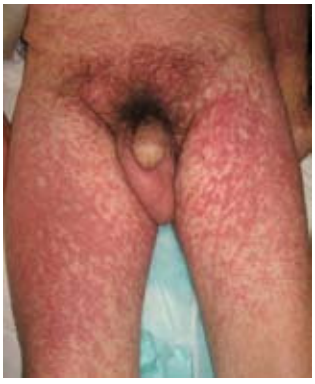

Figure 2.

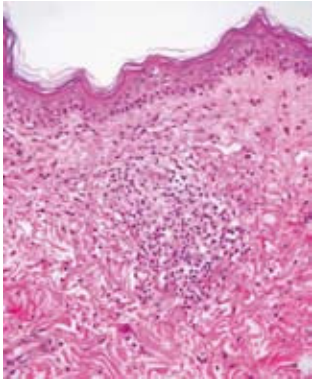

Figure 3. Hematoxylin-eosin, ×20.

What Was the Diagnosis?

Diagnosis

Hypersensitivity syndrome secondary to ceftazidime.

Clinical Course and Treatment

Forty-eight hours after withdrawal of the ceftazidime, the patient was afebrile, the facial edema had resolved, and the skin rash had reduced, leaving a residual desquamation. The patient received a fourth-generation quinolone as an alternative antibiotic and intravenous corticosteroid therapy at a dose of 1 mg/kg body weight, tapered over 30 days, in order to achieve a more rapid resolution of the condition.

Two months after onset, the blood tests had returned to normal values.

Comment

The drug-related eosinophilia with systemic symptoms (DRESS) syndrome, otherwise known as the hypersensitivity syndrome or, more recently, as the drug-induced delayed multiorgan hypersensitivity syndrome, is a toxic dermatosis characterized by a specific skin reaction associated with eosinophilia and systemic manifestations; it has a high mortality.

It is most commonly associated with treatment with aromatic anticonvulsants (phenytoin, phenobarbital, carbamazepine, primidone, lamotrigine, felbamate) and sulfonamides; the overall incidence of hypersensitivity syndrome is of 1 in every 10 000 patients exposed to these drugs.[1]

The case presented is the first DRESS syndrome in the literature associated with the use of ceftazidime, a fourth-generation cephalosporin. This antibiotic is used in hospitals for the treatment of serious bacterial infections.

The clinical signs appear between 1 and 5 weeks after the first dose of the causative agent. Initially the patient presents an influenza-like condition with widespread, painful lymphadenopathies. Facial or periorbital edema then develops, associated with a violaceous and pruritic morbilliform rash that progresses to exfoliative dermatitis, spreading in a craniocaudal direction until it reaches a state of erythroderma. The palms and soles and the mucosas are usually respected. The prognosis is determined by the associated systemic involvement, and the liver is the organ most frequently affected.[2,3]

Blood tests reveal leukocytosis with hypereosinophilia in 90% of cases, and atypical lymphocytes are found in the peripheral blood in 40% of cases.[4]

The prognosis of the hypersensitivity syndrome is variable. Mortality, principally due to liver failure, is 10%, and increases with delays in the diagnosis. Complete recovery is the rule in the remainder of cases, though the rash and abnormal blood test results can persist for weeks or even months after withdrawing the drug.[5]

Early withdrawal of the causative agent is the only universally accepted intervention to control this toxic dermatosis. The administration of intravenous corticosteroids at a dose of 0.5 to 2 mg/kg, depending on the severity of systemic involvement,[3,6] is a treatment that appears to improve the long-term prognosis.

Conflicts of Interest

The authors declare no conflicts of interest.

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