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# A CASE OF CEFTRIAXONE-INDUCED TOXIC EPIDERMAL NECROLYSIS IN GENITAL AREA

## *GENİTAL BÖLGEDE SEFTRİAKSONA BAĞLI GELİŞEN TOKSİK EPİDERMAL NEKROLİZİS VAKASI*

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**ABSTRACT**
We present a 2-year-old Turkısh boy who was treated with ceftriaxone several days for acute tonsillitis, complicated with toxic epidermal necrolysis (TEN) that was initially diagnosed as drug eruption. The advantages of a long half-life, wide spectrum, high tissue penetration rate, and a good safety profile, make ceftriaxone, a third-generation cephalosporin, a frequent choice in the treatment of childhood infections. To the best of our knowledge, this is the first case of ceftriaxone-induced toxic epidermal necrolysis in genital area in the English literature.
***Key words:*** Drug hypersensitivity, adverse drug reaction, toxic epidermal necrolysis, ceftriaxone

**ÖZET**
Akut tonsillit nedeniyle seftriakson ile tedavi edilen ve ilaç erupsiyonu sonrası toksik epidermal nekrolizis (TEN) gelişen bir olguyu sunduk. Uzun yarılanma ömrü, geniş spektrumu, yüksek doku penetrasyon hızı, güvenilirliliği bir üçüncü kuşak sefalosporin olan seftriaksonu çocukluk çağı enfeksiyonlarında tercih edilen bir ajan yapmıştır. Bilgimiz dahilinde bu vaka İngilizce literatür genital bölgede seftriaksona ikincil TEN gelişen ilk vakadır.
***Anahtar kelimeler :*** İlaç hipersensitivitesi, ters ilaç reaksiyonu, toksik epidermal nekrolizis, seftriakson

## INTRODUCTION

Toxic epidermal necrolysis (TEN) is a rare, potentially life threatening disorder characterized by widespread epidermal death (2,5). The majority of reported cases were the result of idiosyncratic drug reactions (1). In the present case, TEN was caused by ceftriaxone therapy.

To the best of our knowledge, this is the third case of ceftriaxone-induced TEN in the English literature. First case an 84-year-old man developed toxic epidermal necrolysis (TEN) due to ceftriaxone, a third generation cephalosporin, involving 72% of the body surface area (7) , second case a 70-year-old woman of Iranian descent who presented with toxic epidermal necrolysis that was initially diagnosed as a scald burn. Further anamnesis prompted by spread of the lesions during hospitalization revealed that the patient had been receiving ceftriaxone for several days (3). But our case is the first case of ceftriaxone-induced toxic epidermal necrolysis in genital area of a child in the English literature.

5x4 cm boyutlu kitle.

## CASE

A 2-year-old boy was admitted with complaints of weakness and fatigue. His personal history revealed treatment with ceftriaxone 50 mg/kg per day, 2 day previously, for tonsillitis. The patient's parents stated that the weakness had begun on the second day of ceftriaxone therapy. He had no chronic disease. He had not used any drugs, except analgesics drugs, in the previous 2 months. He had no history of vaccination in the last two months. During this period, other medications, including herbal remedies and vitamins had not been used. The only drugs he had used was ceftriaxone and paracetamol. Physical examination revealed a weight of 12 kg (50 percentile), and a height of 88 cm (50-75 percentile). Blood pressure was 90/60 mmHg. His general appearance was moderate and seemed weak, and his pharynx was hyperemic. No additional sounds or murmurs were detected upon cardiac and pulmonary examinations. The liver and the spleen were non-palpable. The neurological examination was normal, along with all the other systems. Laboratory examination revealed: AST, 20 IU/L (normal range, 10-40 IU/L ); ALT, 25 IU/L (normal range, 13-40 IU/L); γ glutamyl transferase (GGT), 20 U/L (normal range, 9-50 IU/L); alkaline phosphatase (ALP), 50 IU/L (normal range, 40-140 IU/L); total bilirubin, 1.2 mg/dL; and direct bilirubin, 0.2 mg/dL. Total protein, albumin, globulin, lactate dehydrogenase, amylase and fasting blood glucose levels were normal. The complete blood count revealed a normal number of leukocytes, erythrocytes and platelets. Peripheral blood smear revealed 60 % neutrophils, 30 % lymphocytes, 8 % eosinophils, and 2 % monocytes. The erythrocyte morphology was normal with no atypical cells. Urine analysis, prothrombin time and activated partial thromboplastin time were all in the normal range. Cytomegalovirus IgM, and Epstein-Barr virus viral capsid an-

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tigen values were negative. Evaluating personal history, physical examination and the laboratory findings together, we made a prediagnosis of ceftriaxone induced toxic epidermal necrolysis or drug eruption. Penile dermal biopsy was planned and done. Ceftriaxone administration was ceased immediately. Pulse methylprednisolone administration was begun at 40 mg/kg in the first 3 day. A proton pump inhibitor was added to the drug regimen. His vital functions were normal. Cutaneous examination revealed hyperemia and bullas involving both medial aspect of the left thigh and complete penis (Figure 1).

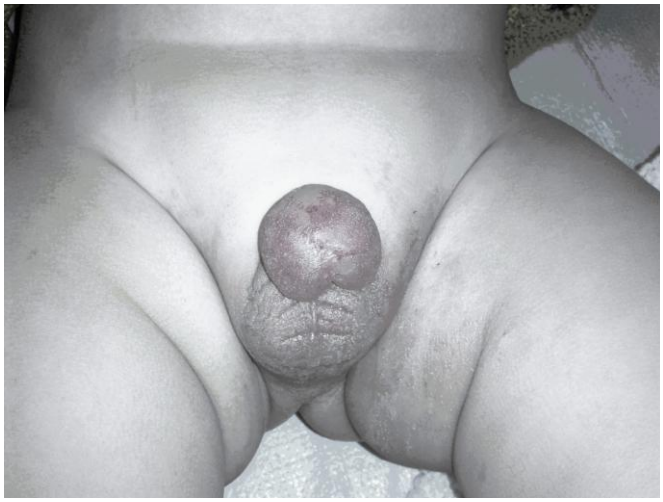

**Figure 1**. The picture of the lesion.

The pathology result was consistent with toxic epidermal necrolysis (Figure 2). On further questioning, burn was ruled out as a causal factor. The patient reported that 2 days prior to admission, he had been discharged from another hospital with a diagnosis of tonsillitis, and he had been receiving ceftriaxone for 2 days.

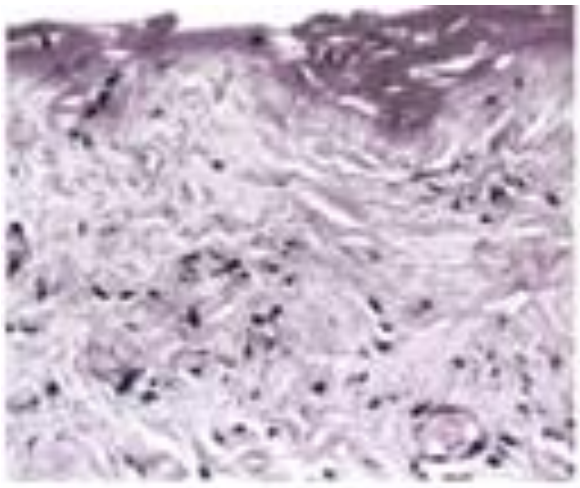

**Figure 2**. Pathologic specimen showing TEN (H&E x200).

After the pathologic specimen investigation the final diagnosis was TEN due to ceftriaxone. Treatment with intravenous hydrocortisone was initiated. Local treatment included vaseline gauze dressings that were changed once a day. Study of the cutaneous lesions demonstrated re-epithelization with successful wound healing.

## DISCUSSION

Ceftriaxone is a generally well tolerated. In clinical trials, the following adverse reactions, antibioatic considered to be related to ceftriaxone therapy were observed: Central nervous system: fever, chills, headache, dizziness ; Dermatological: rash, pruritus; Gastrointestinal: diarrhea, nause, vomiting, sludging in the gallbladder, cholelithiasis, pseudomembranous colitis; Genitourinary : vaginitis,casts in urine; Hematologic: eosinophilia, leukopenia, thrombocytopenia, thrombocytosis, bleeding, neutropenia; Hepatic: transient elevation in liver enzymes, jaundice, elevation in serum bilirubin; Local: pain at injection site; Renal: elevated blood urea nitrogen and serum creatinine (4).

(TEN) is a rare exfoliative disorder with an estimated annual incidence of 1-2 per million(5) Reported mortality rates vary from 20 to 60 percent(1). The most common cause of TEN is idiosyncratic drug reaction, although viral, bacterial, and fungal infections, as well as immunization, have been described(1). The drugs most frequently involved are nonsteroidal anti-inflammatory agents, chemotherapeutic agents, antibiotics, and anticonvulsants (1,6,9) . Among the cephalosporins, ceftazidime , cefuroxime , cephalexin , and cephem have been implicated (6). The pathogenesis of TEN is still not fully clear but is believed to be immune-mediated, as re-challenging an individual with the same drug can result in rapid recurrence of TEN (6) . The widespread epidermal death is thought to be a consequence of keratinocyte apoptosis (8). A pivotal role of cytotoxic T lymphocytes has been suggested (1). Recent studies indicated that TEN may be an MHC-class -I-restricted specific drug sensitivity leads to clonal expansion of CD8+ cytotoxic lymphocytes with potential for cytolysis (6) .

The clinical course of TEN is characterized by a prodromal phase with influenza-like symptoms followed by intense erythema, urticarial plaques, and bullae which progress over a day or two to a more generalized epidermal slough (1,3,6). There is often severe involvement of the mucosal surfaces that may precede the skin lesions. Higher vulnerability to infections, progressive neutropenia and thrombocytopenia and sepsis may cause death.

## CONCLUSSION

TEN is an acute, life-threatening, exfoliative disorder with a high mortality rate. Due to the high risk of mortality, management of TEN requires rapid diagnosis, identification, interruption of the culprit drug, specialized supportive care ideally in an intensive care unit. Also using antibiotics carefully especially in children is very important.

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