Toxic Epidermal Necrolysis: A Case Report

Toksik Epidermal Nekrolizis: Bir Olgu Sunumu

Toksik Epidermal Nekrolizis / Toxic Epidermal Necrolysis

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Özet

Steven's Johnson Sendromu (SJS) ve toksik epidermal nekroliz (TEN), ciddi klinik tablolara ve mortaliteye sebep olabilen, deri ve mukozaların akut seyirli ve şiddetli reaksiyonlarıdır. Burada üst solunum yolu enfeksiyonu nedeniyle parasetamol, kodein fosfat ve klorfeniramin içeren tablet kullanımından sonra toksik epidermal nekroliz tablosu gelişen ve mortalite ile sonuçlanan olgu sunulmuştur. Çocuk hastalarda SJS ve TEN gibi ciddi klinik tablolara neden olabilecek durumlar göz önünde bulundurulmalı, gereksiz ilaç kullanımından kaçınılmalıdır.

Anahtar Kelimeler

Steven-Johnson Sendromu; Toksik Epidermal Nekrolizis; İlaç Yan Etkileri

Abstract

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, acute reactions of the skin and mucosa that can result in serious clinical outcomes and morbidity. We report a case of TEN resulting in mortality, following the use of tablets containing paracetamol, codeine phosphate, and chlorpheniramine for an upper respiratory tract infection. Conditions such as SJS and TEN that can lead to serious clinical outcomes should be considered in juvenile patients, and unnecessary drug use should be avoided.

Keywords

Stevens-Johnson Syndrome; Toxic Epidermal Necrolysis; Drug Side Effects

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Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute and severe reactions of the skin and mucosa that can lead to serious clinical outcomes and morbidity. The pathogeneses of SJS and TEN are unclear, although there is evidence of an association with humoral and cell-mediated immunity. Due to the similarity between the clinical and histopathological findings and etiology, the two diseases are regarded as being two variants of the same process, differing solely in terms of the degree of surface area affected [1]. There is no specific treatment other than support therapy. Drugs that may be responsible should be discontinued, appropriate treatment should be administered if infection is involved.

Case Report

A 15-year-old girl with no known previous history of disease or drug allergy had been started by physician at another institution, on treatment including paracetamol, codeine phosphate, and chlorpheniramine (A-ferin capsules, Bilim Drug Company, Istanbul) due to an upper respiratory tract infection. Approximately 12 hours after drug administration, a red eruption developed, not rising above the surface of the skin, starting from the neck and also involving the inside of the mouth, lips, and eyes, and spreading over the entire body. After four days of monitoring at a private hospital, parenteral antihistaminic and intravenous immunoglobulin (IVIG), 400 mg/kg per day for three days, was administered. However, the cutaneous and mucosal findings persisted and worsened, and the patient was referred to our hospital. Informed consent was received from the family and the patient was admitted to the intensive care unit.

Upon physical examination, body temperature was 37°C, pulse 153 min, respiratory rate 21/min, and blood pressure 128/71 mmHg. Bullous lesions, eroded in places, covered approximately 50% of the body surface (Figure 1). Nikolsky's sign was positive. Laboratory examination results were: Hemoglobin:10.3 gr/dl, White blood cells: 4000/mm³, Platelet: 275.000/mm□, C-reactive protein:84 mg/dL, and procalcitonin 0.15 ng/mL. Varicella zoster virus, cytomegalovirus, herpes virus, hepatitis A, B, and C, Mycoplasma pneumonia, and Chlamydia pneumonia serologies were negative. No pathological growth was observed in the throat, urine, blood, or stool specimens. TEN was diagnosed and empiric antibiotic therapy was started. On the advice of the dermatology department, i.v. antihistaminic and i.v. methylprednisolone at a dosage of 1 mg/kg per day were administered for three days. No improvement was observed, and methylprednisolone was increased to 3 mg/kg per day and was administered at that dose for five days. Membranous conjunctivitis was determined upon ocular examination, and topical autologous serum drops were applied. A decrease in skin and mucosal lesions was observed on the fifth day of corticosteroid therapy. The patient's body temperature subsequently increased. Acinetobacter baumannii growth was determined by blood culture, and colistin at 5 mg/kg was added to the treatment. Hypotension occurred, and the patient was started on inotropic support with dopamine and dobutamine. However, cardiopulmonary arrest developed on the 12th day, and the patient died.



Figure 1. Erosion was present in the skin, eyelids, and oral mucosa

Discussion

SJS and TEN have an acute course, and manifest as severe reactions of the skin and mucosa that can lead to serious clinical outcomes and morbidity. These two diseases are regarded as being two variants of the same process, differing solely in terms of the degree of surface area involved. SJS is a more active form of the disease with a milder course involving less than 10% of the body surface area and characterized by mucous membrane erosions and vesicles. TEN represents the more extreme end of the spectrum, affecting more than 30% of the body surface, with the accumulation of erosions and vesicles resembling burns. If 10-20% of the skin is involved, and in the presence of widespread macules or flat, atypical target lesions, this is known as SJS/TEN overlap syndrome [2].

The increased keratinocyte cell death in TEN is due to Fas ligand (FasL) and Fas (CD95) expression. Any triggering agent, such as a drug, can increase keratinocyte production of apoptotic ligands such as FasL and cause apoptosis through Fas-FasL binding. Higher FasL levels have been reported in the sera of patients with TEN compared to patients with maculopapular eruption and healthy controls [3].

The annual incidence of SJS is estimated at 0.4-1.2/1.000.000 and that of TEN at 1.2-6/1.000.000 [4]. While there are various factors in the etiology, the most common cause is drug administration. Drug use is identified in 70-80% of cases. The most commonly implicated drugs are antibiotics, non-steroidal anti-inflammatory drugs, and anticonvulsants. A second common cause is infection. It has been reported in association with agents such as hepatitis, Yersinia, measles, varicella, herpes simplex, herpes zoster, Mycoplasma pneumoniae, and Escherichia coli [5].

TEN exhibits an acute onset. There is a prodromal phase lasting one to three days before disease onset, involving fever, cough, sore throat, myalgia, and stinging in the eyes. Following this prodromal phase, painful cutaneous eruptions appear, generally beginning on the face and upper part of the trunk and spreading rapidly over the entire body. Nikolsky's sign is positive. Mucous membranes are involved in approximately 90% of cases. Erosions are most commonly seen in the oral mucosa, and diffuse erythema, vesiculation, and diffuse erosions are seen in the lips, conjunctiva, genital, and anal mucosa. Conjunctival erosions may be present, and can cause corneal ulceration and blindness. Odynophagia, dysphagia, dysphonia, dyspnea, earache, and nasal obstruction may occur in the event of ear, nose, and throat involvement.

There is no specific treatment modality other than support therapy. Drugs that may be responsible should be discontinued, and if infection is present this should be treated appropriately. Support therapy consists of fluid electrolyte replacement, nutrition support, wound care, and prevention of sepsis, the most important cause of mortality. Regulation of environmental temperature is important. The patient must be approached in accordance with rules regarding asepsis. Long- and short-term corticosteroid therapy is thought to modify immunological events involved in the pathogenesis of the disease. IVIG therapy has been shown to inhibit Fas-associated keratinocyte apoptosis. Metry et al. [6] reported a response to IVIG therapy in one to seven days and a decrease in new vesicle formation in juvenile patients. A dose of 1-3 g/kg per day can be used for three to five days. Other treatment options that can be tried include plasmapheresis for the purpose of suppressing cytotoxicity, cyclophosphamide, cyclosporine, n-acetyl cysteine, and infliximab. Improvement following hemoperfusion therapy was reported in seven children with TEN in 2014, and hemoperfusion was emphasized as a potential alternative in severe cases of TEN with no improvement despite steroid and IVIG therapy [7].

In conclusion, conditions such as SJS and TEN that can lead to serious clinical outcomes should be considered in pediatric patients, and unnecessary drug use should be avoided.

Competing interests

The authors declare that they have no competing interests.

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