Clinical Notes

Toxic epidermal necrolysis due to procaine penicillin

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In toxic epidermal necrolysis (TEN), a wide layer of skin is peeled and an immature skin layer appears. In a short period, an epidermal necrolysis characterized by scalded appearance of skin due to febrile toxic reaction develops. The mortality rate of this disease is high (20-70%), due to dramatic drug reactions of the skin. The disease resembles mostly to erythema multiforme (EM), Steven Johnson syndrome (SJS), and staphylococcal scalded skin syndrome (SSSS). Toxic epidermal necrolysis is more prevalent in adults, though it can be encountered in all ages. It can be evaluated as an upper respiratory tract infection at first sight, since its initial symptoms are fever, conjunctivitis, or pharyngitis.[5] The main cause of mortality in this disease is systemic infections, such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Adverse effects of drugs (especially sulfonamides), infections, malign diseases, and graft versus host disease are mainly blamed as causes of TEN. The early histopathological finding of TEN is the presence of necrotic keratinocytes in the dermal-epidermal junction. Inflammatory cells can be seen in skin biopsies. Furthermore, Nikolsky phenomenon can also be used for diagnosis. The disease is evaluated as a burn case in many centers. Early diagnosis, timely interventions, and sufficient supportive therapy may save the life of these patients.[1,2]

A 9-year-old female child was bitten by dogs. Injuries by dog bite were seen in her hairy skin and in the femoral region. She was first hospitalized at a state hospital and received rabies vaccine program. After 4 doses, she was discharged. Ten days after discharge, she had fever and sought for a doctor. She was then diagnosed with acute tonsillopharyngitis, and procaine penicillin 800.000 IU was started as treatment. Skin eruptions appeared within 24 hours after the first dose of the drug. Parenteral antihistaminic and prednisolone were administered for allergic reaction, however, her complaints continued and she was transferred to our emergency service. On admission, she was in bad condition but conscious. Arterial blood pressure was 60/90 mmHg, temperature was 41°C, heart rate was 132/dk, and breath count was 24/dk. Maculopapularly eruptions with extensive bullous lesions in places were present in 87% of the body (**Figure 1**). Nikolsky phenomenon was positive. Wide erosions and hemorrhagic clot were observed at oral mucosa and lips. Bilateral hyperemia of conjunctiva, burning, and hurt complaints were present. On examination, other systems were normal. Laboratory results were normal except for lactate dehydrogenase 557 U/L (normal range 240-480 U/L) and sodium 126 mmol/L (normal range 132-145 mmol/L). Urine analyses revealed 7-8 leukocytes and 10-12 erythrocytes. In our patient, results of cultures (urine, blood and lesion) were negative. On peripheral, smear lymphocytes was 24%, monocytes was 75%, and band formation was 6%. She was put in burn care unit with primary diagnoses of TEN, SJS, and SSSS. Fluid replacement was started. Necrotic skin was cleaned and dressed. Consultations were asked from dermatology and ophthalmology clinics. Silver sulfadiazine cream and chloramphenicol pomade were applied. We elevated all extremities to regress edema. Benzydamine hydrochloride spray and novo cream consisting of glycerin were started for oral care, and tobramycin drop and a native tears gel were started for the eyes. Tramadol hydrochloride and famotidine were ordered for her pain and prophylaxis for stress ulcers. Systemic antibiotics (ceftriaxone and clindamycin) were administered. Skin biopsy taken from the gluteus region, revealed the tissue covered with acantholytic stratified squamous epithelia, vascular sections of various sizes in papillary dermis, and collagen sections in the reticular dermis. On the third day of treatment, her temperature was still high, thus, her antibiotic was changed to Meropenem (20 mg/kg x 3 days). Her fever was then controlled. On the seventh day, she started oral alimentation, and was mobilized on the tenth days of hospitalization. Except for daily dressings, other medications were ceased on the fifteenth day, and she was discharged with a complete cure on the twentieth day.

Mucocutaneous erosions are the most important feature of TEN, however, it can also present as systemic disease. Patients with HIV-1 infection, systemic lupus erythematosus, and bone marrow transplantation is the

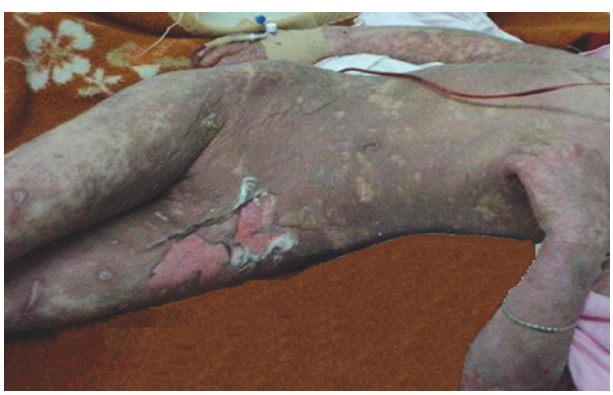

Figure 1 - Maculopapularly eruptions together with extensive bullous lesions.

risk groups for TEN. In our opinion, the fact that our patient was bitten by dogs was the factor facilitating the development of this clinical entity. Among diseases, it mostly resembles to SSSS, EM, and SJS. It may also show resemblance to a relatively less extent, with autoimmune bullous diseases such as, pemphigus and pemphigoid, scarlatina, and boric acid intoxication. We also hospitalized our patient with primary diagnoses of SSSS, EM, and SJS. We reached to the definite diagnosis by the evaluation of all laboratory results, opinion of other related clinics, and results of biopsy together. These diseases are possible to differentiate considering some special features.

In a study carried out by Elias et al[3] TEN was determined to cause necrosis in all layers of epidermis and threaten the life more seriously. In our case, drug associated necrotic and bullous reaction developed. All epidermal layers were involved, and necrosis was developed in the involved part of epidermis. In Becker's study,[4] symptoms of TEN were fever (100%), conjunctivitis (32%), itching (28%), and pharyngitis (25%); and the mucosal membranes were affected in one to 3 days before skin lesions appear. The first symptom was fever in our case. Conjunctivitis, burn, and itching of the eyes, pharyngitis and difficulty in chewing, and swallowing were developed later. These symptoms lasted for 7 days. Our patient had the first burn in her mouth and throat then developed skin lesions. It could not be determined where the skin lesions first started. In a study carried on children, it was reported that 46-90% of the skin, and 60% of the eyes were involved.[5] Skin involvement was 87% in our case. Various rates of mortality associated with TEN have been reported. Revuz et al,[2] in a study consisting of 87 patients determined mortality rate as 25%. They determined systemic infections as the main cause of death and aged, size of the involved skin part and serum urea-nitrogen concentration as the most important prognostic factors. Our treatment lasted long (20 days) due to the patient's young age, a recent trauma by dog bite and large skin involvement (87%).

In conclusion, TEN is a disease characterized by extensive epidermolysis, which involves all epidermal layers and can be life threatening. The extent of the involved skin and superposed secondary infections are the main factors that increase mortality. It should be treated and followed as a serious burn case. Thus, advanced burn centers are the ideal places for the treatment of these patients.

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