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Toxic Epidermal Necrolysis* (Scalded Skin Syndrome)

A Case Report

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This syndrome is described in 1956 by two separate groups of workers and is characterized by irritability, diffuse erythema and tenderness of the skin followed by exfoliation and a positive Nicolsky's sign.[1, 2] Some drugs[3] or the phage group 2 staphylococci are responsible for the etiology.[4-8] Melish and Glasgow experimentally produced a similar picture by injecting the phage group 2 staphylococci in the newborn mice.[9] Further studies in mice have shown that a toxin, exfoliatin, produced by staphylococci is responsible for this clinical picture.[10-12] Recent publications suggest that toxic epidermal necrolysis may be the part of graft versus host (g.v.h.) reaction in patients with immunologic deficiency.[13]

Toxic epidermal necrolysis is first reported in Turkey by Say and Usubütün in 1962.[14, 15] We will report a case who responded to steroid and supportive therapy and the staphylococci phage group 2 isolated from his skin produced typical lesions of the scalded skin syndrome in the newborn mice. A series of immunological studies have also been carried out on this patient.

Case Report

This 4.5 year old boy was admitted to the hospital with chief complaints of fever and skin rash. A week prior to admission he had a boil in the right arm which was treated with tetracycline and penicillin for 5

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days. 3 days before admission his skin became red, erythematous and the local phycician prescribed Benadryl and boric acid washes. During this treatment his fever was elevated, the skin lesions became generalized and he developed sores around the mouth. The skin began peeling and became very tender.

On Physical Examination

Temperature: 38°. 3 C, pulse 130/ min, weight 14.8 kg. There were crusted lesions around the mouth and lips. Skin exhibited diffuse erythema, desquamation and peeling in axillary areas. There were localized areas of bleeding with bullae formation. The Nikolsky's sign was positive. (Fig. 1) The patient was extremely agitated with a very tender skin.

Figure 1
Typical skin lesions observed on admission

Past History: DPT, BCG, smallpox cholera vaccines followed their usual courses. Measles was uneventful. The parents and two sibling were healthy. There was no history of allergy or immune deficieny in the family.

With these typical findings, a diagnosis of toxic epidermal necrolysis was made. After appropriate cultures were obtained he was treated with corticosteroids, I.V. fluids, penicillin, ampicillin, analgesics and a sterile care was carried out. From the skin lesions, staph, aureus coagulase positive was cultured and ampicillin was changed to prostaphline. On the second admission day, the skin was extremely tender and the fever was

elevated to 41°C. The peeling lesions in hands and palms looked like a glove (Fig. 2). After the second hospital day the lesions begun to regress (Fig. 3). Temperature became normal on the fourth day. Steroids were discontinued on the fifth day and he was discharged home on prostaphline on the 8th hospital day (Fig. 4). The follow-up examination two months after discharge revealed normal physical findings.

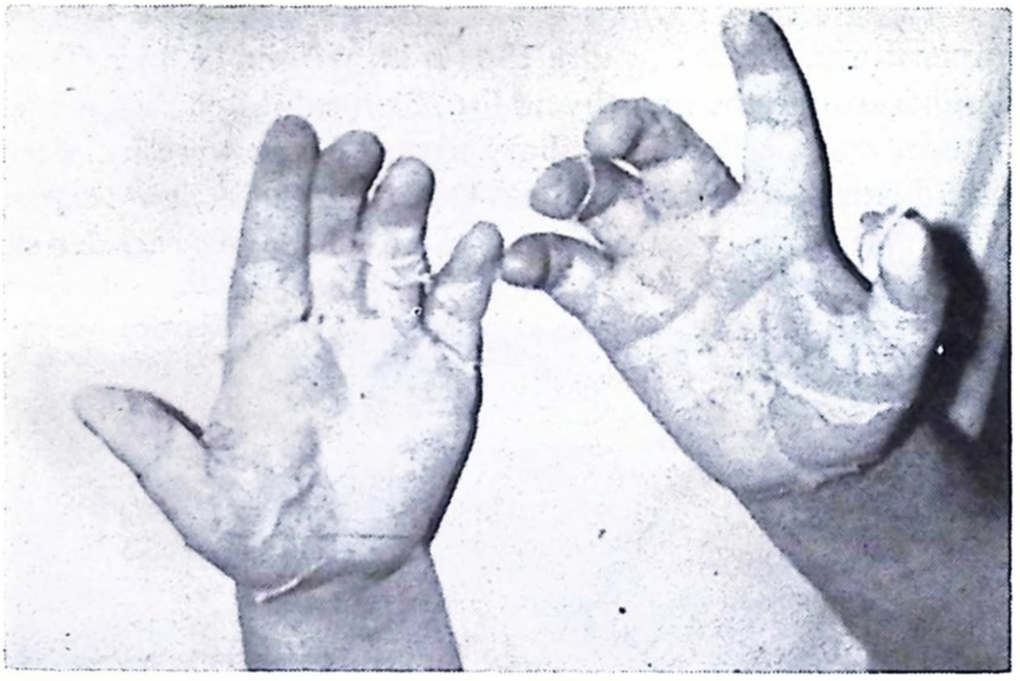

Figure 2
Peeling skin lesions in hands and palms

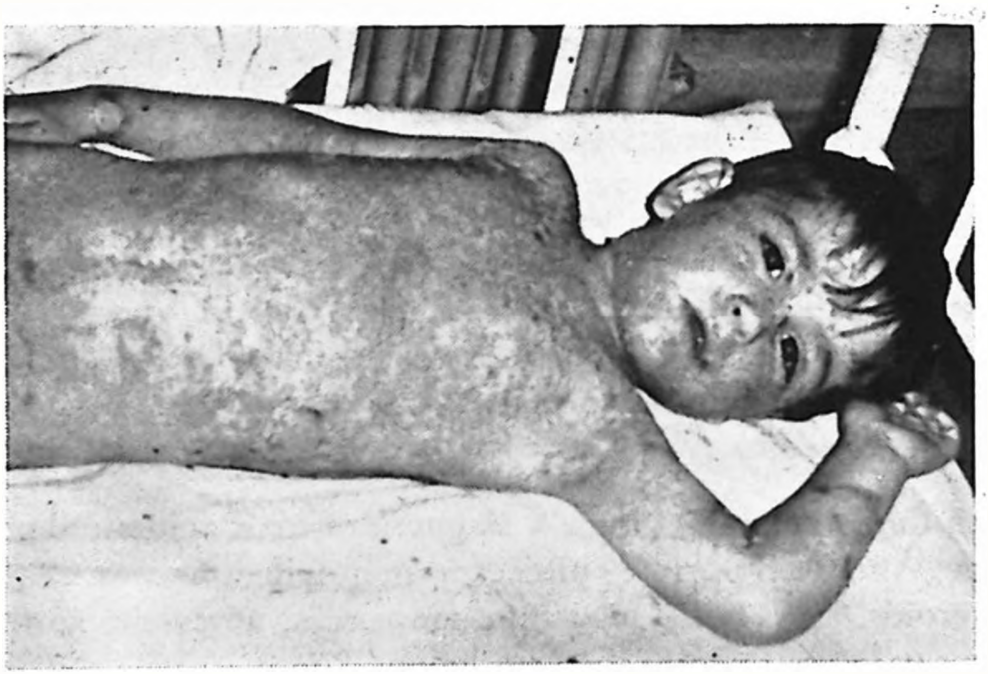

Figure 3
Appearance of the skin lesions on the second admission day

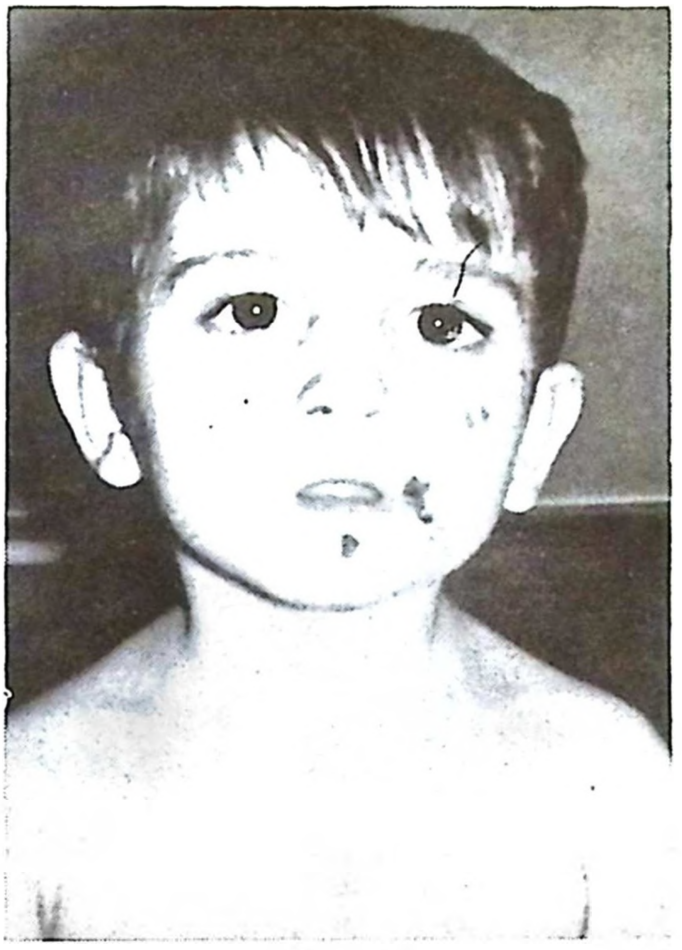

Figure 4
Appearance of the skin on discharge from the hospital

SPECIAL STUDIES-MATERIAL and METHODS and FINDINGS

Laboratody Findings in the Patient were:

Hemoglobin 12.8-14 gm/100 ml., WBC 9600-10200/cmm.[16], absolute PMN 6900-8000/cmm, absolute lymphocyte count 3060-4400/cmm. Urinalysis was normal. There was no growth in blood cultures. The staph. coagulase positive grown from the skin was phage typed at the Microbiology Institute of the Istanbul University and Maryland state Laboratories. Both places reported it as group 2, phage 71. Three-four days old mice were inoculated subcutaneously with this staphylococci with doses of 10^5, 10^6, 10^7, 10^{11} by using 26 gauge needle and the mice were observed at few hourly intervals. Because of canibalism two experiments had to be repeated. Sixteen to-18 hours after inoculation they developed skin lesions characterized with diffuse erythema, peeling and a positive Nikolsky's sign (Fig. 5). Mice inoculated with higher doses of staphylococci (10^7 or 10^{11}) died, those inoculated with lower doses (10^5) developed localized abscesses in the skin (Fig. 6). Injection of staphylococci

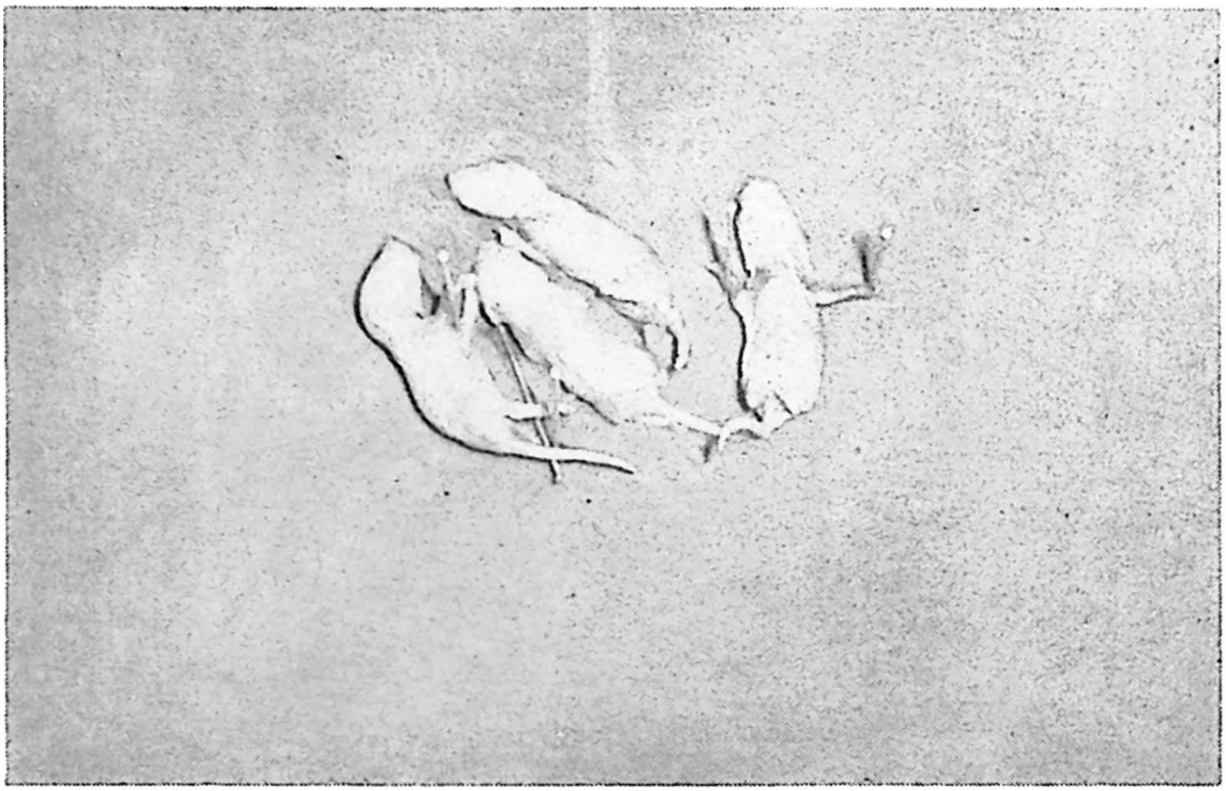

Figure 5

Diffuse erythema and peeling of the skin in mice inoculated with staphylococci cultured from the patients' skin lesions

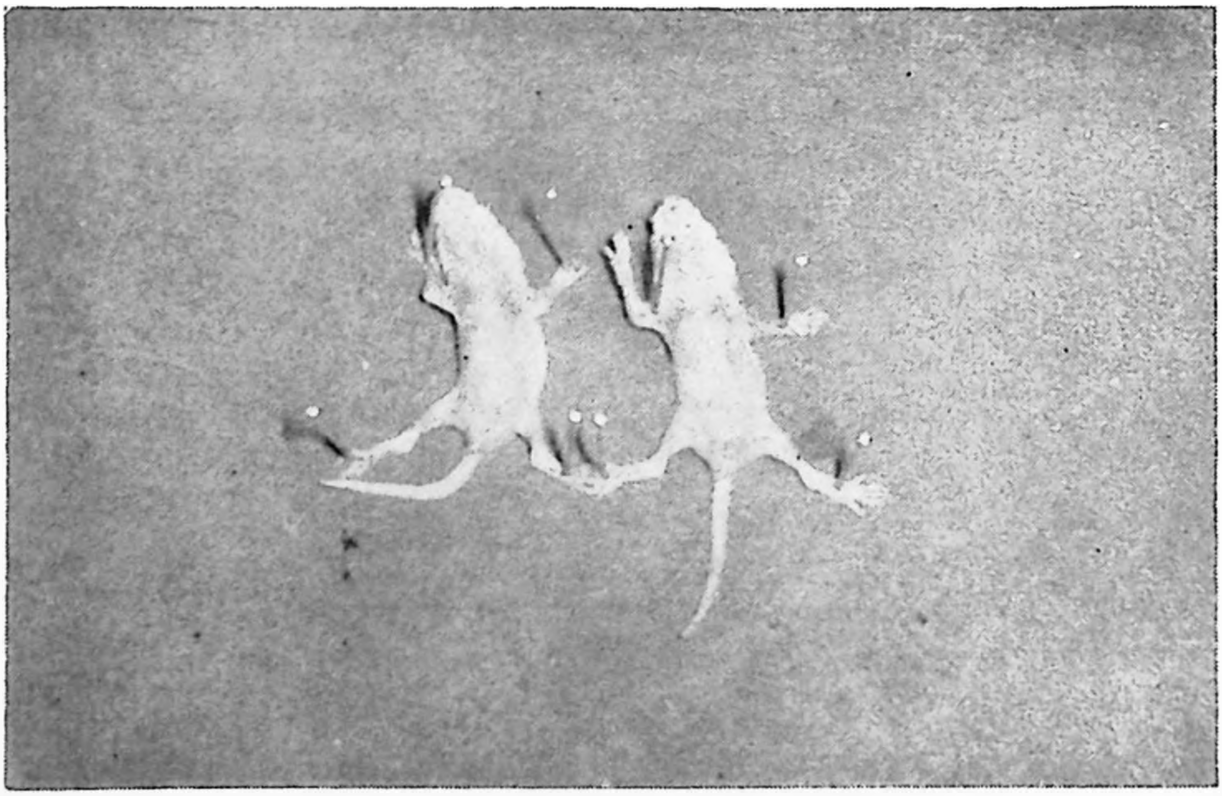

Figure 6

Abscess formation in the mice inoculated with low doses of staphylococci

other than phage group 2 produced localized staphylococci abscesses without peeling of the skin.

The immunoelectrophoresis[17] was normal. Quantitative immunoglobulins[18]: IgG 1860 mg, IgM 122 mg, IgA 140 mg, β_1C 45 mg/100 ml. In vitro lymphocyte studies were done by using phytohemagglutinin (PHA), candida, streptokinase-streptodornase (SKSD) and allogeneic lymphocytes.[19, 20] Incorporation of tritiated thymidine (H_3Tdr) into DNA was measured on the 3rd day for PHA, 4th day for mixed leukocyte cultures (MLC) and 7th day for SKSD and candida. Lymphocytes from a healthy child of the same age were used in control cultures. The results were expressed as counts per minute per million of lymphocytes (CPM x 10^3 / 1 x 10^6 lymphocytes) and compared with the control. The patient's in vitro lymphocyte response was within normal limits (see table). For investigation of delayed hypersensitivity, skin tests were done. An induration more than 5 mm. at the end of 48 hours was considered as positive. The PPD (1 unit/0.1 ml- Refik Saydam Merkez Hıfsıssıhha Enst.) and SKSD (50 units streptokinase, 12.5 units streptodornase/0.1 ml-Lederle Labs) were negative. PHA (10 µg/0.1 ml-PHA-P-Burroughs-Welcome Labs) and candida undiluted 500 PNU/ml- Hollister Stier Labs) were positive.

The results of tests for cellular and humoral immunity did not disclose any evidence of immune deficiency in this patient at the time of these studies. The etiology was staph. Phage group 2 which produced similar picture in newborn mice. The patient recovered after cortiosteroid and antibiotic therapy in addition to supportive treatment.

TABLE I

IN VITRO LYMPHOCYTE STUDIES (CPM x 10^3/1 x 10^6 LYMPHOCYTES)

	PHA	Unstimulated	SI	Candida	Unstimulated	SI	SKSD	SI
Patient	516.03	1.21	423.6	42.9	4.09	10.4	19.59	4.7
Control	616.28	1.13	543.4	9.51	3.21	2.9	10.62	3.3

MLC

Patient's lymphocytes x control's mitomycin-C treated lymphocytes	= 3.25
Patient's lymphocytes	= 0.58
SI	= 5.5

(The response is considered positive for PHA if SI > 20, for MLC if SI > 2.5, for antigens if SI > 2).

Discussion

Toxic epidermal necrolysis is seen in different age groups and the causative agent is generally staph aureus-coagulase positive phage group 2. In the newborn it is described as a form of Ritter's disease.[4] In adults some drugs such as sulfonamides, phenobarbital, phenolphthalein, aspirin, phenacetine, and antibiotics are claimed. In one case a viral etiology is reported.[4] The staphylococcal etiology is more common in infants and the course is more severe in children under one year of age.[4, 6, 9] Sometimes it is triggered by viral infections.[21]

The primary pathological lesion is epidermal necrolysis with cleavage within the layers of the epidermis or with a detachment of the epidermis at the dermal- epidermal junction. The corium is not involved. Although some flaccid bullae may be seen, rapid separation of the epidermis in sheets is the distinguishing feature. Because of the typical lack of involvement of the corium, healing of the skin is often quite complete ten days after the onset of desquamation.[6]

Typical clinical picture usually lasts for about 2-7 days, then dramatically temperature returns to normal and tenderness of the skin disappears. In the management general supportive care with isolation and a sterile nursing technique in addition to local and systemic antibiotics, intravenous fluids, sedation and glucocorticoids is very important. Drugs administered prior to the development of this disease should be discontiuned in order to eliminate their possible role in the etiology. Clinical course and the outcome of the disease depends upon the immune response of the host in this disease of multifactorial etiology.[21]

Streilein and Billingham reported that toxic epidermal necrolysis could be produced in animals as a result of graft versus-host disease.[22] It is also reported in a patient with the graft-versus-host reaction following a bone marrow transplantation.[23] Toxic epidermal necrolysis was observed in two other patients with graft-versus-host disease by Ammann et al.[13] One was following a bone marrow transplant and the other was in an infant with unsuspected immunodeficiency who required neonatal exchange transfusion for hyperbilirubinemia. We have observed it in an acute leukemic patient under heavy immunosuppressive chemotherapy who developed graft-versus-host reaction manifested by toxic epidermal necrolysis following a blood transfusion.[24]

In some cases of toxic epidermal necrolysis the exact etiology can not be ascertained. In our patient staph. aureus phage group 2 has been cultured from the skin and the history revealed use of antibiotics (tetracycline and penicillin) and boric acid prior to the full blown picture of

toxic epidermal necrolysis. The staphylococci cultured from his skin produced similar lesions in the newborn mice. In the treatment of the patient corticosteroids and antibiotics were used in addition to supportive therapy. Special immunological tests showed no evidence of immunodeficiency in this patient.

Summary

A 4.5 year old boy with toxic epidermal necrolysis is presented. Staph. aureus phage group-2 was cultured from his skin. With the same organism, in the newborn mice a similar picture was produced experimentally. The patient showed no evidence of immunodeficiency by various immunological tests.

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