TOXIC EPIDERMAL NECROLYSIS (SCALDED SKIN SYNDROME)

With Special Reference to Contact with Kerosene Resulting in a Clinically Similar Condition *

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Toxic epidermal necrolysis, which was first described in 1956 by Lyell [1] in England and independently by Lange and Walker [2] in South Africa, was thought to be an extremely rare condition. However, the number of new cases reported during the past three years would indicate that it is not as rare as was formerly thought. The three cases which we present here are, to our knowledge, the first to be reported from Turkey.

Reports

Case I. K. B., the one and a half year old daughter of healthy parents, was admitted to Hacettepe Children's Hospital with complaints of redness and peeling of the skin and formation of bullae.

History : Three days prior to admission the child developed fever, and red patches, resembling burns, had appeared on the skin of her neck and the upper part of her trunk. Following this, the skin started to peel. According to the parents. the child had not been given any medication, including sulfonamides.

Physical examination : Her throat was hyperemic and her temperature was 38.3 C. The skin had peeled in large pieces from the area of the forehead, chin, neck and shoulders. Normal skin around the lesions also seemed to separate easily. Peeled areas were red and covered with small bleeding cracks. The back, which showed only erythema on admission, was covered with many bullae within 24 hours. The chest had peeled in patches of different sizes and depths.

Because of the following facts developed in the case history, this condition was diagnosed as toxic epidermal necrolysis : 1. the skin lesions progressed rapidly and after a very short time the skin presented a scalded - like appearance; and 2. the occurence of preceding symptoms such as a low fever and an upper respiratory infection. Once the diagnosis was made, steroid therapy was started immediately. The child received 5 mg. of prednisolone three times a day, the dose having been calculated at one and one half mg./kg. per day. Also, in order to prevent secondary infections, 40 mg./kg. of oxtetracylin were given daily. The following day improvement was evident in the skin lesions. No new bullae formed after the treat-

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ment was begun. On the second day redness decreased. Eruptions began to disappear and the lesions began to dry up. On the third day redness had almost completely disappeared. New skin started forming in scattered areas. On the fourth day the skin was dry and the redness had disappeared completely. Prednisolone was then reduced to 5 mg. twice a day. On the fifth day, except for the old lesions on the feet and legs, the skin lesions were cured. Prednisolone was then reduced to 5 mg. per day. A week later steroid therapy was stopped altogether and the patient was discharged from the hospital without skin lesions. A skin biopsy was obtained before treatment with steroids was begun and was reported to be characteristic of toxic epidermal necrolysis.

Case 2: M. C., an 11 month old boy, was brought to the hospital with complaints of irritability and drowsiness. The physical examination revealed classical symptoms of meningeal irritation. A lumbar puncture was performed and an obviously purulent fluid was obtained. Smears made from the spinal fluid showed no organisms, but the culture subsequently revealed meningococcus. Except for peripheral leucocytosis, other laboratory findings were within normal limits. Initially the patient was given 100 mg./kg. of Gantrisin, 250,000 I. U. of penicillin every three hours, and 50 mg./kg. of chloramphenicol per day. On the fifth day of treatment a widespread erythema was observed on the chest and a day later three bullae appeared in the same area, the largest being approximately five centimeters in diameter (figure 1). The same day these lesions ruptured,

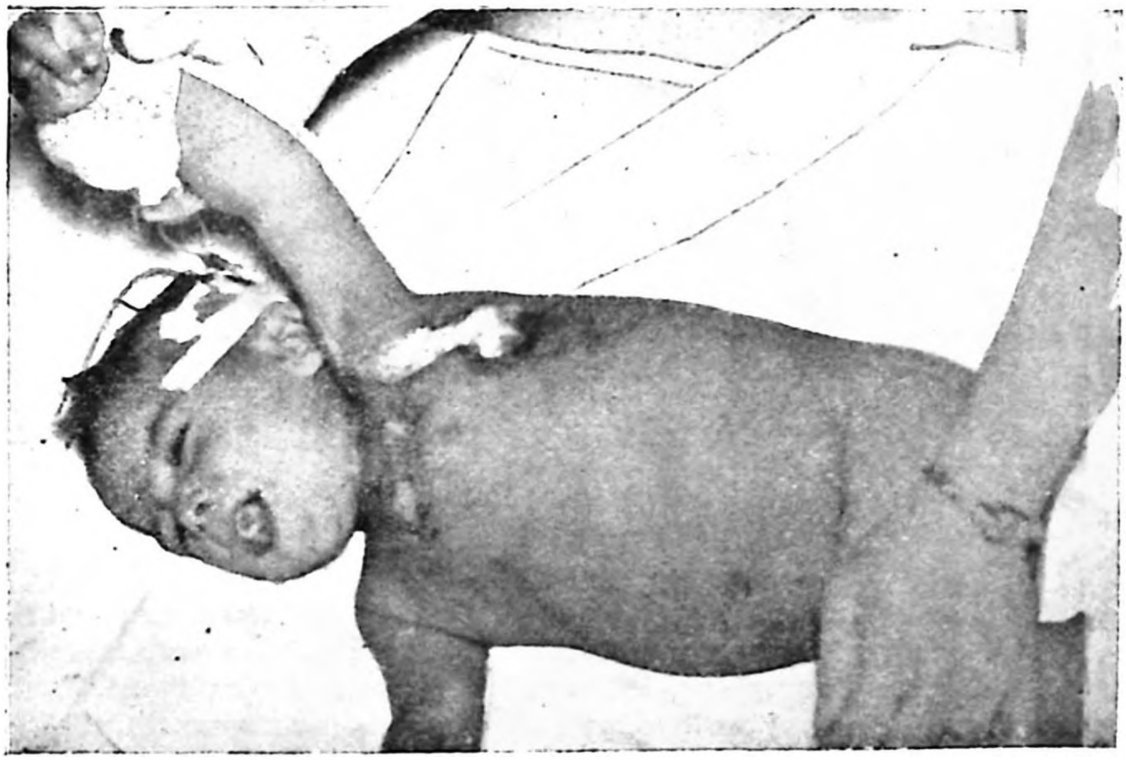

Figure 1.

and the fluid obtained from them showed no growth of pathogenic organisms. The smears were also negative. Also, on this day similar lesions appeared in the gluteal area. After the lesions ruptured, the appearance of the skin resembled that of «scalded» skin. In the area around the lesions, Nikolsky's sign was negative. The Gantrisin was discontinued at this time and the following day the patient was given 2 mg./kg. of Prednisolone per day. Within three days there was marked improvement and the dosage was decreased. The patient was sent home after one week of steroid treatment. A skin biopsy was not performed.

Case 3 : M. O., a 22 month old male, was brought to the Hacettepe Children's Hospital with principal complaints of skin lesions on the abdomen and left thigh. The past history revealed that he was in good health until 24 hours before admission. The previous evening the parents noticed a sudden occurrence of erythema on the right thigh. In the morning they found the area blistered and immediately brought the child to the hospital. The physical examination on admission revealed a large blister about 6 centimeters in diameter on the right thigh. There was also an erythematous area on the right side of the abdomen with a few early bullae (figure 2). Further questioning of the parents revealed that the child

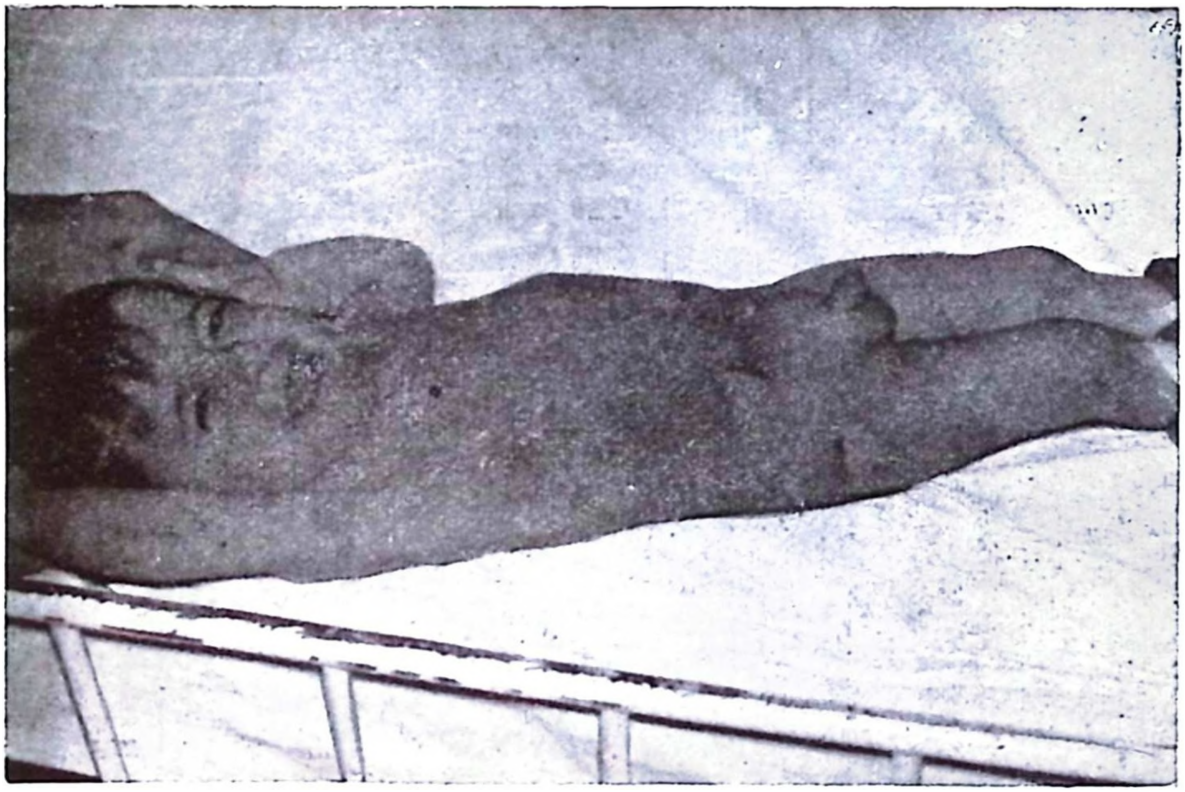

Figure 2.

had been given no medication prior to the illness. He had not been exposed to strong heat, water, or to kerosene. Multiple smears and cultures were made from the fluid taken from unruptured bullae and no organisms were found. Routine laboratory examinations of the blood and urine revealed no abnormalities. A skin biopsy showed necrolysis of the squamous cells in the stratum malpighii of the epidermis, polymorph nucleated cells and a few lymphocytes in the sub - epidermal

area. The epidermis was separated from the dermal layer, but there was no pathology in the the dermal layer (figures 3 and 4).

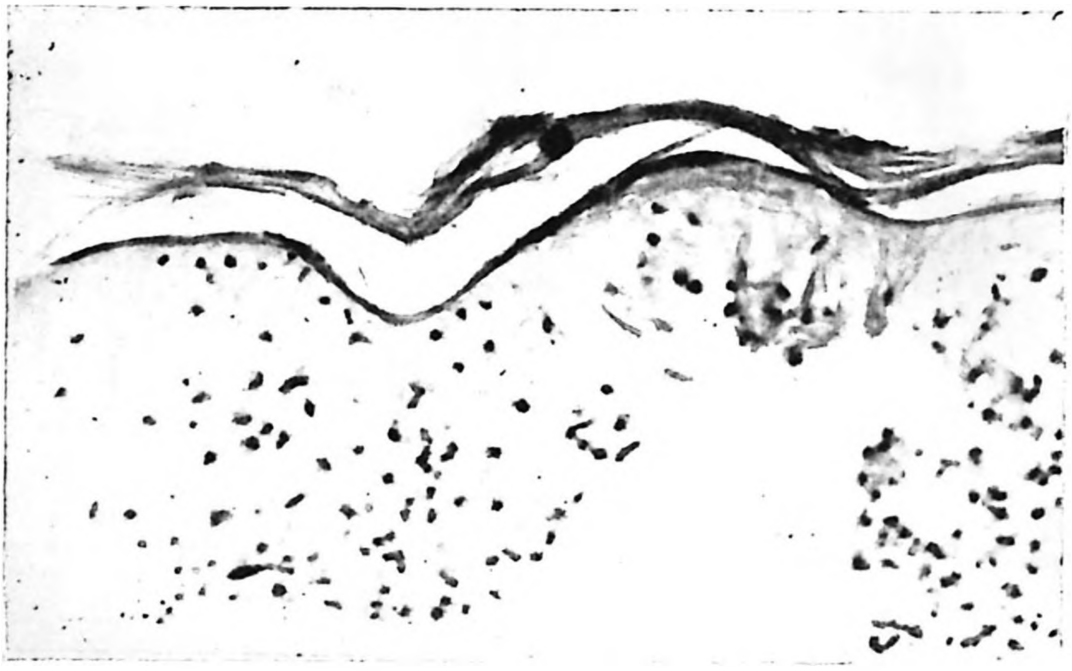

Figure 3. Necrolysis can be seen in the epidermis.

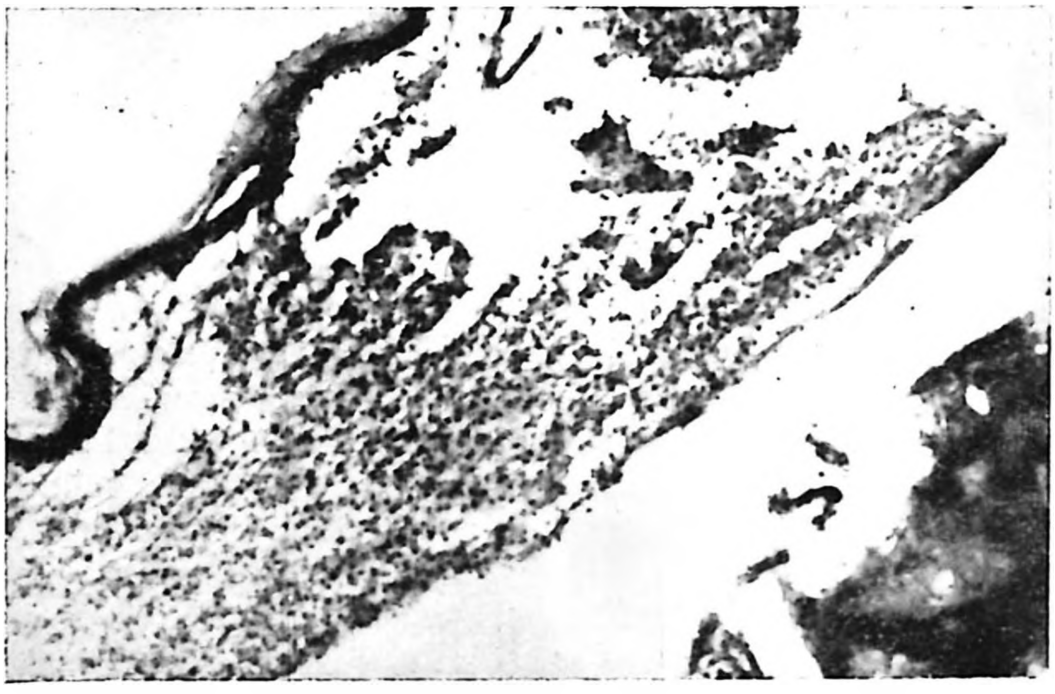

Figure 4. There are many polymorphic leukocytes and some lymphocyte infiltration into the subepidermal area.

The patient was given 2 mg./kg. of prednisolone per day. No new lesions appeared after this treatment was begun, and the initial lesions healed rapidly. The child was discharged after three days in good condition.

Discussion

At the time of this writing, 34 cases of toxic epidermal necrolysis have been published.[1,2,5] Usually, this disease has a sudden onset, although in some cases prodromal symptoms such as vomiting, diarrhea, sore throat, back aches, conjunctivitis and upper respiratory tract infections occur two or three days prior to to the onset of the disease. In one of Frain - Bell and Koblenzer's[3] cases, it is reported that a cat had scratched the patient's cheek. The general condition of the patient varies: some look well on first examination but deteriorate rapidly during the course of the illness, while others are gravely ill from the beginning. Our cases were mild. At first the disease was thought to be almost always serious, but the succeeding reports included so many mild cases that at present the condition is considered to be a mild one in the majority of patients. Patients usually have normal temperatures throughout the course of the disease, although sometimes a fever persists for one or two days.

Steroid therapy elicits sudden improvement in both the lesions and in the general condition of the patient. We were impressed by the favorable and rapid effects of steroids on our patients. We must emphasize, however, that our cases were quite mild and that there are reports in the literature of similar rapid recoveries without the use of these drugs.

In general, the severity of the disease is related to the dissemination of the lesions. Frain - Bell and Koblenzer [3] have described the course of the lesions very precisely, and we shall quote them here :

«The first change appears to be an erythema, perhaps with some degree of edema, resembling sunburn. This erythematous change may then rapidly spread over the surface of the body and merge with the next stage of loosening and separation of the skin. Fluid then collects under this loosened skin to form irregular flaccid bullae. Not uncommonly, extensive loosening of the skin appears without the formation of bullae. Within the next 24 hours the loosened skin will have started to separate and leave raw, red, denuded, oozing areas, sometimes involving practically the entire surface of the trunk and limbs. At all phases and even in the early stages, the child's skin appears to be extremely tender and he will resent any attempt at movement. This tenderness may even be present in the as yet apparently uninvolved portions of the skin. This combination of initial erythema and edema with irregular loosening of the skin, with or without flaccid bullae, followed by denudation leaving raw, red areas

produces an appearance, as Lyell pointed out, identical with the effects of scalding of the skin.

The duration of the next stage is variable, and, if the patient survives, complete healing of the affected skin usually occurs within an average of eight to twelve days.»

In almost one - third of the early case reports, death occurred in the three to four days following the onset of the disease. It was observed at that time that early treatment with steroids seemed to improve the chances of recovery. In a series of six cases, two of the three patients who died had not been given steroid therapy, whereas the three patients who had been given steroids recovered in a very short time. [3] From our review of the literature, we feel it is justified to say that steroid therapy seems to be of benefit in serious cases. We certainly need more data on the effects of steroid therapy in the treatment of this disease before making more definite statements.

Twenty of the published cases involved children, the youngest of which was a two week old baby. There seems to be no marked sex preference. A recurrence of the condition in the cases reported has not been observed.

Histologically, the disease is characterized by involvement of the epidermis only, although in some cases the mucosa was reported to be affected. In our patients we failed to observe any changes in the mucosa. Histologic examinations reveal partial or complete necrolysis of the epidermal cells, but nothing more than vasodilation and edema affect the dermis.

From the point of view of its clinical course, the disease can easily be differentiated from pemphigus with bullae and peeling, epidermolysis bullosa, dermatitis herpetiformis and erythema multiforme. Although the etiology of the disease is unknown, it seems to be related to a toxic process. Recently a fatal case was reported in which a twelve year old girl developed toxic epidermal necrolysis and leukopenia after sulfadimethoxine (Madribon) therapy. [5] Because of this report we discontinued the use of Gantrisin although we have no conclusive evidence that this was the cause of her condition. In most of the cases reported, however, there is no history of drug administration prior to the onset of the disease. On the other hand, it is well known that physical agents, contact with vesicants, and similar noxious substances could result in similar clinical pictures. We will mention here three additional cases which resembled toxic epidermal necrolysis clinically, and which were caused by contact with kero-

sene. One of these was that of an eight year old girl who was riding in a truck, the canvas sides of which were soaked in kerosene. Her dress became impregnated and within three hours there were erythema and bullae formations which exactly resembled the «scalded skin» as seen in toxic epidermal necrolysis. Following this we observed two more children, ten and twelve years of age, who developed symptoms after spilling kerosene on their shirts. In these three cases, steroid therapy was used to good effect. Unfortunately, skin biopsies were not obtained due to parental objections, so we were in no position to compare these histologically with toxic epidermal necrolysis. In each of these three cases, the skin of the upper part of the abdomen and back were involved, and also in two of the cases, the patients had lesions of the chest and thigh. We have found it necessary to question the parents of our patients rather closely about prior contacts with kerosene on the part of the patient. We recommend this especially in countries where kerosene is still widely used in and around the home.

Summary

The authors present three cases diagnosed as toxic epidermal necrolysis and discuss the early use of steroid therapy in the treatment of this disease. Three additional cases are reported in which the patients suffered exposure to kerosene prior to developing symptoms which closely resembled toxic epidermal necrolysis.

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