EPIDERMOLYSIS BULLOSA HEREDITARIA LETALIS *

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Epidermolysis bullosa hereditaria letalis is a very rare skin disease. The bullae characteristic of this disease may be present at birth or appear soon afterwards. There also may be degeneration of the nails as well as ulceration of the mucous membranes. To date all cases of this condition have terminated fatally, with one exception.

Our purpose in publishing this case is twofold: first, it is a rare condition generally, and second, this is the first recorded case in Turkey.

Case Report

Baby Ö, a male newborn infant, was transferred to our hospital from the Ankara Maternity Clinic at the age of eleven hours. The infant was the product of a normal pregnancy and delivery and was thought to be at term. Immediately after birth, while the baby was receiving his initial cleansing, erythematous areas were noticed over all four extremities and it was observed when these areas were rubbed that the skin came off in patches.

The family history was non-contributory. The parents were not, so far as they knew, related. The patient's sister, 6 years of age, and brother, 3 years of age, are in good health.

On admission physical examination revealed a body weight of 2700 grams. There was hyperemia on the back of both hands and over the wrists. In these areas, and also in the inguinal region and on the extensor surfaces of both legs and feet, there were scattered bullae, some of which were sloughing. Linear ulceration was present on the palate. There were dystrophic changes of the distal phalanx of the fourth toe of the right foot, and in addition there were dystrophic changes of most of the nails.

Over the next few hours after admission many new bullae appeared and meanwhile some of the old ones ruptured, leaving an erythematous weeping surface. It was observed that the slightest trauma to the skin was sufficient to produce bullae and that these lesions spread

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rapidly to the chest, abdomen and gluteal areas. Figure 1 shows the appearance and distribution of these lesions.

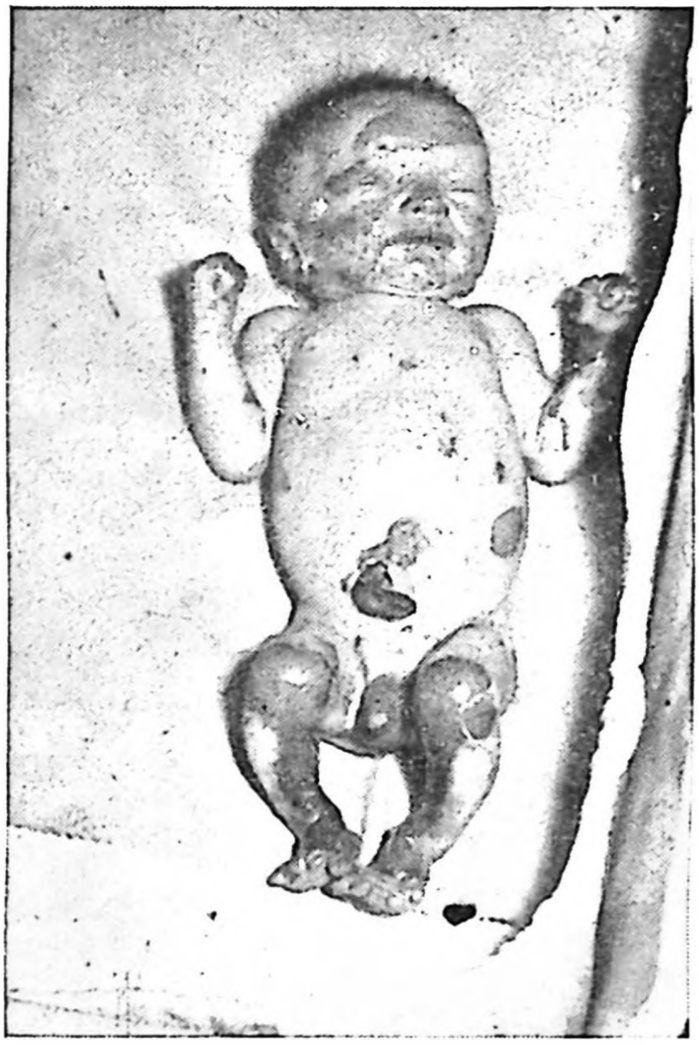

Fig. 1.

Despite extensive treatment with antibiotics, the spread of the disease could not be prevented. On the second day of life the baby stopped taking formula and was given fluids intravenously; plasma and blood were also given. Cortisone was started but on the third day crepitant râles were heard over both lung fields and during that same evening the infant expired.

Laboratory examinations revealed that the urine was cloudy in appearance with no abnormalities on microscopic examination, but the protein was 2 plus. Hemoglobin was 17 grams per 100 cc, RBC, 5.2 mil. and WBC 5200 per cubic mm. Serology was negative. Cultures from unruptured bullae were negative. Smear of the bullous fluid showed no eosinophilia nor other cellular elements.

Immediately after death an autopsy, performed by Prof. M. Köksal, revealed that the skin was edematous at the dermo-epidermal

border. The upper layer of the dermis showed round cell infiltration. There was cloudy swelling of the liver cells and in the kidneys hydropic degeneration of the tubular epithelium. Hydropic swelling of the mucosal cells of the intestines was also seen. There was widespread bronchopneumonia in the lungs.

Discussion

Epidermolysis bullosa was first described by von Hebra[1] in 1870. In 1932 Cockayne[2] classified this disease into two categories: Epidermolysis bullosa simplex and epidermolysis bullosa dystrophica. Finally, in 1935, Herlitz[3] added a new category which he called epidermolysis bullosa hereditaria letalis. In his paper he described 14 cases from the literature, added 8 of his own and suggested that this was a new entity. Leland and Hirschl[4] reviewed the literature in 1954, collected 34 cases published up to that time, and added 2 of their own cases, who were twins. Since then Frank and Kern[5] published another case that same year and in 1955 Henderson[1] described four cases and Lucini[8] described another case. In 1957 Silver[9] described two cases in siblings, making a total of 48 cases published to date.

In differentiating the three forms of the disease, it may be noted that in the simplex form the disease is inherited as a dominant character. Although in this form the slightest trauma may produce bullae, they heal without scarring or pigmentation. There are no dystrophic changes of the nails and the mucous membranes are not involved. It usually appears during infancy but fades away after puberty.

The dystrophic form is a recessive condition. Lesions first appear during infancy but the course is more severe. Lesions always leave scars when they heal and in this form dystrophic changes of the nails are not uncommon, as are lesions of the mucous membranes. However it is usually not a fatal disease.

Epidermolysis bullosa hereditaria letalis resembles the simplex form in regard to the absence of scar formation and is similar to the dystrophic form in that there may be mucous membrane lesions. It differs from both in that it almost always terminates fatally.

Opinions vary regarding the etiology and pathogenesis of this condition. Generally authors believe that there is degeneration and a decrease in the elastic tissues of the skin. For this reason slight trauma, which might ordinarily produce hyperemia in normal skin, produces bullae in these patients. According to Elliot,[1] there is congenital irritability of the vascular bed and because of this, trauma produces rapid transudation, degeneration and bulla formation. Engman and

Mook[10] consider that the primary defect is in the papillary and subpapillary layers of the skin. They think that there is either absence or anomaly of the elastic tissue as well as edema of the cornified layers of the skin. Beck,[11] on the other hand, suggests that edema of the upper layer of the corium produces the degeneration and the disappearance of the elastic tissues. Other authors propose some sort of endocrine involvement. Weiner and Orman[12] feel that there must be a hereditary defect of the vascular wall while Langhof[13] considers a change in the hyaluronidase - heparin ratio to be responsible for the symptoms observed. Lamb and Halpert[14] report that histologic studies on their patient revealed normal hair follicles, sweat and sebaceous glands, as well as normal appearing elastic fibers. Elastic structures were also found to be normal in appearance in Lewis's[7] case.

The differential diagnosis in this condition is not difficult. Recently Lewis[7] has, in some detail, discussed the differential diagnosis of bullous lesions in the newborn period. Among the conditions which should be considered he suggests congenital syphilis, Ritter's disease, varicella, variola, pemphigus neonatorum, incontinentia pigmenti etc. Syphilis is the disease responsible for most of the bullae seen at birth although with better antenatal care the incidence is being markedly reduced. These lesions appear on the palms and the soles and contain cloudy, somewhat purulent material. Diagnosis is easily established either by serogical tests or by dark-field examination of material from a lesion. Ritter's disease starts with local hyperemia and, as is usually the case with pemphigus neonatorum, cultures of material from the lesions usually show staphylococci or streptococci. Chickenpox or smallpox in the neonatal period may be diagnosed on the basis of the appearance of the disease in the mother toward the end of her pregnancy. In our opinion, if the possibility of syphilis is eliminated, the most likely diagnosis in an infant with bullae present at or soon after birth is epidermolysis bullosa of this variety. If nail deformities appear promptly, then the diagnosis is almost certain. The presence of porphyrinuria is consistent with this diagnosis since increased urinary porphyrin excretion has been demonstrated in this disease.

The prognosis of this condition is poor. Infants are usually lost during the first three or four months of life because of secondary infection or fluid and electrolyte problems. Until Silver's case, only Calnan's[6] and Henderson's cases had lived as long as six months and Kagen[15] had reported a child who survived 16 months. At the time of Silver's report his older patient was surviving at 30 months of age and her younger sibling was 9 months old. Silver reported the use

of estrogens, hydrocortisone, and testosterone, none of which were thought to have any beneficial effects. He attributed the survival of the patient to the free use of antibiotics and to the careful use of aseptic techniques, in so far as possible, in the management of the patient during the early months of life. He also suggests that the condition in these cases might not have been as severe as is usually the case in others. He suggested also that the use of any ointment seemed harmful to the skin but that the lesions seemed to improve somewhat after transfusions.

Conclusion

As is apparent from the discussion above, there is no specific treatment in this disease. Careful hospital management should provide adequate fluid, electrolytes, calories and vitamins, as well as keeping the infant in an environment as clean as possible. Broad spectrum antibiotics should be given, but should be changed from time to time. Steroids and other hormones do not seem worth while.

Summary

A case of epidermolysis bullosa hereditaria letalis, admitted to the Hacettepe Children's Hospital at 11 hours of age, has been presented and is the first such case reported in Turkey. A brief review of the history, theories of etiology, and classifications, and a discussion of various forms of therapy have been presented.

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