EPIDERMOLYSIS BULLOSA HEREDITARIA LETALIS

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Epidermolysis bullosa is a rare chronic hereditary skin disorder characterized by the formation of vesicles and bullae which develop spontaneously or as a result of slight trauma. Although several varieties have been described, there are three main clinical types.

The simple non-scarring type appears in infancy or childhood in otherwise normal children. The bullae develop mainly over parts exposed to trauma, such as the hands and feet. There is no involvement of the mucous membranes or nails. It is dominant in inheritance.

The dystrophic type is more severe and appears at, or soon after birth. Scarring usually follows and the mucous membranes are involved together with deformity and loss of finger and toe nails. Both recessive and dominant inheritance sub-types have been described.

The third type, epidermolysis bullosa hereditaria letalis, was first described by Herlitz (1935). The bullae appear at birth or soon after. They are extensive and progressive, but some may heal without scarring. The mucous membranes are involved and the nails may be lost or deformed. This type is recessive in inheritance, and death usually occurs within a few months.

The clinical features of epidermolysis bullosa hereditaria letalis have been reviewed in articles (Davidson, 1940; Leland and Hirschl, 1954; Lewis, Steven and Farquhar, 1955; Silver, 1957). Silver stated that 46 cases had been reported, and added a further case showing all the features of the disease except the usual fatal outcome, the child being alive at 30 months.

It is the purpose of this paper to present two further fatal cases of the disease, and to describe additional pathological features indicating a more widespread epithelial disorder.

Case Reports

Case 1. M.H., a girl, was delivered prematurely, weighing 1,820 g., following a mild accidental haemorrhage in a twin pregnancy on January 16, 1957, at the Royal Women's Hospital. The other twin, a boy,

weighing 2,550 g. was normal. The mother had one normal child aged 18 months. The family history was normal.

Immediately after birth there were raw red areas on the back of both feet and ankles, and around the wrist. Strands of mucous membrane were hanging from the mouth.

On the next day, bullae developed on the buttocks, the fingers of the left hand and the back of the right hand (Fig. 1). The skin could be removed by light pressure (Nikolsky's sign). The nails of two toes on the left foot, and one on the right, separated over the next few days.

She was given A.C.T.H. gel 20 mg. daily for four days from January 17, without any influence on the developing bullae. A solution of penicillin and streptomycin sprayed on the lesions produced better drying and healing than vaseline gauze dressings. Despite parenteral antibiotics, the skin lesions became infected with

FIG. 1.—Case 1: showing extensive ulceration of the back of the right hand and fingers and small lesions on the trunk.

FIG. 2.—Case 1: showing lifting of the epithelial lining of a bronchiole by fluid. This lesion is essentially the same as that seen in the skin. (H. and E. $\times 83$.)

Staphylococcus aureus. The infant's condition gradually deteriorated, she became moderately jaundiced, further skin lesions developed, and she died nine days after birth.

Autopsy Findings

MACROSCOPIC. Autopsy was performed four days after death. The body was kept in a refrigerator at 4° C.

Large areas of skin were ulcerated. One ulcer on the left side of the chest measured 6 cm. in diameter. There were other areas of ulceration around the mouth, on both sides of the nose, on the elbows, hands, feet, buttocks and lower part of the back. In the left thalamus there was an area of icteric staining 4 mm. in diameter. The aortic intima showed marked jaundice. Both lungs contained a moderate amount of air. The right upper lobe was congested and solid. Patchy areas of congestion were seen in the left lower lobe. The trachea and main bronchi were congested and contained a large amount of tenacious mucus. The thyroid was smaller than normal. The material in the intestine was partly clay coloured and partly brown. The gall bladder was distended and contained colourless fluid. The liver was of normal size, and had sharp edges. The other organs appeared normal.

MICROSCOPIC

Lungs: Some alveoli contained oedema fluid and there were patchy interstitial inflammatory infiltrations. In a few there were fibrin and occasional red cells. The alveolar capillaries were intensely congested. Masses of bacteria were seen throughout the lungs. Some bronchi and bronchioles had an intact columnar epithelial lining. In others this lining was lifted from the lamina propria by fluid (Fig. 2). However, most bronchioles and an occasional small bronchus had no epithelial lining. They were filled by masses of degenerate columnar epithelial cells mixed with amorphous material.

Trachea: The epithelial lining appeared normal. There was no separation from the lamina propria by fluid.

Skin: At the site of a bullous lesion the epidermis was lifted from the underlying tissues and bacteria were seen. There was some haemorrhage in the dermis immediately beneath the area where the epithelium had lifted and very little inflammatory cellular infiltration was seen.

Liver: Small plugs of bile were seen in and between the parenchymal cells, and there was moderate congestion of the sinusoids.

Pancreas: Eosinophil leucocytes were conspicuous in the interstitial tissues.

Suprarenals: There was marked congestion of the medulla and the inner half of the cortex. Haemorrhages were present in the fibrous tissue behind the gland.

Kidney: Haemorrhages were present around the pelvis. The heart, thyroid and spleen showed no significant abnormality.

Case 2. J.L., a girl weighing 3,685 g. was delivered spontaneously at term on February 19, 1957, at the Royal Women's Hospital. The mother had a normal child aged 6 years. The family history was normal.

At birth, the infant had a blister on the chin and there was a raw area on the back of the left hand. Over the next three days large superficial bullae developed (Fig. 3), especially over the buttocks, and six finger nails commenced to separate. One week after delivery bullae were present around the umbilicus, on the back of the neck and on the shoulders. There were three small ulcers on the palate. Some bullae healed without scarring. Nikolsky's sign was positive. When aged 3 weeks she was admitted to the Royal Children's Hospital, Melbourne. Despite local treatment to the skin and parenteral chemotherapy the skin lesions became infected with *Pseudomonas pyocyanea*, the infant's condition deteriorated, further skin lesions developed and she died at the age of 5 weeks.

Autopsy Findings

MACROSCOPIC. Autopsy was performed nine hours after death by Dr. Alan Williams at the Royal Children's Hospital, Melbourne.

Large areas of ulceration covered by coagulum were present on the trunk, face and limbs. The lungs were congested. The trachea and main bronchi were inflamed and contained mucus and aspirated food. The thymus was atrophic.

FIG. 3.—Case 2: showing extensive lesions on arm, trunk, buttocks and leg.

MICROSCOPIC. The lungs showed scattered intra-alveolar haemorrhages, patchy collapse and small areas of early bronchopneumonia. Scattered inflammatory infiltrations were seen around the renal pelvis, and in the medulla and cortex of the kidney. In the skin taken from an apparently normal area, there was a complete absence of rete pegs. The basal layer consisted of cells which appeared flatter than normal and the change from the nucleated cells to those at the surface was unusually abrupt.

Discussion

These two cases of epidermolysis bullosa hereditaria letalis are described because of the rarity of the disease, and to record lesions of epithelial surfaces other than the skin. Leland and Hirschl (1954) have already described vesicular lesions in the trachea, bile ducts and pancreas, but tended to regard them as artifacts. In the first case presented here, there is direct evidence of vesicular lesions in the bronchioles and indirect evidence of involve-

ment of the common bile duct. Consideration has been given to the possibility of post-mortem changes causing the appearances in the lungs, particularly because of the long interval between death and autopsy. There were no unusual post-mortem changes in other organs, however, and the pulmonary lesions were essentially the same as those observed in the skin. In the early lesion a clear fluid separated the columnar epithelial lining from the lamina propria in the terminal bronchioles, and in a very occasional small bronchus. With rupture of the vesicle, fluid passed downwards into the lung, and masses of degenerate epithelial cells filled bronchiolar lumina which were devoid of epithelial lining.

In this case also the presence of jaundice, mucocele of the gall bladder, bile thrombi in the liver, and clay-coloured material in parts of the bowel, indicated obstruction of the common bile duct, above the origin of the cystic duct. It is considered likely that the obstruction resulted from the presence of one or more vesicular lesions, or degenerate cellular material from such lesions, filling the lumen of the duct. No other lesions in the smaller ducts of the liver or pancreas were found microscopically.

Summary

Epidermolysis bullosa hereditaria letalis is a rare hereditary skin disorder. The skin lesions develop after birth, and eventually lead to death in infancy.

The present study indicates that bullous lesions in the skin are not the only abnormality as similar findings also indicate probable involvement of the extra-hepatic bile ducts.

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