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Protein-losing Enteropathy in a Child with Junctional Epidermolysis Bullosa and Pyloric Atresia

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We report on a newborn boy with junctional epidermolysis bullosa and pyloric atresia. Blisters were found on his skin at birth, especially in places exposed to pressure, and appeared later on his mucous membranes. Epidermolysis bullosa was confirmed by electron microscopy. Radiography revealed pyloric atresia, and a gastroduodenostomy was carried out at 7 days of age. A connective tissue septum was found between his ventricle and duodenum. The skin changes were mild, and the clinical course was determined by his protein-losing enteropathy. He died at 66 days of age from pseudomonas sepsis. ***Key words: nutrition; hypoproteinemia; blister.***

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Epidermolysis bullosa associated with pyloric atresia has been recognized recently as an autosomal recessive entity. This association is phenotypically variable, and the clinical outcome may be determined as much by protein-losing enteropathy as by the skin disease.

CASE REPORT

A Pakistani boy (Fig. 1A) was born after a normal pregnancy in the 38th week. His mother was 19 years old and healthy. The parents were consanguineous, but family history revealed no previous cases of epidermolysis bullosa. His weight at birth was 2,220 g and his length 50 cm. Apgar-scores were 5/1, 7/5.

Blisters were observed on his skin from birth. The blisters (Fig. 1A and B) appeared upon pressure on the left lateral side of his body, buttocks, knees and left calcaneal region. The largest blisters were about 1 cm in diameter and all contained clear yellowish fluid. Nikolsky sign and blister spreading phenomenon were negative. Finger and toe nails were dystrophic and some of the nails fell off (Fig. 1C). The blisters

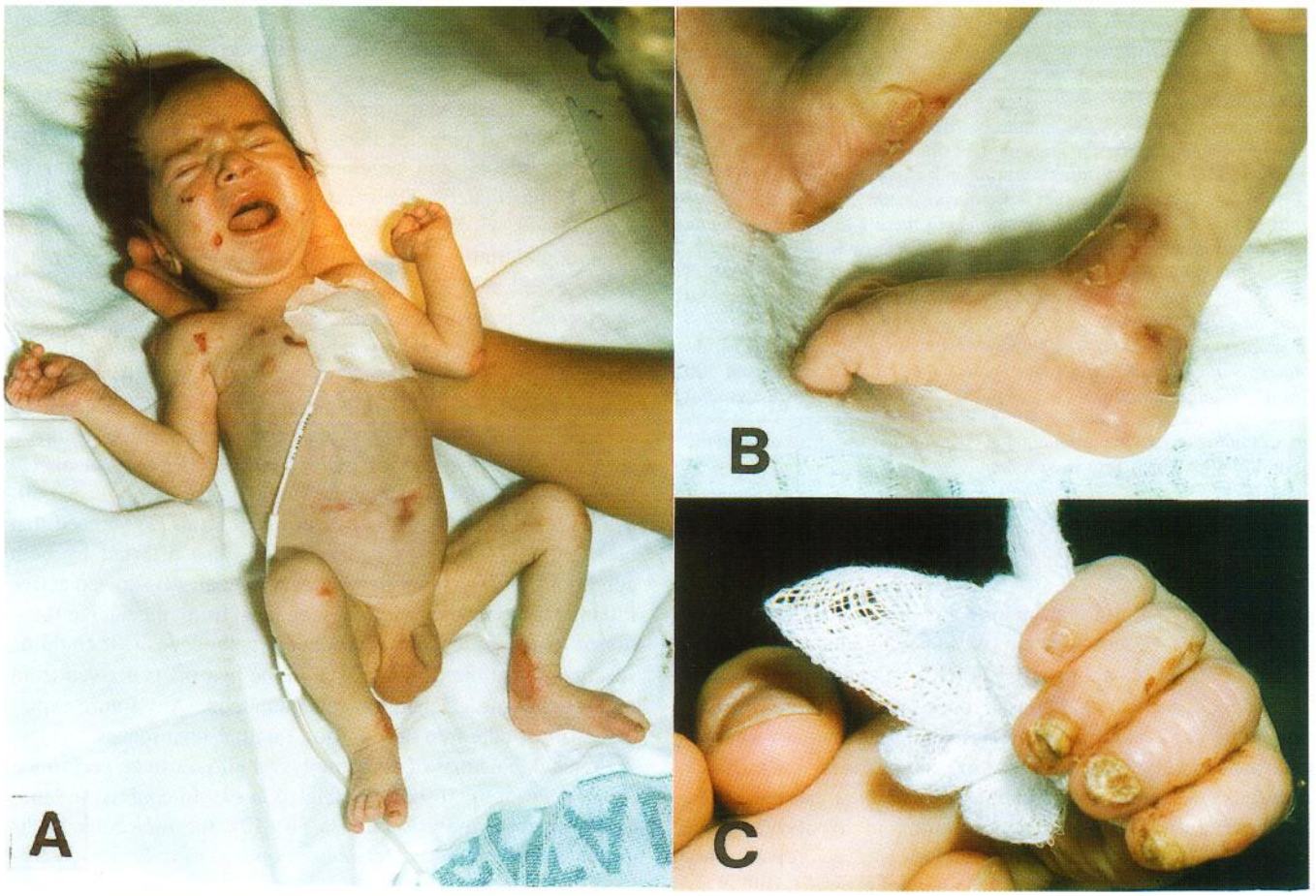

Fig 1. A) The boy with junctional epidermolysis bullosa. Note the scarcity of skin lesions. B) Close-up of feet with ruptured blisters. C) Dystrophic nails.

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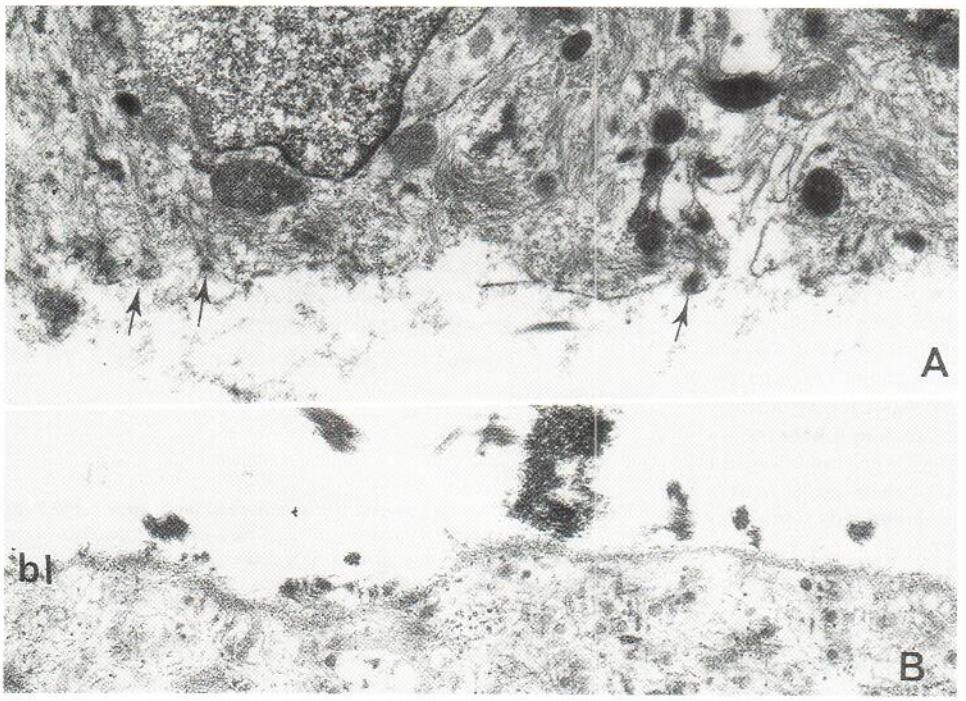

Fig. 2. Electron microscopy of skin. A) The blister roof, consisting of basal cell membrane. Hemidesmosomes are scarce (*arrows*). B) The blister floor covered by continuous basal lamina (*bl*).

healed without scarring, while new blisters appeared repeatedly during the first month of life in skin and later also in the mucous membranes. After the first month only a few new blisters developed. Electron microscopy demonstrated that the blisters were located between the basal lamina and the basal cell membrane (Fig. 2), confirming the diagnosis "junctional epidermolysis bullosa".

Vomiting led to the suspicion of pyloric atresia. The pyloric atresia was diagnosed by X-ray examination of the abdomen, showing a single gastric bubble. Operation showed that the pylorus was completely obstructed by a thick fibrous septum, and a gastroduodenostomy was performed. Histologically the septum consisted of connective tissue with central necrosis and calcifications, but there was no sign of acute inflammation. Because of severe failure to thrive both before and after the operation the boy received parenteral nutrition. In the third week of life he developed intractable bloody diarrhoea, hypoproteinemia and oedema. This persisted despite total parenteral nutrition and supplementation with albumin. Laboratory examination showed total serum protein values around 30 g/l and serum albumin between 50 and 300 µmol/l. Immunoglobulin G was around 7 µmol/l. Despite parenteral nutrition as mentioned above, antimicrobial treatment and a trial with phenytoin, severe hypoproteinemia persisted, and the patient died on the 66th day after birth from pseudomonas sepsis.

DISCUSSION

Epidermolysis bullosa with pyloric atresia has been reported in 47 children (1–4), most of them (90%) having junctional epidermolysis bullosa. A sibling was similarly affected in one fourth of the cases, and parental consanguinity was found in 10 cases (including (1, 2) and this report), making autosomal recessive inheritance likely. Most patients have more severe skin changes than those observed in our patient, who, on the other hand, had extensive mucosal involvement resulting in hypoproteinemia and failure to thrive. A severe protein-losing enteropathy has been reported in 4 other patients by Ishigami et al. (5), Bull et al. (6) and De Groot et al. (7). The child reported by Ishigami et al. (5) had very mild skin changes, like our case. In these cases measurement of serum albumin and alpha-1-antitrypsin in stools is important in giving the prognosis. Hypoproteinemia may result from dermal or gastrointestinal involvement or both and we propose that it may be the most important prognostic sign in this disorder.

Therapy should be initiated as early as possible, since it is still not possible to pinpoint the 20% who will survive (1). This includes surgery and parenteral nutrition, which should be started immediately. There is a loss of proteins through both mucosa and skin, and this should be replaced by albumin and immunoglobulins. Adequate nutrition is of as great importance to these children as it has been shown to be to children with dystrophic epidermolysis bullosa (8).

A thick, fibrous septum was found between the ventricle and duodenum, but whether the septum was primarily developmental or secondary to inflammatory processes could not be determined histologically. At least two studies argue against a secondary pathogenesis of pyloric atresia: Dennery et al. (2) reported identical twins, both of whom had epidermolysis bullosa with pyloric atresia, and Lestringant et al. (1) showed that one fourth of the cases had a sibling, also affected by both conditions. On the other hand, Dennery et al. (2) showed active inflammation in the stenotic segments from the above-mentioned twins, arguing for a secondary pathogenesis. It could be speculated that the fibrous tissue in the pylorus is derived from organisation of detached mucous membrane. Any future explanation must take into account the familial recurrences.

Prenatal diagnosis of epidermolysis bullosa can be performed using electron microscopy of fetal skin (9). In contrast to other forms of epidermolysis bullosa (10–12), the molecular background of junctional epidermolysis bullosa is only just emerging. Recently mutations were found in the $\gamma 2$ chain gene of laminin-5 (13). However, much remains to be done, and it is important to keep DNA on these infants for future research.

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