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Letter to the Editor

Diaphragmatic Hernia and Epidermolysis Bullosa in Two Sibs

To the Editor:

The association of congenital diaphragmatic hernia (CDH) with epidermolysis bullosa, a skin disorder characterized by blister formation, which is induced by minor trauma, with variable inheritance patterns, has to our knowledge not been reported before. Two cases presented in our Neonatal Unit with both conditions.

PATIENT I

A 2,620 g male infant was delivered at 38 weeks of uneventful pregnancy by vacuum due to fetal distress. Apgar scores were one and 4 at one and 5 minutes, respectively. The infant had severe respiratory distress and a scaphoid abdomen. He required immediate intubation and was transferred to the intensive care unit. Chest film showed a left diaphragmatic hernia. Generally he looked normal; his length, weight, and occipitofrontal circumference (OFC) were appropriate for gestational age. The infant was covered by large blisters mainly over the limbs which ruptured easily.

After intubation, the peribuccal area, mouth, and oropharynx became covered by the same type of lesions. Any manipulation caused blistering over the entire body. The patient died 3 hours later of refractory hypoxia in spite of assisted ventilation.

PATIENT II

Four years earlier, the same couple had had a 3,500 g term girl who was delivered by cesarean section due to acute fetal distress. She showed immediate respiratory distress and chest film documented massive left diaphragmatic hernia. She also had the same skin lesions described above. She died at 4 hours of refractory hypoxia. No other malformations were detected.

FAMILY

In both cases, the parents declined consent to a skin biopsy, autopsy, or chromosome studies. Both parents were Moslems from the Jerusalem area. They were the first cousins. They had a healthy girl, now 3 years old, who was delivered vaginally at term with uneventful neonatal history and normal development.

The mother has 4 unmarried sisters, 2 healthy brothers, and another brother who was delivered at home and who died soon after birth without further relevant information. She also has 2 healthy half-sisters one of whom is married to a distant relative. She had 3 early neonatal deaths (delivered at home in undetermined conditions).

The father has 2 brothers who are married to first cousins with normal children.

Diaphragmatic hernia was listed among the possible causes of neonatal death reported in this family, but no definite conclusions could be drawn. Epidermolysis bullosa was not reported in other relatives.

DISCUSSION

Epidermolysis bullosa has been reported in association with pyloric atresia [Bull et al., 1983] and congenital muscle dystrophy [Kletter et al., 1989]. Chromosomal abnormalities [David and Illingworth, 1976], de Lange syndrome [Rose-Spencer et al., 1981], and Fryns syndrome [Fryns, 1987] were described in association with CDH. The list of cardiovascular, urinary, central nervous system (CNS), and other malformations associated with CDH is growing [Benjamin et al., 1988].

The exact type of epidermolysis bullosa was not determined histologically in our patients. No chromosome study was done on either case to exclude small deletions which could behave as autosomal recessive disorders in consanguinous marriages. Parental chromosomes were normal.

Bochdalek diaphragmatic hernia occurs mainly on the left side. The incidence of this malformation is around one in 2,500 live births. [Harrison and Delormier, 1980]. Some cases represent autosomal recessive inheritance [Hitch et al., 1989]. The incidence of epidermolysis bullosa is around one in 50,000 [Haber et al., 1985]. The likelihood of a merely coincidental association between both conditions in a consanguinous family is remote.

Tracing the family history, close consanguinity and recurrence of the anomaly make a single autosomal recessive gene the most plausible explanation for the occurrence of this condition in 2 sibs with a recurrence risk of 25%. Another explanation can also include a coincidental homozygosity of 2 different autosomal genes. In fact, the likelihood of homozygosity at any locus in the 2 cases is 1/16 and it is not outside the realm of possibility that the 2 conditions are distinct.

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