CASE REPORT

Epidermolysis bullosa and congenital pyloric atresia

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SUMMARY

The association between epidermolysis bullosa (EB) and pyloric atresia (PA) is rare but well documented. Herein, we report a case of EB associated with congenital PA. A female baby, weighing 1480 g, was born vaginally to a 31-year-old gravida 7 lady at 33 weeks of gestation. Polyhydramnios was detected on antenatal assessment. The parents were non-consanguineous Saudis with no family history of significant illness. At birth, well-demarcated areas of peeled skin were present over knees, left leg and periumbilical region. Systemic examination revealed no other abnormality. On second day, the patient developed recurrent vomiting and abdominal distension. An abdominal X-ray revealed a single gastric gas bubble suggesting pyloric obstruction. Following gastroduodenostomy, the baby developed severe sepsis with multiorgan dysfunction and expired on 25th day of life. Skin biopsy showed cleavage within lamina lucida.

At birth, her Apgar Score was 7 and 8 at 1 and 5 min, respectively. The physical examination revealed well-demarcated, erythematous areas of peeled skin over knees, left lower leg and foot and periumbilical region (figures 1 and 2). Small blisters were also noted over the skin of forehead, chin, earlobes and back of the trunk. The blistering lesions were well circumscribed and contained clear fluid. Puncturing and derroofing of the lesions exposed an erythematous base. Similar bullous lesions were noted in the oral mucosa. By 12 h of life, the skin over the left arm elbow also began to peel off following minimal trauma. Systemic examination revealed no other abnormality.

By second day of life, it was evident that the baby could not tolerate feeding. After starting oral supplements through an orogastric tube, large non-bilious, straw-coloured, gastric fluid was aspirated. Subsequently, the patient developed recurrent vomiting and the abdomen became distended.

BACKGROUND

The coexistence of genetically-mediated epidermolysis bullosa with pyloric atresia (EB-PA) is extremely rare. All three variants of EB, simplex, junctional and dystrophic, have been associated with PA. EB-PA has recently been described as a separate, hemidesmosomal variant rather than a form of junctional EB. The cutaneous involvement consists of localised or widespread blister formation. Skin peeling follows spontaneously or after minimal trauma. PA usually presents itself with non-bilious vomiting and abdominal distension.

EB-PA is inherited as an autosomal recessive disorder. The three genes in which mutation is known to cause EB-PA are integrin- β -4 (ITGB4), integrin-A-6 (ITGA6) and plectin (PLEC1). Diagnosis of EB depends on examination of skin biopsy by transmission electron microscopy and/or immunofluorescent antibody/antigen mapping. Plain abdominal X-rays and gastrointestinal (GI) contrast series confirm pyloric stenosis.

The course of EB-PA is usually severe; extensive lesions generally have a fatal outcome in the neonatal period due to sepsis and fluid loss.

CASE PRESENTATION

A female baby, weighing 1480 g, was born by vaginal delivery to a 31-year-old gravida 7 lady at 33 weeks of gestation. An antenatal diagnosis of polyhydramnios was documented in late pregnancy. Antenatal karyotyping was not performed. The parents were non-consanguineous Saudis with no family history of bullous disease or congenital malformations.

INVESTIGATIONS

Relevant blood investigations were unremarkable.

A plain abdominal X-ray revealed a dilated stomach with single gastric gas bubble; no air was seen in the duodenum (figure 3). An upper GI series had revealed dilation of stomach with no

Figure 1 Clinical photograph taken after the birth showing multiple, variable-size bullae with skin peeling characteristic of epidermolysis bullosa.

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Figure 2 Clinical photograph taken after the birth showing a large area of skin peeling over the right knee.

contrast beyond the pylorus. This confirmed the diagnosis of pyloric obstruction.

Histopathological findings of a skin biopsy obtained on day 2 were compatible with EB; dermal-epidermal cleavage was noted without inflammatory cells. Full-thickness epidermis made roof of the blisters.

An ultrasound of the abdomen did not show any renal malformations.

Figure 3 A plain abdominal X-ray showing a single large gastric air bubble, with no air distal to pylorus.

TREATMENT

Total parenteral nutrition with amino acids, lipid emulsion, dextrose, nutritional supplements and electrolytes was provided. After stabilising her general condition, exploratory laparotomy was performed on day 3. A distended stomach with thickened pylorus (PA) was found, and gastroduodenostomy was performed.

Care of the skin involved opening of blisters using a sterile needle. She was also treated with regular skin cleanings, dressing with antiseptics and topical antibiotics. All broken skin areas were covered in that manner and the dressings only needed to be changed once or twice every week. All the tape on the skin was removed by soaking it in liquid paraffin. Empirical antibiotic cover comprised of amoxicillin and cefotaxime.

OUTCOME AND FOLLOW-UP

Postoperatively, the baby developed severe sepsis with multiorgan dysfunction. Vancomycin and ceftazidime were used to cover methicillin-sensitive *Staphylococcus aureus* and *Enterobacter* species. Despite appropriate infection control, assisted ventilation, wound care and nutritional support, the neonate expired on the 25th day of life.

DISCUSSION

EB represents a heterogeneous group of rare inherited disorders characterised by fragility of the skin and mucous membrane, which manifest by spontaneous or post-traumatic blister formation and skin peeling. The incidence of EB is 1 case/50 000–500 000 live-births. Depending on the ultrastructural level of basement membrane cleavage responsible for blistering, three major varieties of EB have been identified: simplex EB (epidermolytic), junctional EB (lucidolytic) and dystrophic EB (dermolytic).¹ All three types of EB have been described to coexist with congenital PA (EB-PA), although junctional EB has been reported most frequently. In addition, two more rare forms of EB, EB with PA and EB with muscular dystrophy, have been more recently described as hemidesmosomal EB.²

Among the subtypes, EB-PA is a particularly rare form of EB. The exact prevalence remains unknown. Lestringant *et al*³ collected 41 cases of EB-PA reported in the literature until 1992 and added one of their own. More than 100 cases of EB-PA have been reported worldwide.^{4–10}

Clinical features may be apparent at birth or may appear later. The skin may show localised or extensive areas of peeling or blistering with little or no trauma. Significant oral and mucous membrane involvement is common. Congenital absence of skin (aplasia cutis congenita) is present in approximately 20% of cases.¹¹ Additional features of EB-PA may include fusion of the skin between the fingers and toes, nail dystrophy, scarring alopecia, contractures and dilated cardiomyopathy. PA is usually suspected when neonates develop recurrent non-bilious vomiting and abdominal distension.

Extracutaneous manifestations include involvement of genitourinary, respiratory and GI tracts. In particular, genitourinary malformations such as dysplastic/multicystic kidney, hydronephrosis/hydroureter, ureterocoele, duplicated renal collecting system and absent bladder are relatively frequent.¹² Regular follow-up is needed in monitoring urinary symptoms because ureterovesical obstruction usually occurs after the neonatal period. Atresias involving multiple regions of GI tract may occur simultaneously.¹³ Polyhydramnios, secondary to PA, is usually evident by third trimester in pregnancies with an affected fetus.

The condition is inherited as an autosomal recessive disorder. EB-PA can be caused by mutation in three genes: ITGB4 in 80%, ITGA6 in 5% and PLEC1 in 15%.^{14–16}

The course of EB-PA is usually severe and often fatal in neonatal period. In those who survive, the condition may improve with time; some affected individuals have little or no blistering later in life. However, many affected individuals living past infancy experience blistering and formation of granulation tissue around the mouth, nose, fingers and toes, and occasionally in the trachea, leading to stridor.

Diagnosis is usually suspected based on clinical findings of skin blistering and gastric outlet obstruction. The most precise means of diagnosing inherited EB involves the assessment of a combination of ultrastructural and antigenic features by transmission electron microscopy, immunofluorescence antigenic mapping and EB-related monoclonal antibody studies. Molecular genetics are available but not necessary to confirm the diagnosis.

PA is diagnosed by the presence of a single gastric gas bubble on plain abdominal X-ray. Upper GI series with Gastrografin show a 'single bubble sign' representing pyloric obstruction.

For pregnancies at risk, prenatal diagnosis can be established by examining DNA from chorionic villi or amniotic fluid cells¹⁷ or by using monoclonal antibodies.¹⁸ With the routine use of prenatal ultrasound scan, polyhydramnios and fetal gastric dilation may be detected long before the time of delivery.

There is no definite treatment for EB-PA. If a prenatal diagnosis is established, a caesarean section should be considered to reduce trauma during delivery. Surgical intervention is needed to correct PA. Mothers need education and training in proper handling of neonates. Skin care is of paramount importance; protection of skin from poorly fitting clothing and use of atraumatic sterile dressings may avert further skin peeling. Supportive measures including antibiotics and antiseptics to prevent wound infections, fluid and electrolyte balance and nutritional support improves outcome. Prevention of secondary complications such as growth delay, anaemia, zinc deficiency, osteopaenia/osteoporosis and scarring of skin and mucosal surfaces should be addressed. Psychological support should be provided to caretakers to avoid rejection and child abuse.

Genetic counselling is crucial for families with a strong history of EB-PA. Molecular genetic testing of the parents will establish heterozygous carrier status. Assuming that the parents are obligate carriers, and EB-PA an autosomal recessive disorder, there is a 1 in 4 chance at conception for each baby of the affected parents of getting the disease.

In most cases, the course of EB-PA is usually relentless and fatal despite surgical correction of concomitant PA. The prognosis of this disease is poor due to prematurity, extensive skin blistering with fluid and electrolyte imbalance, respiratory distress syndrome, malnutrition, sepsis, persistent vomiting and diarrhoea and associated significant genitourinary disease.

Contributors AAM was involved in manuscript writing. AH and SA were involved in manuscript writing and literature search.

Learning points

- Pyloric atresia (PA) should be suspected in neonates born with vesico-bullous lesions on the skin.
- Genetic counselling should be provided to families at risk for developing epidermolysis bullosa with PA.
- Psychological support should be provided to caretakers to avoid rejection and child abuse.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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