CASE REPORTS

Syndromic Association of Pyloric Atresia and Epidermolysis Bullosa (Carmi Syndrome) – A Case Report

Z Marjanovic, A Slavkovic, I Djordjevic

ABSTRACT

Epidermolysis bullosa (EB) is an inherited, autosomal recessive, bullous disease, characterized by blisters followed with skin and mucosal erosions. We present a case of a male infant with pyloric atresia associated with junctional EB (Carmi syndrome). The patient underwent urgent laparotomy after prompt stabilization. Postoperative course was uneventful. Nine months later, the patient died in the paediatric intensive care unit from respiratory distress syndrome. Prognosis is usually very poor. Death usually occurs during the first year of life, as a result of septic complications.

Keywords: Complications, epidermolysis bullosa, pyloric atresia

Asociación Sindrómica de la Atresia Pilórica y la Epidermolisis Bullosa (Síndrome de Carmi) – Un Reporte de Caso

Z Marjanovic, A Slavkovic, I Djordjevic

RESUMEN

La epidermólisis bullosa (EB) es una enfermedad hereditaria, autosómica recesiva, y bullar, caracterizada por ampollas acompañadas de erosiones de las mucosas y la piel. Presentamos el caso de un niño con atresia pilórica asociada con EB juntural (síndrome de Carmi). El paciente fue sometido a laparotomía urgente después de una rápida estabilización. Curso postoperatorio transcurrió sin incidentes. Nueve meses más tarde, el paciente murió en la unidad de cuidados intensivos pediátricos de síndrome de dificultad respiratoria (SDR). El pronóstico es generalmente muy pobre. La muerte ocurre generalmente durante el primer año de vida, como consecuencia de las complicaciones sépticas.

Palabras clave: Complicaciones, epidermolisis bullosa, atresia pilórica

West Indian Med J 2013; 62 (2): 149

INTRODUCTION

Epidermolysis bullosa (EB) is an inherited, autosomal recessive, bullous disease, characterized by blisters followed with skin and mucosal erosions, caused by mutations in the hemidesmosomal genes ITGA6 and ITGB4 (1−3). Familial predisposition has also been proven. Numerous subtypes of EB are described and divided into three major groups: EB simplex (EBS), dystrophic EB (DEB) and junctional EB (JEB). Junctional epidermolysis bullosa is further divided into three subgroups: Herlitz, non-Herlitz and JEB with pyloric atresia (Carmi syndrome). Patients with the severe form of JEB have the poorest prognosis with an estimated mortality rate of 87% during the first year of life, predominantly due to immunologic disorders and recurrent pulmonary and urinary tract infections. It is important to prevent infections and skin erosions.

From: Clinic of Paediatric Surgery, Clinical Center, Nis, Serbia.

Correspondence: Dr I Djordjevic, Knjaza Milosa 58−64 I/15, 18220 Aleksinac, Serbia. E-mail: ivonadj74@gmail.com

CASE REPORT

A male preterm infant was born at 36 weeks gestation, by normal vaginal delivery. The body weight at birth was 2900 grams and body length 50 cm. The family history of the boy's

mother revealed two spontaneous abortions and one normal delivery five years previously. This was of a female baby born at 27 weeks gestation, with multiple skin erosions and diagnosed antenatally with polyhydramnios. The baby died 24 hours after birth due to respiratory distress syndrome (RDS) and prematurity (1450 g). Although skin biopsy was not done, the blisters and erosions were highly suspicious of EB.

The male patient was admitted to hospital 48 hours after birth due to persistent vomiting and salivation, with no stools, a suspicion of *ileus meconialis,* with prenatally diagnosed polyhydramnios.

Nasogastric tube was introduced and standard laboratory and biochemical analyses were made. Urea 13.9 mmol/L, glycaemia 2.29 mmol/L, lactate dehydrogenase (LDH) 1008 U/L, serum electrolytes, total proteins, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (gamma GT,) amylase, blood gas parameters, as well as blood count were within the normal range.

Babygram revealed no air-fluid levels and no pneumoperitoneum. The stomach was very dilated with no gas in the intestine (Fig. 1). Ultrasound examination diagnosed a

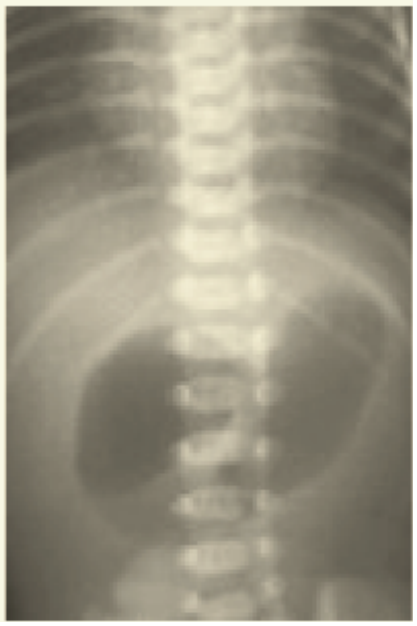

Fig. 1: Abdominal X-ray shows single gas field bubble, very distended stomach and no gas in distal portions, suggesting pyloric atresia.

very dilated stomach with no gas in the other parts of the intestinal tract (Fig. 2). Endoscopic examination revealed pyloric atresia.

The abdomen was opened by transversal laparotomy. The incision along the anterior gastric wall revealed an atretic 5 mm long pyloric canal. The duodenum was opened distally from the obstruction, and a gastroduodenal latero-lateral two-layer anastomosis was created. A nasogastric tube was placed through the anastomotic site. Almost im-

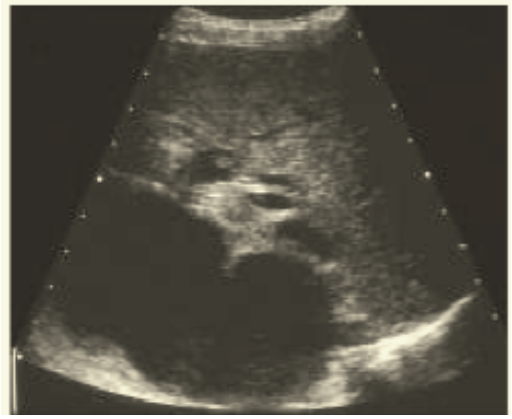

Fig. 2: Ultrasound examination reveals very dilated stomach with no gas in the duodenum and other parts of the intestines.

mediately after the placing of an intravenous cannula and the nasogastric tube, small blisters appeared on the underlying skin in the region of their fixation. At the end of the intervention on the index finger (where the pulse oximeter was placed), right elbow and the right foot, bullous changes were observed, the largest 3 x 3 cm in diameter (Fig. 3). On the

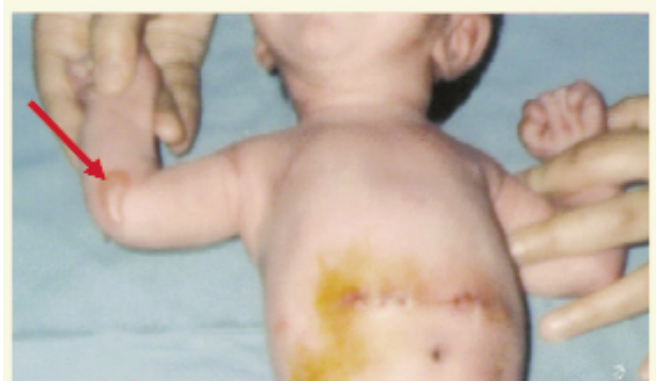

Fig. 3: Bullous changes on the right elbow.

fifth postoperative day, the nasogastric tube was removed and oral feeding started. The patient had regular stools. Skin biopsies confirmed the diagnosis of EB (Fig. 4). Recovery

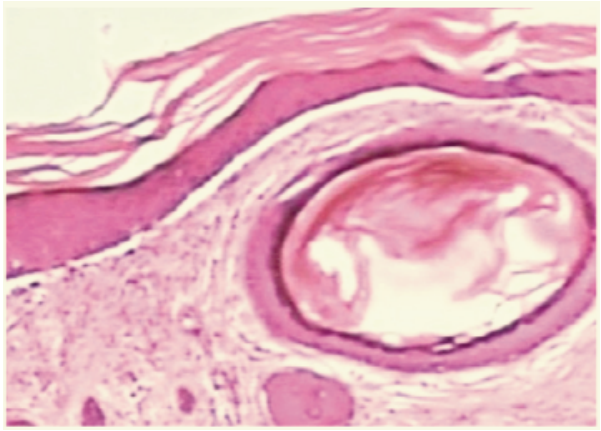

Fig. 4: Histopathologic findings showing epidermo-dermal separation at the level of their junction.

was uneventful. But nine months later, the patient died in the paediatric intensive care unit from RDS and sepsis.

DISCUSSION

Junctional epidermolysis bullosa-pyloric atresia (JEB-PA) [Carmi syndrome] represents a syndromic association of skin fragility and congenital gastrointestinal atresia, most frequently pyloric, although duodenal atresia with skin fragility has also been reported (4). Familial predisposition has been proven. In our case, death of a previous female infant with cutaneous changes supports this conclusion, although skin biopsy was not done.

Patients with Carmi syndrome can also present with erosions and subepithelial cleavage in the respiratory, gastrointestinal and urinary tracts (5). The diagnosis is made easily on plain abdominal X-ray: single gas field bubble representing the distended stomach with no gas in the distal portions. However, the most precise diagnosis is gastroduodenal passage of contrast to duodenum.

Prenatal ultrasound may indicate the presence of polyhydramnios and severe gastric dilatation. In 1990, Carmi and Meizner described the "snowflake sign", specific ultrasonographic picture of the amniotic fluid associated with epidermolysis (6). In all patients with snowflake amniotic fluid, Carmi syndrome should be suspected.

Electron microscope examination is essential for the definitive diagnosis of EB showing the exact level of tissue separation that cannot be confirmed by light microscopy. Caesarean section should be considered to reduce the skin trauma of the affected fetus during delivery (7).

It is generally considered that fetal intestinal obstruction may be the result of scar formation due to recurrent damage of the pyloric mucosa. Mucosal damage may initiate scarring of the gastric outlet, resulting in the formation of pyloric membrane or atresia.

Surgical treatment depends on the type of pyloric atresia. In Type 1, excision of the membrane (Heineki-Mikulicz pyloroplasty) is recommended. Gastroduodenostomy and excision of the atretic segment is the treatment of choice for Type 2 (8). Gastrojejunostomy is not recommended because of the possibility of jejunal ulcers due to acid gastric juice. Dank *et al* reported 51 patients who underwent surgery with average survival time about 70 days. Although intestinal obstruction is surgically corrected, mortality rate remains over 90% (9) during the first year of life because of electrolyte imbalance, protein-losing enteropathy, skin and respiratory infections and septicaemia.

The treatment of patients with Carmi syndrome is multimodal including surgical intervention and symptomatic management: meticulous "minimal touch" principle is recommended, antibiotics and antiseptics are administered to prevent secondary wound infections, correction of water and electrolyte disturbance, nutritional support, even gastrostomy when necessary and appropriate doses of calcium (Ca), zinc (Zn), iron (Fe) and vitamin D.

During anaesthesia, movement of the patient should be reduced to a minimum; the face mask should be coated with petroleum jelly gauze in order to reduce local skin trauma, appropriate dressing to protect the skin from mechanical forces, the patient should be very carefully intubated with no-cuff endotracheal tube and adhesive parts of the electrodes during the electrocardiogram (ECG) monitoring should be removed. The greatest challenge may be to maintain a secure airway to prevent the formation of new blisters in the respiratory tract. To reduce the risk of new laryngeal and tracheal blisters, it may be necessary to use a tracheal tube which is a half or full size smaller than recommended. During extubation, the anaesthesiologist has to verify whether new erosions are in the oropharynx. Postoperatively, nurses and parents should be trained on how to manage these infants and neonates (10).

Despite all the efforts undertaken, prognosis is still very poor and death usually occurs during the first year of life, usually from septic complications.

REFERENCES

1. Jae-Hong K, Hwa-Young P, Hae-jin L, Minseob E, Choi EH. Case of epidermolysis bullosa with pyloric atresia. Ann Dermatol 2011; **23:** 41−4.
2. Pfendner E, Uitto J. Plectin gene mutations can cause epidermolysis bullosa with pyloric atresia. J Invest Dermatol 2005; **124:** 111–15.
3. Charlesworth A, Gagnoux-Palacios L, Bonduelle M, Ortonne JP, DeRaeve L, Meneguzzi G. Identification of a lethal form of epidermolysis bullosa simplex associated with a homozygous genetic mutation in plectin. J Invest Dermatol 2003; **121:** 1344–8.
4. Maman E, Maor E, Kachko L, Carmi R. Epidermolysis bullosa, pyloric atresia, aplasia cutis congenita: histopathological delineation of an autosomal recessive disease. Am J Med Genet 1998; **78:** 127–33.
5. Pfendner E, Uitto J, Fine JD. Epidermolysis bullosa carrier frequencies in the US. J Invest Dermatol 2001; **116:** 483−4.
6. Meizner I, Carmi R. The snowflake sign. A sonographic marker for prenatal detection of fetal skin denudation. J Ultrasound Med 1990; **9:** 607–9.
7. Hayashi AH, Galliani CA, Gillis DA. Congenital pyloric atresia and junctional epidermolysis bullosa: a report of long-term survival and a review of the literature. J Pediatr Surg 1991; **26:** 1341–5.
8. Muller M, Morger R, Engbert J. Pyloric atresia: a report of four cases and review of the literature. Pediatr Surg Int 1990; **5:** 276−9.
9. Dank JP, Kim S, Parisi MA, Brown T, Smith LT, Waldhausen J et al. Outcome after surgical repair of junctional epidermolysis bullosa-pyloric atresia syndrome: a report of 3 cases and review of the literature. Arch Dermatol 1999; **135:** 1243−7.
10. Sahebpo AA, Ghafari V, Shokohi L. Pyloric atresia associated with epidermolysis bullosa. Indian Pediatr 2008; **45:** 849−51.