Curr Pediatr Res 2016; 20 (1&2): 268-272 *ISSN 0971-9032*
www.currentpediatrics.com

A case of gastric rupture in non-neonatal child with incontinentia pigmenti and intestinal neuronal dysplasia, is there any correlation?

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Abstract

Gastric rupture is extremely rare in childhood beyond the neonatal period and the etiology of this condition in preschool children remains obscure. We report a case of 6 year old girl who sustained sudden and lethal gastric rupture. The young patient was affected by Incontinentia Pigmenti (IP), a genetic disease; she had an episode of nausea and vomiting the day before admission to the emergency ward. Abdominal X-ray showed free air in the abdominal cavity, an emergency laparotomy detected a wide perforation of posterior gastric wall. The post-operative course was complicated by a cardiac arrest and an autopsy was performed. Histological examination showed ulcerations and erosions in gastric mucosa with thrombosis in the blood vessel in the submucosa and it suggested Intestinal Neuronal Dysplasia (IND) type B. An eventual correlation between the three diseases that affected our patient was investigated. After a review of literature we have found that the presence of IP not appears to be associated with the other two diseases; so, in our case, it can be considered as a pre-existing pathology. About IND, even if it was never described any case in which this condition has determined gastric rupture, we think, on the basis of clinical and histological findings, that it has determined an increase of pressure at gastrointestinal level, with serious stomach distension until fatal gastric rupture.

Keywords: Gastric rupture, Childhood, Incontinentia pigmenti, Intestinal neuronal dysplasia, Autopsy.

Accepted October 20, 2016

Introduction

Spontaneous rupture of stomach sometimes occurs in the neonatal period but it is rarely seen beyond the neonatal period; currently the etiology of this condition in preschool children remains obscure [1]. All articles on spontaneous idiopathic gastric rupture in pre-school age children have only been reported in Japanese and Chinese literature and there are isolated European cases [2,3]. These cases showed several common features. The clinical manifestations include severe abdominal pain, distension, vomiting and respiratory distress and they progress rapidly with high rate of mortality.

From a pathophysiological point of view gastric rupture can cause a Tension Pneumoperitoneum (TP), than develops as air is trapped within the peritoneal cavity and cannot escape.

The trapped air is under tension leading to rising intraperitoneal pressure, this condition can determinate cardiovascular effects as decrease of venous return through the inferior vena cava, with cardiac output reduction; compression of the aorta and mesenteric vasculature [4,5].

About pulmonary effects, it's important to stress the role of the diaphragm to balance pressure between thoracic and abdominal cavities [6]. In cases of gastric rupture TP can determinate diaphragm elevation and respiratory failure [4].

Incontinentia Pigmenti (IP) also known as Bloch-Sulzberger syndrome, is a rare X-linked dominant inherited genodermatosis, usually lethal in males even in the prenatal period [4,7]. IP is caused by mutations in the NEMO gene (IKK-gamma), located in Xq28 locus.

IP is considered to be a syndrome of multisystem polydysplasias; it affects ectodermal and mesodermal tissues, such as skin, eyes, teeth and central nervous system. There are around 800 registered cases worldwide and the estimated incidence is about 1 to every 40.000 children. The estimated prevalence of IP was stated to be 0.2 in 100,000 based on the data available literature published during the period of 2000–2013 [5,8]. Infant mortality is associated with bacterial infection, and malfunction of the central nervous system [6,9].

Intestinal Neuronal Dysplasia (IND) is a clinical condition characterized by a malformation of enteric plexus. It was first described by Meier-Ruge in 1971 [7,10] and, in 1983, Fadda et al. sub classified it into two clinically and histologically distinct subtypes [8,11]. Type A occurs in less than 5% of cases and is characterized by congenital aplasia or hypoplasia of the sympathetic innervations; it presents acutely in the neonatal period with episodes of intestinal obstruction, diarrhea and bloody stools. Type B (95% of cases) is characterized by malformation of the parasympathetic of submucous and myenteric plexuses with hyperganglionosis [9,12].

The incidence of this disease is of approximately 1 in every 7,500 newborns, but there is a great variability in frequency of isolated IND between different countries, with reported rates between 0.3 and 40% of all rectal suction biopsies [10-15]. About pathogenesis there is no consensus, in fact it is unclear whether IND is due to primary factors such as gene abnormalities, or secondary changes due to enterocolitis and constipation [13,14,16,17]. From a clinical point of view, patients with IND Type B present with intractable constipation and grossly slowed intestinal transit time. In particular, it may occur alone or associated with other neuropathies, such as Hirschsprung's disease, but clinical features are variable and children can show different degrees of chronic constipation ranging from slight constipation to severe cases with abdominal distension and vomiting [15-20].

We report a case of child affect by Incontinentia Pigmenti, who presented a lethal gastric rupture with a histological suspect of Intestinal neuronal dysplasia type B.

Case Report

A 6 year old girl was admitted to pediatric department because of lethargy, nausea, vomiting, crying spells and general discomfort the day before admission. No history of trauma was reported. Her past clinical history was characterized by diagnose of Incontinentia Pigmenti when she was 12 month old (spastic tetraparesis, mental retardation, speech/language delays, nystagmus and alteration of visual evoked potentials -VEP). On examination, she was listless, dehydrated and the abdomen was progressively becoming distended and tensed. Laboratory examination showed leukocytosis (WBC 18.620/mmc), hyperglycemia and an increase of amylase (221 U/L). By nasogastric tube gas with digested blood material flowed. Abdominal X-ray showed free air in the abdominal cavity (Figure 1), dilated bowel loops, fecal impaction and colonic interposition between the liver and diaphragm. There was uncertainty about the diagnosis because of the unusual presentation, with a delay in the transfer to a pediatric surgery unit. The child's general condition deteriorated rapidly: comatose state, acute abdomen with hernia of umbilicus and rectum. A transverse supra-umbilical laparotomy was performed, the peritoneal cavity was filled with cloudy and brownish fluid and a perforation at the posterior wall of the stomach was detected. The intra-operative course was complicated by a cardiac arrest that was treated by successful resuscitation. The gastric lesion was sutured. However, the post-operative course was complicated by a new fatal cardiac arrest.

An autopsy was performed and tissue samples were taken for subsequent histological examination.

Macroscopically we have found: signs of gastric perforation with suture stitches; hemorrhagic effusion in gastric cavity and pouch of Douglas; many gastric ulcerations (Figure 2); decreased bowel wall thickness and alternation of dilated and partial obstructed sections; atrophy of the cerebral cortex; signs of acute respiratory distress and left ventricular hypertrophy.

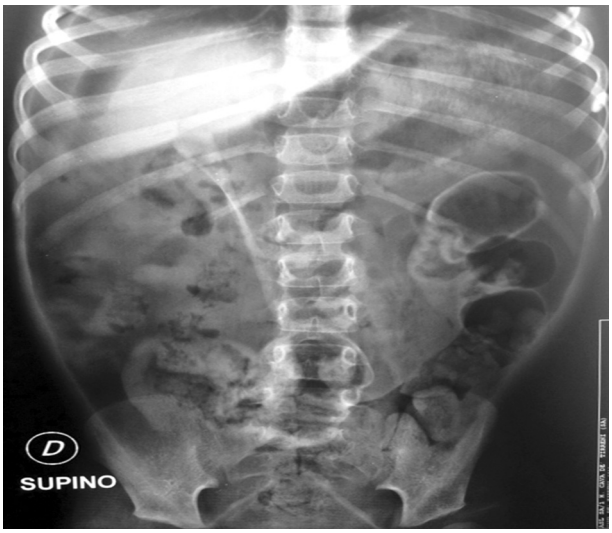

Figure 1. *Abdominal X-ray showed free air in the abdominal cavity*

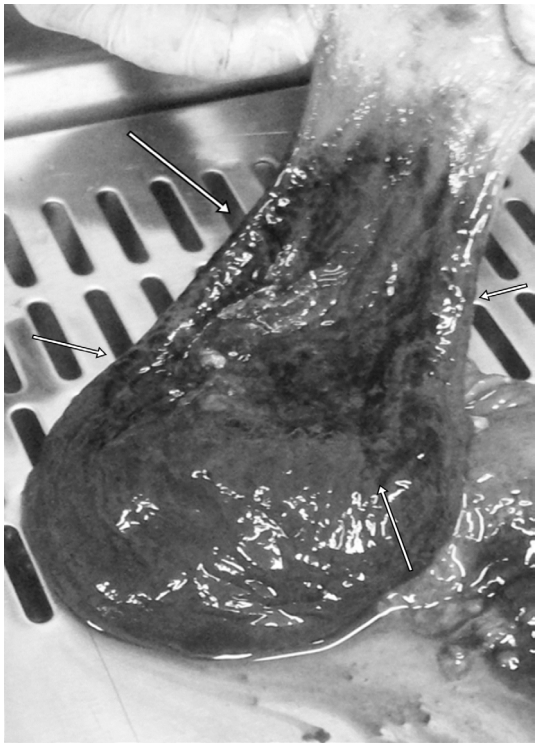

Figure 2. *Macroscopic examination of gastric mucosa: gastric ulcerations and hyperemia areas (arrows)*

Histological examination showed ulcerations and erosions in gastric mucosa with thrombosis in the blood vessel in the submucosa. The muscle layer of the colon showed areas of unequal thickness and the tunica submucosa showed areas of sclerosis and abundance of lymphatic nodules. Furthermore, tissue samples were characterized by accumulations of giant ganglia (>10 unit) in thickened bowel segments. They were observed segments of the colon where the muscle layer is thinned and at this level it was seen reduction or absence of neuronal elements. Also the small intestine tissue samples showed accumulations of neuronal elements.

Discussion

The case that we have reported presents three different diseases: gastric rupture, incontinentia pigmenti and IND; so it is characterized by pathologies that have not a known association in literature.

Nevertheless, we think that, in the present case, gastric rupture occurred because of a synergic action between gastric lesions and vomiting IND-induced, instead the presence of IP can be considered as a pre-existing pathology that does not appear to be associated with the other two diseases.

Rupture of a normal stomach occurs because of increased intragastric pressure until the tensile strength of the stomach wall is exceeded. The gastric wall becomes large and thin and its blood vessels becomes extended, constricted and even obstructed, resulting in ischemia [18,19,21,22]. It has also been reported that increase of the intra-abdominal pressure after labored coughing or vomiting, blunt abdominal trauma, ulcers, tumours, cardiopulmonary resuscitation and the Heimlich maneuver can precipitate rupture [1,19,20,22,23].

In this case, there was no history of trauma or any other underlying diseases.

The literature search suggests that perforation along the lesser curve, such as in this case, is usually due to a distended stomach [21,24].

The patient of our case presented, at post mortem histological examination, ulcerations and erosions in gastric mucosa with thrombosis in the blood vessel of submucosa.

From the other hand, the same examination showed areas of unequal thickness in the muscle layer of the colon and areas of sclerosis and abundance of lymphatic nodules of the tunica submucosa. Furthermore, tissue samples were characterized by accumulations of giant ganglia (>10 units) in thickened bowel segments of both colon and small intestine.

On the basis of these findings, we have suspected a diagnosis of IND type B.

In literature there is lack of consensus in diagnostic criteria of IND; initially diagnosis was based on AChE histochemistry of nerve fibers in rectal suction biopsies [22,25]. However the AChE activity in the lamina propria mucosae has been shown to be an age-dependent phenomenon that disappears on maturation of the submucosal plexus; so, at present, the most commonly used diagnostic criteria are: (1) more than 20% of 25 submucosal ganglia must be giant ganglia containing 9 or more ganglion cells and (2) the patient must be older than 1 year, as before that age, giant ganglia may be misinterpreted due to the fact that immature ganglia often have an incomplete differentiation in nerve cells [23-29].

In addition to histology, IND diagnosis is coherent with clinical presentation of our little patient. In fact IND usually presents with intractable constipation and grossly slowed intestinal transit time, even if clinical features are variable and children can show different degrees of chronic constipation ranging from slight constipation to severe cases with abdominal distension and vomiting [16,17,19,20]. About IP, we do not know what the role of this pathology was in the presented case.

Clinically IP is characterized by cutaneous findings, classically subdivided into four stages: vesiculobullous, verrucous, hyperpigmented, and atrophic [27,28,30,31]. Stage 1, known as inflammatory or vesiculobullous stage, is characterized by the development of papules, vesicles and pustules on an erythematous base, this phase can be confused with herpes simplex, varicella or impetigo [29,32]. The vesicular stage occurs in 90-95% of patients. In most patients (>90%) lesions are present at birth or develop during the first two weeks of life and then disappear by 4 months of age [30,33]. The skin lesions generally regress spontaneously [31,34]. The hair may also be affected in IP: scarring alopecia, usually on the vertex, is the most common manifestation of hair involvement, in addition, the hair can be sparse in infancy and later have a dull appearance and brittleness [32,35]. Although ocular manifestations in Incontinentia pigmenti Syndrome are not the most common (with a frequency of 35 to 77% on the studied populations), they are often highly debilitating [33,34,36,37]. Ocular abnormalities are typically divided into retinal (foveal hypoplasia, anomaly of retinal pigment epithelium, retinal vascular non-perfusion, neovascularization, vitreous hemorrhage and retinal detachment) and nonretinal manifestations (strabismus, nystagmus, optic nerve atrophy, conjunctival pigmentation, iris hypoplasia and uveitis) [33,35-40]. The central nervous system disorders in patients with IP can have a major impact on quality of life. In the literature, neurological manifestations have been reported approximately in 18 to 36% of cases forming one of the major causes of morbidity and mortality of the condition [38,39,41,42]. Seizures, delayed psychomotor development, hemiplegia, hemiparesis, microcephaly, Neuronal heterotopias (normal neurons found in abnormal locations), spasticity, cerebral atrophy and mental retardation are the major reported neurological findings [28,31,32,35,40,43].

It was not found any association between IP and gastric lesions/rupture or between IP and IND, except for a single case in which it was observed incontinentia

pigmenti and segmental dilation of colon, even if as isolated event [41,44]. About IND, it can be associated to various gastrointestinal and not gastrointestinal diseases, such as anorectal malformations, intestinal malrotation, congenital short small bowel, hypertrophic pyloric stenosis, necrotizing enterocolitis, intestinal atresia, diffuse intestinal angiomatosis, microvillus agenesia, vesical dysfunction and megacystis, mental retardation, short stature, facial dysmorphia, Down's syndrome, histiocytosis, hearing loss [42,45]. In our knowledge, it was never described any case in which IND has determined gastric rupture. Nevertheless, on the basis of clinical and histological findings, we have hypothesized that IND has determined an increase of pressure at gastrointestinal level, with serious stomach distension. Therefore, in our opinion ulcerations and erosions of the gastric wall predisposed this patient to gastric rupture during vomiting. What was the role of IP in the pathophysiological sequence above described is uncertain, so, at present, we don't know if the association between IP and IND can be considered as isolated event, as previously reported in literature, or not. We hope further investigations can solve these questions.

Conclusion

Gastric rupture in children, although rare, is rapidly progressive with high mortality and can be easily misdiagnosed. Early diagnosis and treatment, with a clear knowledge of possible favoring conditions will reduce complications and mortality. The pathological findings provide us some insights to consider the pathogenesis of gastric rupture in childhood.

Finally, we recommend autopsy and histological analysis to identify possible associations between rare pathologies, such as IND and gastric rupture of our case. In fact, we think that knowledge of these associations could avoid dangerous delay in treatment.

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Special issue: Pediatric Research
Editor: Abdulla A Alharthi, Department of pediatric nephrology, Taif University, Saudi Arabia