SURGERY

Megacystis-microcolon-intestinal hypoperistalsis syndrome associated with cystic fibrosis and meconium peritonitis in a female neonate 4 days of age – case report and review of the literature

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Abstract

We present a case of megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) in a four days old female infant who presented with abdominal distension, bilious vomiting, massive hematuria and feeding intolerance which was first interpreted as Prune Belly Syndrome (PBS), referred to our department after iatrogenic gastric and colonic perforation. Berdon syndrome or MMIHS is a rare congenital anomaly characterized by a massive enlarged bladder, distended abdomen, microcolon, functional obstruction of the gastrointestinal tract, and malrotation.

Keywords: megacystis, microcolon, intestinal obstruction, hypoperistalsis

Introduction

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is a rare autosomal recessive disorder first described by Berdon in 1976. It is characterized by abdominal distension, distended non-obstructive urinary bladder, microcolon, intestinal hypoperistalsis and malrotation of the small intestine [1]. Until 2011, 227 cases of MMIHS have been reported in the literature with a female incidence of 2.4:1 compared to Prune Belly Syndrome (PBS) with male predominance [2,3]. MMIHS may be misdiagnosed as PBS due to the common characteristics such as: flaccid abdominal wall, dilation of the urinary tract, intestinal malrotation, cryptorchidism, urachal remnants and familial incidence [4]. We present a female infant diagnosed with MMIHS and cystic fibrosis which is a unique case referred to our clinic after iatrogenic perforation of the sigmoid colon and gastric rupture.

Case report

A preterm female infant delivered at 35 weeks of gestation by an uncomplicated caesarian section, to a gravida 2, para 2 mother with a birth weight of 2460 g presented with abdominal distension due to an enlarged bladder, massive hematuria, failure to pass meconium and feeding intolerance. No history of pathological findings during pregnancy follow-up, except for a very distended bladder which was repeatedly drained. The first pregnancy was uneventful and no medications were used. The patient was referred for surgical consultation on the 2nd day of life with the suspicion of Prune Belly Syndrome (Figure 1). The bladder had been drained through ultrasound guided puncture three times in utero. Abdominal ultrasound revealed a distended bladder and bilateral uretero-hydronephrosis. Cystography revealed a very distended bladder without reflux (Figure 2). Blood samples were in the normal range. Initial investigations revealed Hb 12 g/dl, total WBC 9800/mm³.

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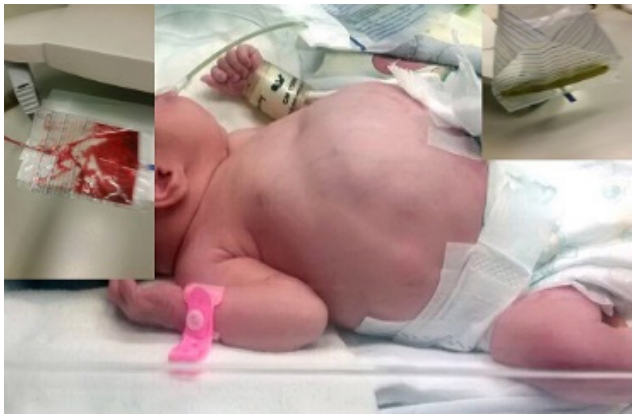

Figure 1. Abdominal distension. Appearence with massive hematuria (top left corner) bilious aspirate (top right corner).

The infant was transferred back to the neonatal ward with a rectal tube inserted and recommendation of bladder instillations with saline, antibiotics and hemostatic twice daily. On the 4th day of life the neonate developed bilious vomiting, massive abdominal distension and was transferred to our clinic. Thoraco-abdominal X-ray revealed an important pneumoperitoneum and the contrast studies revealed a gastric and distal colon perforation (Figure 3).

Blood samples revealed total WBC of 23000 and a CRP of 12.6, Blood urea was 49 mg/dl and serum creatinine was 1.10 mg/dl**.**

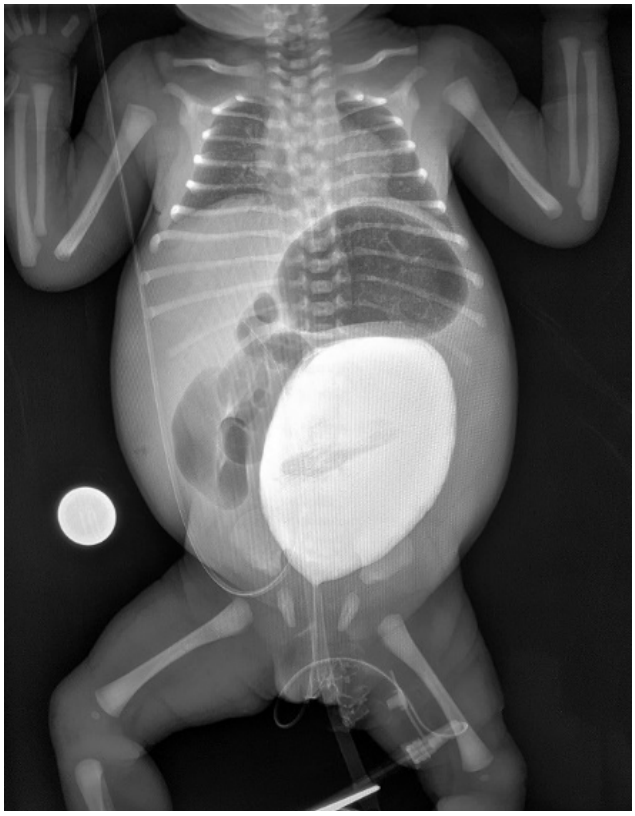

Figure 2. Enlarged bladder filled with contrast.

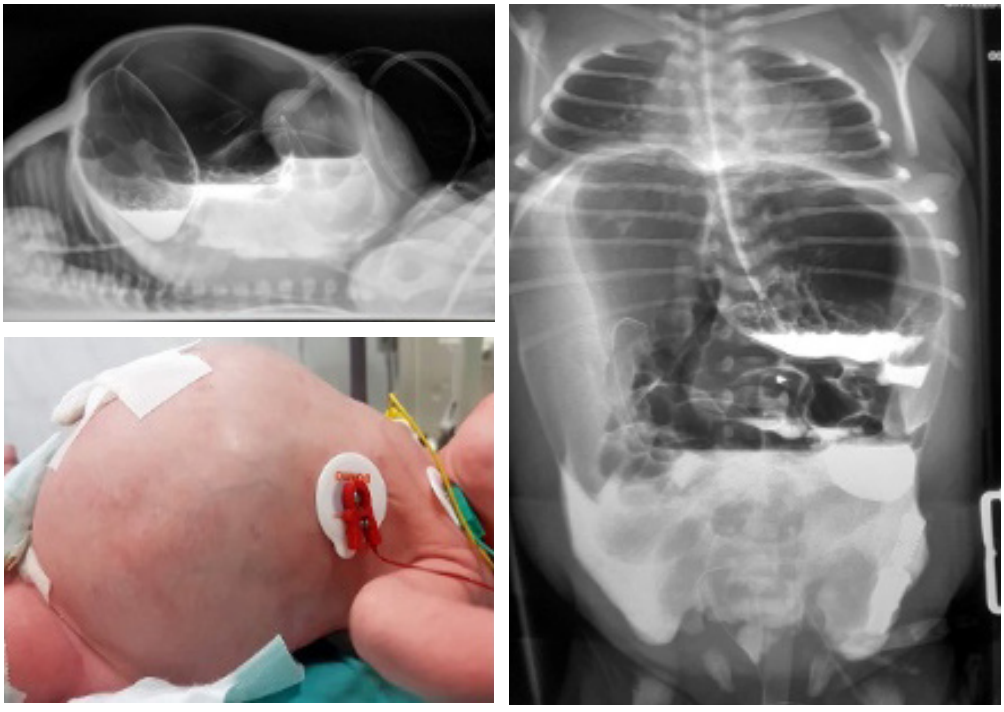

Figure 3. Massive abdominal distension with contrast leakage through the gastric perforation. Lateral (top left) and antero-posterior views (right).

After an adequate brief resuscitation, an emergency laparotomy was performed during which the following were found: an enlarged urinary bladder (Figure 4), malrotation with a small caliber colon which had been perforated by the rectal tube in the sigmoid flexure developing meconium peritonitis (Figure 5), a gastric perforation on the great curvature with gastric and bilious content in the abdominal cavity (Figure 6), dilated jejunum and ileum with a very small caliber terminal ileum containing meconium plugs (Figure 7).

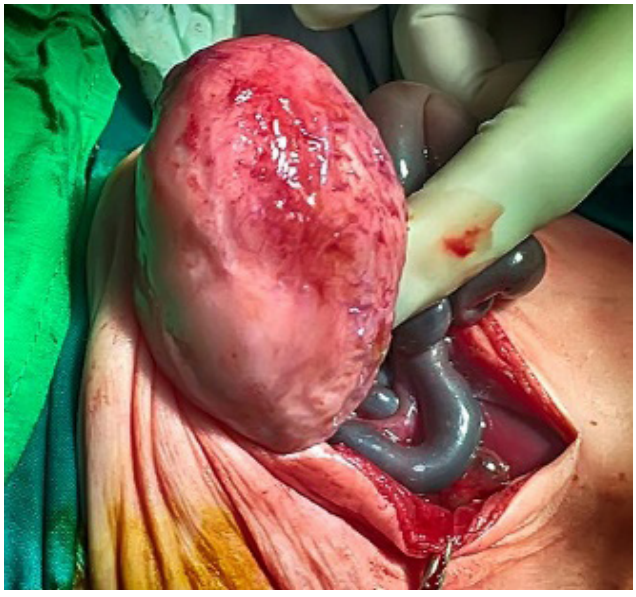

Figure 4. Dilated bladder and small caliber bowel.

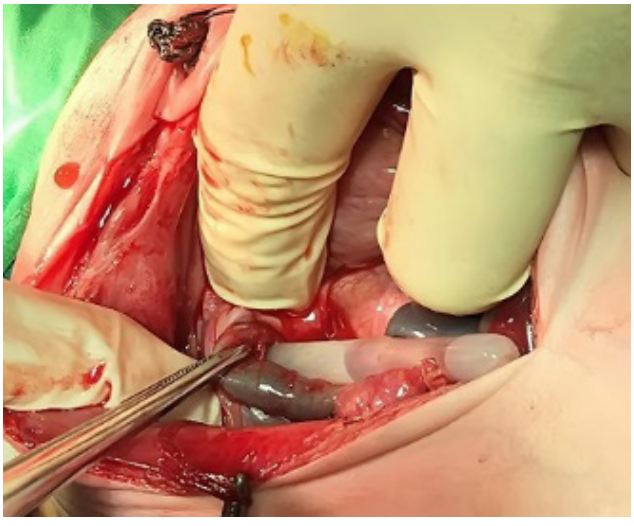

Figure 5. Perforation of the sigmoid colon with rectal tube in the peritoneal cavity.

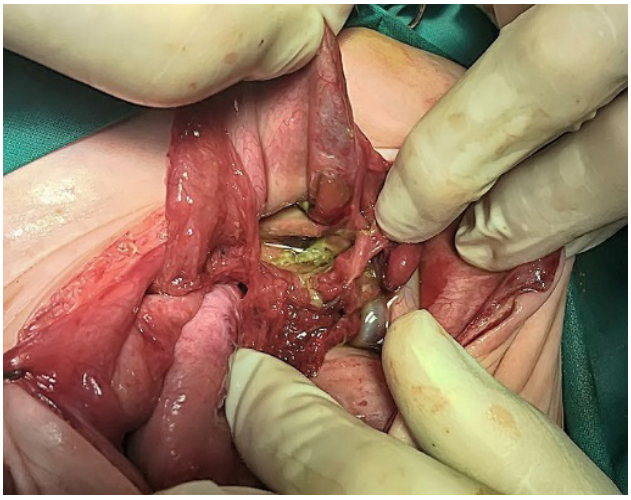

Figure 6. Gastric perforation.

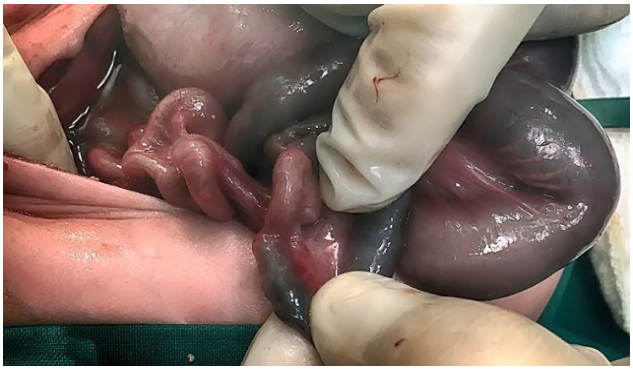

Figure 7. Very small terminal ileum with meconium plugs in it.

The diagnosis of Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome (MMIHS) was confirmed. Gastric and sigmoid wall repair was performed in double layer. Malrotation correction, appendectomy and terminal ileostomy was performed. Postoperatively, the ileostomy failed to function with intermittent low output and the infant continued to have bilious aspirates and feeding intolerance, forcing us to put her on TPN (total parenteral nutrition). Genetic testing was performed using the DNA extraction technique followed by PCR technique using the IVD Cystic Fibrosis-Nuclear Laser Medicine Diagnostici. In the CFTR gene, G542X mutation was found -Homozygotic type which confirmed the diagnosis of cystic fibrosis and explained the difficult bowel movements. This mutation is a class 1 mutation that affects biosynthesis and it is the second most frequent in Europe. The mutation is also associated with a severe phenotype of disease.

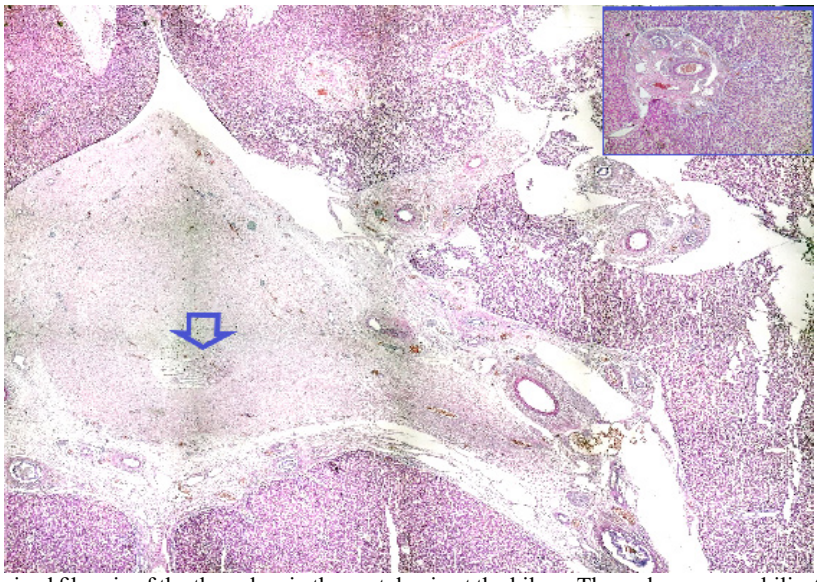

Figure 8. Liver with organized fibrosis of the thrombus in the portal vein at the hilum. Through re-permeabilisation of the thrombus there is a very small lumen (blue arrow). The portal veins in the portal spaces are collapsed and with hypo perfused (insert) HEx5.

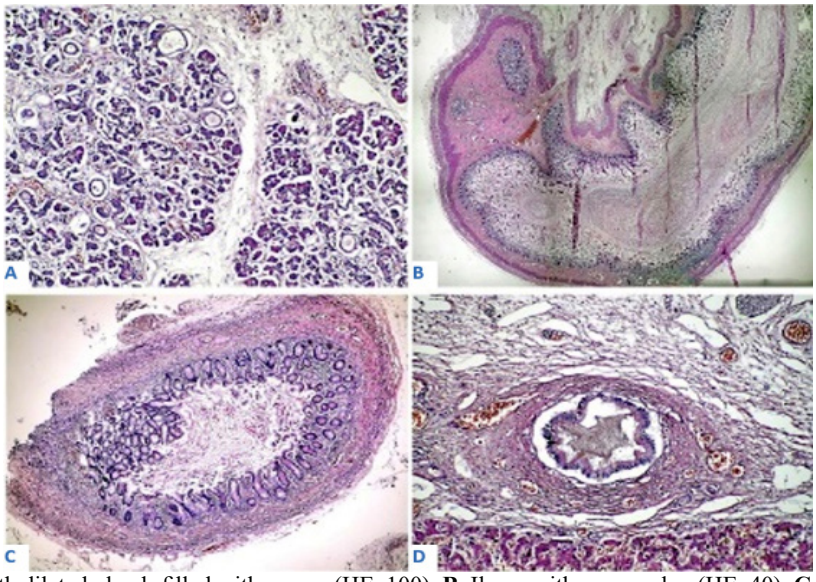

Figure 9. A. Pancreas with dilated glands filled with mucus (HEx100); **B.** Ileum with mucus plug (HEx40); **C.** Small caliber colon with mucus plug (HEx40); **D.** Major intrahepatic biliary duct with mucus plug and bile (HEx200).

Urinary output was good and the hematuria resolved progressively after daily instillations through urinary catheter. The patient was recovering well, nevertheless, after 2 months of TPN in the intensive care unit she developed sepsis due to urinary and central venous catheters. Urinary cultures were positive for *Serratia marcescens* and blood cultures were positive for *Staphylococcus epidermidis* and *Klebsiella pneumoniae*. Despite all efforts to resuscitate, the infant died due to acute cardio-respiratory distress.

The histopathological examination confirmed the clinical diagnosis of MMIHS, and in addition revealed a second diagnosis of cystic fibrosis to our surprise. The histopathological diagnosis following clinical autopsy was: Berdon Syndrome, Cystic fibrosis, major intrahepatic portal vein thrombosis with portal fibrosis secondary to TPN and secondary thrombophilia (Figure 8, Figure 9).

Discussion

MMIHS or also known as Berdon Syndrome is a rare congenital disease characterized by the distension of the urinary bladder leading to severe abdominal distention, microcolon, intestinal dysmotility and malrotation. The disease was first reported in 1976 by Berdon et al [1]. So far 227 cases of MMIHS have been reported with a female predisposition among neonates, F:M ratio of 2.4-4:1, including familial cases [3,5,6]. The prenatal diagnosis can be suspected by the appearance of the bladder on ultrasound, though confusion with Prune Belly Syndrome (PBS) may occur.

Review of literature reveals a significant overlapping of clinical features between PBS and MMIHS, and also the possibility of a common pathogenesis has been suggested [7]. Common clinical characteristics between MMIHS and PBS are dilation of the urinary tract, lax abdominal wall, intestine malrotation and familial incidence. Oliveira et al. stated the possibility that PBS and MMIHS are manifestations of the same underlying process and that intestinal hypoperistalsis-microcolon is the distinguishing feature between the two syndromes [4]. Other differential diagnosis for MMIHS is posterior urethral valves, but this has its pathognomonic ultrasound appearance of "key-hole" sign.

The exact pathogenesis is not fully understood but several factors including genetic, neurogenic, myogenic and hormonal abnormalities have been reported to play a role in the development of this syndrome [3]. The frequent occurrence in families with consanguineous parents and in siblings of an affected child suggests an autosomal recessive mode of inheritance like cystic fibrosis. Familial cases of MMIHS have been linked to mutations in MYH11, a gene that encodes smooth muscle myosin heavy chain, and LMOD1, another gene expressed exclusively in smooth muscle [8,9].

Newborns with MMIHS present in the first days of life with abdominal distention, bilious emesis, failure to pass meconium and voiding problems which are similar to the clinical features in neonates with intestinal obstruction [10]. If non obstructive distention of the urinary bladder, microcolon and hypoperistalsis of the intestines present together, as in our case, it steers the physician and radiologist to the diagnosis of MMIHS [3,10]. Prognosis of MMIHS is very poor, most of these patients survive with an average life expectancy of 3.6 months, nevertheless some case reports document prolonged survival rate [6,11-13]. Death is mainly caused by sepsis, malnutrition or multiple organ failure.

Our patient was admitted with both peritonitis and pneumoperitoneum due to iatrogenic colonic perforation and gastric rupture, which most likely were caused from insertion of rectal tube and nasogastric tube. These preoperative complications contributed to a decreased prognosis with a prolonged recovery period and more difficult to manage treatment options.

Meconium ileus is pathognomonic for neonates with cystic fibrosis, diagnosed through specific laboratory tests such as sweat chloride test [3]. Other causes of congenital mechanical obstruction, acquired mechanical obstruction and functional obstruction should first be eliminated. Diagnosis of Hirschsprung's disease, drugs, endocrine disorders and sepsis should also be considered. Small bowel or colon atresia are not usually associated with a distended bowel. Hirschprung's disease has the usual aspect of a normal distal colon with the distention of proximal colon. Meconium plug syndrome is usually a transient entity which is resolved by a contrast enema. All these diseases should be considered when treating a newborn with failure to pass meconium. Postmortem histopathological examinations revealed a positive diagnosis for cystic fibrosis, nevertheless this suspicion was not raised due to the fact that meconium ileus has not to our knowledge been associated with megacystis, microcolon, malrotation and peritonitis as in our case. The coexistence of these entities only worsened the prognosis. To our knowledge this is the first case reported of a neonate diagnosed with MMIHS and cystic fibrosis.

Without these complications and with the knowledge of the associated cystic fibrosis, the survival of our patient could have been improved significantly. Iatrogenic perforation of the colon in this case should teach us to always consider MMIHS as a possible diagnosis if inserting a rectal tube leads to perforation of the colon.

The available therapeutic options for MMHIS are prokinetic drugs, gastrointestinal hormones (gastrin, cholecystokinin and secretin) [12] total parenteral nutrition (TPN) due to intestinal hypomotility, repeated bladder catheterization and surgical palliative procedures like gastrostomy, ileostomy, vesicostomy and multi-organ transplantation, but none of them is curative [6,12,14]. TPN usage in MMIHS patients leads to metabolic complications, hypertriglyceridemia as a result of hepatotoxicity, as well as hepatic failure and sepsis [12]. Bladder function may not improve after transplantation and the patient may need clean intermittent catheterizations [15].

Physicians must consider MMIHS in each prenatal ultrasonography or MRI that show bladder dilatation with or without hydronephrosis, especially if the fetus is female, as well as post-delivery with neonates presenting abdominal distention that resolve promptly after inserting a catheter into the bladder. We should be aware of this presentations for timely diagnosis and appropriate treatment. Importantly, urinary bladder catheterization should always be performed before laparotomy in every neonate with intestinal obstruction and abdominal distension.

Conclusions / Learning Points

• Any Infant with Meconium ileus or peritonitis, improper or absent bowel movements combined with MMIHS-like symptoms should be investigated for possible cystic fibrosis.

• MMIHS and PBS have overlapping clinical presentations leading to difficulties in differentiation.

• Physicians should be aware of the possibility of gastric or colon perforations in MMIHS patients, therefore insert nasogastric and rectal tubes with caution in these patients.

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