

Megacystis Microcolon Intestinal Hypoperistalsis Syndrome

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Abstract

Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS) is a congenital disease distinguished by a markedly dilated acontractile bladder and a microcolon with dysfunctional peristalsis in the absence of mechanical obstruction. While the exact pathophysiology of MMIHS is not yet fully understood, the literature suggests a combination of genetic, neurogenic, and myogenic causes contribute to the disease. Most patients are diagnosed in utero or as neonates. Fetal US often suggests MMIHS. However, the diagnosis is often confirmed on fetal MRI. Advances in total parenteral nutrition, intestinal rehabilitation, and intestinal transplant have helped improve patients' survival.

Keywords: renal, gastrointestinal, congenital

Case Summary

A late premature neonate was born with abdominal distention. Pregnancy was complicated by polyhydramnios. Prenatal imaging (not available) showed a markedly enlarged urinary bladder and abdominal distention.

Imaging Findings

Abdominal radiograph (Figure 1) showed a markedly distended abdomen with small-caliber air-filled loops of bowel. Contrast enema (Figure 2) showed microcolon, while voiding cystourethrogram (Figure 3) showed an enlarged bladder.

Diagnosis

Megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS), also known as Berdon syndrome.

The differential diagnosis of neonates presenting with symptoms of bladder obstruction, an enlarged bladder, symptoms of bowel obstruction, and failure to pass meconium should include Hirschsprung disease, prune-belly syndrome, chronic intestinal pseudo-obstruction, multisystemic smooth muscle dysfunction syndrome, and MMIHS.

Discussion

MMIHS is a rare and often fatal condition of the newborn. It is characterized by a distended bladder in the absence of a mechanical obstruction, a microcolon, and decreased or absent intestinal peristalsis.¹ There have been >750 patients reported in the literature since the condition was first described by Berdon et al in 1976.² Girls are affected more commonly than boys. One meta-analysis analyzed 227 patients with MMIHS. Of

those included in the study, 70.6% were in females.³

The pathophysiology of the syndrome remains uncertain, with genetic, neurogenic, and myogenic causes all having been implicated. Despite the uncertainty of the exact pathogenesis, "an enlarged, acontractile bladder in a child with bowel motility problems" is considered diagnostic.⁴ Evidence supporting a genetic cause of disease includes 6 gene mutations as having been identified in patients with MMIHS and lineage tracing showing both autosomal-dominant and autosomal-recessive inheritance patterns. Additionally, parental consanguinity has been recognized as contributing to the autosomal-recessive inheritance pattern.⁵ Gene mutations associated with MMIHS include ACTG2, LMOD1, MYH11, MYL9, MYLK, and PDCL3. However, other genes may be involved.⁶

The evidence for a neurogenic etiology of disease is based on the absence of interstitial cells of Cajal (ICCs). Patients with MMIHS and Hirschsprung disease may each present with failure to pass meconium in the neonatal period. While both diseases are associated with abnormal innervation of the affected

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Disclosures: The authors have no conflicts of interest to disclose. None of the authors received outside funding for the production of this original manuscript and no part of this article has been previously published elsewhere.

Figure 1. Abdominal radiograph showing a markedly distended abdomen with a relative paucity of bowel gas. The visible loops of bowel (arrow) are small caliber in the right upper quadrant.

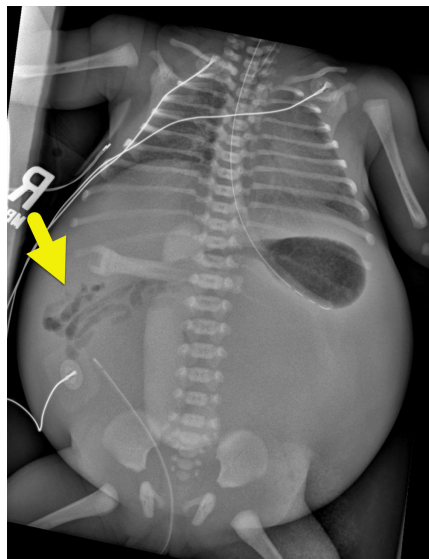
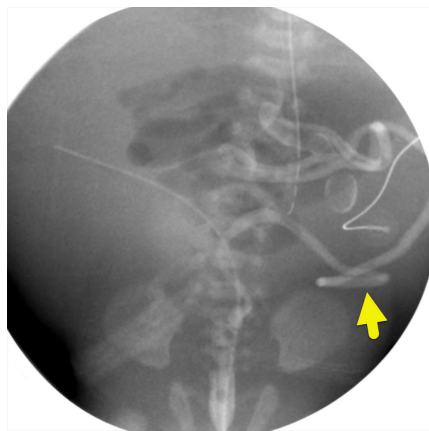


Figure 2. Water-soluble contrast enema showing a very small microcolon (arrow). Dilated air-filled loops of bowel are not yet opacified.



colon, Hirschsprung disease is defined by a lack of ganglion cells, while patients with MMIHS lack ICC. Absence of the ICC results in decreased facilitation of neuroexcitatory signaling to the myenteric plexus, ultimately resulting in the hypoperistalsis and voiding dysfunction seen in MMIHS.¹

Finally, experiments with mice lacking the $\alpha 3$ subunit of nicotinic acetylcholine receptors have contributed to the myogenic theory of disease in MMIHS.¹

These studies have shown that excessive storage and poor utilization of glycogen within smooth muscle cells in the bowel and bladder contribute to degenerative changes and excessive intercellular connective tissue between muscle cells. These changes result in dysfunctional peristalsis and bladder contraction.¹ The murine experiments are supported by confirmed reports of intestinal myopathy in patients with MMIHS.

Patients with MMIHS present in the neonatal period with abdominal distention, hypoactive or absent bowel sounds, bilious vomiting, constipation, and an inability to void spontaneously or pass meconium.¹ Laboratory values may reveal anemia, hyperkalemia, hyperbilirubinemia, and elevated creatinine and urea.⁷

Diagnosis is often first suspected on second trimester fetal US. Findings of MMIHS include megacystis with or without hydroureteronephrosis, oligo- or polyhydramnios, and/or vesicoureteral reflux (VUR).^{1,8} It is important to note that MMIHS cannot be diagnosed with evidence of megacystis alone. It must be accompanied by microcolon and intestinal dysmotility. If there is suspicion based on fetal US, fetal MRI may be used to identify additional characteristics that would raise suspicion for MMIHS, including a microcolon, dilated esophagus, shortened bowel, and malrotation.⁷⁻⁹ Early identification of MMIHS in the antenatal period is helpful in providing parents time to make an informed decision regarding care, find a postnatal care team, and coordinate any medical and surgical interventions after delivery.⁸ After birth, fluoroscopy and US are used to confirm the diagnosis. Upper GI shows dilation of the stomach and proximal small bowel, diminished peristalsis, and intestinal hypomotility.⁸⁻¹⁰ Shortened bowel length and intestinal malrotation are also common features of the syndrome.⁸ Contrast enema during the neonatal period shows microcolon, which may or may not be associated with malrotation.⁹ Of note, a

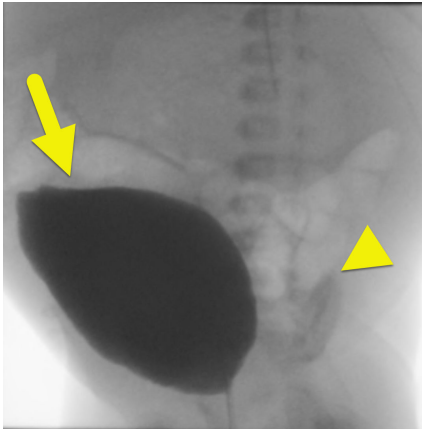
microcolon may be a transient finding secondary to bowel hypomotility and disuse while in utero, and over time the colon may assume a normal caliber or dilate.⁸ Due to peristaltic dysfunction, meconium ileus may subsequently develop and be seen on contrast enema studies. However, this is ultimately a result of bowel dysmotility rather than abnormal meconium consistency. Finally, postnatal US or voiding cystourethrogram will show megacystis and urinary tract dilation, which include hydronephrosis, hydroureters, and VUR.⁸ Differential diagnosis of these renal findings should include other etiologies of bladder outlet obstruction such as megacystitis megaureter, posterior urethral valves, and urethral atresia. However, evidence of megacystis with concomitant presentation of bowel obstruction signs and image findings should point to a diagnosis of MMIHS.

Historically, options for management were limited and associated with a poor prognosis and death in the first year of life. Early treatment options included use of prokinetic drugs, GI hormones, and parenteral nutrition. Unfortunately, these treatments provided little to no improvement, and death resulted mostly from malnutrition and multiorgan failure secondary to sepsis.⁵ Advances in therapy with implementation of intestinal rehabilitation, management of the complications of total parenteral nutrition, and multivisceral transplant have helped improve survival for patients with MMIHS.^{5,8} Currently, 5- and 10-year survival rates have improved to 63% and 57%, respectively.⁵

Conclusion

MMIHS is a congenital disease distinguished by a markedly dilated acontractile bladder and a microcolon with dysfunctional peristalsis in the absence of mechanical obstruction. While the exact pathophysiology of MMIHS is not yet fully understood, the literature suggests a combination

Figure 3. Oblique image from voiding cystourethrogram showing a large bladder (arrow) extending well beyond the iliac crest (arrowhead). There is no vesicoureteral reflux.



of genetic, neurogenic, and myogenic causes contribute to the disease. Most patients are diagnosed in utero or as neonates. Fetal US often suggests MMIHS. However, the diagnosis is often confirmed on fetal MRI. Advances in total parenteral nutrition, intestinal rehabilitation, and

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