Journal of Pediatric Surgery 51 (2016) 1565–1573

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Megacystis microcolon intestinal hypoperistalsis syndrome: Case series and updated review of the literature with an emphasis on urologic management☆,☆☆,★

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ARTICLE INFO

Article history:
Received 21 March 2016
Received in revised form 14 June 2016
Accepted 19 June 2016

Key words:
MMIHS
Berdon
Megacystis
Microcolon
Hypoperistalsis

ABSTRACT

Introduction: Megacystis microcolon intestinal hypoperistalsis (MMIHS) is a rare disorder characterized by distended nonobstructed bladder, microcolon, and decreased intestinal peristalsis. MMIHS has a particularly poor prognosis; however, when appropriately managed, survival can be prolonged.
Study design: A systematic review (1996–2016) was performed with the key words "megacystis microcolon intestinal hypoperistalsis syndrome." In addition, a case series of four patients is presented as well as algorithms for the diagnosis and treatment of MMIHS.
Results: 135 patients with MMIHS were identified in the literature. 73% (88/121) of the patients were female, 65% underwent diagnostic biopsy (64/99), and 63% (66/106) were identified with prenatal imaging. The majority of patients were treated with TPN as well as gastrostomy or ileostomy and CIC, however 15% (18/116) received multivisceral or intestinal transplant, and 30% (22/73) had a vesicostomy. The survival rate was 57% (68/121).
Conclusion: Appropriate management of MMIHS patients is crucial. An enlarged, acontractile bladder in a child with bowel motility problems should be considered diagnostic. Bladder distension can be managed with CIC or vesicostomy in addition to prophylactic antibiotics if frequent urinary tract infections are present. These patients often require gastrostomy or ileostomy as well as total parenteral nutrition. This management has led to significant improvement in survival rates.

Megacystis microcolon intestinal hypoperistalsis syndrome, also known as Berdon syndrome, is a rare disorder of both bladder and bowel motility. MMIHS is characterized by a distended nonobstructed bladder, microcolon, and decreased intestinal peristalsis [1–3]. It is part of a spectrum of chronic intestinal pseudoobstruction disorders, characterized by intestinal hypoperistalsis but, unlike the more common Hirschsprung's disease, ganglion cells are present on rectal biopsy [4,5]. MMIHS is considered to represent the most severe form of these disorders and is typically a fatal diagnosis [2,4]. It was first reported by Dr. Berdon in his 1976 publication of 5 female patients born with enlarged bladders with no mechanical obstruction, decreased gastrointestinal peristalsis, and abundant ganglion cells on colonic biopsy [1]. Given the low incidence of MMIHS, the majority of data regarding presentation, management, and outcomes are recorded in small case series. It is of particular importance for pediatric surgeons to have an awareness and basic understanding of MMIHS as appropriate management can significantly improve the prognosis of these patients.

1. Materials and methods

We performed a Pubmed search for the term "megacystis microcolon intestinal hypoperistalsis syndrome." This search identified 101 articles. 10 additional articles were identified through the references of the original search, with a specific focus on articles relating to urologic management of MMIHS. Of the 111 articles screened, 15 were excluded because they were published in a non-English language, and 6 were excluded because they did not address the gastrointestinal or urologic management of MMIHS. Therefore, 90 articles were used in the quantitative and qualitative study analysis.

We also reviewed our pediatric urologic database (IRB 15-0258) to identify patients diagnosed with MMIHS at the University of Chicago Comer Children's Hospital in the past 10 years. Four patients were

Abbreviations: CIC, clean intermittent catheterization; CIPO, chronic intestinal pseudoobstruction; DMSA, dimercaptosuccinic acid scan; MMIHS, megacystis microcolon intestinal hypoperistalsis syndrome; TPN, total parenteral nutrition; UTI, urinary tract infection; VCUG, voiding cystourethrogram.

☆ Conflict of interest statement: none of the authors has any conflicts of interest to report, financial or otherwise.

☆☆ Funding sources: no funding was received for this work.

★ Ethical approval: Pediatric urology database retrospective review; IRB 15-0258.

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http://dx.doi.org/10.1016/j.jpedsurg.2016.06.011
0022-3468/

identified, and their electronic medical charts were thoroughly reviewed with particular emphasis on diagnosis, management, and outcome in order to write the following case series.

2. Case series

2.1. Case 1

The first case describes a female infant delivered at 38 weeks with prenatal imaging notable for fetal gastric dilation, bladder distension, and bilateral hydronephrosis as well as polyhydramnios. Following delivery, these findings were confirmed on ultrasound and a voiding cystourethrogram showed a massively enlarged bladder and no evidence of urethral obstruction or stricture. A Foley catheter was placed and drained approximately 150 cm^3 of urine. A KUB shortly after delivery showed an absence of bowel gas distal to the stomach and a single gastric bubble. Additionally, the patient had no meconium passage. She was made NPO and placed on tube feeds because of concern for gastric outlet obstruction. On day of life two, the patient went to the operating room for an exploratory laparotomy for suspected jejunal atresia. During the procedure, the patient was noted to have malrotation, thick meconium present in the proximal jejunum, and a very thickened and enlarged bladder.

Over the next month, the patient was continued on TPN, started on clean intermittent bladder catheterization (CIC), and began prophylactic amoxicillin for UTIs. A repeat VCUG was unchanged and spinal MRI was normal. The patient continued to have no bowel production and lower gastrointestinal imaging was notable for microcolon. A rectal biopsy was done with ganglion cells present and no evidence of Hirschsprung's. At two weeks, the patient was taken back to the operating room and underwent ileostomy creation. At two months of age, an MR enterography study found grossly diminished peristalsis of the small bowel affecting the distal segment. Based on her course and these findings, the patient was diagnosed with MMIHS. She remained stable on TPN and CIC and had a gastrostomy tube placed at two and a half months of age. She was discharged home at four months.

Between four and ten months of age, the patient has been readmitted ten times for various infections including Klebsiella upper respiratory infection, multiple *Escherichia coli* UTIs, gram negative sepsis, and septic shock. A recent abdominal ultrasound demonstrated bilateral grade 3 hydronephrosis (Fig. 1). Because of her multiple infections, she was placed on sulfamethoxazole-trimethoprim antibiotic prophylaxis. She is currently doing relatively well and is 10 months of age.

2.2. Case 2

The second case describes a female infant who was also found on prenatal ultrasound to have bilateral hydronephrosis and a large, distended bladder. Based on these findings, MMIHS was suspected. The patient was born via cesarean section at 34 weeks and suffered from respiratory distress secondary to a massively dilated abdomen. A urethral catheter was placed shortly after delivery and she was subsequently started on CIC and ampicillin prophylaxis. A lower gastrointestinal series on day of life one showed small bowel rotation, microcolon, and possible partial duodenal obstruction. A VCUG demonstrated a large bladder and renal ultrasound was notable for bilateral hydronephrosis. Based on these findings, the diagnosis of MMIHS was confirmed. On day of life three, she underwent a laparotomy for malrotation correction, intestinal biopsy, ileostomy formation, and gastrostomy tube placement. The biopsy results were normal with ganglion cells present and she was started on TPN. At three weeks of age, a repeat renal ultrasound showed slightly decreased hydronephrosis bilaterally with a persistently enlarged bladder.

Urodynamic studies at five weeks demonstrated a large, oblong bladder with increased capacity and failure to empty with no reflux (Figs. 2, 3). At 7 weeks, a renal ultrasound showed left grade 4 hydronephrosis and right grade 1 hydronephrosis. The patient has been placed on trimethoprim-sulfamethoxazole prophylaxis and continues with intermittent catheterization with no clinically significant infections to this point. An MR enterography study done at five weeks showed aperistaltic bowel in the distal ileum and robust peristalsis in the proximal bowel. She was transitioned to gastrostomy tube feeds and was discharged at four months on tube feeds as well as oral breast feeding once daily. Since her discharge, the patient has been admitted to the hospital three times for emesis and difficulty with her tube feeds and once for central line infection. The patient is currently 18 months old.

2.3. Case 3

The third case describes a patient diagnosed with hollow visceral myopathy and megacystis megaureter syndrome as an infant who has been successfully managed and is currently 20 years old. The patient was found to have intestinal failure and megacystis on imaging shortly after birth and underwent colectomy, ileostomy, and gastrostomy tube placement around two years of age and was also started on TPN at that time. Since then, she has been followed closely by both pediatric gastroenterology as well as pediatric urology.

Urologically, she has been managed with daily self-catheterization and prophylactic antibiotics. Routine imaging with ultrasound has shown a stably enlarged bladder and chronic bilateral hydronephrosis (Fig. 4). Her hydronephrosis has progressed from grade 2 bilaterally at age 11 to grade 3 right hydronephrosis and grade 2 left hydronephrosis at age 17. Urodynamic studies at age 15 found a large bladder capacity of 1 L with emptying to partial completion. Despite management with prophylactic antibiotics, her course has been complicated by multiple UTIs.

The patient continues TPN; however, she consumes a regular diet orally during the day which she tolerates well. Her weight has remained around the 5th percentile, height at the 10th–25th percentile, and BMI at the 5th–10th percentile. Her course has been complicated by multiple ileostomy and gastrostomy tube revisions and hospitalization for acute or chronic intestinal pseudoobstruction. She takes prophylactic metronidazole to prevent small bowel bacterial overgrowth and omeprazole for gastric reflux symptoms. This case represents a rare prolonged survival of a patient with MMIHS. Overall, she is doing very well with her management with TPN, intermittent catheterization, and antibiotic prophylaxis.

2.4. Case 4

The fourth patient was born following an uncomplicated pregnancy and developed intestinal obstruction and feeding difficulty during the first year of life. There is no record of prenatal imaging performed or abnormal findings. At 17 months, he underwent a 15 cm colonic resection for obstruction; however, he continued to have persistent feeding intolerance and abdominal distension. Rectal biopsies were taken at 20 months of age with ganglion cells present. The patient also underwent a jejunostomy and had a gastrostomy tube placed at this time. The patient's parents stated that the patient's older sister had presented similarly with multiple episodes of constipation, colonic obstruction, and abdominal distension. She underwent rectal biopsy which was negative for Hirschsprung's and unfortunately died at age 3.

Over the following nine months, the patient continued to have difficulty maintaining adequate nutrition resulting in PICC line placement and initiation of TPN. In addition, the patient suffered from three infections including two UTIs during this time. Following the second UTI at 29 months, a VCUG was done and was notable for an enlarged bladder with difficulty emptying. Based on the patient's gastrointestinal symptoms, enlarged bladder, and family history, the diagnosis of MMIHS was made. The patient was started on CIC and prophylactic antibiotics.