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An Unusual Presentation of Megacystis-Microcolon-Intestinal-Hypoperistalsis Syndrome

Case

A 13 month old girl, with background of congenital megacystis requiring intermittent catheterisation, right duplex kidney and constipation presented to A+E with a short history of lethargy, vomiting and fever. She appeared lethargic and pale with a slightly distended abdomen. Initially a diagnosis of gastroenteritis was entertained but she quickly deteriorated with tachycardia and hypotension, and was transferred to intensive care. She went on to develop decompensated shock with multi-organ failure including AKI stage 3, transaminitis, coagulopathy with leukoencephalopathy on MRI. She was intubated and ventilated, received significant fluid resuscitation, intravenous antibiotics, inotropes and required haemofiltration. Blood and urine cultures were negative. She developed bloody diarrhoea and abdominal x-ray showed a dilated colon with bowel wall thickening, without features of obstruction. She improved slowly with a period of bowel rest, parenteral nutrition and neuro-rehabilitation.

As a neonate she had been admitted to intensive care for bilious vomiting and delayed passage of meconium. She was described to have been managed for constipation from birth requiring laxatives.

Attempts to establish feeds induced bloody diarrhoea and pyrexia. Contrast enema showed a distended featureless loop of sigmoid colon with tortuous proximal descending colon. This was felt not to be typical of megacystis microcolon as the areas of colonic narrowing were segmental. Endoscopic assessment revealed an enterocolitis. Histology showed severe inflammation with granulation tissue in the descending colon and ganglion cells were identified in the submucosa. Rectal strip biopsies were normal and adequately ganglionated. Genetics were sent for exome sequencing and identified a de novo heterozygous pathogenic ACTG2 missense variant, 275, a known pathogenic mutation. A diagnosis was made of Megacystis-Microcolon-Intestinal-Hypoperistalsis Syndrome (MMIHS).

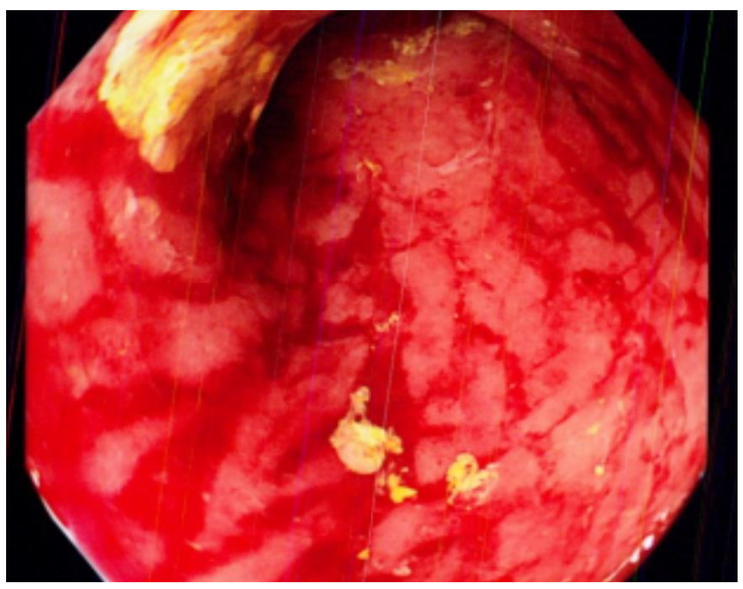

Image 1: Enterocolitis seen on endoscopic assessment.

Discussion

MMIHS is a rare syndrome consisting of a dilated bladder without obstruction, a microcolon and intestinal dysmotility. The condition was first described by Walter Berdon in 1976 and a recent systematic review in 2011 identified 227 reported cases between 1976 and 2011.[1] The condition is often suspected antenatally with megacystis being found on ultrasound. Neonatally these children present with symptoms of bladder and bowel obstruction including distended abdomen, inability to void, delayed passage of meconium and bilious vomiting.[2] The prognosis is variable with intestinal dysfunction leading to dependence on parenteral nutrition. Defunctioning of the colon is reported in most affected individuals or they go on to require multivisceral transplantation for survival and PN autonomy.

ACTG2 mutation has been identified in 44.1% of cases of MMIHS making it the commonest known genetic cause of MMIHS.[2] ACTG2 affects actin γ 2 smooth muscle and can present with varying degrees of visceral myopathy including MMIHS and chronic intestinal pseudo-obstruction.[3]

Conclusion

This was an unusual presentation in an older infant with symptoms suggestive of a Hirschprung's-like enterocolitis leading to a diagnosis of MMIHS with identification of de novo ACTG2 missense variant associated with the condition. This case highlights the importance of taking a neonatal history and the diagnostic power of whole exome sequencing in children with congenital GI disorders.

Key Learning Points

- Neonatal history is significant in helping to identify rare diagnoses
- Chronic constipation from birth is a red flag for underlying pathology
- Whole exome sequencing is a powerful diagnostic tool in children with congenital GI disorders

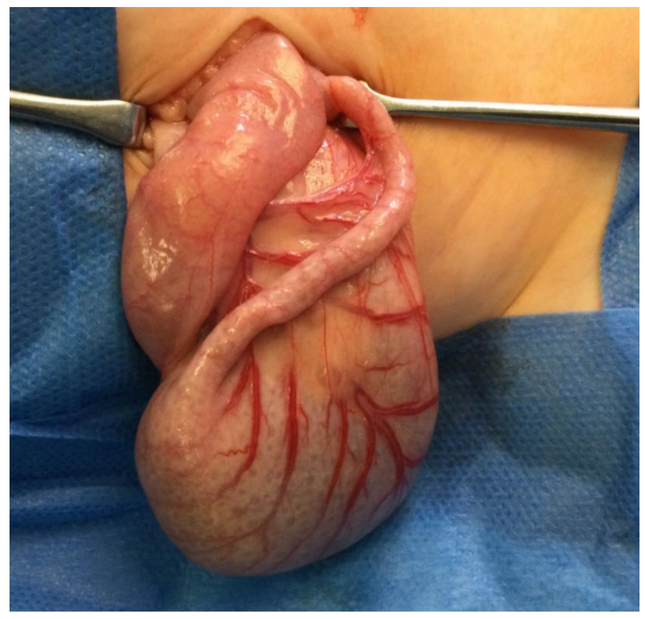

Image 2: Microcolon with pneumatosis visible during surgery to for a defunctioning ileostomy.

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3. Hashmi S, Barka V, Yang C, Schneider S, Svitkina T, Heuckeroth R. Pseudo-obstruction-inducing ACTG2R25C Alters Actin Organization and Function. JCI Insight. 2020;5(16):e140604