Enteritis with pneumatosis intestinalis following rotavirus immunisation in an infant with short bowel syndrome

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SUMMARY

Rotavirus vaccines now form part of the national immunisation schedule in many countries. Contraindications to its use are few but do not currently include infants with short bowel syndrome (SBS). We present a nearly 3-month-old boy with SBS who developed enteritis with pneumatosis intestinalis following administration of the Rotarix vaccine.

BACKGROUND

The present case suggests a novel adverse reaction to rotavirus immunisation. It further highlights the need to methodically consider the risk–benefit equation with regard to universal rotavirus immunisation in the short bowel syndrome (SBS) population. The benefit of acute gastroenteritis risk reduction needs to be weighed against the serious risk of loss of intestinal length in this vulnerable group. Further research in this area is urgently needed.

CASE PRESENTATION

An 11-week-old boy had SBS with an ileostomy secondary to long-segment Hirschsprung's disease. He was born at 38 weeks gestation with a birth weight of 3588 g via elective caesarean section for gestational diabetes mellitus. His family history was significant for maternal total colonic Hirschsprung's disease. He was admitted to the neonatal intensive care unit (NICU) at 29 hours of age for bilious vomiting. At that point, the patient was commenced on broad-spectrum intravenous antibiotics and made nil by mouth.

A contrast study revealed a small calibre colon which raised the possibility of Hirschsprung's disease. His clinical condition deteriorated and he proceeded to laparotomy, which revealed a mid-transverse colonic perforation, and a dilated caecum and proximal small bowel. An ileostomy was initially formed 15 cm proximal to the ileocaecal valve. Subsequently, histology showed no ganglion cells at the stoma site and a further ileostomy was fashioned 42 cm distal to the duodenojejunal flexure where there were ganglion cells present in the submucosa.

Following discharge from the NICU, the patient progressed satisfactorily on the paediatric ward. His parenteral nutrition was cycled gradually and his enteral nutrition cautiously advanced with good tolerance and acceptable weight gains. The

patient's enteral nutrition initially consisted of expressed breast milk. He was transitioned to an extensively hydrolysed formula with high medium chain triglyceride content once maternal breast milk supply ceased at 1 month of age.

On day 75 of life, the patient was given the Rotarix vaccine in accordance with the national immunisation schedule.¹ His other immunisations due at 2 months of chronological age were given 7 days prior. At the time of Rotarix immunisation, the patient was having daily stoma outputs of 40–50 mL/kg/day consistently.

Three days following Rotarix immunisation, the patient developed increased stoma losses of >70 mL/kg/day. Even though his abdomen remained benign on examination, the increased losses persisted for 3 days and on the fifth day following Rotarix immunisation, the patient developed bloody stomal output and became lethargic. His clinical observations remained within normal limits.

INVESTIGATIONS

An abdominal ultrasound performed to investigate for intussusception did not reveal intussusception but identified small bowel wall thickening and markedly diffuse circumferential echogenic small bowel wall consistent with pneumatosis intestinalis (figure 1). The large bowel was visualised during this examination and noted to be of normal appearance. Pneumoperitoneum and portal venous gas were absent on a subsequent plain abdominal film. He had a mildly raised C reactive protein (CRP) count of 7 mg/L and a drop in platelet count to $216 \times 10^9/L$ (having previously been $>400 \times 10^9/L$). There was no evidence of polycythaemia on repeat serological testing. Blood and stomal cultures were obtained and the patient was managed non-operatively with intravenous antibiotics (Tazocin) and cessation of enteral feeds.

DIFFERENTIAL DIAGNOSIS

The patient here presented had clinical and sonographic evidence consistent with necrotizing enterocolitis (NEC), with increased and bloody stomal outputs, bowel wall thickening suggestive of an inflammatory reaction as well as compromised mucosal integrity allowing entry of pathogenic organisms into the bowel wall leading to the development of pneumatosis intestinalis.² The alternative diagnosis considered was Hirschsprung's-associated

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Figure 1 Ultrasonography showing pneumatosis intestinalis with arrows pointing out two examples of intramural gas in the patient's small intestine.

enterocolitis potentially triggered by administration of rotavirus vaccine which has proven immunogenicity in the SBS population.³

TREATMENT

Blood and stoma cultures were obtained and the patient was managed non-operatively with intravenous antibiotics (Tazocin) and cessation of enteral feeds. Enteral feeds were recommenced 48 hours after cessation and the patient completed a 6-day course of Tazocin for this illness.

OUTCOME AND FOLLOW-UP

Over the next three days, his stoma output returned to baseline and his CRP and platelet counts normalised. In total, three stoma samples were obtained on days 5, 6 and 8 following immunisation and these remained negative for multiple, common pathogenic bacteria and viruses including rotavirus group A and B RNA (by PCR testing).

Repeat ultrasound performed 9 days after the initial scan revealed no pneumatosis intestinalis or intestinal wall thickening. The patient has continued to progress well with grading up of enteral feeds, cycling of parenteral nutrition and good physical and developmental gains.

DISCUSSION

Contraindications to Rotarix administration include uncorrected congenital malformations of the gastrointestinal tract which may predispose the infant to intussusception.⁴ Other precautions include previous hypersensitivity reactions to any component of the vaccine, acute gastroenteritis and underlying immunodeficiencies.⁴ There is, however, relative paucity of data on the safety of rotavirus immunisation in infants with SBS. In a case series⁵ of pentavalent rotavirus vaccine (RotaTeq) in infants with non-Hirschsprung's disease-related SBS, one infant developed NEC following sequential administration of two RotaTeq immunisations resulting in a 2 cm terminal ileal resection. Of note, however, in the other eight cases, vaccine administration was generally well tolerated aside from a transient increase in stoma outputs without significant associated sequelae. In a separate case series⁶ examining the safety of monovalent rotavirus immunisation in 15 infants with intestinal failure, no serious adverse event was observed. In a case-controlled study of eight infants,³ the pentavalent rotavirus vaccine was well tolerated among infants with prior bowel resections. That study included one infant with total colonic Hirschsprung's disease.

The clinical concern in this case, irrespective of the actual diagnosis, was the potential loss of viable small intestine in an immune-competent patient with SBS. This patient had risk factors for NEC, which included multiple courses of intravenous antibiotics and formula feeding.⁷ On the other hand, long-segment Hirschsprung's disease is a known risk factor for Hirschsprung's-associated enterocolitis.⁸ A previous study has demonstrated the difficulty in differentiating NEC from Hirschsprung's-associated enterocolitis.⁹

Direct causality as a result of rotavirus immunisation cannot be proven, although the temporal relationship with the patient's illness, and biological plausibility, raise the possibility of a cause-effect relationship particularly as a similar event occurred neither prior to nor since the immediate aftermath of rotavirus immunisation. The absence of rotavirus RNA on repeat stoma cultures is in keeping with published data, which found viral shedding following Rotarix immunisation in as few as 35% of recipients.⁴

Learning points

- ▶ There may be risk of serious complication following rotavirus immunisation in infants with short bowel syndrome (SBS), including further loss of intestinal length in children with already compromised functional bowel.
- ▶ This risk should be discussed as part of the informed consent process prior to rotavirus immunisation in infants with SBS.
- ▶ Further research in a large cohort of patients is warranted to weigh the benefits of gastroenteritis risk reduction against the potential loss of intestinal length following immunisation in this at-risk patient population.

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