CASE REPORT

Pneumatosis intestinalis in a preterm infant: should we treat all intestinal pneumatosis as necrotising enterocolitis?

Siu Jun Chew,¹ Rajadurai Samuel Victor,^{1,2,3,4} Krishna Revanna Gopagondanahalli,^{1,4} Suresh Chandran^{1,2,3,4}

¹Department of Neonatology, KK Women's and Children's Hospital, Singapore

²Duke NUS Medical School, Singapore

³LKC School of Medicine, Singapore

⁴YLL NUS School of Medicine, Singapore

Correspondence to

Associate Professor Suresh Chandran, schandran1312@yahoo.co.uk

RSV and SC contributed equally. SJC and KRG contributed equally.

Accepted 16 March 2018

SUMMARY

Gastric pneumatosis is a very rare site of pneumatosis intestinalis (PI), and we report this finding in a preterm female infant with cyanotic congenital heart disease. The infant was stable initially on nasal intermittent mandatory ventilation; however, torrential pulmonary flow through a large patent ductus arteriosus prompted closure using oral ibuprofen. After an episode of haematochezia, she developed PI, affecting mainly the gastric wall and small intestine with portal venous gas. Her bowel movements were regular, with no abdominal distension or significant gastric aspirates. She was haemodynamically stable with negative infective markers. Management consisted of endotracheal intubation and ventilation, gastric decompression and broad-spectrum antibiotics. Both the gastric and intestinal pneumatosis resolved within 24 hours and she made an uneventful recovery. If PI is not due to necrotising enterocolitis, enteral nutrition can be initiated early and prolonged course of broad-spectrum antibiotics could have been avoided.

BACKGROUND

Pneumatosis intestinalis (PI) is a rare form of an air leak into the gastric and intestinal wall, and used as an imaging sign often in sick preterm infants to diagnose necrotising enterocolitis (NEC). We report here a 34+5 weeks gestational age female infant born with a cyanotic congenital heart disease (CCHD), total anomalous pulmonary venous drainage (TAPVD). After a course of oral ibuprofen to close a large patent ductus arteriosus (PDA), she developed an episode of haematochezia and pneumatosis of gastric and intestinal walls with portal venous gas (PVG). There were no abdominal signs or feed intolerance; gastric aspirates were negligible and haematological parameters were unremarkable. Following gastric decompression and elective intubation and ventilation to reduce gastrointestinal intraluminal pressure, a rapid resolution of pneumatosis within 24 hours was noted. Indomethacin or ibuprofen-induced PI, which developed in the presence of gastrointestinal ischaemia due to CCHD and diastolic drift due to large PDA and gastric emphysema due to nasal intermittent mandatory ventilation (NIMV), can resolve rapidly with conservative management. In

contrast, NEC needs bowel rest for 14 days and other supportive measures. Having knowledge of the benign nature of indomethacin-induced pneumatosis, especially against the background of gut ischaemia, in a clinically stable infant, could facilitate conservative management for a short period and thereby preventing prolonged deprivation of enteral nutrition.

CASE PRESENTATION

A female infant, twin 2 of dichorionic diamniotic pregnancy, was born at 34+5 weeks gestation to a 33-year-old mother. The antenatal scan of both twins was unremarkable. Twin two was small for gestational age and weighed 1629 g. She was born with a vigorous cry with Apgar score of 9 and 9 at 1 and 5 min of life, respectively. She was admitted for establishment of feeds to the special care nursery and was stable in room air. On day 1 of life, enteral feeds were initiated with breast milk and graded up to full feeds by day 7. She developed respiratory distress on day 10 of life and was noted to have a cardiac murmur. An echocardiography showed supracardiac TAPVD and a haemodynamically significant large PDA. She was transferred to neonatal intensive care unit and remained stable in NIMV support. Echocardiographic evidence of increased pulmonary blood flow through PDA impelled a closure using oral ibuprofen. On day 14 of life, she was given oral ibuprofen and continued for 3 days. On day 17, she had an episode of haematochezia. There were no significant gastric aspirates and her bowel movements were normal. Her blood pressure was stable and there was no tachycardia. An X-ray of the abdomen was requested.

INVESTIGATIONS

An X-ray of her abdomen showed marked gastric and distal intestinal linear pneumatosis with PVG (figure 1A,B). Her blood counts and C reactive protein were normal. The liver and renal function tests were unremarkable. There was no acidaemia and she was haemodynamically stable. The blood and stool cultures were sterile.

DIFFERENTIAL DIAGNOSIS

Indomethacin-induced pneumatosis intestinalis. Fulminant necrotising enterocolitis.

To cite: Chew SJ, Victor RS, Gopagondanahalli KR, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224356

Figure 1 (A) The frontal radiograph shows air in the stomach wall outlining the greater curvature of the stomach (long arrows) and linear pneumatosis over the distal intestine (arrow head). Portal venous gas noted (short arrows). (B) Lateral decubitus X-ray showing the linear pneumatosis on the gastric wall (long arrows), distal intestine (arrow head) and portal venous gas (short arrows).

TREATMENT

Medical management included (1) gastric decompression, (2) switching ventilation from NIMV to endotracheal intubation, (3) bowel rest and (4) empirical antibiotics. An X-ray of the abdomen done after 5 hours of diagnosis showed marked improvement in the degree of intramural gas in the walls of the stomach and intestine (figure 2). A near-complete resolution of gastric and intestinal pneumatosis and absorption of PVG with normal gut gaseous pattern was noted within 24 hours of diagnosis (figure 3). Antibiotics were discontinued after 5 days with negative blood and stool cultures. Feeds were initiated with expressed breast milk and were graded up to full feeds over the following week. She had normal bowel patterns and was transferred to the cardiothoracic unit for surgical repair of TAPVD.

OUTCOME AND FOLLOW-UP

She underwent surgical repair of TAPVD and was discharged home well.

DISCUSSION

Pneumatosis intestinalis is the radiological finding of gas in a linear or cystic form within the gastrointestinal wall and gastric pneumatosis is a rare site of PI in infants.¹ Gastric pneumatosis has been reported with gastric outlet obstruction, NIMV, intramural feeding catheter placement and rarely with fulminant NEC.¹⁻⁴ PI describes the collection of gas intramurally within the bowel wall.⁵ PI is a radiological diagnosis often made in a sick preterm infant with suspicion of NEC and it is a standard practice to use Bell's classification to diagnose, stage and treat NEC.^{6,7} Nelson described mechanisms involved in extraluminal gas collections in the gastrointestinal tract as being either: (1) related to infection of the visceral wall by gas forming organisms (emphysematous gastritis) or (2) secondary to obstruction in gastrointestinal tract (gastric emphysema).⁸ Emphysematous gastritis has been described in NEC and erosive gastritis.⁴ It is characterised by cystic or bubbly appearance intramurally secondary to gas production by bacteria.^{4,9} Patients with emphysematous gastritis are usually critically ill with higher mortality and morbidity.^{1,5} On the other hand, gastric emphysema is caused by an increase in intragastric pressure that leads to superficial mucosal tear, followed by air escaping intramurally, which has been reported in infants on NIMV or in cases

of gastric outlet obstruction.^{10,11} Gastric pneumatosis has been described following malpositioned orogastric tube intramurally.³ In gastric emphysema, the radiological gas pattern appears as

Figure 2 Follow-up abdominal X-ray done 5 hours after the initial radiograph shows marked improvement in the degree of intramural gas noted in the stomach wall and in the walls of the intestines. The portal venous gas in the liver has largely resolved with only a small amount still visible.

Figure 3 Abdominal X-ray showing near complete resolution of gastric pneumatosis and portal venous gas with normal intestinal gas pattern after 24 hours of diagnosis.

linear streaks of gas around a distended stomach and along the intestine as noted in figure 1.^{4,9} In contrast to emphysematous gastritis, gastric emphysema has a better prognosis with resolution of intramural gas within 24 hours of conservative management, as reported in this case.^{10,11} The gastric and intestinal submucosal air getting drained into the portal vein through gastric and mesenteric veins can explain the PVG visualised on diagnosis of GP and PI.^{12,13} In the presence of PVG, NEC is staged as II B in modified Bell's staging criteria in a moderately ill preterm infant, which warrants off feeds and antibiotics for 14 days.^{6,7} Kosloske reported PVG as the best indicator of intestinal gangrene and have specificity and positive predictive value close to 100%.¹⁴ Cikrit *et al* found an increased survival rate of infants with PVG and NEC when laparotomy was performed early for PVG.¹⁵ PVG was considered as an ominous sign in the past but is currently a relative indication for surgery in NEC.¹⁶

The pathogenesis of gastric pneumatosis is multifactorial in this reported case, which includes an ischaemic gastric and intestinal mucosa due to CCHD and large PDA causing ductal steal, gastric distension due to NIMV predisposing to gastric mucosal tear and direct mucosal injury caused by oral ibuprofen. Cyanotic heart disease has been linked to GP in a neonate with hypoplastic left heart syndrome by Krueger *et al*,¹⁷ non-invasive ventilation such as NIMV is one of the causes of gastric emphysema, especially in face of ischaemic mucosa. Ting *et al* reported a case of gastric pneumatosis associated with the use of indomethacin in a preterm neonate while on synchronised NIMV.¹ Increase in intragastric pressure and dilatation of the stomach

has been reported, after positive pressure ventilation without tracheal intubation, possibly due to high cricopharyngeal pressures. The rise of intragastric pressure by NIMV in a damaged gastric mucosa after ibuprofen use can cause submucosal dissection of air as noted in our case.¹ Ibuprofen is a well-recognised drug that causes gastric and intestinal mucosal injury. Prostaglandin has a critical role in maintaining the gastric mucosal defence system. Use of cyclooxygenase inhibitors (COX-inhibitors) like ibuprofen can damage the gastric mucosa by inhibiting prostaglandin, thereby causing GP. Ibuprofen can also cause direct mucosal cellular injury independently of prostaglandins via the 'trapping' theory.¹⁸ Ibuprofen-induced small intestinal injury was proposed to go through the following steps: COX-inhibitors absorbed into the enterocytes inhibit mitochondrial oxidative phosphorylation; resultant dysfunction of the tight intracellular junctions and increase in intestinal permeability can finally expose the enterocytes to bile, pancreatic secretions and intestinal bacteria causing inflammation and ulceration.¹⁸ One episode of haematochezia in the reported case could be due to ibuprofen-induced distal intestinal mucosal ulceration.

Identifying PI from non-NEC causes is paramount. Conservative management leads to radiographic clearance and resolution of clinical symptoms in PI without systemic signs/symptoms and normal haematological and biochemical parameters.^{11,12} If the infant remains asymptomatic and stable, with resolution of pneumatosis in X-ray, feeding can be restarted early. In contrast, a progressive PI may imply a sign of fulminant NEC, needing prolonged gut rest and antibiotics, haemodynamic support and surgery if perforation occurs.⁴ Trivedi *et al* reported 32 cases of gastric pneumatosis, but only one had fulminant NEC, which required laparotomy. This exemplifies the rarity of NEC-causing GP.¹⁹ A detailed history of CCHD, large PDA, NIMV, use of ibuprofen and rapid resolution of pneumatosis with conservative management in a preterm infant could lead to a non-NEC diagnosis, hence facilitating early feeding.

Learning points

- ▶ Aetiology of isolated gastric pneumatosis (GP) is multifactorial and prognosis is generally good. In preterm small for gestational age infants, rarely GP could be an extension of pan-necrotising enterocolitis, where the outcome is extremely poor.
- ▶ GP and pneumatosis intestinalis (PI) can be prevented by avoiding nasal intermittent mandatory ventilation (NIMV) especially in babies with cyanotic congenital heart disease (CCHD) and large patent ductus arteriosus, both contributing to gastric and intestinal mucosal hypoxaemia.
- ▶ Linear pneumatosis in X-ray points to a diagnosis of gastric emphysema and cystic pneumatosis to emphysematous gastritis.
- ▶ Ibuprofen is a known cyclooxygenase inhibitor (COX-inhibitor) causing mucosal ulceration, bleeding and perforation. In a hypoxic infant due to CCHD, the effect of ibuprofen could be profound, causing gastric and intestinal pneumatosis and even perforation. Avoid the use of ibuprofen in infants with CCHD.
- ▶ Treatment of COX-inhibitor-induced GP and PI is supportive: (1) stop feeds and (2) if respiratory support is required, intubate and ventilate, not to continue with NIMV and follow-up with serial abdominal X-rays.

In conclusion, the following indicators in this case favour a benign form of GP/PI—the absence of systemic signs, non-bilious aspirates, normal bowel pattern following resolution of pneumatosis within 24 hours and unremarkable haematological parameters against a background of CCHD, NIMV and ibuprofen use. We should also facilitate early enteral nutrition to prevent nutritional compromise in these preterm infants, thereby promoting growth and reducing the risk of central line sepsis and parenteral nutrition-related complications. Unnecessary and prolonged course of broad-spectrum antibiotics should also be avoided.

Acknowledgements We would like to thank A/Prof Harvey Teo Eu Leong, department of diagnostic imaging, KK Women's and Children's Hospital, Singapore for reporting the X-rays and Ms Vivian Chua, Medical writer, SingHealth Academy for assistance in editing the manuscript.

Contributors SJC: manuscript preparation and review of literature. KRG: manuscript preparation and literature review. RSV and SC: Manuscript preparation, literature review and involved with antenatal planning, delivery and management of the case.

Funding We authors declare that there was no grant for this research from any funding agency.

Competing interests None declared.

Patient consent Guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 Ting YJ, Chan KL, Wong SC, *et al.* Gastric pneumatosis in a premature neonate. *AJP Rep* 2011;1:11–4.
- 2 Bhargava P, Parisi M. Gastric pneumatosis and portal venous gas: benign findings in hypertrophic pyloric stenosis. *Pediatr Radiol* 2009;39:413.
- 3 Mandell GA, Finkelstein M. Gastric pneumatosis secondary to an intramural feeding catheter. *Pediatr Radiol* 1988;18:418–20.
- 4 Duran R, Vatansever U, Aksu B, *et al.* Gastric pneumatosis intestinalis: an indicator of intestinal perforation in preterm infants with necrotizing enterocolitis? *J Pediatr Gastroenterol Nutr* 2006;43:539–41.
- 5 Heng Y, Schuffler MD, Haggitt RC, *et al.* Pneumatosis intestinalis: a review. *Am J Gastroenterol* 1995;90:1747–58.
- 6 Bell MJ, Ternberg JL, Feigin RD, *et al.* Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Ann Surg* 1978;187:1–7.
- 7 Kliegman RM, Walsh MC. Neonatal necrotizing enterocolitis: pathogenesis, classification, and spectrum of illness. *Curr Probl Pediatr* 1987;17:219–88.
- 8 Nelson SW. Extraluminal gas collections due to diseases of the gastrointestinal tract. *Am J Roentgenol Radium Ther Nucl Med* 1972;115:225–48.
- 9 Soon MS, Yen HH, Soon A, *et al.* Endoscopic ultrasonographic appearance of gastric emphysema. *World J Gastroenterol* 2005;11:1719–21.
- 10 D'Cruz R, Emil S. Gastroduodenal emphysema. *J Pediatr Surg* 2008;43:2121–3.
- 11 López-Medina G, Castillo Díaz de León R, Heredia-Salazar AC, *et al.* Gastric emphysema a spectrum of pneumatosis intestinalis: a case report and literature review. *Case Rep Gastrointest Med* 2014;1–5.
- 12 Chesley P, Stark R, McAdams R, *et al.* Isolated gastric pneumatosis in a premature infant following steroid exposure. *J Pediatr Surg Case Rep* 2014;2:436–8.
- 13 Abboud B, El Hachem J, Yazbeck T, *et al.* Hepatic portal venous gas: physiopathology, etiology, prognosis and treatment. *World J Gastroenterol* 2009;15:3585–90.
- 14 Kosloske AM. Indications for operation in necrotizing enterocolitis revisited. *J Pediatr Surg* 1994;29:663–6.
- 15 Cikrit D, Mastandrea J, West KW, *et al.* Necrotizing enterocolitis: factors affecting mortality in 101 surgical cases. *Surgery* 1984;96:648–55.
- 16 Molik KA, West KW, Rescorla FJ, *et al.* Portal venous air: the poor prognosis persists. *J Pediatr Surg* 2001;36:1143–5.
- 17 Krueger M, Ramsauer T, Dittrich S, *et al.* Gastric pneumatosis in a neonate with hypoplastic left heart syndrome. *Pediatr Radiol* 2006;36:571.
- 18 Matsui H, Shimokawa O, Kaneko T, *et al.* The pathophysiology of non-steroidal anti-inflammatory drug (NSAID)-induced mucosal injuries in stomach and small intestine. *J Clin Biochem Nutr* 2011;48:107–11.
- 19 Travadi JN, Patole SK, Simmer K. Gastric pneumatosis in neonates: revisited. *J Paediatr Child Health* 2003;39:560–2.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow