CASE REPORT

Hepatic portal venous gas in Crohn's disease

Georgina Cunningham,¹ Georgina Cameron,¹ Peter De Cruz^{1,2,3}¹Department of Gastroenterology, St Vincent's Hospital, Melbourne, Victoria, Australia.²Department of Gastroenterology, Austin Health, Melbourne, Victoria, Australia³Department of Medicine, The University of Melbourne, Austin Academic Center, Melbourne, Victoria, Australia**Correspondence to**Dr Peter De Cruz,
ppdecruz@gmail.com

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SUMMARY

Hepatic portal venous gas (HPVG) is a rare finding that has only been reported previously among 25 patients with Crohn's disease in the English literature. We present a case of a 27-year-old woman with Crohn's disease who presented with fever, abdominal pain and per rectal bleeding and was found to have HPVG at the time of presentation most likely due to an enterovenous fistula. She was managed with intravenous antibiotics, corticosteroids and infliximab and subsequently made a full recovery. HPVG is most likely a manifestation of penetrating Crohn's disease, is overall associated with a low mortality rate and can be managed conservatively in the majority of cases associated with Crohn's disease. Although surgery has been suggested for cases of enterovenous fistulae in the past, this is the first case to suggest that use of antitumour necrosis factor therapy may arrest associated gastrointestinal bleeding and avoid the need for surgery.

BACKGROUND

Hepatic portal venous gas (HPVG) was first described in 1955 in infants with necrotising enterocolitis. Historically it was thought to be an ominous sign indicating likely ischaemic bowel with poor prognosis. However, due to increased sensitivity of imaging modalities, it has been described with increasing frequency in other pathologies, and in these instances the patient may be able to be treated conservatively.¹ HPVG has also been very rarely described in Crohn's disease, with only 25 cases to our knowledge published in the English literature to date. In this paper a case of HPVG in a patient with Crohn's disease associated with an enterovenous fistula is discussed and the literature is reviewed.

CASE PRESENTATION

A 27-year-old woman with a history of Crohn's disease and autoimmune hepatitis presented acutely unwell with fevers, rigours, vomiting, abdominal pain and diarrhoea while being treated with prednisolone for a flare of terminal ileitis. Colonoscopy a month prior had shown mild inflammation involving the distal 8 cm of rectum and severe inflammation with deep ulceration involving the terminal ileum.

INVESTIGATIONS

On admission, inflammatory markers were raised and an abdominal CT scan showed gas locules in the left lobe of the liver (figures 1 and 2), but no obvious perforation.

Figure 1 CT cross-sectional image of hepatic portal venous gas in left lobe of liver.

TREATMENT

The patient initially responded to conservative management with intravenous hydrocortisone, ciprofloxacin and metronidazole and did not show any signs of bowel necrosis. However, on the fourth day of her admission she had significant lower gastrointestinal bleeding associated with haemodynamic instability and required blood transfusion.

Figure 2 CT coronal image of hepatic portal venous gas in left lobe of liver.

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Table 1 Cases of HPVG in Crohn's disease

Case	Prior colonoscopy	Prior barium enema	Duration before detection HPVG	Blunt abdominal trauma	Evidence of sepsis	Observation	Antibiotics	Surgery	Immunosuppression	Outcome
Reiner <i>et al</i> ⁸			NA		✓		✓	✓	Prednisolone	Survived
Sadhu <i>et al</i> ¹¹		✓	At same time			✓				Survived
Gosink ¹²			NA		✓			✓		Survived
Pappas <i>et al</i> ¹³	✓	✓	At same time				✓			Survived
Huycke <i>et al</i> ¹⁴	✓		<1 day		✓		✓	✓	Intravenous methylprednisolone	Survived
Katz <i>et al</i> ¹⁵		✓	At same time				✓		Initially 40 mg prednisolone daily, intravenous steroids, discharged on 20 mg prednisolone daily	Survived
Ajzen <i>et al</i> ⁹			NA		✓			✓		Died
Kirsch <i>et al</i> ¹⁶			NA		✓		✓			Survived
Venugopal <i>et al</i> ¹⁷			NA		✓			✓	5 mg prednisolone daily for erythema nodosum	Survived
Delamarre <i>et al</i> ¹⁸	✓	✓	12 days		✓		✓		5 ASA and prednisolone 30 mg daily	Survived
Al-Jahdali <i>et al</i> ¹⁹			NA		✓		✓	✓	Intravenous methylprednisolone initially, discharged on 30 mg prednisolone	Survived
Hong <i>et al</i> ²⁰			NA		✓		✓	14 days prior		Survived
Hong <i>et al</i> ²⁰			NA				✓			Represented 2 weeks later, laparotomy, died secondary to ischemic gut (CMV)
Hong <i>et al</i> ²⁰			NA		✓		✓			Represented with abdomen pain 4 weeks later, resolution of HPVG but underwent small bowel resection, survived
Brandon <i>et al</i> ²¹			NA		✓			✓		Survived
Nesher <i>et al</i> ²²				✓		✓			5 ASA preaccident	Survived
Niki <i>et al</i> ²³			NA			✓				Survived
Paran <i>et al</i> ²⁴			NA	✓		✓				Survived
Thethy <i>et al</i> ²⁵	✓		3 months		✓	?	?	?	Previously well controlled on mesalazine	Survived
Ng <i>et al</i> ²⁶			NA		✓		✓	✓	Discharged on mesalazine and azathioprine	Survived
Alqahtani <i>et al</i> ²⁷	✓		30 min				✓		Previously on azathioprine	Survived
Salyers <i>et al</i> ²⁸	✓		2.5 h			?	?	?	?	Survived
Lim <i>et al</i> ¹⁰			NA		✓			✓	On azathioprine and 5ASA prior to flare when budesonide started, stabilised on mesalazine and 6-mercaptopurine	Survived
Rao <i>et al</i> ³³	✓		Hours				✓		6-mercaptopurine and adalimumab	Survived
Rao <i>et al</i> ³³	✓		Hours		✓		✓		5 ASA and prednisolone	Survived
Cunningham <i>et al</i> (2014) [†]	✓		Weeks		✓		✓		Discharged on infliximab	Survived
Total=26	Total=9 (34%)	Total=4 (15%)	Average <24 h	Total=2 (8%)	Total=16 (62%)	Total=4 (15%)	Total=15 (58%)	Total=9 (35%)		Mortality rate=8%

ASA, acetylsalicylic acid; CMV, cytomegalovirus; HPVG, hepatic portal venous gas; NA, not applicable. †Cunningham G, Cameron G, De Cruz P Hepatic portal venous gas in Crohn's disease. *BMJ Case Reports* 2014.

OUTCOME AND FOLLOW-UP

CT angiography (performed at the time of bleeding) demonstrated vivid bowel wall enhancement within the terminal ileum in keeping with the known deep ulceration. There was no contrast extravasation to confirm an arterial source of bleeding. The previously identified portal venous gas had resolved. The bleeding settled spontaneously. The patient was discharged home on 6-mercaptopurine, prednisolone and a 2-week course of ciprofloxacin 500 mg twice daily and metronidazole 400 mg three times daily. Unfortunately, she represented 2 weeks later with a repeat episode of lower gastrointestinal bleeding requiring further blood transfusion. Clinical and endoscopic remission was subsequently achieved with standard induction and maintenance infliximab and there was no further gastrointestinal bleeding. Complete mucosal healing assessed endoscopically has been maintained for 3 years since the initial gastrointestinal bleed.

DISCUSSION

The finding of hepatic portal venous gas on radiological imaging has traditionally been regarded as an indicator of ischaemic bowel and prognostic marker associated with high mortality. In a review of 64 cases of HPVG by Leiberman *et al*,² mortality was reported to be as high as 75% and urgent surgical intervention was therefore recommended for all cases unless secondary to ulcerative colitis as all five cases with ulcerative colitis had survived with conservative treatment. However, in 2001, due to an increased number of cases reported that were being managed conservatively, Kinoshita *et al*¹ revisited the literature and found the mortality to be 39%. The difference in mortality rates, and the increasing number of cases of HPVG reported in the literature secondary to non-fatal conditions, is most likely due to the increased availability and sensitivity of imaging modalities, namely CT scanning³ and MRI.⁴ Abdominal ultrasound is also sensitive in detecting HPVG which may at times only be seen on ultrasonography. In relation to abdominal ultrasound the continuous passage of bubble-like echoes, flowing from the portal and intrahepatic portal radicles and inferior vena cava towards the cardiac chambers is akin to passage of bubbles in an aquarium and has prompted the term 'aquarium sign'.^{5 6}

HPVG is defined as linear radiolucencies extending to within 2 cm of the periphery of the liver.⁷ Two main hypotheses have been postulated in relation to how HPVG is formed; first, that gas embolisation may be secondary to elevated intraluminal pressure and mucosal disruption, and second, that gas-producing organisms may be present within the portal venous system secondary to sepsis.² Of those with sepsis, enterovenous fistulisation between the bowel and portal vein has been described in three previous cases.^{8–10} We describe a case with a febrile illness associated with raised inflammatory markers at the time of presentation. Blood cultures were negative most likely because empiric antibiotics had already been started. To the best of our knowledge our case is the fourth ever case of enterovenous fistulisation in Crohn's disease described in the literature. Nonetheless we acknowledge that although the previous case reports of HPVG associated with Crohn's disease have not specifically attributed the development of sepsis to enterovenous fistulation it does remain the most likely underlying mechanism for the development of sepsis in the majority of the previously described cases.

To date the English literature describes 26 cases of HPVG in patients with Crohn's disease including our case (see table 1).^{8–28} Of these, 15 (58%) had prior colonoscopy, barium enema study or blunt abdominal trauma and the time frame between potential mucosal trauma and detection of HPVG was

most often reported within 24 h. The number of cases that showed evidence of sepsis was 16 (62%) and a substantial number were treated with antibiotics (58%). Most of the cases were managed conservatively (73%), the majority with antibiotics, but four cases with observation alone.^{11 22–24} In two cases^{20 23} no predisposing factors were identified and it was presumed Crohn's alone was the cause.

In relation to our case, we believe that the presence of HPVG in association with large-volume gastrointestinal bleeding is also most likely explained by the development of an enterovenous fistula secondary to a microperforation within the known area of terminal ileal ulceration. The pathogenesis behind such cases of haemorrhagic type Crohn's disease previously reported in the literature remains poorly understood.²⁹ Although our patient had undergone colonoscopy, this was weeks prior to presentation, and 67% of patients who had undergone a colonoscopy in this literature review had HPVG reported within 24 h.

Based on the literature the mortality rate among Crohn's disease patients with HPVG appears to be relatively low. Nonetheless two deaths have been reported among the 26 cases both in association with ischaemic gut, one of whom was elderly.^{1 20} In both cases there was radiological evidence of bowel perforation. The accumulating evidence suggests that the management of HPVG should centre on the underlying cause. Surgery is required for patients who have clinical or radiological evidence of free perforation or ischaemic gut³⁰ and earlier recourse to surgery should also be considered in elderly patients.²⁰ However, the majority of cases in Crohn's disease do not require surgery^{10 11 13 15 16 18 20 22–24 27 28} and those who have known risk factors for developing HPVG such as recent enteroscopy, barium enema or blunt trauma may be able to be simply observed. If symptomatic, a trial of antibiotics may be given and if there is no response only then should surgical intervention be considered. In a previous case report by Lim *et al*¹⁰ it was concluded that HPVG caused by an enterovenous fistula is an indication for urgent surgery. In our patient's case having excluded an intra-abdominal collection on abdominal imaging, standard induction therapy with infliximab 5 mg/kg administered at 0, 2 and 6 weeks followed by maintenance therapy every 8 weeks was administered. Empiric antibiotics ciprofloxacin 200 mg intravenous twice daily and metronidazole 500 mg intravenous three times a day were given concurrent until the patient was afebrile and there was a downward trend in her inflammatory markers. Our patient responded to infliximab and concurrent antibiotics and avoided the need for surgery. Antitumour necrosis factor therapy (TNF) therapy has been demonstrated to rapidly induce mucosal healing^{31 32} and this case suggests that among patients with Crohn's disease associated with HPVG, surgery may be able to be avoided provided early anti-TNF therapy is administered to induce mucosal healing.

Patient's perspective

I feel the infliximab saved my life, it worked quickly to restore my quality of life and I was able to resume working etc with in 8 weeks of starting the treatment (this had been something I had been unable to do due to symptoms for at least 4 months prior). Since this episode I have not quite returned to my physical capabilities and still feel quite fragile but considering what I manage to do I am doing very well. Three years later I am in endoscopic remission with no sign of Crohn's.

Learning points

- To the best of our knowledge this is one of only four reported cases of enterovenous fistulisation associated with hepatic portal venous gas (HPVG).
- In the setting of Crohn's disease HPVG most probably represents a manifestation of deep penetrating disease associated with free perforation or enterovenous fistulisation.
- This case reinforces the message that HPVG does not necessarily warrant urgent surgical exploration but may be treated conservatively, especially in Crohn's disease where the mortality rate is relatively low.
- Antibiotics may be of benefit given the underlying association of HPVG with sepsis.
- This case also suggests that antitumour necrosis factor therapy agents may be of benefit in Crohn's patients with HPVG to rapidly induce mucosal healing.

Contributors GCu, GCa and PDC provided patient care and collected data; GCu drafted this manuscript; GCa and PDC contributed to the synthesis of this manuscript; PDC provided study supervision and critically reviewed the manuscript.

Competing interests None.

Patient consent Obtained.

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