

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.elsevier.com/locate/radcr](http://www.elsevier.com/locate/radcr)

## Case Report

# Pediatric milk protein allergy causing hepatic portal venous gas: Case report

Zaid Siddique, DO\*, Ryan Thibodeau, MPH, Abtin Jafroodifar, MD, Ravikumar Hanumaiah, MD

Department of Radiology, State University of New York, Upstate Medical University, Syracuse, NY 13210

## ARTICLE INFO

## Article history:

Received 16 September 2020

Revised 29 October 2020

Accepted 2 November 2020

## Keywords:

Hepatic portal venous gas

Milk protein allergy

Necrotizing enterocolitis

Intramural bowel gas

## ABSTRACT

Hepatic portal venous gas (HPVG) is a rare imaging finding in infants and usually indicative of a severe disease process such as necrotizing enterocolitis, bowel ischemia, or bowel wall rupture / infarction. The diagnosis of HPVG may have serious implications such as parenteral nutrition, antibiotics and even surgery. In this case, we present an 8-week-old male with a history of prematurity presenting with HPVG, later concluded to be caused by milk protein allergy. Milk protein allergy is a rare cause of HPVG, but it should be recognized due to its benignity and potential prevention of unnecessary testing and interventions.

© 2020 Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Introduction

Radiologic evidence of hepatic portal venous gas (HPVG) in an infant is usually associated with a serious underlying abdominal disease necessitating urgent interventional action. When making the diagnosis of HPVG this can have serious implications to the clinician and may suggest serious etiology such as necrotizing enterocolitis, ischemic colitis or bowel wall rupture. It is important however to also consider benign causes of HPVG. In this case we present a very common benign condition of infancy which may also cause HPVG.

Cow's milk allergy (CMA) is one of the most common food allergies amongst young children (2%-5%) and approximately 3% of all newborn infants will suffer from CMA within the first year of life [1]. Ingestion of milk protein leads to in-

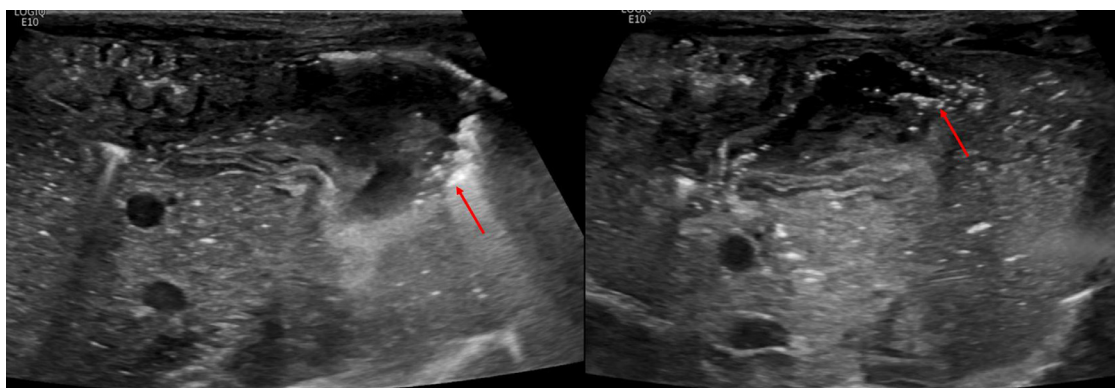
flammation within the intestinal mucosa characterized by eosinophilic and mast cell infiltration [2]. Inflammation and intestinal motility abnormalities disappear after milk protein is eliminated from the diet [2]. We present an unusual case of HPVG in a pediatric patient caused by milk protein allergy.

## Case report

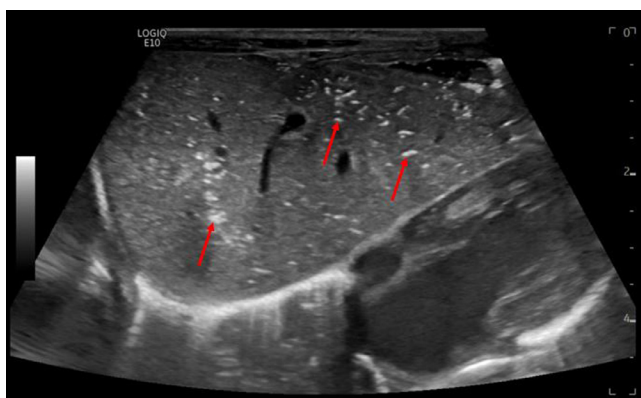
In this case we present an 8-week-old male with a past medical history of prematurity (33 weeks), gastroesophageal reflux disease, vomiting, and poor weight gain. Patient had a reported birth weight of 4 lbs, 2 oz (1.87 kg) and the most recent weight following admission was 4.3 lbs (1.98 kg). Patient was exclusively breastfed and has had issues with emesis since birth. The mother estimates that the patient continues to spit

\* Corresponding author. (Z.Siddique)

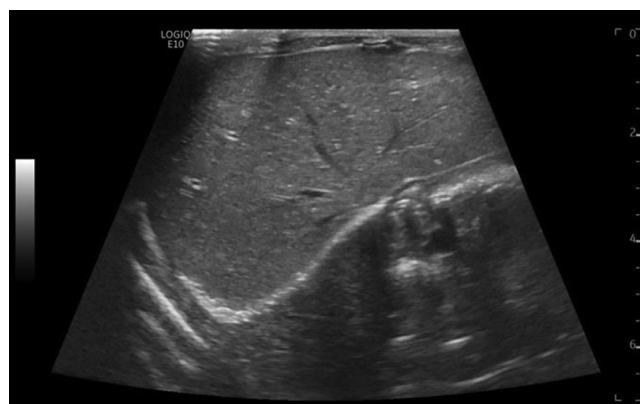
E-mail addresses: [zsiddiqu@upstate.edu](mailto:zsiddiqu@upstate.edu) (Z. Siddique), [thiboder@upstate.edu](mailto:thiboder@upstate.edu) (R. Thibodeau), [jafrooda@upstate.edu](mailto:jafrooda@upstate.edu) (A. Jafroodifar), [HanutmaiR@upstate.edu](mailto:HanutmaiR@upstate.edu) (R. Hanumaiah).<https://doi.org/10.1016/j.radcr.2020.11.002>1930-0433/© 2020 Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)



**Fig. 1 – Ultrasound of the pylorus in the transverse plane. There are multiple echogenic foci (red arrow) present within the wall of the stomach consistent with intramural pneumatosis.**



**Fig. 2 – Ultrasound of the liver in the transverse plane showing multiple echogenic foci within the liver consistent with hepatic portal venous gas.**



**Fig. 3 – Ultrasound of the liver in the transverse plane showing near complete resolution of echogenic foci which were previously seen.**

up one-third to one-half of every feed despite reflux precautions and starting on omeprazole 2 weeks prior. The patient initially presented to their primary care provider and underwent ultrasound for suspected hypertrophic pyloric stenosis which was ruled out; however, it did show echogenic foci in the liver suggestive of portal venous gas.

On arrival to the hospital, the patient was mildly hypothermic and labs were significant for hyperbilirubinemia with a total bilirubin of 3.0 mg/dL and direct bilirubin of 0.4 mg/dL. All other labs were within normal limits. The patient was once again suspected to have hypertrophic pyloric stenosis or a structural anomaly causing gastroesophageal reflux. A repeat ultrasound to assess the pylorus showed a normal appearing pyloric sphincter with contents flowing freely from the stomach into the duodenum. An incidental finding of multiple echogenic foci consistent with air was seen within the liver, portal vein branches, and stomach wall (Figs. 1 and 2). The differential diagnosis of necrotizing enterocolitis, ischemic bowel, and bowel rupture was considered; however, the patient had a benign physical examination and extensive workup for sepsis including labs and cultures were negative. Given the low suspicion for sepsis the patient was not started on antibiotics. The patient was also evaluated for possible esophageal and upper gastrointestinal (GI) structural anomaly

with fluoroscopic upper GI series; which showed unobstructed contrast flow through the upper GI tract and no malrotation. Newborn metabolic screening tests were performed and negative.

During the hospital stay, the patient was noted to have a bloody bowel movement which was confirmed with fecal occult blood test. The patient was suspected of having a milk protein allergy despite being exclusively breastfed, likely related to the mother's consumption of cow milk protein and bovine protein. The mother was counselled on eliminating cow milk protein from her diet however, she found this impractical and decided to switch to hydrolyzed protein formula. Once switching to hydrolyzed formula, the patient had decreased spit ups and resolution of blood in the stool. A repeat ultrasound was done a few days later and showed near complete resolution of air within the liver and portal vein (Fig. 3).

## Discussion

HPVG in infancy is a rare diagnosis and commonly associated with severe disease processes such as necrotizing enterocol-

itis (NEC), bowel ischemia, bowel infarction, and bowel wall rupture. However, less severe disease processes such as hypertrophic pyloric stenosis and milk protein allergy can also cause HPVG.

NEC is the most common GI condition in premature infants, occurring within the first few days following birth with approximately 90% of affected neonates developing it within 10 days [3]. NEC is a multifactorial disease that occurs through hypoxic ischemic injury of a neonate's immature GI tract and subsequent alterations in the microbiologic intestinal flora [4]. GI hypoperfusion in preterm infants occurs when blood is shunted away from the bowels to better aid in the perfusion of critical organs. This leads to proliferation of pathogenic intestinal flora secondary to breakdown of the mucosal barrier, causing mucosal and/or transmural gas. The etiologies of GI hypoperfusion are variable, but may include patent ductus arteriosus, sepsis, polycythemia, in utero cocaine exposure, perinatal or postnatal asphyxia, respiratory distress syndrome, congenital heart disease, umbilical catheter use, and exchange transfusions [5]. Urgent diagnosis of NEC is needed as patients often require parenteral nutrition, antibiotics, and surgery. The best diagnostic imaging clue includes dilated bowel loops with pneumatosis, portal venous gas, and free intraperitoneal air. The diagnosis of NEC needs to be quick and accurate in order to help treat the patient [3].

Air is often visualized using abdominal ultrasound or, in severe cases, on abdominal radiographs. On ultrasound, HPVG appears as hyperechogenic foci within the portal veins or liver parenchyma in a singular or linear arrangement. While ultrasound is frequently the preliminary study of choice because it is rapid, inexpensive, and lacks radiations; A CT scan is the gold standard for HPVG despite the comparable sensitivity and accuracy to ultrasound [6]. Not only does CT allow for the detection of small volumes of gas (particularly on the lung-window setting), but it may also provide information on the etiology of the HPVG [6].

There are several proposed mechanisms of HPVG. The most prevalent and accepted theories include migration of air bubbles through the portal capillaries due to increased intestinal loop pressure, presence of gas-producing bacteria in inflammatory areas within bowel (such as enteritis), and breakdown of the intestinal mucosal membrane with subsequent migration of gas-producing bacteria within the mucosal wall [6]. The hydrogen gas produced within the bowel wall after bacterial translocation leads to pneumatosis intestinalis which is seen as lucencies on radiograph within the bowel wall [4]. The hydrogen gas then travels from the bowel wall through the mesenteric veins to the portal vein, intrahepatic branches and eventually to the peripheral liver parenchyma in a non-dependent fashion, predominantly in the left lobe and anterior right lobe [5].

It is important to consider benign causes of HPVG in infants such as milk protein allergy. CMA is one of the most common food allergies amongst young children (2%-5%) and approximately 3% of all newborn infants will suffer from CMA within the first year of life [1]. Milk allergy leading to HPVG is rarely reported in literature. In our case, milk protein allergy was determined to be the cause of HPVG, by excluding other causes. Soon after cessation of ingesting milk protein allergen, the patient's symptomatology and ultrasonographic evidence

of HPVG resolved. While symptoms typically occur with cow's milk, this is also seen with breast milk fortified with cow's milk and soy-based formulas (soy protein allergy) [7]. Breast-feeding mothers may be required to eliminate cow milk protein, bovine protein (milk and protein) and occasionally other protein sources such as soy from their diet in order to continue breastfeeding [8]. In cases of milk protein allergy leading to pneumatosis intestinalis, it rarely progresses to bloody stools and necrotic bowel [7]. These symptoms are extremely rare in infants younger than 6 weeks of life and those weighing less than 2 kg. Despite no known mechanism of the development of pneumatosis intestinalis in the setting of milk allergy, the cause may be due a local inflammatory reaction within the bowel, thereby resulting in introduction of luminal gas into the bowel wall with subsequent migration of this air into the portal system.

The presence of HPVG in an infant is usually concerning given the associated morbidity and mortality and frequent necessity of immediate intervention. However, as our case demonstrates HPVG can be from a benign cause and may not require surgical evaluation and/or treatment. Besides food allergy, other causes of HPVG in a pediatric patient that may not necessitate surgery includes acute enterocolitis, acute viral gastroenteritis (rotaviruses and adenoviruses), anemia, post-operative changes from bowel surgery, metabolic liver disease leading to hepatic injury, and ventricular septal defects [9]. While ultrasound in these patients showed signs of HPVG, there was complete resolution of the HPVG without the need for surgery [9]. While it is imperative to work up HPVG for the usual serious etiology, benign causes of HPVG including milk protein allergy, should be also kept in mind. These benign causes of HPVG should be considered if severe bowel disease is not apparent or if the patient is otherwise asymptomatic. Recognizing benign causes of HPVG may prevent unnecessary testing and interventions.

---

## Conclusion

The presence of HPVG in infants is often concerning for severe GI pathology, such as necrotizing enterocolitis, bowel ischemia or bowel rupture. These conditions often require extensive medical interventions such as parenteral nutrition, antibiotics and even surgery. However, it is important to consider benign causes of HPVG which do not require significant medical intervention. Milk protein allergy is a rare cause of HPVG, but it should be recognized in infants due to its benignity and potential in preventing unnecessary testing and interventions.

---

## Patient Consent Statement

No consent was obtain for this case report since this is a retrospective study with no patient identifiers.

Formal consents are not required for the use of entirely anonymised images from which the individual cannot be identified- for example, xrays, ultrasound images, pathology

slides or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.

## REFERENCES

- [1] Terheggen-Lagro SWJ, Khouw IMSL, Schaafsma A, Wauters EAK. Safety of a new extensively hydrolysed formula in children with cow's milk protein allergy: a double blind crossover study. *BMC Pediatr* 2002;2(1):10. doi:[10.1186/1471-2431-2-10](https://doi.org/10.1186/1471-2431-2-10).
- [2] Borrelli O, Barbara G, Di Nardo G, Cremon C, Lucarelli S, Frediani T, et al. Neuroimmune interaction and anorectal motility in children with food allergy-related chronic constipation. *Am J Gastroenterol* 2009;104(2):454–63. doi:[10.1038/ajg.2008.109](https://doi.org/10.1038/ajg.2008.109).
- [3] Epelman M, Daneman A, Navarro OM, Morag I, Moore AM, Kim JH, et al. Necrotizing enterocolitis: review of state-of-the-art imaging findings with pathologic correlation. *Radiographics* 2007;27(2):285–305. doi:[10.1148/rg.272055098](https://doi.org/10.1148/rg.272055098).
- [4] Thompson Alecia M, Bizzarro Matthew J. Necrotizing enterocolitis in newborns. *Drugs* 2008;68(9):1227–38. doi:[10.2165/00003495-200868090-00004](https://doi.org/10.2165/00003495-200868090-00004).
- [5] Abboud B, El Hachem J, Yazbeck T, Doumit C. Hepatic portal venous gas: physiopathology, etiology, prognosis and treatment. *World J Gastroenterol* 2009;15(29):3585–90. doi:[10.3748/wjg.15.3585](https://doi.org/10.3748/wjg.15.3585).
- [6] Nelson AL, Millington TM, Sahani D, Chung RT, Bauer C, Hertl M, et al. Hepatic portal venous gas: the ABCs of management. *Arch Surg* 2009;144(6):575–81 discussion 581. doi:[10.1001/archsurg.2009.88](https://doi.org/10.1001/archsurg.2009.88).
- [7] Gordon PV, Swanson JR, Attridge JT, Clark R. Emerging trends in acquired neonatal intestinal disease: is it time to abandon Bell's Criteria? *J. Perinatol.* 2007;27(11):661–71. doi:[10.1038/sj.jp.7211782](https://doi.org/10.1038/sj.jp.7211782).
- [8] Brill Herbert. Approach to milk protein allergy in infants. *Can. Fam. Physician* 2008;54(9):1258–64 PMID: 18791102; PMCID: PMC2553152.
- [9] Barczuk-Fałęcka M, Bombiński P, Majkowska Z, Brzewski M, Warchol S. Hepatic portal venous gas in children younger than 2 years old - radiological and clinical characteristics in diseases other than necrotizing enterocolitis. *Pol J Radiol* 2017;82:275–8 Published 2017 May 19. doi:[10.12659/PJR.89999](https://doi.org/10.12659/PJR.89999).