# Variceal Hemorrhage in the Setting of Chronic Non-Cirrhotic Portal Hypertension After Neonatal Instrumentation

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Case in Point

**Introduction.** A 43-year-old woman with longstanding thrombocytopenia previously attributed to an idiopathic thrombocytopenia purpura secondary to prior *Helicobacter pylori* infection, presented to the emergency department with acute-onset large volume hematemesis concerning for portal venous hypertension.

Portal venous hypertension (PVH) can lead to rapid, life-threatening gastrointestinal bleeding. Although it is most often a consequence of liver cirrhosis in the developed world, a spectrum of non-cirrhotic etiologies has been identified in the pre-, intra-, and post-hepatic systems including portal vein thrombosis, polycystic liver disease, autoimmune cholangiopathies, and right sided heart failure[1]. While non-cirrhotic portal hypertension (NCPH) only accounts for 3% to 6% of patients with portal hypertension in Western countries like the United States, the incidence is on the rise[3]. There is a growing body of literature examining iatrogenic causes, particularly umbilical vein central access which can lead to portal vein disease in neonates or chronic PVH during childhood with widely varying reported incidences ranging 1.3% to 43% of patients undergoing umbilical vein catheterization[2]. Here, we present an atypical case of adult onset NCPH and variceal bleeding due to prolonged umbilical vein catheterization in early infancy, highlighting a previously unknown complication and the need for further investigation.

**Case Description.** The patient presented to the emergency department with hematemesis following 24 hours of abdominal discomfort self-treated with bismuth subsalicylate. She had no known history of chronic liver disease, nor did she have any identifiable risk factors for common causes of cirrhosis. On evaluation, she was tachycardic but otherwise hemodynamically stable. Her exam was notable for dried blood along the corner of her mouth, splenomegaly, and mild epigastric tenderness, but no hepatomegaly, peritonitis, caput medusae, or fluid wave.

Laboratory tests revealed anemia to hemoglobin of 9 g/dL (reference range 12-15.3 g/dL), thrombocytopenia of 111 g/dL (reference range 150-450 g/dL), an elevated BUN-to-creatinine ratio, coagulopathy with elevated international normalized ratio to 1.3 (reference range 0.8-1.2), and hypoalbuminemia to 2.9 g/dL (reference range 3.5-5 g/dL). Due to concern for a portal hypertension-related bleed, she was started on octreotide and antibiotics, resuscitated judiciously with 1 unit of packed red blood cell, and admitted to the step-down unit for further monitoring.

Urgent upper endoscopy demonstrated stigmata of portal hypertension including recent bleeding from high-risk esophageal varices, which were banded. Computed tomography (CT) abdomen and pelvis showed multiple large esophageal varices and splenomegaly, but a normal liver. Magnetic resonance imaging (MRI) noted diminished portal venous flow initially thought to represent thrombosis. However, CT venogram revealed an obliterated portal vein with no thrombosis, along with severe periesophageal thoracic and abdominal varices, perisplenic and peripancreatic vascular congestion, and significant periportal vein collateralization.

Previous extensive autoimmune and hypercoagulable workup performed during her initial thrombocytopenia evaluation had been negative, and given the absence of confirmed thrombosis, no further hypercoagulability work was pursued. Transjugular liver biopsy with pressure measurements was obtained. The portosystemic pressure gradient was 2, indicating no intrahepatic portal hypertension. Liver biopsy revealed minimal fibrosis and no evidence of cirrhosis.

Upon broad questioning related to potential risk factors, she disclosed that she was born prematurely and had a prolonged neonatal intensive care unit stay of more than 6 weeks, with multiple weeks of umbilical vein catheterization for hyperbilirubinemia, further complicated by sepsis. The prolonged umbilical vein catheterization was then the presumed cause of her abnormal anatomy. She was placed on a non-selective beta blocker and discharged from the hospital. She required rebanding 4 weeks later but has had negative surveillance endoscopy since, with no further bleeding in the last 2 years while on non-selective beta blocker monotherapy.

**Discussion.** Noncirrhotic portal vein hypertension (NCPH) is defined as intrahepatic portal hypertension in the absence of cirrhosis[3]. While this is a diagnosis of exclusion and there is no specific test to confirm NCPH, the current criteria for NCPH include signs of portal hypertension, and histological exclusion of cirrhosis. Recognized signs of portal hypertension include gastric-esophageal varices and variceal bleeding, systemic collateralization on imaging, ascites, thrombocytopenia, and splenomegaly[3].

Our patient's chronic thrombocytopenia, splenomegaly, varices with hemorrhage, and presence of chronic collateralization in the setting of a non-cirrhotic liver biopsy meets the diagnostic criteria of NCPH. There are many causes of NCPH, including chronic infections like Hepatitis B or C, medications and toxins such as azathioprine, autoimmune conditions such as Crohn disease or autoimmune hepatitis, prothrombotic conditions like antiphospholipid syndrome, and genetic predispositions including Turners or HLA-DR3. Given that our patient had none of these risk factors, we argue that her NCPH and eventual variceal hemorrhage are related to prolonged umbilical vein catheterization leading to obliteration of the portal vein. There are geographical differences in mean age, occurrence rates, and gender predominance for NCPH, thought to be secondary to varying socioeconomic conditions[1]. In Western countries, there are studies showing mean age at

diagnosis of 42 years, with significant variation within the first standard deviation (±19 years) and slight female predominance[1,5]. This differs from developing countries, particularly India, where there is a male predominance and mean age of 30-35 years[1]. While variceal bleeding is the most common presenting symptom of NCPH, most patients are asymptomatic at diagnosis and identified during workup for idiopathic thrombocytopenia or splenomegaly[5].

Our patient, a 43-year-old woman, fits the typical NCPH patient population in Western countries. While the diagnosis was made after presenting with variceal hemorrhage, she was previously evaluated for chronic thrombocytopenia that was attributed to idiopathic thrombocytopenia purpura secondary to a prior *Helicobacter pylori* infection. We argue that this is more likely reflective of chronic undiagnosed portal hypertension, again fitting the classic NCPH picture.

While NCPH in the fifth decade of life secondary to prolonged umbilical vein catheterization has so far not been established in the literature, it is consistent with a growing body of evidence suggesting a link between perinatal interventions involving the umbilical vein and subsequent complications of the portal-hepatic system[2]. More common acute injuries include portal vein thrombosis, necrotizing hepatic injury from irritating drugs, and direct injury to surrounding structures such as the colon, liver parenchyma, and even the heart from traumatic misplacement[2]. When there is injury to the portal-hepatic system, it typically presents during childhood with a mean age of 4-years-old, with one-third of patients experiencing acute gastrointestinal bleeding[4]. The delay in this patient's presentation was likely due to her extensive chronic collateralization, prolonging her compensation. This is further supported by her low portosystemic pressure gradient which, despite esophageal variceal rupture, was only 2mmHg, suggesting a longstanding and extensive periportal collateral network.

As the incidence of neonatal umbilical vein catheterization and other interventions grows[4], it is likely that the adult population with chronic injuries to their portal-hepatic system, including non-cirrhotic portal venous hypertension, will grow as well. Future studies are needed to examine their long-term impacts, and clinicians will need to include perinatal and pediatric history of hospitalization and interventions in their diagnostic evaluation of non-cirrhotic portal hypertension.

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