Rare is now common-newer diagnostic modalities revealing Neonatal Portal Vein Thrombosis frequently

Ramesh Choudhary[1*], Dhanraj Bagri[2], Romesh Gauttam[3], Vivek Kumar Athwani[4]

[1]Associate Professor, [2,3]Assistant Professor, [4]Medical Officer, Dept. of Pediatrics, SMS Medical College, Jaipur, Rajasthan, India

***Corresponding Author: Ramesh Choudhary**
Email: drrameshchoudhary@yahoo.co.in

Abstract
Neonatal portal vein thrombosis (PVT) previously described rarely due to diagnostic modalities and awareness among clinicians. In about 50% of children with PVT, etiology remains unknown, Mechanical and chemical damage to a vessel wall by a catheter is believed to initiate the thrombotic process, making UVC placement the major risk factor for PVT. Application of unhygienic substance like cow dung, ghee and local sepsis are preventable causes of PVT.

Keywords: Neonate, Portal Vein, Abdominal Distension, Umbilical Sepsis.

Introduction
Neonatal portal vein thrombosis (PVT) previously described by Thompson and Sherlock as exceedingly rare[1] is being revealed frequently now a days. Incidence varies from 1 in 100,000 live births[2] to 36 per 1000 NICU admissions.[3] Despite the reported rarity in the neonatal setting, PVT is the major cause of extrahepatic portal hypertension and gastrointestinal bleeding in children.[4] Portal vein occlusion associated with small periportal collaterals is termed as cavernous transformation of the portal vein (CTPV).[5]

The etiology of neonatal PVT differs from that in children and adults. In adults PVT is most commonly secondary to cirrhosis.[6] PVT is a result of liver transplantation, intraabdominal sepsis, splenectomy, sickle cell anemia, and antiphospholipid antibodies in older children. In about 50% of children with PVT, etiology remains unknown.[7] Mechanical and chemical damage to a vessel wall by a catheter is believed to initiate the thrombotic process, making UVC placement the major risk factor for PVT.[8]

There have been reports of thrombophilia associated with PVT in neonates and children. Case series have reported factor V Leiden, prothrombin gene mutation, protein C deficiency, protein S deficiency, antithrombin deficiency, increased factor VIII, methylene tetrahydrofolate reductase (MTHFR) variants with elevated homocysteine, and elevated lipoprotein.[9]

The long term follow up and clinical importance of thrombosis detected on ultrasound in asymptomatic neonates are not detailed in literature. The spontaneous regression of catheter-related thrombi detected on ultrasound has been reported.[10] If the PVT does not resolve, It may transform into a cavernoma, with dilated pancreatico-duodenal and pre-biliary veins, secondary to portal hypertension.[8] There may be an absence of clinical and laboratory signs with PVT in the neonate. Thrombocytopenia may be seen at the time of diagnosis, but is not specific for PVT.[3] Consumption from the thrombosis or the concomitant clinical risk factors for thrombosis, such as sepsis, may explain the low platelet count in the acute phase. In the late chronic stage, a low platelet count may be secondary to hypersplenism with portal hypertension.[11]

In contrast to adults, liver function is usually normal in children presenting with PVT. There can be mild liver biochemical abnormalities in children with PVT.[8] The extent to which similar abnormalities occur in neonates is less clear. Nine out of 133 (7%) neonates had abnormal liver enzymes as the indication for ultrasound which identified the PVT.[3] A grading system for PVT based on ultrasound findings has been suggested. Grade 1 PVT was defined as non-occlusive PVT with normal liver parenchyma; grade 2 as

occlusive PVT with normal liver parenchyma; and grade 3 as occlusive PVT with ultrasonographic abnormalities of the liver parenchyma.[3]

Investigational radiographic studies in the diagnosis of PVT include abdominal ultrasound, computed tomography (CT), angiography, and magnetic resonance imaging (MRI). Accurate interpretation of the findings identified by each of these modalities can be difficult, especially in the neonates. Ultrasonography has been supplanted by Doppler ultrasound, which improves assessment by providing information on portal vein patency and blood flow characteristics. Doppler ultrasound and especially color flow Doppler is useful for confirming the changes in flow patterns around the thrombus and the resumption of normal flow pattern in follow-up imaging as the thrombosis resolves.[11]

A CT scan accurately identifies PVT and the presence of collateral vessels but requires exposure to radiation and the use of intravenous contrast materials. Similarly, angiogram requires exposure to radiation and intravenous contrast material. MRI performs as least as well or better than CT in diagnosing PVT, without the issues of ionizing radiation exposure and intravenous contrast.[11] In comparing the efficacy of imaging techniques in identifying portal vein patency, Weinreb et al. found MRI superior to CT in visualizing hepatic architecture and vascular anatomy and patency in 27 children undergoing evaluation of suspected liver disease.[11]

The role of anticoagulation in PVT management is unclear. There is an absence of prospective data on anticoagulation in the literature. Multiple strategies have been reported in the literature from observation, anticoagulation, and thrombolysis. The indications for anticoagulation treatment included the presence of a second, occlusive thrombus with liver parenchymal changes or involving two branches of the portal vein, post cardiac surgery. Dosages and lengths of treatment varied significantly.[3] Treatment of symptomatic acute PVT, extending to the main portal vein, by means of regional streptokinase infusion has been reported.[12] After initial treatment with UFH or LMWH, vitamin K antagonists (VKA) with a target INR of 2-3 could theoretically be used to continue anticoagulation therapy. However, the use of warfarin in the neonatal period is problematic. Formula-fed infants will receive large amounts of vitamin K, and will be warfarin resistant. Dosing becomes difficult as there is no commercially available liquid formulation of warfarin.[13]

Given the anticipated difficulties, anticoagulation with warfarin would not be recommended in the neonatal period. LMWH may be preferable to UFH if anticoagulation therapy is used to treat neonatal PVT, given the predictable pharmacokinetics, reduced monitoring requirements, and possibly decreased rate of major bleeding. In a randomized, controlled trial of therapeutic anticoagulation in children, LMWH therapy was compared with UFH and VKA for the treatment of venous thromboembolic events in children. There was a major bleeding rate of 12.5% in the UFH/ VKA versus 5.6% in the LMWH arm.[14] A major bleeding rate of 0.7% of children treated with the low molecular weight heparin, enoxaparin, has been reported.[15]

To Summarize, Neonatal PVT is being revealed frequently due to sophisticated and advanced imaging technologies .There may be no symptoms or laboratory abnormalities. Some patients may have accompanying thrombocytopenia or liver serum biochemical abnormalities. As a result of the lack of symptoms, the diagnosis may not be suspected. Umbilical catheterization and sepsis are risk factors for neonatal PVT. Thrombophilia may be a contributing risk factor. However, neonatal PVT may still occur in the absence of risk factors.Neonates should be followed for at least 5 years after PVT to monitor for the development of portal hypertension in an attempt to avoid presentation with gastrointestinal hemorrhage in childhood. The role of anticoagulation in the management of neonatal PVT is unclear. The role of thrombophilia in neonatal PVT is unclear. Application of ghee or use of herbal preparations should be discouraged.

Conflict of Interest

None.

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References

1. Thompson EN, Sherlock S. The aetiology of portal vein thrombosis with particular reference to the role of infection and exchange transfusion. *Q J Med* 1964;33:465-80.
2. Heller C, Schobess R, Kurnik K, et al. Abdominal venous thrombosis in neonates and infants: role of prothrombotic risk factors e a multicentre case-control study. For the Childhood Thrombophilia Study Group. *Br J Haematol* 2000;111:534-9.
3. Morag I, Epelman M, Daneman A, et al. Portal vein thrombosis in the neonate: risk factors, course, and outcome. *J Pediatr* 2006;148:735-9.
4. Alvarez F, Bernard O, Brunelle F, Hadchouel P, Odievre M, Alagille D et al. Portal obstruction in children. I. Clinical investigation and hemorrhage risk. *J Pediatr* 1983;103:696-702.
5. Fisher MR, Wall SD, Hricak H, McCarthy S, Kerlan RK. Hepatic vascular anatomy on magnetic resonance imaging. *Am J Roentgenol* 1985;144:739-46.
6. Wilson KW, Robinson DC, Hacking PM. Portal hypertension in childhood. *Br J Surg* 1969;56:13-22.
7. Brady L, Magilavy D, Black DD. Portal vein thrombosis associated with antiphospholipid antibodies in a child. *J Pediatr Gastroenterol Nutr* 1996;23:470-3.
8. Kim JH, Lee YS, Kim SH, Lee SK, Lim MK, Kim HS et al. Does umbilical vein catheterization lead to portal venous thrombosis? Prospective US evaluation in 100 neonates. *Radiol* 2001;219:645-50.
9. Uttenreuther-Fischer MM, Vetter B, Hellmann C. Paediatric thromboembolism: the influence of non-genetic factors and the role of activated protein C resistance and protein C deficiency. *Eur J Pediatr* 1997;156:277e81.
10. Neonatal portal vein thrombosis: Diagnosis and management S. Williams, A.K.C. Chan / Seminars in Fetal & Neonatal Medicine 16 (2011) 329-339
11. Stringer DA, Krysl J, Manson D, Babiak C, Daneman A, Liu P. The value of Doppler sonography in the detection of major vessel thrombosis in the neonatal abdomen. *Pediatr Radiol* 1990;21:30-3.
12. Rehan VK, Cronin CM, Bowman JM. Neonatal portal vein thrombosis successfully treated by regional streptokinase infusion. *Eur J Pediatr* 1994;153:456-9.
13. Veldman A, Nold MF, Michel-Behnke I. Thrombosis in the critically ill neonate: incidence, diagnosis, and management. *Vasc Health Risk Manag* 2008;4:1337-48.
14. Massicotte P, Julian JA, Gent M. An open-label randomized controlled trial of low molecular weight heparin compared to heparin and coumadin for the treatment of venous thromboembolic events in children: the REVIVE trial. *Thromb Res* 2003;109:85-92.
15. Ignjatovic V, Najid S, Newall F, Summerhayes R, Monagle P. Dosing and monitoring of enoxaparin (low molecular weight heparin) therapy in children. *Br J Haematol* 2010;149:734-8.

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