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Radiology Section

Ultrasound and Computed Tomography Features of Non Cirrhotic Portal Hypertension caused due to Non Cirrhotic Portal Fibrosis and Extrahepatic Portal Vein Obstruction: A Retrospective Study

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ABSTRACT

Introduction: Non Cirrhotic Portal Hypertension (NCPH) encompasses a wide range of disorders that are characterised by increased portal pressure with the absence of cirrhosis of liver. The disorders are classified anatomically based on the site of blood flow obstruction into prehepatic, hepatic and posthepatic causes. These numerous and variable aetiological factors and the lack of standardised diagnostic criteria, makes NCPH under-recognised both clinically and pathologically and often being falsely labelled as cryptogenic cirrhosis. Therefore, it is important for radiologists to be aware of the imaging features that constitute NCPH for its early recognition, so that appropriate management can be carried out.

Aim: To assess the distinct ultrasound and Computed Tomography (CT) features of the two main causes of NCPH: Non Cirrhotic Portal Fibrosis (NCPF) and Extrahepatic Portal Venous Obstruction (EHPVO).

Materials and Methods: This retrospective observational study included all radiologically diagnosed cases of NCPH who underwent ultrasound and CT examination at the Institution between June 2020-June 2021. A total of 10 patients met the inclusion criteria. The various imaging features of NCPF and EHPVO were analysed and tabulated.

Results: The study showed male predominance with males and females being seven and three, respectively. The mean age of the patients in the study was 35.1 years. The common cause in both NCPF and EHPVO was idiopathic. The most characteristic imaging finding in EHPVO was cavernous transformation of the portal vein seen in all cases and that in NCPF being dilatation of the spleno-portal axis and mural thickening of the main portal vein seen in all the cases.

Conclusion: The present study demonstrated the characteristic imaging features of NCPF and EHPVO which are leading cause of NCPH, facilitating radiologist to identify the conditions and not label cases with Portal Hypertension (PHT) as cryptogenic cirrhosis.

Keywords: Cavernous transformation of portal vein, Portal biliopathy, Portosystemic shunts, Spleno-portal axis

INTRODUCTION

The NCPH encompasses a wide range of disorders. These disorders are classified anatomically by the site of resistance to blood flow as prehepatic, hepatic and posthepatic causes, with the hepatic causes further classified into presinusoidal, sinusoidal and postsinusoidal. Amongst these various aetiological factors of NCPH, the two significant reasons are NCPF and EHPVO [1]. PHT is a late manifestation in majority of the aetiological factors, however in NCPF and EHPVO, PHT is the only and predominant manifestation [1]. EHPVO being a childhood disorder is characterised by chronic obstruction of the extrahepatic portal vein with or without involvement of the intrahepatic portal vein branches, splenic vein and/or the superior mesenteric vein. The term EHPVO implies chronicity and is characterised by cavernous transformation of the portal vein [2]. EHPVO is further common in rising countries affecting children and young adults and is the most common cause of paediatric PHT. The aetiology of majority of the cases is idiopathic despite a thorough laboratory and clinical work-up [3]. The causes in paediatric population include infections, abdominal trauma, umbilical vein cannulation, congenital anomaly such as congenital portal vein stenosis/atresia and prothrombotic states. The causes in adult population include prothrombotic state, abdominal trauma/surgery, local inflammatory conditions such as pancreatitis and liver abscess [2].

NCPF comprises a group of diseases of unknown aetiology that are characterised by fibrosis of the small and medium branches of the portal vein resulting in increased portal pressure in the absence of cirrhosis of liver. It is a vascular condition of the liver wherein the pressure gradient between the portal vein and the intrabdominal inferior vena cava is greater than 5 mmHg [4]. NCPF, similar to EHPVO, is also more common in the developing countries than in developed countries. The exact aetiology of NCPF in most cases is unknown, however, infection and prothrombotic states have been implicated as a common cause in the eastern and western population respectively. Other causes include exposure to trace metals and chemicals such as chronic exposure to arsenic and vinyl chloride polymers, autoimmune and genetic factors [5]. With numerous and variable aetiological factors and lack of standardised diagnostic criteria, NCPH is under-recognised both clinically and pathologically and often being falsely labeled as cryptogenic cirrhosis. Therefore, it is important for radiologists to be aware of the imaging features that constitute NCPH for its early recognition, so, appropriate management can be instituted. The purpose of the present study was to assess the distinct ultrasound and CT features of the two main causes of NCPH: NCPF and EHPVO.

MATERIALS AND METHODS

This retrospective observational study was carried out on patients that were radiologically diagnosed as NCPH within the period of June 2020 to June 2021 in MVJ Medical College and Research Hospital, Hoskote, in rural India. Data collection

and analysis was done in the same duration i.e., June 2020 to June 2021.

Inclusion criteria: Cases of NCPH with NCPF and EHPVO as the cause.

Exclusion criteria: Cases of PHT due to cirrhosis of liver, cases of NCPH due to other causes.

A total of 10 patients were included in the study after the inclusion and exclusion criteria were fulfilled. All patients underwent ultrasound and CT at the Institution, ultrasound examination was carried out with GE Voluson E6 machine and CT (unenhanced and contrast-enhanced series) was performed with a GE BRVIO CT scanner 16-slice. Contrast administration was i.v. injection of 1.5 mL/kg of non ionic contrast medium, Iohexol, at 300–400 mg/mL through a power injector at a rate of 3-3.5 mL/s.

Imaging analysis

The CT images were interpreted by two experienced radiologists, both with an experience of at least five years in interpreting CT. The ultrasound and CT features that have been accepted in literature as associated with NCPH were analysed in the cases. The imaging features that were analysed in EHPVO include: cavernous transformation of the portal vein, portal biliopathy, hepatic changes, splenic changes, presence of porto-systemic collaterals and ascites [2]. In NCPF, the features include: features of PHT, mural thickening of the portal vein, intrahepatic portal vein abnormalities, hepatic changes, splenic changes and ascites [5].

STATISTICAL ANALYSIS

The data obtained from the study was tabulated in Microsoft Excel (2019 version) and the results were expressed in percentages and the data was depicted in tables.

RESULTS

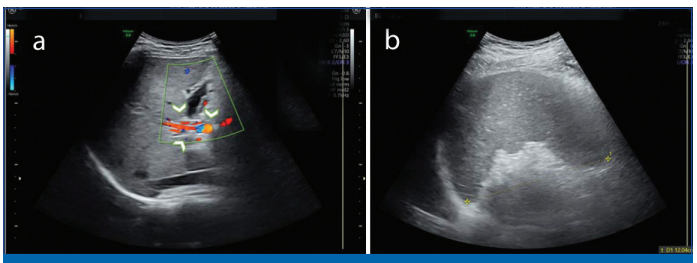
Of the 10 patients who met the inclusion criteria, five patients had NCPF and five patients had EHPVO. The mean age of patients with NCPF in the study was 42.4±17 years and that in EHPVO 27.8±8.5 years, wherein the presentation of EHPVO occurred more than a decade (14.6 years) earlier then NCPF. There was male predominance in both the conditions. The causes of NCPF in the study population included idiopathic causes (n=3), prothrombotic state (n=1) and hepatic abscess (n=1). The cause of EHPVO was idiopathic (n=2), local inflammatory causes like pancreatitis (n=1) and multiple hepatic abscesses (n=1) and prothrombotic state (n=1). All patients included in the present study had well preserved liver function, except for one patient with clinical features of jaundice had raised levels of direct bilirubin and alanine aminotransaminase/aspartate aminotransferase levels [Table/Fig-1].

Characteristic	NCPF (n=5)	EHPVO (n=5)
Age (years) Mean±SD	42.4±17	27.8±8.5
Sex		
Male	3	4
Female	2	1
Clinical features		
Gastrointestinal bleeding	2	2
Left hypochondrium pain due to splenomegaly	5	4
Ascites	2	4
Jaundice	0	1
Anaemia	0	0
Cause		
Idiopathic	3	2
Prothrombotic event	1	1
Local inflammatory	1	2
Blood tests		
Deranged liver function test	-	(N=1)
Direct bilirubin (mg/dL)	-	2.5
Alanine aminotransaminase (U/L)	-	78.2
Aspartate aminotransferase (IU/L)	-	81.0
Haemoglobin (g/dL)	10.7 (8.2-15.9)	10.28 (7.8-13.2)
Platelet count (×10^5/mL)	0.87 (0.58-1.2)	0.84 (0.64-1.0)

[Table/Fig-1]: Characteristics of patients with Non Cirrhotic Portal Hypertension (NCPH).

Features of EHPVO	USG, n (%)	CT, n (%)
Cavernous transformation of the PV	5 (100)	5 (100)
Porto-systemic collaterals	2 (40)	2 (40)
Portal biliopathy/PCC	3 (60)	3 (60)
Extrinsic indentation	-	2 (40)
Upstream dilatation	3 (60)	3 (60)
Displacement of extrahepatic duct	-	
Hepatic changes		
Compromised portal perfusion	-	1 (20)
Smooth hepatic atrophy	-	-
Splenic changes		
Splenomegaly	5 (100)	5 (100)
Gamma-gandy bodies	2 (40)	2 (40)
Ascites	4 (80)	4 (80)

[Table/Fig-2]: Ultrasound and CT features of Extrahepatic Portal Venous Obstruction (EHPVO).



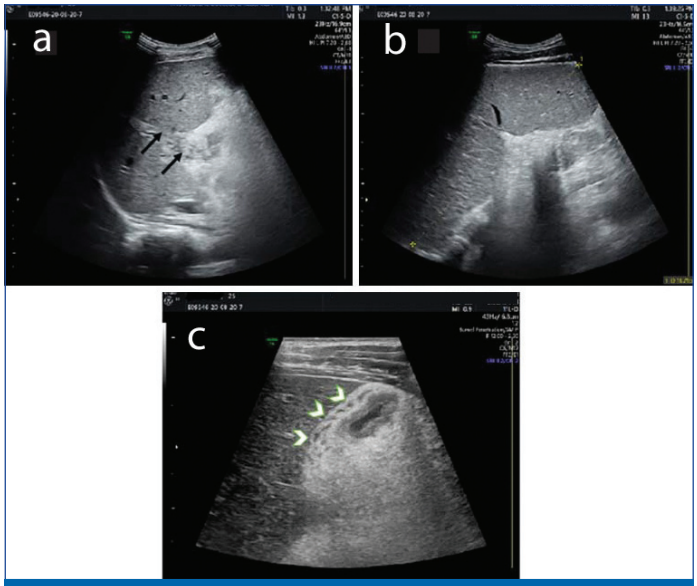
[Table/Fig-3]: An 18-year-old male with EHPVO. (a,b) Ultrasound and colour doppler images demonstrates cavernous transformation of the portal vein (arrow heads) on the left image and splenomegaly with hyperechoic Gamma-Gandy bodies on the right image.

EHPVO: The liver appears normal in all patients on both ultrasound and CT, expect for mild increase in parenchymal echogenicity in two patients. Minimal to mild ascites was seen in four out of five cases of EHPVO in the present study [Table/Fig-2].

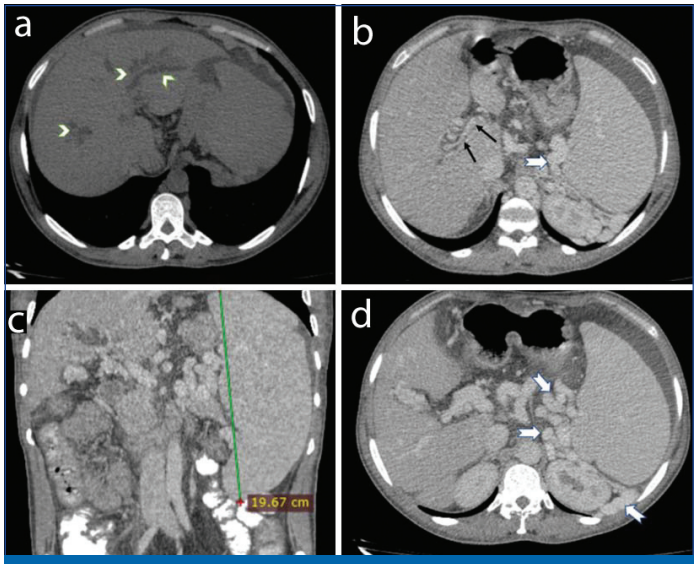
'Cavernous' transformation of the portal vein, a characteristic feature of EHPVO seen as serpiginous vascular channels replacing the portal vein, is the most frequent finding both on ultrasound and CT, seen in all of the cases [Table/Fig-3-6]. Three of five patients showed features of portal biliopathy with intrahepatic biliary radicle dilation seen in all the three cases [Table/Fig-5]. Splenomegaly was seen in all five cases with a mean size of the spleen being 17.4 cm [Table/Fig-3-6]. Two of five cases showed porto-systemic collaterals [Table/Fig-5] in the form of perigastric, oesophageal, para-oesophageal, pericholecystic [Table/Fig-4], epi and para choledochal, splenic and spleno-renal.

NCFP: Similar to EHPVO ascites was only minimal to mild and was comparatively seen less frequently in about two out of five cases [Table/Fig-7].

Mural thickening of the portal vein [Table/Fig-8-10] was considered when the wall thickness was >3 mm and was seen in all cases of NCPF in the present study. Features of PHT i.e., dilated spleno-portal axis [Table/Fig-8,11] and splenomegaly [Table/Fig-8,10,11] were seen in all the cases and abdominal varices was seen in four cases. The mean spleen size in these cases was 17.2±3.6 cm



[Table/Fig-4]: A 25-year-old male with EHPVO. Ultrasound demonstrates; a) Cavernous transformation of vessels (black arrows); b) Splenomegaly with gamma-gandy bodies; and c) Multiple perichoelcytic collaterals (white arrow heads).



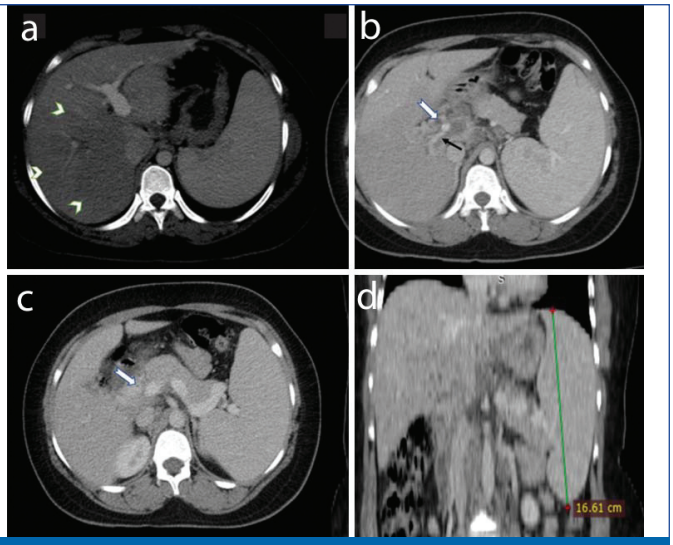
[Table/Fig-5]: a) Axial non contrast CT demonstrates dilatation of the right and left intrahepatic biliary radicles (white arrow heads)- portal bilopathy; b) Axial contrast enhanced CT demonstrates few collaterals at the porta and retropancreatic segment replacing the portal and splenic veins (black arrow) consistent with cavernous transformation; c) Coronal contrast enhanced CT demonstrates gross splenomegaly; d) Axial contrast enhanced CT demonstrates multiple, tortuous, dilated porto systemic collateral vessels at the splenic hilum, adjacent to the tail of pancreas, splenorenal regions (white arrows).

and one of the cases showed the gamma-gandy bodies. Hepatic changes include mild smooth atrophy of the left lobe of the liver with hypertrophy of the caudate lobe [Table/Fig-11] and hepatic arteriopathy is seen in one case.

DISCUSSION

The NCPH comprises a wide range of vascular conditions leading to PHT associated with normal or slightly elevated Hepatic Venous Pressure Gradient (HVPG), whereas the portal venous pressure gradient between the portal vein and inferior vena cava is comparable or higher than cirrhotic PHT [3].

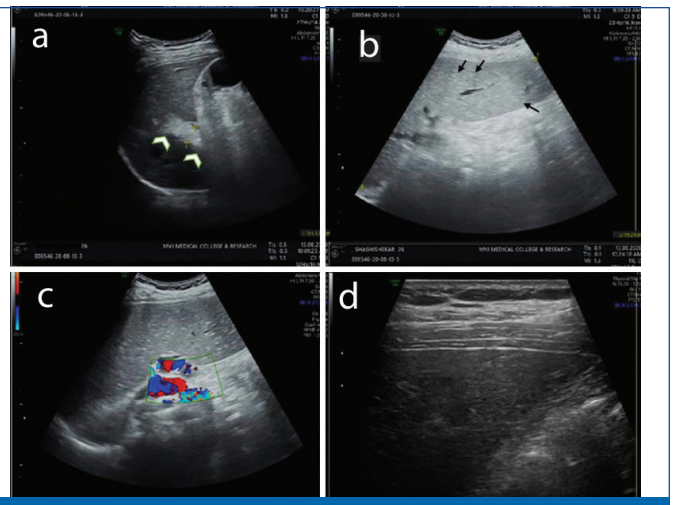
EHPVO is a primary vascular disease that excludes acute or chronic portal vein thrombosis occurring along with cirrhosis and hepatocellular carcinoma. It is an important cause of NCPH with a preserved liver function. EHPVO is a disease of children and young adults with early age of acute or recurrent infection with thrombotic origin leading to thrombosis of the portal vein which in turn leads EHPVO [6]. Although EHPVO is a childhood disorder, a study was conducted by Amarapurkar P et al., to determine the aetiology, clinical presentation, and outcome of adult primary EHPVO in India



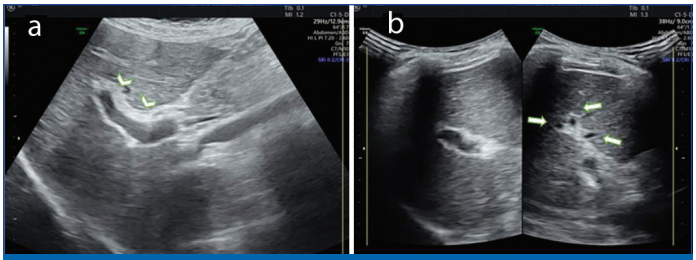
[Table/Fig-6]: a) Axial contrast enhanced CT liver demonstrates areas of relative hypoattenuation on PV phase (white arrow heads); b) Right branch of PV is significantly attenuated. MPV is also significantly attenuated and replaced by multiple collaterals at porta and in pericholedochal region (black arrow); b,c) Pericholedochal collaterals are causing significant luminal narrowing of the CBD in its supraduodenal and intrapancreatic segments (white arrow) suggestive of portal biliopathy;(d) Coronal contrast enhanced CT demonstrates splenomegaly.

Features of NCPF	USG, n (%)	CT, n (%)
Portal hypertension	5 (100)	5 (100)
Splenomegaly	5 (100)	5 (100)
Abdominal varices	3 (60)	4 (80)
Dilatation of the spleno-portal axis	5 (100)	5 (100)
Intrahepatic portal vein abnormalities		
Pruning of the intrahepatic branches	-	1 (20)
Occlusive thrombosis	-	-
Extrahepatic portal veins abnormalities		
Mural thickening of portal vein	5 (100)	5 (100)
Hepatic changes		
Atrophy	1 (20)	1 (20)
Perfusion anomalies	-	-
Hepatic arteriopathy	-	1 (20)
Splenic changes		
Splenomegaly	5 (100)	5 (100)
Gamma-Gandy bodies	2 (40)	2 (40)
Ascites	2 (40)	2 (40)

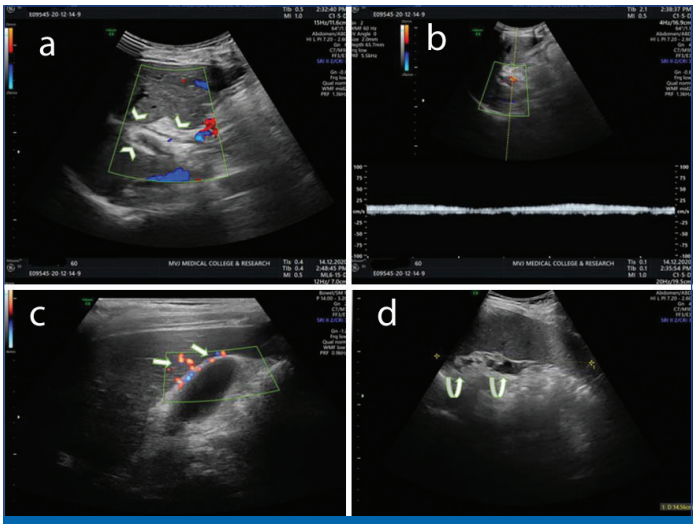
[Table/Fig-7]: Ultrasound and CT features of Non Cirrhotic Portal Fibrosis (NCPF).



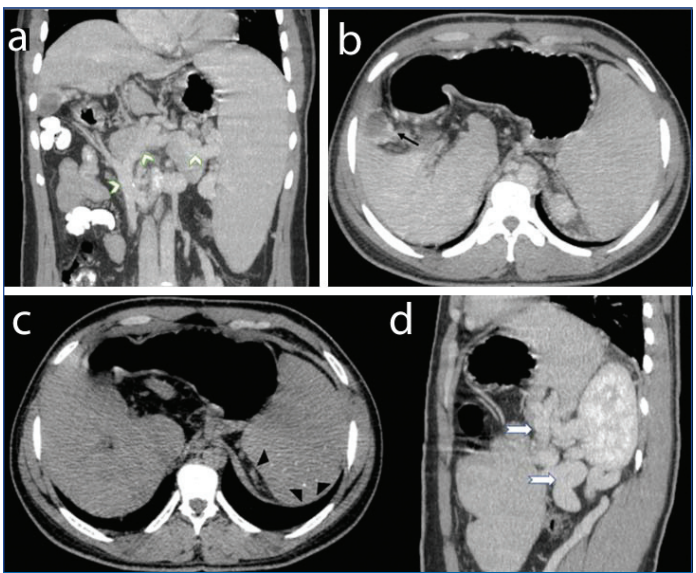
[Table/Fig-8]: a) Ultrasound demonstrates periportal echogenicity (white arrow heads) along main portal vein its right and left branches and few segmental branches; b,c) Spleen is enlarged in size with tiny echogenic foci, Gamma-Gandy bodies (black arrows) and show dilated and tortuous splenic vein; d) Liver demonstrates normal smooth outline.



[Table/Fig-9]: a,b) Ultrasound demonstrates periportal echogenicity (white arrow heads) along the MPV on the left image; with abrupt cut-off of the segmental and subsegmental branches (white arrows) suggestive of pruning of the intrahepatic portal veins on the right image.



[Table/Fig-10]: a,b) Colour doppler and spectral analysis demonstrates periportal echogenicity (white arrowheads) along main portal vein its right and left branches and few segmental branches, significantly narrowing its lumen with monophasic hepatofugal flow; (c) Colour doppler demonstrates pericholecystic collaterals (white arrows); (d) Splenomegaly and dilated and tortuous splenic vein (curved arrows) are seen at the splenic hilum.



[Table/Fig-11]: a,b) Coronal contrast enhanced CT demonstrates lack of visualisation of the entire length of the MPV and right and left main branches of the portal vein and intrahepatic portal venous branches. Moderate dilatation of the splenic vein (white arrow) at the splenic hilum, prominent pericholecystic (black arrow) and gross splenomegaly. Mild atrophy of left lobe of the liver (segments–II and III); (c) Numerous, tiny hyperdense foci in splenic parenchyma–Gamma-Gandy bodies; (d) Sagittal contrast enhanced CT demonstrates extensive, dilated and tortuous splenorenal collateral vessels.

and concluded that adult EHPVO accounted for 3.3% of patients with PHT with age of presentation in second to fourth decade and the major causative factors identified were prothrombotic conditions while, in one-third of patients, no risk factors could be identified [7]. In this study, the age of presentation was in the second and third decade of life and the cause of EHPVO in this study was local inflammatory causes (n=2), idiopathic (n=2) and prothrombotic state (n=1) which was in concordance with previous study by Amarapurkar P et al., [7].

The Imaging Features of EHPVO

Cavernous transformation of the portal vein and formation of portosystemic shunts: The EHPVO is characterised by cavernous transformation of the portal vein, which is the formation of extensive portoportal collaterals in order to preserve the hepatopetal flow. However, these collaterals are insufficient to bypass the splenomesentric inflow leading to portosystemic shunt formation and splenic enlargement. The portal cavernoma show monophasic hepatopetal flow with loss of normal respiratory undulations on Doppler study [2,3,8]. This study showed similar finding with portal cavernoma and splenomegaly seen in all patients and portosystemic collaterals seen in 40% of the cases.

Portal biliopathy/Portal cavernoma cholangiopathy: In a study by Dhiman RK et al., on 12 patients with portal biliopathy described it as varicoid, fibrotic, or mixed, depending on the appearance of the bile duct at the point of obstruction [9]. The investigators in these studies proposed that varicoid portal biliopathy is biliary obstruction caused by large collateral veins that compress and distort the extrahepatic bile duct, while fibrotic portal biliopathy is a result of smaller intramural collaterals visible as narrowed, thickened, and densely enhancing bile ducts. In this study, it was found that external indentation of the biliary tree in two of the patients and bile duct thickening in one of the patients which were causing upstream dilatation of the biliary radicles.

Hepatic changes: As EHPVO is a prehepatic vascular insult, the liver parenchymal morphology i.e., the size, architecture and volume can be normal. However, there is a relative reduction in portal venous flow to the periphery of liver along with compensatory increase in arterial blood flow. These circulatory changes lead to better perfusion of the central liver. This is seen as a transient difference in hepatic attenuation and peripheral arterial concentration of contrast material on CECT. Thus, liver parenchymal volume redistribution, parenchymal extinction and smooth hepatic atrophy ensues. On ultrasound, these morphological changes may be misdiagnosed as cirrhosis, especially, if, colour Doppler evaluation is not performed or when the collateralisation around the liver is subtle [10]. In this study, it was found that one patient with similar findings of transient difference of hepatic attenuation with peripheral concentration of contrast on CT study.

Splenic artery aneurysms: Splenic artery aneurysm is a rare complication of EHPVO, however they are clinically significant due to their high propensity for spontaneous rupture. It is known to occur due to the haemodynamic change resulting from PHT [11]. There were no cases of splenic artery aneurysms in the present study.

NCPF: NCPF usually presents in young males between third and fourth decade of life with gastrointestinal haemorrhage, left upper quadrant mass and pain due to massive splenomegaly, anaemia and thrombocytopenia with a preserved liver function. The variceal bleeding in NCPF is said to be well tolerated when compared to other causes of varices, probably because of well-preserved hepatic function. Arora A and Sarin SK hypothesised that repeated microthrombotic insults to the small or medium-sized portal veins in young adults leads to the development of NCPF [5].

In the present study, it was found that all NCPF patients had preserved liver function, showed male predominance and presented in their third to sixth decade of life. This was in concordance with the literature [12].

The imaging features of NCPF

PHT: Splenomegaly, abdominal varices and splenoportal axis dilatation: There is massively enlarged spleen, with the splenic weight reaching upto 1500 g. In a study carried out by Furuichi Y et al., comparing NCPF and liver cirrhosis, it was found that the spleen

size was very large in NCPF when compared to liver cirrhosis [13]. The enlarged spleen may show Gamma-Gandy bodies denoting long standing PHT. The splenoportal axis is dilated and patent and there are abdominal varices. These findings were consistently found in all patients with NCPF in present study.

Extrahepatic Portal vein abnormalities: There is mural thickening of more than 3 mm of the portal vein axis and displays increased echogenicity with thickening of the larger portal tracts. Portal vein calcification, partial or complete thrombosis has also been reported. These changes are suggestive of periportal fibrosis. In some cases, the periportal hyperechogenicity alternates with hypoechoic stirpes giving it a layered appearance of the portal tracts [5]. In this study, all patients with NCPF demonstrated portal vein mural thickening, this was in concordance with previous studies.

Intrahepatic portal vein abnormalities: The intrahepatic portal vein radicles show smooth and regular tapering with abrupt cut-off of the segmental and subsegmental branches giving it a "withered tree" appearance [3]. In this study, it was found that there was one case wherein, there, was abrupt cut-off of the segment and sub-segmental branches of the main portal vein.

Hepatic changes: In advance cases of NCPF, the liver turn atrophic which may be due to reduced portal venous blood supply to the periphery. Nodularity of the liver may also develop in advance cases making it difficult to differentiate between advanced NCPF and cirrhosis of liver. Liver parenchymal perfusion anomalies are another feature documented in NCPF. This is characterised by heterogeneous portal perfusion showing decreased enhancement of the liver at the periphery with compensatory increase in the arterial perfusion at the periphery. These changes are more appreciable on arterial phase than on venous phase and are considered to be distinctive for NCPF [5]. One patient in this study showed smooth atrophy of the left lobe of the liver.

Limitation(s)

The sample size of the study was very small to obtain statistical significance. A larger study sample size and long-term follow-up is likely to throw more light onto the disease pathogenesis and the imaging implications.

CONCLUSION(S)

The present study demonstrates the characteristic imaging features of NCPF and EHPVO which are leading cause of NCPH. The distinctive ultrasound and CT features of EHPVO include cavernous transformation of the portal vein, portosystemic collaterals formation and splenomegaly. NCPF is characterised by dilatation of the speno-portal axis, mural thickening of the portal vein, abrupt cut-off of the intrahepatic portal vein branches and splenomegaly. Therefore, in cases with PHT and absence of cirrhosis, the radiologist should be aware of these conditions before labeling them as cryptogenic cirrhosis.

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