PICTORIAL REVIEW

Multimodality imaging of obliterative portal venopathy: what every radiologist should know

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ABSTRACT

Obliterative portal venopathy (OPV) is an important cause of non-cirrhotic portal hypertension, which is often erroneously misdiagnosed as cryptogenic cirrhosis. It has a worldwide distribution with majority of cases hailing from the Asian subcontinent. However, recently the disease has gained global attention particularly because of its association with human immunodeficiency virus infection and use of antiretroviral drug therapy (didanosine). As the name suggests, the disorder is characterized by sclerosis and obliteration of the intrahepatic portal vein branches (with attendant periportal fibrosis) leading to portal hypertension amid intriguingly little liver dysfunction. It primarily affects young adults who present with clinically significant portal hypertension in the form of episodes of variceal bleed; however, contrasting liver cirrhosis, the liver function and liver structure remain normal or near normal until late in the disease process. Radiological findings during advanced disease are often indistinguishable from cirrhosis often warranting a liver biopsy. Nevertheless, recent studies have suggested that certain imaging manifestations, if present, can help us to prospectively suggest the possibility of OPV. At imaging, OPV is characterized by a wide range of intrahepatic and/or extrahepatic portal venous abnormalities with attendant changes in liver and splenic volume and stiffness. We shall, through this pictorial review, appraise the literature and illustrate the germane radiological manifestations of OPV that can be seen using different imaging modalities including ultrasonography, CT, MRI, elastography and hepatic haemodynamic studies.

It is important to recognize that not all varices mean liver cirrhosis. Although liver cirrhosis constitutes the commonest cause of portal hypertension, we should be aware that portal hypertension can occur in the absence of liver cirrhosis—a condition termed as non-cirrhotic portal hypertension (NCPH).[1,2] NCPH represents a heterogeneous group of (primarily vascular) disorders where portal hypertension manifests amid absent liver cirrhosis. Pathologically, the insult is either pre- or intrahepatic involving the main portal vein or its smaller branches and/or the perisinusoidal area.[1–3]

Obliterative portal venopathy (OPV) represents an important cause of NCPH that is characterized by sclerosis and obliteration of the medium-sized portal venous branches leading to portal hypertension.[1–10] Liver biopsy characteristically shows phlebosclerosis and periportal and perisinusoidal fibrosis amid absent cirrhosis (Figure 1).[1–3] Although, the exact aetiology is contentious, infections and prothrombotic states have been implicated in eastern and western patients, respectively.[1,2] Additionally, xenobiotic exposure, autoimmune and genetic factors have also been incriminated.[1–4] Although the disease has a worldwide distribution, it continues to remain poorly understood primarily owing to its relative rarity.[1–3,5–8] Another potential reason is the use of diverse terminologies under which the entity has been described from various parts of the globe, such as non-cirrhotic portal fibrosis in India, idiopathic portal hypertension in Japan and hepatoportal sclerosis in the USA.

More recently, the disease has gained global attention because of escalating number of cases being reported in human immunodeficiency virus (HIV)-infected patients.[1–3,8–10] Also, US Food and Drug Administration has recently issued a warning regarding the potential association of OPV in patients with HIV on didanosine (antiretroviral therapy).[3]

OPV primarily affects young patients usually in their third or fourth decades of life. The affected individuals typically present with clinically significant portal hypertension characterized by multiple episodes of well-controlled upper

Figure 1. (a) Atrophic small portal tract (arrow) showing absent portal vein [haematoxylin and eosin stain (HE), ×200]. (b) Two small portal tract (arrows) approximations (×100, HE). (c) Portal and central vein approximation (×100, HE). (d) Parenchymal extinction suggested by portal–portal and portal–central approximation (Masson's trichrome stain, ×200).
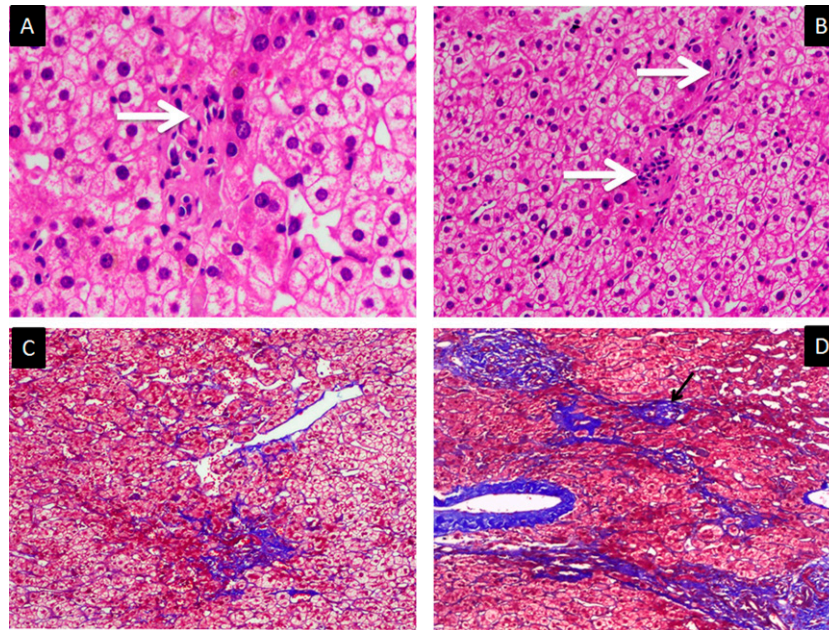
gastrointestinal (GI) bleed, massive splenomegaly and/or hypersplenism.[1–3] Advanced stages of the disease are often indistinguishable from liver cirrhosis especially on imaging. However, discrimination from cirrhosis is crucial in clinical practice because of differences in management. Management of OPV is primarily symptomatic, that is, focused on management of an acute episode of variceal bleed. The risk of rebleeding and bleeding-related mortality is low. Intriguingly, in contrast to liver cirrhosis, the liver function and liver structure remain normal or near normal until late in the disease process leading to a better prognosis and higher survival rates; the 10-year survival rate is around 86–95%.[1,2] Development of jaundice, ascites and hepatic encephalopathy is uncommon and if at all is seen only after an episode of GI bleeding.[1,2] Liver failure and the incidence of developing hepatocellular carcinoma are also much lower.[1–3,8–10] Nonetheless, in 20–33% of patients, the liver gradually atrophies and shows functional decompensation, occasionally needing liver transplantation.[1,2]

Figure 2. Transabdominal ultrasonography showing dilated portal vein in a non-cirrhotic liver with prominent periportal hyperechogenicity (arrows) suggesting periportal fibrosis.
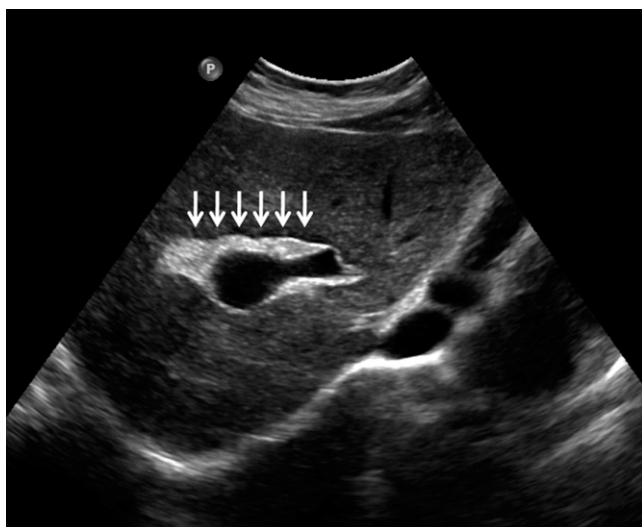

Figure 3. Transabdominal ultrasonography in a 24-year-old male with obliterative portal venopathy showing attenuated left portal vein (LPV) with a "layered" appearance (arrows) secondary to alternating hyperechoic and hypoechoic bands in the periportal region.
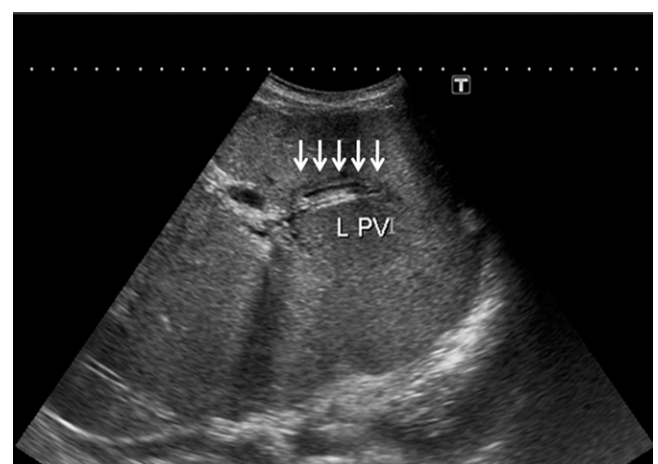
Figure 4. (a, b) Coronal CT maximum intensity projections show dilatation of the splenoportal axis with an unusually dilated coronary vein (arrow) serving as an afferent for a large tuft of paraoesophageal varices (arrowheads). Note the liver volume and contour is preserved. (c) Liver biopsy showing atretic portal tract with the absence of portal vein profile [haematoxylin and eosin stain, ×200]. (d) The same tract in Masson's trichrome stain with no parenchymal activity (arrow) (Masson's trichrome stain, ×200).
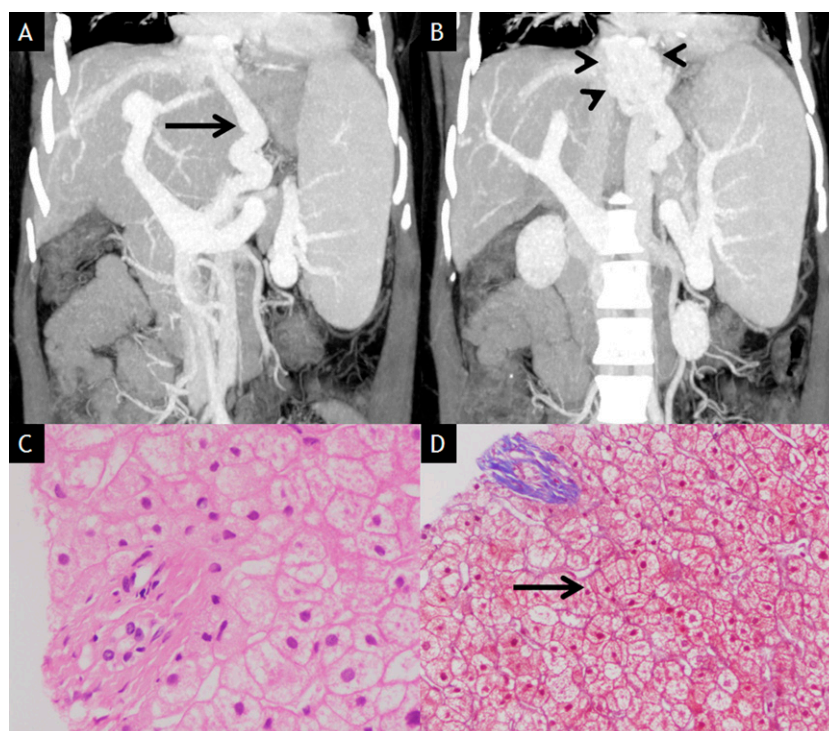

Although limited literature is available on the radiological manifestations of OPV, recent studies have suggested certain imaging manifestations to be more prevalent in OPV that can allow discrimination from cirrhosis. Moreover, use of newer techniques, including transient elastography, can allow prospective non-invasive diagnosis of OPV based upon the differential changes in liver and splenic stiffness. The aim of this review is to appraise the imaging findings of OPV described in

Figure 5. (a) Coronal-unenhanced CT in a 24-year-old female with obliterative portal venopathy showing a massively enlarged spleen containing multiple calcified Gamna–Gandy bodies. The liver shows a smooth contour. (b, c) Transabdominal ultrasonography of the same patient showing a smooth contoured liver (thick arrow) with a dilated portal vein (arrows).

Figure 6. (a) Smooth shrunken liver (arrows) in a patient with obliterative portal venopathy (OPV). (b) Liver biopsy of the same patient showing a sclerotic portal tract (arrow) [haematoxylin and eosin stain (HE), ×200]. (c) A different patient with advanced OPV exhibiting markedly atrophic nodular liver (arrow) (Stage III as per the classification of Nakanuma et al[11]) indistinguishable from cirrhosis. (d) Periportal fibrous expansion (arrow) and atrophic hepatocytes (arrowheads) (HE, ×200) are seen on liver biopsy.
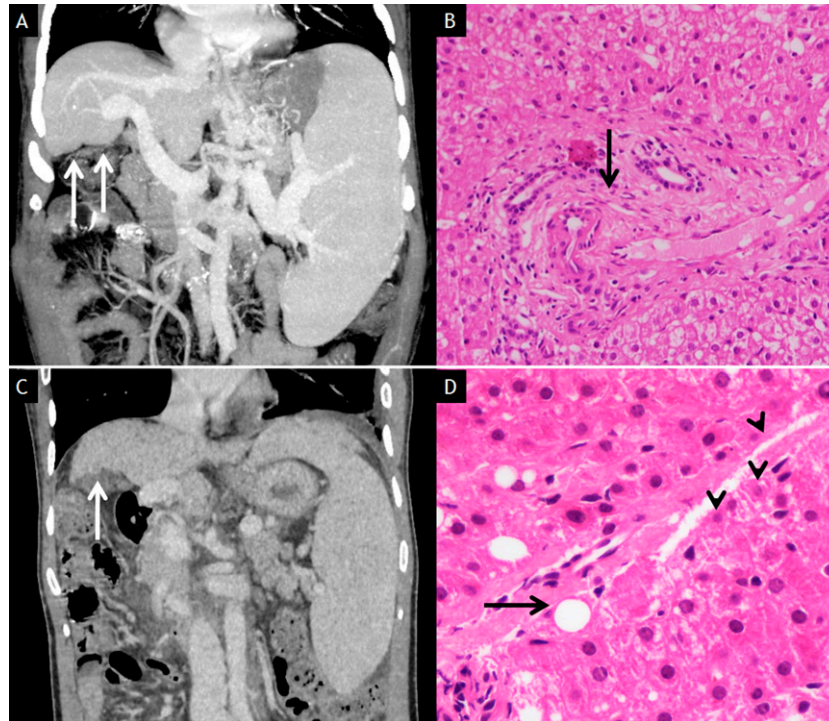
ULTRASONOGRAPHY

Abdominal ultrasonography is usually the first step in imaging evaluation of patients with OPV.[1,2] Typically, patients with OPV manifest stigmata of portal hypertension, such as splenic enlargement, abdominal varices and dilatation of the splenoportal venous axis even as the liver remains normal in size, contour and echotexture. The portal vein axis displays mural thickening (>3 mm) with increased echogenicity and thickening of the larger portal tracts (Figure 2), changes suggesting periportal fibrosis.[1] At times, this periportal hyperechogenicity alternates with hypoechoic stripes resulting in a "layered" appearance of the larger portal tracts (Figure 3).[4] The intrahepatic portal vein radicles show smooth and regular tapering with a sudden cut-off

Figure 7. Axial contrast-enhanced CT in a 24-year-old female with obliterative portal venopathy showing arterial hyperperfusion (arrows) along the liver periphery on the late arterial phase scan. Note the liver is smooth but shows volume redistribution in the form of left lobe enlargement.
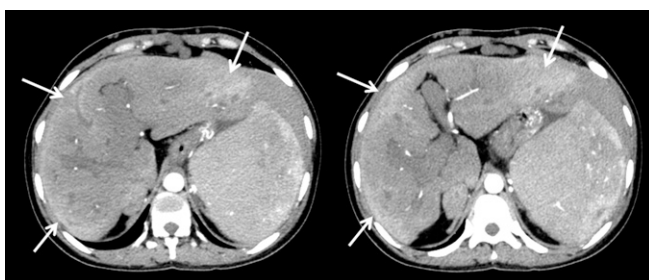

Figure 8. (a) Arterial phase CT showing increased hepatic arterial inflow in the form of several arteries near the liver hilum (arrows). (b) Another 35-year-old male with obliterative portal venopathy showing increased hepatic arterial inflow in the form of unusually dilated right hepatic artery extending up to the liver periphery with attendant subcapsular arterial proliferation (portal arteriopathy).
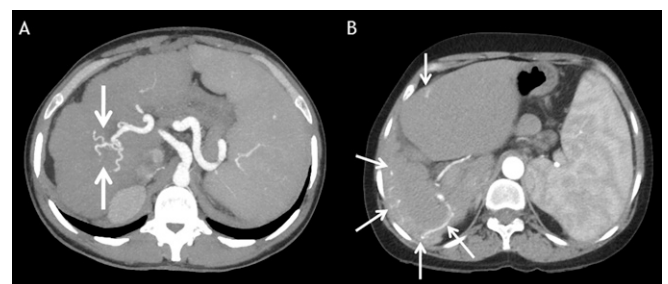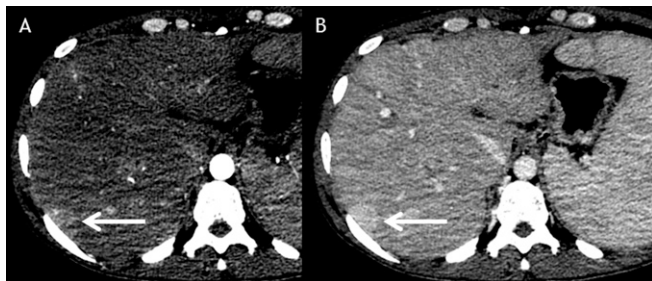
Figure 9. (a, b) Contrast-enhanced CT in a young patient with obliterative portal venopathy depicting an arterial hypervascular subcapsular focal nodular hyperplasia-like nodule (arrows), which retains contrast on subsequent portal venous phase. Note splenic enlargement amid a non-nodular liver.

of the segmental and/or subsegmental branches, popularly termed as the "withered-tree" appearance.[1]

Apart from substantiating portal hypertension, Doppler ultrasound plays an important role in assessing the patency of the splenoportal axis and hepatic veins that are pivotal to exclude other causes of NCPH, such as extrahepatic portal venous obstruction (EHPVO) or Budd–Chiari syndrome etc.[1–3] EHPVO is an important cause of NCPH, which is characterized by complete cavernomatous transformation of portal vein resulting in pre-hepatic portal hypertension.[1,2] Cavernomatous transformation of the portal vein can be readily depicted on Doppler ultrasound that has an overall sensitivity and specificity of 95%.[2] These patients may manifest concomitant changes of biliary dilatation (portal biliopathy) owing to engorged paracholedochal and epicholedochal varices compressing the biliary tree.[1,2] Although a very small subset of patients with OPV can also present with cavernomatous transformation of portal vein, patients with EHPVO typically present much earlier with a bimodal age of presentation at 3 years (for those secondary to umbilical sepsis) and after 8 years of age (for the idiopathic variety).[1,2] Budd–Chiari syndrome causes NCPH owing to obstruction of the hepatic venous outflow tract. Doppler ultrasound findings range from partial or complete obliteration of the hepatic veins, intraluminal echogenicity, with absent flow/flow reversal or continuous flow (the "pseudoportal" Doppler signal) upstream of a stenosis. By
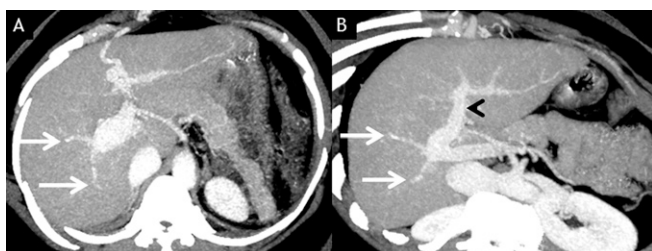
contrast, patients with OPV show patent hepatic veins on Doppler ultrasound.

Advanced OPV wherein the liver is atrophic and nodular cannot be, however, readily differentiable from cirrhosis. Nevertheless, newer techniques such as contrast-enhanced ultrasonography and transient elastography have shown promising results for differentiating the two entities.[5–7] Contrast-enhanced ultrasonography using perflubutane microbubble, although not widely practiced, has shown that the presence of delayed periportal enhancement to be a characteristic feature of OPV.[5]

TRANSIENT ELASTOGRAPHY

When available ultrasonography assessment of liver stiffness using transient elastography (FibroScan®; Echosens, Paris, France) can be a vital tool that can be employed for differentiating OPV and cirrhosis.[6,7] As opposed to liver cirrhosis, patients with OPV exhibit a relatively soft liver and a hard spleen, and, consequently, the liver stiffness is low (mean, 5.9 kPa) and the spleen/liver stiffness ratio increased. Whereas the opposite is true for liver cirrhosis, where the liver is hard (mean, 7.8–10.2 kPa) and spleen/liver stiffness ratio is low owing to low splenic stiffness.[1,6,7]

CT

Imaging features of OPV on CT and MRI include a non-nodular liver with enlarged caudate lobe ± atrophic right lobe and preserved liver volume amidst features of portal hypertension (Figure 4).[8,10] The spleen in OPV gets massively enlarged at portal pressures comparable to other disorders of portal hypertension (Figure 5).[1–3] Splenic weight can reach as high as 1500 g (700 g in cirrhosis).[1] In a recent study comparing OPV and cirrhosis, the spleen size was found to be very high in the OPV group (area, 102.5 cm^2, median value) when compared with liver cirrhosis (44.0 cm^2).[6] It is not uncommon that patients report having a longstanding mass in the left hypochondrium (owing to massive splenic enlargement).[1,2] Enlarged spleen may display multiple Gamna–Gandy bodies on CT or MRI. Gamna–Gandy bodies are fibrosiderotic splenic nodules impregnated with iron and calcium—signs of long-standing portal hypertension.

Figure 10. (a, b) Axial and axial-oblique maximum intensity projection images depicting conspicuous attenuation of the right-sided portal venous branches (arrows) whilst the left portal venous system is normal (arrowhead).

Figure 11. (a, b) Axial contrast-enhanced CT in a 26-year-old male with obliterative portal venopathy showing intraluminal filling defects/thrombi (arrows) within the right portal vein branches. Note caudate lobe enlargement with attendant Segment IV atrophy and splenomegaly.
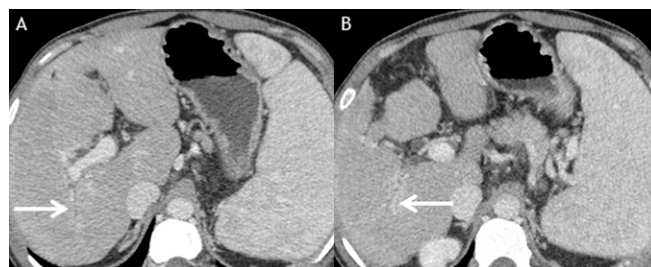
Figure 12. A 34-year-old male with obliterative portal venopathy (OPV). (a) Axial contrast-enhanced CT showing abrupt termination of the posterior branch of right portal vein (arrow) with non-visualization of segmental branches. Note caudate lobe enlargement and periportal space widening with periportal fat proliferation (arrowhead) simulating early liver cirrhosis. (b) Biopsy-confirmed OPV; shown here is a proximated portal tract and central vein (bracket area) owing to parenchymal loss.
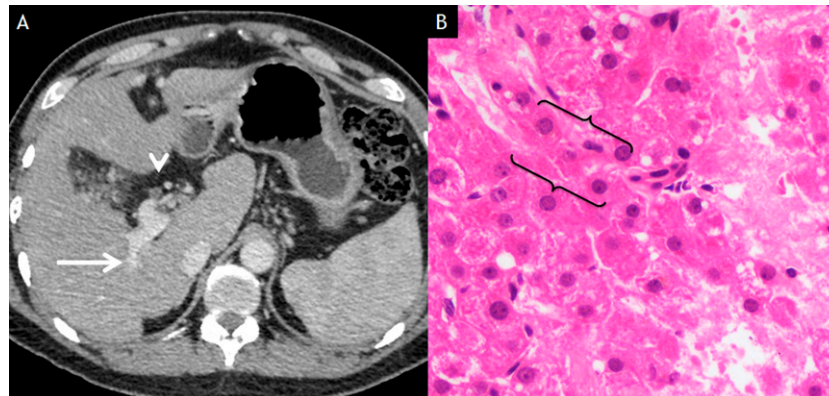
Macroscopically, the liver tends to remain normal until late in the disease process, however, as the disease progresses, the liver turns atrophic and/or nodular (Figure 6). Liver atrophy is presumably owing to reduced portal venous blood supply to the periphery.[1,2,8,9] Parenchymal loss is not necessarily progressive, and the hepatic functional reserve mostly remains preserved.[1,2] Based on gross and imaging features, Nakanuma et al[11] proposed four stages of the disease. Stage I: non-atrophic liver without subcapsular parenchymal atrophy; Stage II: non-atrophic liver with subcapsular parenchymal atrophy; Stage III: atrophic liver with subcapsular parenchymal atrophy; and Stage IV: with concurrent occlusive portal venous thrombosis.[1–3] Advanced OPV and liver cirrhosis can be indistinguishable; however, Glatard et al[8] reported that the combination of caudate lobe enlargement and medial segment (Segment IV) atrophy is significantly more frequently associated with cirrhosis. Enlargement of the gallbladder fossa owing to early atrophy of Segment IV is an early feature of liver cirrhosis (expanded gallbladder fossa sign), whereas preservation of Segment IV until late in the disease process could be a feature favouring OPV.[10] Although patients with OPV can manifest with a normal, atrophic or even hypertrophic Segment IV.[8,9]

Intrahepatic portal venous obliteration leads to impaired hepatic haemodynamics, which, on imaging, manifests as parenchymal perfusion anomalies. This is characterized by heterogeneous portal perfusion with decreased enhancement of the liver periphery. However, there is compensatory increase in the arterial perfusion at the liver periphery (Figure 7). These perfusional changes are more appreciable on arterial phase than on venous phase and are believed to be unique for OPV.[9] Also, patients may show increased arterial inflow in the form of hepatic arterial enlargement (at the hilum or within the hepatic parenchyma) or the presence of several arteries at the hilum (Figure 8). On liver specimens, these hypertrophic arterial changes have been termed as portal arteriopathy.[8] Additionally, liver parenchyma can show arterial hypervascular focal nodular hyperplasia-like nodules, which are believed to be a response to haemodynamic disturbances from decreased portal venous inflow and reciprocal increased arterial inflow (Figure 9).[1,8,10]

Intrahepatic and/or extrahepatic portal venous abnormalities constitute the commonest imaging manifestations of OPV. Intrahepatic portal abnormalities can be seen in the form of attenuation or pruning of the intrahepatic branches when

Figure 13. (a, b) Contrast-enhanced and contrast-unenhanced CT images in a patient with obliterative portal venopathy showing partial luminal thrombosis of the extrahepatic portal vein (arrow) with attendant mural calcifications involving the splenoportal axis (arrowheads). (c) Ultrasonography image of the same patient showing mural thickening of the extrahepatic portal vein (arrows). The portal vein is also dilated.
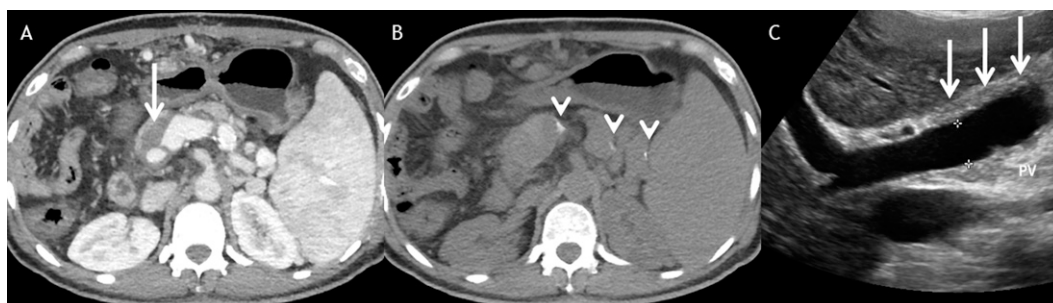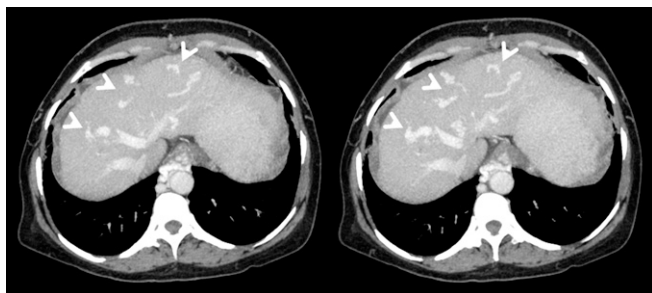
Figure 14. (a, b) CT maximum intensity projections showing tortuous intrahepatic venous collaterals (arrowheads) in a patient with obliterative portal venopathy even in the presence of patent hepatic veins.

Figure 15. (a) A 26-year-old male showing excessive periportal hyperintensity (arrows) on T_2 weighted MRI. Note the spleen is enlarged amid an otherwise normal looking liver. (b) Liver biopsy shows an atretic portal tract without any vascular profiles (arrow) (haematoxylin and eosin stain, ×200) in keeping with obliterative portal venopathy.
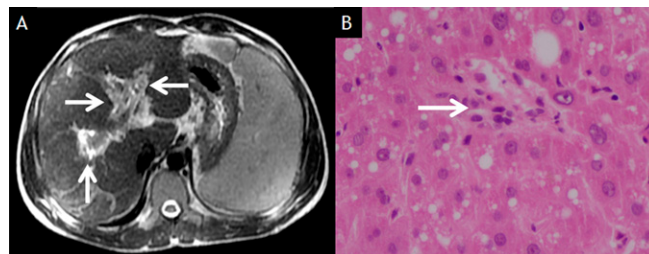

compared with adjoining other intrahepatic branches, occlusive thrombosis either in the form intraluminal filling defect, abrupt termination or lack of contrast enhancement (Figures 10–12). Extrahepatic portal vein abnormalities include mural thickening, calcifications, or partial or complete thrombosis (Figure 13).[8,9] Glatard et al[8] reported intrahepatic portal abnormalities in 58% patients with OPV and 2% patients with cirrhosis, and extrahepatic portal vein abnormalities in 43% patients with OPV *vs* 12% patients with cirrhosis, respectively. Intrahepatic veno-venous collaterals have also been reported on splenovenography studies (Figure 14).[1,2,8–10]

MRI

MRI in patients with OPV is also conspicuous in detecting stigmata of portal hypertension in the form of splenic enlargement (with or without Gamna–Gandy bodies), abdominal varices and dilated portal venous axis. As with CT, MRI findings in non-advanced disease include relatively enlarged caudate lobe amid the absence of liver nodularity and preserved liver volumes. However, during advanced stages, liver contour changes and decreased liver volume make differentiation from cirrhosis unfeasible.[10]

Krishnan et al[10] in their study reported increased periportal signal intensity on T_2 weighted images in 6 of their 18 (33.3%) patients with OPV. These changes on MRI correspond to the periportal changes that can be identified on sonography and

have been attributed to periportal fibrosis. Additionally, this periportal hyperintensity on T_2 weighted sequence may also signify aberrant neovascular proliferation adjoining the portal vein radicals (Figure 15).[10]

In addition, benign focal nodular hyperplasia-like liver nodules are also better discernible on contrast-enhanced MRI (Figure 16). Krishnan et al[10] in their study identified liver parenchymal nodules in 2 of 18 (11.1%) patients. One of these patients had two T_2 hyperintense lesions (1.5-cm each), which demonstrated arterial hyperenhancement and remained hyperintense on delayed phase images. By contrast, the other patient displayed multiple subcentimetre lesions that were hyperintense on T_1 weighted images and isointense on other sequences. Two additional lesions that were hyperintense on T_1 and T_2 weighted images (measuring 2.0 and 2.6 cm, respectively) were also recognized; however, these did not show any arterial phase enhancement. The fact that one of these lesions completely resolved whilst the other showed a significant decrease in size on the follow-up MRI performed after 18 months corroborated a presumed benign aetiology.

HEPATIC HAEMODYNAMIC STUDY

Confounding cases may warrant hepatic vein catheterization and measurement of the venous pressure, which is a well-established technique to differentiate OPV from cirrhosis (Figure 17).

Figure 16. (a–c) Dynamic contrast-enhanced MRI in a young patient with obliterative portal venopathy depicting an arterial hypervascular subcapsular focal nodular hyperplasia-like nodule (arrows) retaining contrast on subsequent phases. Note prior partial splenic artery embolization changes (asterisks) for symptomatic hypersplenism.
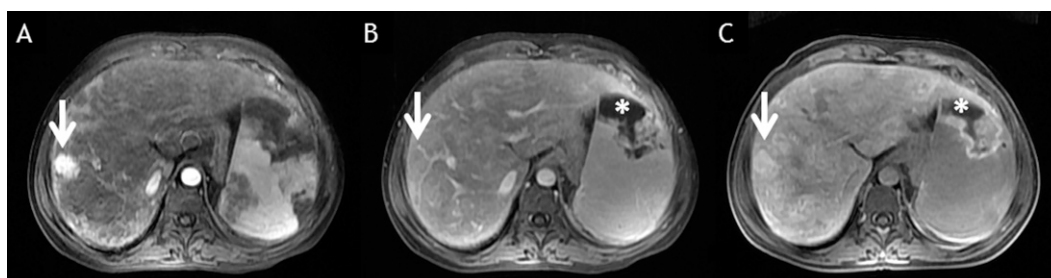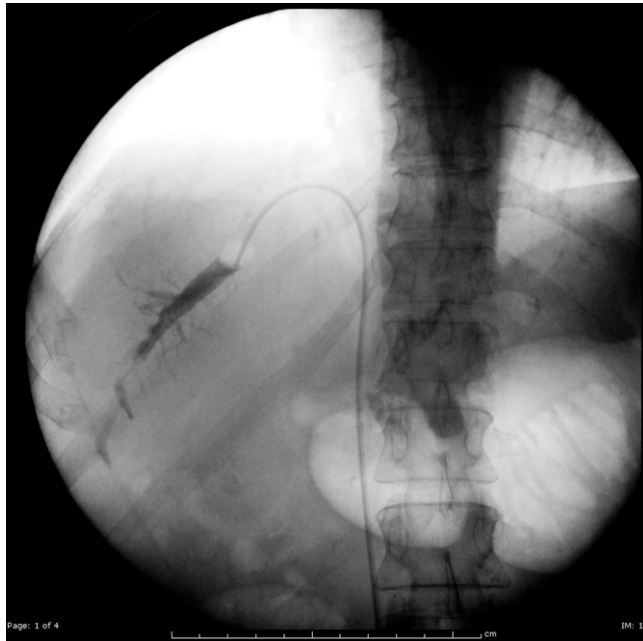
Figure 17. Hepatic vein catheterization while evaluating hepatic venous pressure gradient in a suspected case of obliterative portal venopathy.

Hepatic venous pressure gradient (HVPG) when normal (<5 mmHg) or near normal (<10 mmHg) strongly argues against the diagnosis of cirrhosis. Whereas, elevated HVPG signifies increased sinusoidal resistance owing to fibrosis and structural damage in cirrhosis.[7]

SUMMARY

To conclude, OPV is an important cause of NCPH that is often erroneously diagnosed as cryptogenic cirrhosis. As radiologists, we should have a high level of suspicion, especially in patients who present with portal hypertension but who do not have other clinical features of cirrhosis, such as ascites, jaundice, encephalopathy and transaminitis etc. In addition, history of HIV infection and/or treatment with didanosine should also alert the radiologist to its possibility. Differentiation from cirrhosis is pivotal, as these patients only require symptomatic treatment for variceal bleed with secondary prophylaxis to prevent rebleed. The overall prognosis remains good with high 10-year survival rates of 86–95%. Only occasionally, progressive structural and functional decompensation may warrant liver transplantation. Although, a confident diagnosis mandates liver biopsy, nevertheless, the presence of intrahepatic and extrahepatic portal venous abnormalities, liver perfusion changes (in the form of subcapsular decrease in portal perfusion with compensatory increase in arterial perfusion) in a liver that remains non-nodular until late should favour the possibility of OPV in appropriate clinical settings. Also, increased splenic stiffness and low liver stiffness on elastography helps differentiation from cirrhosis, wherein the liver becomes stiff while the spleen remains relatively soft. HVPG measurement by an interventionist may be required in confounding cases and to follow up these patients.

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