Ductal Plate Malformations: Spectrum of Imaging Findings

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Learning objectives

1. To illustrate the embryology of ductal plate malformations

2. To demonstrate the spectrum of multimodality imaging findings of ductal plate malformations
Background

The ductal plate consists of a layer of bi-potential hepatic precursor cells surrounding portal vein radicals which undergoes remodeling into the intrahepatic biliary tree. Remodeling of these ductal plates occurs during the 12th embryonic week to form bile canaliculi of various sizes beginning from the hilum to the periphery of the liver with successive development of initially the larger ducts, the segmental ducts, the interlobular ducts and finally the smallest bile ductules. Any surplus bile ducts are degraded or resorbed. Dysmorphogenesis of ductal plates can result in ductal plate malformations (DPMs) and the level of involvement determines the clinical and radiopathological manifestations, and also the level of fibrosis, with fibrosis being a dominant feature with small duct involvement. DPMs include biliary hamartomas, autosomal-dominant polycystic liver disease (ADPLD), Caroli's disease/syndrome, and congenital hepatic fibrosis.

Large-sized ductal involvement includes Caroli's disease, which is characterized by multifocal segmental dilatation of the large intrahepatic bile ducts. Choledochal cysts are sometimes included as ductal plate malformations affecting the large-sized ducts, similar to Caroli’s disease, which is in fact, listed as a type 5 choledochal cyst in Todani’s choledochal cyst classification.

However, the pathogenesis of Caroli’s disease (autosomal recessive and often associated with renal disorders) and choledochal cysts (congenital and not associated with renal disorders) makes it unlikely that these entities are related. Choledochal cysts are most likely related to an anomalous junction of the pancreatic and common bile duct resulting in a common channel causing pancreatic enzymes to reflux resulting in progressive bile duct dilatation from inflammatory changes.

The small ducts are also commonly involved in Caroli's (alongside large ductal involvement). This results in concommittant congenital hepatic fibrosis, and is commonly referred to as Caroli’s syndrome.

Large sized ductal involvement (both simple Caroli's and the syndrome) is also associated with renal abnormalities, most commonly renal tubular ectasia (medullary sponge kidneys) as these share the same genetic defect (PKHD1 gene, chromosome region 6p21).

Medium sized ductal involvement results in Autosomal Dominant Polycystic Liver Disease (ADPLD) where progressive dilatation of abnormal bile ducts in microhamartomas leads to the formation of innumerable liver cysts. The development of
liver cysts lags behind the development of renal cysts. However, patients can present solely with ADPLD without renal involvement.

Small sized ductal involvement results in biliary hamartomas (also called Von Meyenburg complexes) and congenital hepatic fibrosis. Congenital hepatic fibrosis is an autosomal recessive condition and is characterized by aberrant interlobular bile duct proliferation and periductal fibrosis. Portal hypertension is usually the presenting feature of such patients and typically manifests in early adulthood. Clinicopathologic features of this disorder are non-specific, making radiology an important tool in diagnosing this condition. Biliary hamartomas are usually clinically insignificant and composed of one or more dilated duct like structures lined by biliary epithelium and accompanied by a variable amount of fibrous stroma.

Ductal plate malformations have also been implicated in the pathogenesis of biliary atresia since mutations of genes controlling normal bile duct formation have been found in the fetal form of atresia and are considered to carry a worse prognosis. It is thought that ductal plate malformations result in the rupture of bile ducts at the initiation of bile flow and the detergent properties of extravasated bile would then lead to protracted inflammation and sclerosis in the submucosa, causing secondary obliteration and obstruction of the more distal extrahepatic bile duct. However, the pathophysiology of biliary atresia is still not fully understood and certainly there are several other factors including infectious, immunological and/or toxic agents which play an important role in the etiology of this disease, especially the more common neonatal type.

Given that these conditions arise from the same pathological process, it is important to understand that together these disorders form a spectrum and patients can present with features anywhere along this spectrum (as shown in figure 2). Although classifying and categorizing these disorders into separate entities might be merely an attempt in simplifying a complex disease process, doing so allows the radiologist to guide further management of these patients.
Fig. 1: Schematic illustration demonstrating the normal and abnormal embryological development. (a) The ductal plate surrounding the portal vein. (b) Development into a double layered sheath of cells. (c) Normal resorption of primitive biliary duct resulting in the final bile duct network surrounding the portal vein malformation. (d) Insufficient resorption results in large dilated bile duct segments surrounding the portal vein.

**Fig. 2:** Axial T2-weighted MR with spectral fat suppression showing multiple cystic foci around both the large and medium-sized bile ducts with no associated biliary dilatation.

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Findings and procedure details

Large-sized ductal involvement

Ultrasonography findings in large-sized ductal involvement (Caroli’s disease and Caroli’s syndrome) typically show large anechoic well marginated regions with echogenic sludge or stones. MRI cholangiography confirms that these regions communicate with the biliary tree. Caroli’s disease is limited to the intrahepatic bile ducts, however extrahepatic biliary dilatation is seen in up to 53% of patients. This association may be explained by the repeated bouts of cholangitis, stone formation and stone passage that occurs in these patients.

Contrast-enhanced CT and MRI demonstrate segmental intrahepatic saccular or fusiform cystic areas of varying sizes measuring up to 5cm and may be used in confirming a diagnosis of Caroli’s disease by demonstrating the presence of the central dot sign (figures 3 and 4) which represents the fibrovascular bundle within the dilated cystic intrahepatic ducts and is considered a characteristic feature of Caroli’s disease. This is seen as a hyper-enhancing or hyperintense focus however fibrovascular bundles may also be seen as a bulge in the wall of the sacculus or a linear bridging structure.

Caroli’s syndrome is more common and appears very different on imaging when compared to the pure form of Caroli’s disease in view of the presence of congenital hepatic fibrosis (see figure 4).

When suspecting large-sized duct involvement, it is important to look for any associated renal abnormalities such medullary sponge kidneys (also shown in figure 4).

Medium-sized ductal involvement

In ADPLD, massive hepatomegaly with innumerable predominantly simple cysts are present throughout the liver. Although the overall size of the liver is grossly enlarged, the hepatic parenchyma may be significantly compressed or replaced to such a degree that it comprises only a small portion of the overall liver volume (fig 5). Regional ADPLD may also occur making it difficult to distinguish from biliary cystadenoma or cystadenocarcinoma as seen in figure 6.

Two types of cysts may be found, intrahepatic cysts and peribiliary cysts. Intrahepatic cysts are more common and are mostly peripheral, ranging from less than 10mm to 80mm in size whilst peribiliary cysts are typically less than 10mm in diameter and appear as
either discrete cysts, a string of cysts or tubular structures paralleling the path of the portal vessels. The variability in size of these well-defined cysts within one patient is a diagnostic criterion to distinguish ADPLD from other cystic entities of the liver such as hamartomas or Caroli’s disease. Furthermore, these cysts do not communicate with the biliary system since ADPLD is thought to result from progressive dilatation of the abnormal bile ducts in microhamartomas.

Most cysts have imaging features of simple fluid, but hemorrhagic cysts and fluid-fluid levels may also be observed. The cystic walls are smooth and usually show no septations or nodularity. Thin calcifications of the wall may be seen, which is considered to be a sequela of chronic or remote hemorrhage or inflammation. Polycystic kidneys may coexist in up to 40% and multiple pancreatic cysts in 9%.

US, CT or MRI may all be useful in diagnosing ADPLD as they all show characteristics of simple versus complex contents and calcified walls. T1-weighted MR imaging demonstrates low signal intensity fluid-containing cysts, while T2-weighted imaging shows cysts with high signal intensity. Cysts complicated by hemorrhage or infection may be seen as increased T1-weighted signal intensity.

Small-sized ductal involvement

Although congenital hepatic fibrosis and biliary hamartomas are considered to result from small sized ductal involvement the imaging features of these two diseases are very different from each other.

In congenital hepatic fibrosis, ultrasound will demonstrate typical findings of a fibrotic liver with increased or heterogeneous echogenicity, hyperechoic portal triads, and poorly defined portal vessels. Ultrasound can also detect biliary duct and liver parenchymal abnormalities, such as bile duct dilatation, regenerative nodules (fig 7), hepatosplenomegaly, and periportal thickening.

Cross sectional imaging of congenital hepatic fibrosis would demonstrate hypertrophy of left lateral segment and atrophy of the right lobe (fig 8 and 9). CT may also demonstrate associated ductal plate abnormalities (biliary hamartoma, Caroli’s disease), portal hypertension, and renal abnormalities such as medullary sponge kidney (fig 10).

Ultrasound in patients with biliary hamartomas typically shows innumerable tiny hypoechoic or hyperechoic foci measuring less than 10 mm and distributed uniformly throughout the liver, and comet-tail artefacts may also be demonstrated. Biliary hamartomas may also be isoechoic.
On CT, the lesions are depicted as multiple, round, low-attenuation, non-enhancing lesions of less than 1.5 cm distributed throughout the liver. On MRI, the lesions are iso to hypointense on T1-weighted and hyperintense on T2-weighted images (Fig 11). At MR cholangiography, the multiple tiny cystic lesions demonstrate no communication with the biliary tree. The lesions do not show contrast enhancement although they may sometimes demonstrate thin rim enhancement with gadolinium, and this is considered to correlate with the compressed liver parenchyma that surrounds the lesions at histological analysis.

A summary of the pertinent findings distinguishing these related conditions from each other may be found in figure 12.
**Fig. 3:** Axial T1 and T2-weighted MRI showing multifocal large cystic dilatations of segmental intrahepatic bile ducts with the classic central dot sign in a patient with Caroli’s disease. The hepatic parenchyma is normal distinguishing it from Caroli’s syndrome, and the central dot represents the respective segmental/subsegmental hepatic artery and portal vein radicle.

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Fig. 4: Selected CT and MR images showing the central dot sign as well as abnormal liver morphology. The presence of both the central dot sign and congenital hepatic fibrosis led to a diagnosis of Caroli’s syndrome. Bilateral renal tubular ectasia (medullary sponge kidneys) is also noted, together with small intraductal calcifications in the liver on CT.

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Fig. 5: Coronal T1 post contrast and FIESTA images showing multiple cysts with no complex features, causing gross enlargement of the liver. Signs of previous intracystic hemorrhage is seen in one of the cysts at the lower right lobe (arrow).

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Fig. 6: Selected images from axial contrast enhanced CT showing multiple variably sized cysts in segments two and three which remained stable over time. Simple cysts in the kidneys are also noted. The differential here would include a biliary cystadenoma or cystadenocarcinoma however the lack of mural nodularity and complex septations favour a diagnosis of regional polycystic liver disease.

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Fig. 7: Ultrasound showing heterogenous parenchymal texture with an ill-defined hypoechoic node in segment 3 (arrow) and MRI showing abnormal morphology of the liver with a T1 hyperintense lesion demonstrating venous enhancement (arrow) but no arterial enhancement. The lesion is likely to represent a large regenerative nodule in the context of congenital hepatic fibrosis. There is also a large spleen with siderotic nodules (Gamna-Gandy-bodies).

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**Fig. 8:** Selected MR images of a 35 year old female with congenital hepatic fibrosis showing abnormal morphology with an enlarged left lobe and posterior sector atrophy and a small portal vein secondary to hepatofugal flow (seen on colour doppler, not shown). Coronal T1-weighted post-contrast imaging shows large splenorenal portosystemic varices and a large spleen with siderotic nodules (also known as Gamna-Gandy bodies).

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Fig. 9: Two selected axial CT images in a patient with congenital hepatic fibrosis showing an abnormal liver morphology (with hypertrophy of the left lobe), signs of portal hypertension (large portosystemic varices at the gastric funds and around the esophagus), and with end-stage renal atrophy. Note is also made of a TIPS shunt.

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**Fig. 10:** Ultrasound image showing coarse parenchymal texture and selected coronal T2-weighted MR images showing medullary sponge kidneys, abnormal liver morphology and a Todani type one choledochal cyst (arrow) in a one year old baby with congenital hepatic fibrosis.

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**Fig. 11:** Radial MRCP and selected image from an axial T2 weighted sequence with spectral fat suppression. Multiple small T2 hyperintense foci are seen in the liver with little variability in size and with no communication with the biliary tree, consistent with biliary hamartomas.
Fig. 12: Radiopathological classification of ductal plate malformations

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Conclusion

A working knowledge of the principles behind the pathogenesis of DPMs is of paramount importance to general and hepatobiliary radiologists. Clinical imaging plays an important role in the correct diagnosis, stratification of severity, prognosis, and follow-up of DPMs.
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References
