Radiological Imaging in Hepatobiliary and Pancreatic Malignancies

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Contents

Liver malignancies are briefly divided into hypo- and hypervascular lesions. The lesions in hypovascular groups include metastasis from colon, lung, gastric, prostate and transitional cell carcinomas [1, 2] and cholangiocarcinoma. The hypervascular lesions include hepatocellular carcinoma (HCC) and hypervascular metastasis from breast, melanoma, renal, thyroid and neuroendocrine tumour [2, 3].

HCC is the fifth most common malignant neoplasm worldwide and most common liver malignancy. The risk factors for HCC include hepatitis B, C viral infection, alcoholic cirrhosis, cirrhosis from steatohepatitis and hemochromatosis. Clinical presentation would be non-specific; however, it may have right upper quadrant pain, hepatomegaly, ascites and weight loss. Alpha-fetoprotein (AFP) would be elevated with patients with HCC, and it is used for initial diagnosis and monitoring response to treatment [4], but one third of patients will not have elevation of AFP [5].

With the advancement in imaging, it can provide definite diagnosis; however in atypical or equivocal cases, biopsy needs to be done [6–8].

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HCC
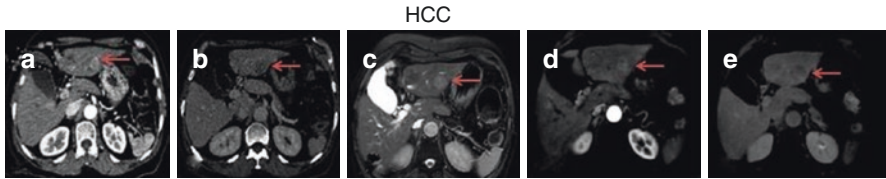
Fig. 4.1 HCC: (**a, b**) contrast-enhanced CT reveals arterially enhancing lesion in the lateral segment, i.e. segment III (**a**), and wash out on porto-venous phases (**b**). On MRI (**c**–**e**), a well-defined T2 hyperintense signal lesion (**c**) which shows rapid wash in on the arterial phase (**d**) and wash out on porto-venous phase (**e**). These imaging findings are classical for hepatocellular carcinoma

Ultrasound (USG) is the first modality when patient experiences right upper quadrant pain. USG would demonstrate coarse nodular liver with irregular nodular surface, with small shrunken right lobe, hypertrophy of the lateral segments and caudate lobe of the liver, ascites, splenomegaly and varices. HCC would be capsulated hypoechoic lesion when <5 cm [9]. Colour Doppler will demonstrate high-velocity signals and portal vein thrombosis [10] (Fig. 4.1).

The typical pattern of enhancement on both CT and MRI scan would be rapid arterial enhancement and wash-out on porto-venous phases and delayed enhancing capsule due to fibrous nature [11]. Arterio-portal shunting is also one of the characteristic features [12]. HCC can cause spontaneous haemorrhage, and surface HCC can rupture leading to hemoperitoneum. On MR imaging it will be hypointense on T1-weighted imaging. It can be hyperintense due to fat, protein or blood content within. On T2 these lesions would be hyperintense with restricted diffusion. Small HCC are <2 cm in size and have classical features, whereas large HCC will not show classical enhancement pattern and will have haemorrhage and necrosis. HCC are known to cause portal vein tumour thrombus which on imaging will enlarge the portal vein, cause arterial enhancement and neovascularity. HCC can have scar, calcification, fat and blood and can be cystic. They can be solitary, well-defined, multiple or diffuse [13].

Fibrolamellar carcinoma occurs in younger patients without underlying liver disease. These on imaging appear as large well-defined lobulated tumours with central scar, calcifications and heterogeneous enhancement [14, 15]. On MRI, these are hypointense on T1-weighted and heterogeneously hyperintense on T2-weighted images [15]. The scar is hypointense on T2 and shows delayed enhancement on post-contrast.

LI-RADS—The Liver Imaging Reporting and Data System is developed by the American College of Radiology with the aim to reduce variability in lesion interpretation, standardizing of the reporting content, improving communication with the clinician and decision-making, outcome monitoring, performance auditing, quality assurance and research [16].

Biopsy is indicated for the nodules which are >1 cm and do not show characteristic pattern on imaging [17–19].

BCLC staging is widely used for HCC since it combines predictor of survival and treatment options.

BCLC staging is widely used for HCC since it combines predictor of survival and treatment options. In radiological stage B of BCLC which is an intermediate group, say, one lesion more than 3 cm or more than three lesions irrespective of size, the best option is transarterial chemoembolization (TACE) [20].

Other liver lesions are discussed in the table.

Liver tumours	Imaging findings
Metastases	On imaging these will be solitary or multiple and well defined which may be hypervascular as in renal cell carcinoma, carcinoid tumour, malignant adrenal tumours, thyroid carcinoma, pancreatic islet cell tumours, NET, sarcomas and melanomas. Calcifications can occur in mucinous colon carcinoma and gastric, breast, renal, carcinoid and lung carcinomas. On MR, these will be hypointense on T1 and hyperintense on T2, except for haemorrhagic lesions which have T1-hyperintense lesions (Fig. 4.2)
Biliary cystadenocarcinoma	On CT these are well-defined intrahepatic masses, which are cystic, with enhancing wall, mural, septal nodules or soft tissue papillary projections on contrast study. On MRI, T1 and T2 show variable signal intensity but will have contrast enhancement similar to CECT
Haemangioendothelioma	Middle age, predominant in females. Lesions are multiple which coalesce to form masses, capsular retraction; tumour enhances peripherally. On MR, hypointense on T1 and homogenous or heterogeneously hyperintense on T2 with peripheral enhancement
Angiosarcoma	Variable enhancement which may be nodular and irregular; may have areas of haemorrhage within. On MR, large mass which may be hypo or hyper due to haemorrhage on T1 and heterogeneously hyperintense on T2 and may show heterogeneous and progressive enhancement on post-contrast

For MRI contrast agents for the liver. There are four types:

1. Extracellular agents
2. Reticuloendothelial agents
3. Hepatobiliary agents
4. Blood pool agents
5. Combined agents

Metastasis
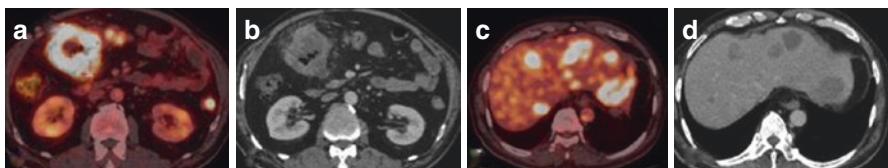
Fig. 4.2 Metastasis: Sixty-year old gentleman with pain in abdomen and mild constipation for 3 months. USG reveals multiple hypoechoic lesions. The above PET/CT images reveals FDG avid lesion in the hepatic flexure (**a**) which on corresponding CECT reveals circumferential heterogeneously enhancing thickening (**b**). Also FDG avid hepatic lesions (**c**) which on CECT (**d**) shows non-enhancing liver lesions. Colonoscopy and biopsy were done which reveal adenocarcinoma

Extracellular agents—Mechanism depends on the gadolinium, which has seven unpaired electrons and is highly paramagnetic resulting in shortening of the T1 and T2 relaxation times of adjacent water protons and causing signal enhancement at T1-weighted imaging and loss of signal at T2-weighted imaging [21, 22]. It is used in lesion detection, characterization and liver vascular anatomy.

Reticuloendothelial agents—Superparamagnetic iron oxides, e.g. ferucarbotran, are currently used as reticuloendothelial agents. They are phagocytosed by macrophages throughout the body but are entrapped by Kupffer cells [23]. They act as negative contrast agent, and due to their superparamagnetic properties, they cause T2 and T2 * shortening [24]. It is used with liver tumours since they are deficient in Kupffer cells and do not exhibit SPIO particle uptake. So after injection of SPIO, the tumour will appear hyperintense since the background is suppressed [25].

Hepatobiliary agents—As they have five unpaired electrons, paramagnetic agents are taken by functioning hepatocytes and excreted in the bile [26]. It shortens T1 and T2 relaxation times of water protons. It is used for characterization of hepatocellular and non-hepatocellular masses since these agents are taken by the hepatocytes (e.g. HCC, focal nodular hyperplasia, hepatic adenoma) and surveillance of the liver for metastasis and functioning of biliary system.

Combined agents—Gadobenate dimeglumine has the property of an extracellular, hepatobiliary and blood pool agent. It is used for HCC, focal nodular hyperplasia and non-hepatocellular lesions, adenoma, metastasis and haemangioma [26].

Cholangiocarcinoma is the second most common malignancy of the biliary system. According to its anatomical origin, it is classified as intrahepatic, hilar or extrahepatic [27].

Intrahepatic CC is an adenocarcinoma that arises from the epithelium of the small intrahepatic bile ducts. Predisposing factors are primary sclerosing cholangitis, *Clonorchis sinensis* infestation, thorium dioxide exposure and congenital biliary anomalies. They are further macroscopically divided into mass form, periductal or intraductal growth. Clinical presentation depends on the location of the mass; peripheral masses are diagnosed late as they cause pain only in late stage where central hilar will cause painless jaundice early. On CT it presents as having a low attenuation mass with incomplete peripheral arterial enhancement that becomes iso- or hypodense on porto-venous phase. Capsular retraction is seen due to fibrosis. There can be ductal dilatation and mural thickening seen in peripheral intrahepatic ducts [28]. On MRI they appear hypointense on T1 and hyperintense on T2. Central area may be hypo or hyper due to fibrosis, mucin or oedema. It shows mild to moderate enhancement with progressive centripetal fill-in of the contrast on delayed phases [29]. On USG it shows solid heterogeneous echotexture mass (Fig. 4.3).

Peripheral CC are primary biliary tumours arising between the right and left and the common hepatic duct up to the cystic duct insertion and also known as Klatskin's tumours [30]. On CT/MR, it will show focal mural thickening with luminal obliteration and peripheral ductal dilatation, periductal thickening with mass, focal liver atrophy, vascular encasement, lymph nodal involvement and distant metastasis.

Cholangiocarcinoma
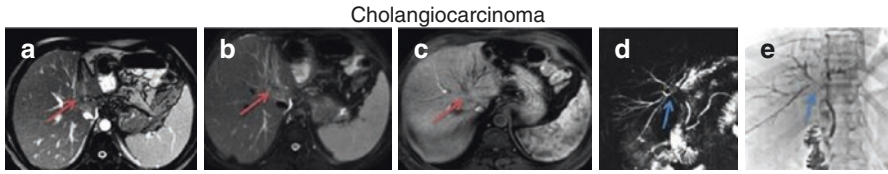
Fig. 4.3 Cholangiocarcinoma: Fifty-eight-year old male with pain in abdomen and progressive pain-less jaundice since 2 months. CECT done outside reveals mass in the left hepatic duct with periportal lymph nodes. MRI abdomen (**a–c**) with MRCP (**d**) done which shows ill-defined altered signal inten-sity mass lesion in the left hepatic duct (↗) extending into the common hepatic duct which shows delayed progressive enhancement, atrophy of the left lobe of liver and mild IHBR dilatation in both lobes. These features are s/o cholangiocarcinoma. MRCP (**d**) reveals stricture (↑) involving the left hepatic duct, confluence and just extending into the right anterior and posterior ductal system s/o type IV block. PTC gram (**e**) done which reveals multiple segmental block s/o type IV block

Distal CC originates between the insertion of the cystic duct in the extrahepatic channel and the ampulla of Vater. On cross-sectional imaging, tumour will show soft tissue density with delayed enhancement and abrupt cut-off and infiltrative thickening of bile duct wall.

4.1   Gall Bladder Carcinoma

It is the most common biliary malignancy worldwide. Most of the patients are diag-nosed in late stages due to vague symptoms. Predisposing factors include choleli-thiasis, porcelain gall bladder, choledochal cyst, congenital cystic dilatation of biliary tree, anomalous pancreatico-biliary junction and low cystic duct insertion and primary sclerosing cholangitis. Clinical presentation includes abdominal pain, fever, weight loss and jaundice [31].

There are three patterns of gall bladder carcinoma:

1. Mass obliterating the gall bladder lumen
2. Focal or diffuse gall bladder wall thickening
3. Intraluminal polypoidal mass [32]

Radiological features in:

1. Mass-forming lesion—On USG it shows heterogeneously hypoechoic mass fill-ing partially or completely. On CT it will show heterogeneously enhancing mass lesion. There may be presence of calcification within the mass or calculi within the gall bladder lumen [33]. On MRI it will show T1 hypointensity and T2 moderate hyperintensity. Similar contrast enhancement is seen as that of CT. CT helps to demonstrate involvement of the hepatic flexure of the colon or regional adenopa-thy. Primary tumour can infiltrate along the bile ducts and biliary system.
2. Focal or diffuse wall thickening—On cross-sectional imaging, it will show asymmetrical, irregular or extensive thickening showing heterogeneous

enhancement. It needs to be differentiated from acute and chronic cholecystitis, xanthogranulomatous cholecystitis and adenomyomatosis.

3. Intraluminal polypoidal mass—It is a mass larger than 1 cm in diameter which is immobile upon changing position on USG.

CT scan is for preoperative staging and MRCP for bile duct and vascular invasion.

4.2   Pancreatic Carcinoma

Pancreatic adenocarcinoma is the most common malignancy of the pancreas.

These tumours are located 60–70% in the pancreatic head, 10–20% in the pancreatic body and 5–10% in the pancreatic tail. They present with pain in abdomen, weight loss and jaundice.

On ultrasound it would be a poorly defined heterogeneous hypoechoic mass. Other indirect signs include dilatation of the pancreatic duct, biliary duct dilatation or both (double duct sign). On CT it will be hypoenhancing mass; tumour in the pancreatic head causes dilatation of CBD and main pancreatic duct, whereas tumour in body of pancreas will cause upstream MPD dilatation. Cross-section imaging will also demonstrate vascular invasion, thrombosis and collateral vessels [34]. On MR it is hypointense on T1 and T2 due to scirrhous fibrotic nature and shows restricted diffusion. Metastases are frequently seen in liver and peritoneum (Fig. 4.4).
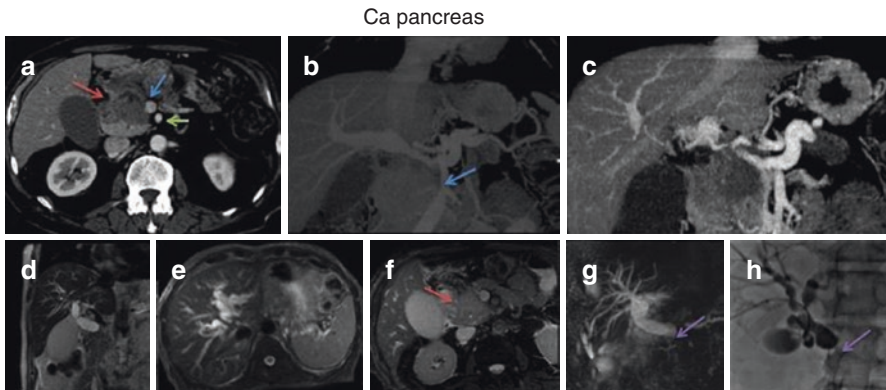
Ca pancreas

Fig. 4.4 Pancreatic cancer: Seventy-year old male with painless jaundice, weight loss. CECT (**a**, **b**, **c**) reveals mass in the head of pancreas (*red arrow*) with abutting SMV (*blue arrow*) = 180° and SMA (*green arrow*) free with double duct sign and multiple periportal lymph nodes. This is s/o head of pancreas malignancy. MRI abdomen (**d**–**f**) with MRCP. (**g**) Mass in the head of pancreas (*red arrow*) which shows hyperintense signal on T2 W and shows heterogeneous post contrast enhancement. MRCP shows stricture (*purple arrow*) involving distal common bile duct s/o type I block. PTC gram (**h**) reveals similar findings

One of the newer modality is endoscopic USG, which has similar findings of USG.

FDG-PET shows high metabolic activity in pancreatic adenocarcinoma. Sensitivity and specificity of FDG-PET (96% and 78%, respectively) were superior to those of CT (91% and 56%), transabdominal US (91% and 50%) and endoscopic US (96% and 67%) [35].

NCCN Guidelines for the Resectability of Pancreatic Adenocarcinoma
Resectable

- -No distant metastasis
- -No SMV/PV abutment, distortion, tumour thrombus, venous encasement
- -Clear fat planes around celiac, SMA, HA

Borderline Resectable

- No distant metastasis
- Venous involvement of SMV or PV consisting of tumour abutting with or without impingement and narrowing of the vessel lumen
- Short-segment venous occlusion resulting from either tumour thrombus or encasement but with suitable vessel proximal and distal to the area of tumour involvement, allowing safe resection and reconstruction
- Gastroduodenal artery encasement up to the HA with either short-segment encasement or direct abutment of the HA, without extension to the CA
- Tumour abutment of the SMA ≤ 180° of the circumference of the vessel wall

Unresectable
Pancreatic Head
• Distant metastases
• SMA encasement >180°, any CA abutment
• Unreconstructible occlusion of the SMV or PV
• Aortic invasion or encasement
Pancreatic Body
• Distant metastases
• SMA/CA encasement of >180°
• Unreconstructible occlusion of SMV or PV
• Aortic invasion or encasement
Pancreatic Tail
• Distant metastases
• SMA/CA encasement >180°
Nodal status
• Metastases to lymph nodes beyond field of resection [36]

Pancreatic neuroendocrine tumour is solid and shows homogenous enhancement, whereas larger tumour shows heterogeneous, cystic-necrotic degeneration and calcification [37]. On MRI these show hypointense signal on T1 and iso- to hyperintense signal on T2. Metastases to the lymph nodes and liver have similar enhancement as primary tumour.

Other tumours include solid pseudopapillary tumour, cystic pancreatic neoplasm, pancreatic lymphoma and metastasis.

Pancreatic tumour	Imaging findings
Serous cystadenoma	Age—seventh decade. Female more than male, asymptomatic. On CT, multicystic, more than six septated by fibrous septae, lobulated, water, soft tissue density, cysts <2 cm, and hallmark feature is central stellate scar which may contain calcification [38]. On MR cluster of tiny cysts with high signal on T2 with intervening septa and scar
Mucinous cystic neoplasms	Age—fifth and sixth decade. Female more than male; body and tail location. Uniloculated or multiloculated cystic mass > 5 cm. On CT, few and large cysts. Walls may be irregular, contains nodularity or septations and may contain peripheral calcification in 15% [39]
Intraductal papillary mucinous neoplasm	Age—seventh decade. Arises from three types of ductal system—main duct, side branch and mixed. On CT, diffuse or segmental dilatation of the main pancreatic duct. On MR, diffuse or segmental dilatation which will be hypointense on T1 and hyperintense on T2. If there are mural nodules, focal solid area, enhancement of the duct wall and main pancreatic duct diameter of 18 mm [40] may suggest features of malignant transformation of main duct IPMN. Similarly, side-branch IPMN. Features that may suggest malignant transformation: mural nodule, solid component, <3 cm
Pancreatic neuroendocrine tumour	Functioning (secretory) and non-functioning (non-secretory). Small tumours, solid and homogenous, and large tumours, heterogeneous cystic-necrotic and calcification. On MR these have low signal on T1 and intermediate to high signal on T2. These enhance avidly [37]

Key Points

- Liver malignancies are briefly divided into hypo and hypervascular lesions.

- Classical HCC on cross-sectional imaging would show rapid arterial enhancement and wash out on portovenous phases and delayedly enhancing capsule due to fibrous nature, in addition on MRI T2 hyperintensity and restricted diffusion.

- LIRADS- Liver Imaging- Reporting and Data System- aim to reduced variability in the lesion interpretation, standardizing of the reporting content, improving communication with the clinician and decision making, outcome monitoring, performance auditing, quality assurance and research.

- Intra hepatic CC- low attenuation mass with capsular retraction, ductal dilatation and mural thickening seen in peripheral intrahepatic ducts and shows mild to moderate enhancement with progressive centripetal fill-in of the contrast on delayed phases.

- Gall cancer has 3 patterns mass obliterating the gall bladder lumen, focal or diffuse gall bladder wall thickening and intraluminal polypoidal mass.

- Pancreatic cancer on cross section imaging hypoenhancing mass, tumour in pancreatic head with dilatation of CBD and main pancreatic duct (double duct sign).

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