

HEPATOCELLULAR carcinoma (HCC), or liver cancer, develops like any other cancer when there is a mutation to the cellular machinery that causes the cell replicate at a higher rate and/or results in the cell avoiding apoptosis. In particular, chronic infections of Hepatitis B and, or C, can aid the development of HCC by repeatedly causing the body's own immune system to attack the liver cells, some of which are infected by the virus, others merely bystanders. This constant cycle of damage followed by repair can lead to mistakes during repair which in turn leads to carcinogenesis. This hypothesis is more applicable, at present, to Hepatitis C. Chronic Hepatitis C causes HCC through the stage of cirrhosis. In chronic Hepatitis B, however, the integration of the viral genome into infected cells can directly induce a non-cirrhotic liver to develop HCC. Alternative, repeated consumption of large amounts of ethanol can have a similar effect. The toxin aflatoxin from certain *Aspergillus* species of fungus is carcinogenic and aids carcinogenesis of Hepatocellular cancer by building up in the liver. The combined high prevalence rates of aflatoxin and Hepatitis B in settings like China and West Africa has led to relatively high rates of HCC in these regions. Other viral Hepatitis, such as Hepatitis A have no potential to become a chronic infection and, thus, are not related to HCC.

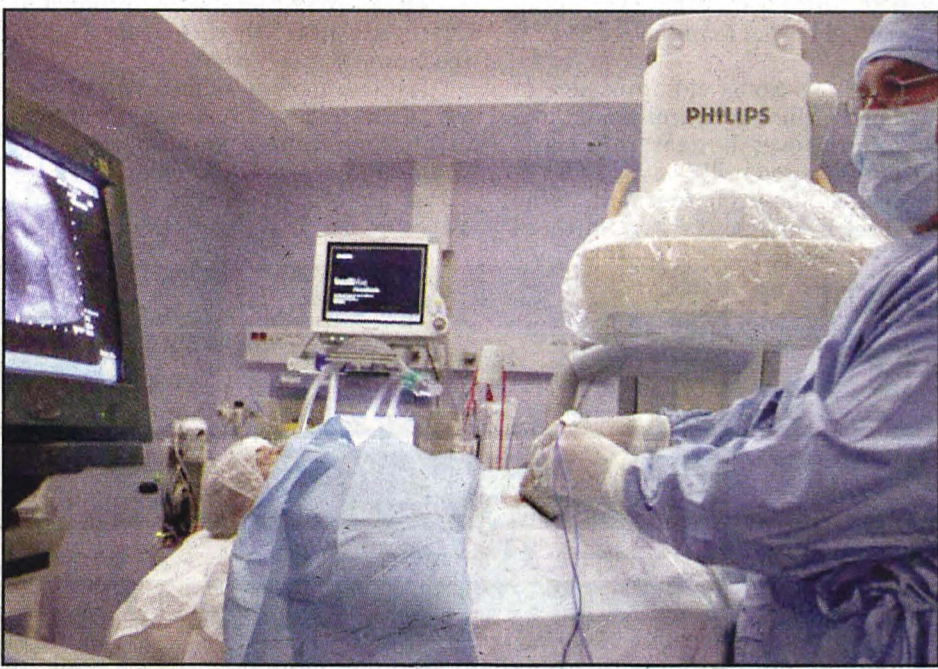
Diagnosis

HCC most commonly appears in person with chronic viral Hepatitis (Hepatitis B or C, 20 per cent) or, and with cirrhosis (80 per cent). These people undergo surveillance with ultrasound due to cost effectiveness. Alpha-fetoprotein is a marker that is useful if is markedly elevated. At levels less > 20 sensitivity is 41-65 per cent and specificity is 80-94 per cent. However, at levels > 200 sensitivity is 31 and specificity is 99 per cent.

Ultrasound, imaging

Ultrasound (pic) is often the first imaging and screening modality used. On Ultrasound, HCC often appears as a small hypo-echoic lesion with poorly defined margins and coarse irregular internal echoes. When the tumour grows, it can sometimes appear heterogeneous with fibrosis, fatty change and calcifications. This heterogeneity can look similar to cirrhosis and the surrounding parenchyma.

In people with higher suspicion of HCC such as rising alpha-fetoprotein and des-gamma carboxyprothrombin levels, the best methods of diagnosis involves a CT scan of the abdomen using intravenous contrast agents and three-phase scanning (before contrast administration, immediately after contrast administration, and again after a delay) to



HCC common in Hep B, C patients

increase the ability of the radiologist to detect small or subtle tumours. It is important to optimise the parameters of the CT examination because the underlying liver disease that most people with HCC have can make the findings more difficult to appreciate.

An alternative to CT imaging study would be Magnetic Resonance Imaging (MRI). MRI has about the same sensitivity for detecting HCC as helical CT. However, MRI has the advantage of delivering high resolution images of the liver without nephrotoxic or ionising radiation. Despite the advantages of MRI, helical CT remains the technique of choice among radiologists due to the high costs and long image acquisition time of MRI.

Classification

Classification of HCC on CT Liver Image Reporting and Data System is the new way to standardise/ classify the HCC lesion found on CT and MRI. Radiologist use this classification system in their imaging reports in order to further characterise suspicious lesions. As rule LR1 and LR2 get continued surveillance. LR3 has variable follow up. LR4 gets close follow up, additional imaging or treatment. LR5 gets treatment. On CT, HCC can have three distinct patterns of growth:

A single large tumour (b) Multiple tumours (c) Poorly defined tumour with an infiltrative growth pattern.

A biopsy is not needed to confirm the diagnosis of HCC if certain imaging criteria are met.

Histopathology

Macroscopically, liver cancer appears as a nodular or infiltrative tumour. The

nodular type may be solitary (large mass). Or multiple (when developed as a complication of cirrhosis). Tumour nodules are round to oval, grey and green (if the tumour produces bile), well circumscribed but not encapsulated. The diffuse type is poorly circumscribed and infiltrates the portal veins or hepatic vein (rarely). Microscopically, there are four architectural and cytological types (patterns) of HCC fibro lamellar, pseudo glandular (adenoid), pleomorphic (giant cell) and clear cell. In well differentiated forms, tumour cells resemble hepatocytes, form trabeculae, cords and nests, and may contain bile pigment in cytoplasm. In poorly differentiated forms, malignant epithelial cells are discohesive, pleomorphic, anaplastic, giant. The tumour has a scant stroma and central necrosis because of poor vascularisation.

Staging

The prognosis of HCC is affected by the staging of the tumours as well as the livers function due to the effects of liver cirrhosis. There are a number of staging classification for HCC available. However, due to the unique nature of the carcinoma in order to fully encompass all the features that affect the categorisation of the HCC, a classification should incorporate tumour size and number, presence of vascular invasion and extrahepatic spread, liver function (levels of serum bilirubin and albumin, presence of ascites and portal hypertension) and general health status of the patient (defined by ECOG classification and the presence of symptoms). Out of all staging classification systems available the Barcelona Clinic Liver Cancer staging classification encompasses all of the above characteristics. This staging classification can be used in order to select people for treatment. The important features that guide treatment include: size, spread (stage), presence of tumour capsule, presence of hepatic metastases, presence of daughter nodules and vascularity of the tumour. MRI is the best staging method to detect the presence of a tumour capsule.

About the authors



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This series on liver cancer concludes next week by examining the treatments and prognosis for the disease.