Current trends in the Radiological Investigation of Hepatic Diseases

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ABSTRACT

Radiological Imaging of the liver plays a central role in the diagnosis and treatment of patients with hepatic disease .Cross sectional imaging techniques such as ultrasound (US), Computerised Topography (CT) and Magnetic Resonance imaging (MRI) all produce high quality images of the liver parenchyma while Plain radiography has very poor sensitivity in the detection of liver disease.

The choice of imaging technique depends on the clinical question, availability, the clinicians' familiarity with the technique and the patient's clinical condition. In general US and CT are the first imaging technique for screening and characterizing most patients with suspected liver disease while MRI is used more as a problem solver when the diagnostic question cannot be answered by either US or CT.

Adequate knowledge of hepatic anatomy as it is depicted by the various imaging modalities is very important in the interpretation of the anatomical changes produced by focal and diffuse pathological processes in the liver.

IMAGING TECHNIQUES

Anatomy: the liver is an accessory digestive organ made up of homogeneous soft tissue parenchyma transverse by vascular channels and bile ducts. It is divided into eight independent segments each of which has its own vascular inflow, outflow and bile drainage. Approximately two thirds of the blood supply to the liver is from the hepatic artery. Venous drainage is through the hepatic vein in the inferior vena cava.

Ultrasound; diagnostic ultrasound makes use of very high frequency sound (1-10 MHz) transmitted from the transducer into the organ. It is particularly suitable for imaging soft tissue and fluid containing structures particularly when there is no intervening bone or air (which is poor transmitters of sound) between the incident beam and the anatomical structure of interest.

On the US images the liver parenchyma has homogeneous echogenicity equal to or slightly greater than that of the kidneys and less than that of the spleen. The vessels are seen as anechoic branching tubular structures. Portal veins are differentiated from other vascular channels by their echogenic walls. Normal intrahepatic bile ducts are not visualized on ultrasound scan. Doppler ultrasound is used to demonstrate the velocity and the direction of blood flow. US is relatively cheap and easily available therefore it is first technique used to screen for liver disease.

Computerized Tomography: This is a digital cross sectional imaging technique that uses a highly collimated X-ray beam and an array of detectors moving through an arch o 360 degrees to image the subject in contiguous slices. The detector measure the X-rays transmitted through the subject and these measurements are converted to number known as CT number, attenuation values or Hounsefield units. The computer produces images in shades of grey based on these numbers.

The liver is uniformly grey on CT with density greater than that of the spleen (HU 65). The portal vasculatures are not identified unless they are outlined by fat.

Contrast enhanced CT is done following a bolus injection of intravenous (IV) contrast during rapid CT scanning. There is immediate perfusion of the hepatic artery and increase in density(enhancement) of the parts of the liver it supplies (arterial phase), portal vein perfusion and maximal liver parenchyma enhancement is delayed for 1 to 2 minutes because of the transit time of the contrast medium through the Gastrointestinal tract (Portal phase)

CT is slightly superior to US in the direction of focal lesions in the liver especially when it is combined with selective injection of contrast into the hepatic artery or superior mesenteric artery, namely CT angiography and CT arterio-portography respectively.

Magnetic Resonance Imaging: MRI is based on the ability of a small number of protons within the body to absorb or emit radio waves (signals) when the body is placed in a strong magnetic field. Different tissues absorb and emit radio waves (signals) at different detectable and characteristic rates. Signal intensity depends on the hydrogen atom concentration and the chemical environment of the tissue (known as magnetic relaxation times T1 and T2) the emitted signals are processed digitally to produce cross sectional anatomic images.

On the MRI brightness of the image depends on the intensity of the radio wave signal, structures are described as having high or low intensity signal or signal void. Tissues that contain little hydrogen such cortical bone generate little or no MR signal and appear black while tissues high in hydrogen such as fat have high signal intensity and appear white.

The normal liver appearance on MR depends on the scanning protocol. On T1 weighted images (TIWI) the normal liver is of slightly higher signal intensity than the spleen and most focal lesions appear as lower intensity defect while on T2 weighted images (T2W1) the normal liver is less than or equal to the spleen in signal and strength and most lesions appear as high intensity foci.

MRI of the liver is used primarily as a problem solving technique rather than as a survey procedure, because it is the best imaging test for liver lesion detection and characterization and does not use ionizing radiation. It is also preferred to CT when there is contradiction to intravenous IV iodinated contrast medium [(2).] In MRI, Gadolinium chelates are used similar to iodinated contrast media in CT, for vascular imaging, to enhance organs and to accentuate pathology.

Radio-Isotope Imaging (Nuclear imaging): this makes the use of radio-pharmaceutical

agents which are radioactive isotopes used alone or in combination with a physiologically active compound. After administration (intravenously, orally or through inhalation) the radio-pharmaceutical agent is selectively taken up by the tissue of interest which then becomes “radioactive” and begins to emit rays from the resident isotope. The pattern of radioactive substance emission is recorded using a gamma camera and forms the basis of the radioisotope or nuclear image. Regions of high concentration of the radio-pharmaceutical tend to appear dark and are called ‘hot’ arrears whereas those areas devoid of radio-pharmaceuticals are called ‘cold’ areas.

Nuclear imaging of the liver is by intravenous injection of technetium-99m labeled albumin or sulphur colloid. These are selectively trapped by Kupffer cells in the liver and reticuloendothehal cells in the spleen to produce images of the liver and the spleen. Nuclear imaging of the liver is inferior to CT and MRI for lesion detection but it is useful in the definitive diagnosis of focal nodular hyperplasia and carvenous haemangiomas.

Position Emission Tomography (PET) a variation of the nuclear imaging techniques, often used to evaluate metastatic liver disease. A greater metabolic activity in malignant tissue is accompanied by a higher glucose uptake relative to that of normal tissue. 18F-flouro-2-deoxy-D glucose (FDG) PET scan identifies this focal increase in glucose uptake and allow for detection of malignant foci. Fusion of PET and CT images acquired at the same time helps to accurately localize the greater metabolic activity. The disadvantage of this procedure is the high cost and poor availability.

Angiography: Celiac artery or selective hepatic artery angiography is now largely performed as a preliminary to catheter placement during interventional procedures. It has been replaced by US, CT and MRI in lesion detection Angiography is also done as part of pre operative assessment of primary and secondary neoplasm.

DIFFUSE LIVER DISEASES

The liver response to injury and toxin may be in the form of fatty infiltration, (**fatty liver**) or diffuse parenchyma destruction fibrosis and regenerative nodules that replace normal liver parenchyma (**cirrhosis**)

Fatty liver: lowers the density of the liver on CT, (HU less than 40) thereby making the liver appear less dense than spleen and on post contrast images, fatty liver enhances less than normal liver. On ultrasound there is increased parenchyma echogenicity with poor visualization of portal vessel walls. The distribution of fat may be diffuse or focal. In either case the internal architecture of the liver is not affected and thre is no masseffect.

Cirrhosis: imaging finding in cirrhosis are those of heterogeneous parenchyma, coarse liver architecture and irregular margins of the liver. The role of imaging is to differentiate the regenerating nodules in the cirrhosis from dysplastic nodules which are precursors of hepatocellular carnoma (HCC). This may not be possible on ultrasound or CT and imaging guided needle biopsy may be required for histological diagnosis.

On contrast enhanced CT or MRI studies, dysplastic nodules and HCC demonstrate early arterial phase enhancement versus non enhancing regenerating nodules. MRI is superior to CT in this regard.

Portal Hypertension is a result of sustained increase in portal vein pressure that results in formation of porto-systemic collateral vessels. Imaging (US) signs of portal hypertension include increased portal vein diameter (> 13mm) and the flow velocity within the portal vein of less than 20cm/s in 80% of cases splenomegaly and ascites are usually present. The most specific evidence of portal hypertension is identification of porto-systemic collateral vessels.

Portal vein thrombosis: may be secondary to cirrhosis or portal vein invasion or compression by tumor. On US and CT the thrombosis is seen as a hyperechoic or hyperdense plug within the portal vein. On MRI, the acute thrombus is hyperintense on TIWIs and isointense when chronic.

Budd Chiari syndrome; obstruction to the hepatic various outflow may be due the presence of congenital web in IVC or thrombosis of the hepatic vein. It has a characteristics appearance on contrast enhanced CT images. In the easily phase the central liver enhances strongly while the peripheral liver enhances weakly. On delayed images the periphery of the liver is enhanced whereas contrast has washed out of the central liver. Multiple benign hepatic nodules (up to 3cm) may develop. Color Doppler shows no flow in one or more hepatic veins or IVC. Characteristic intrahepatic veno-venous collaterals develop and portal hypertension may occur.

Passive liver congestion: occurs in right heart failure and constrictive pericarditis. On US scan the IVC and hepatic vein dilate (hepatic vein diameter more than 10mm) spectral Doppler show an abnormal pattern of continuous blood flow rather than their normal triphasic pulsatility in the hepatic veins and IVC.

Haemochromatosis : may be hereditary or secondary to excessive iron intake. CT demonstrates diffuse increase in density (up to 130 HU) MRI is more sensitive to hepatic iron overload because of the magnetic effect of iron. There is marked diffuse low signal intensity on TIWIs

Gas in portal venous system: this often accompanies life threatening conditions such as haemorhagic pancreatitis, bowel ischaemia in adults and necrotizing enterocolitis in infants. Imaging reveal air in the portal tracts as hypodense branching tubular structures that extends to the liver capsule Air in the biliary tracts is more central and does not extend to within 2cm of the liver capsule. These findings can also be demonstrated on the plain radiograph.

FOCAL LIVER DISEASES

The major challenges in imaging focal lesions of the liver is to differentiate benign from malignant liver masses because of considerable overlap in imaging appearances. Most cysts can be characterized definitely by ultrasound or CT, however solid masses may need imagine guided biopsy for the final diagnosis even with optimal imaging technique.

M**etastasis:** they have a wide spectrum of appearances on all imaging studies. They may be solid, cystic or complex; vascular or avascular; may be sharply marginated or poorly defined. However multiplicity of lesions tends to be characteristic of matastatic deposits.

Cavernous haemangioma: the tumor has large thin walled blood filled vascular spaces separated by fibrous septae. Most are smaller than 5cm, and the size tend to be stable over time. US demonstrates a well defined uniformly hyperechogenic mass. Doppler signal is usually absent because of the very sluggish flow while CT shows a well defined hypodense mass which enhances from the periphery post IV contrast and gradually becomes isodense or hypodense compared to liver parenchyma as blood pools in the mass.

Radionuclide scanning with Technitium -99 labeled red blood cells show prolonged intense activity on delayed images and is highly specific in the diagnosis of cavernous haemangioma.

MRI appearances are not specific but following IV administration of gadolinium it enhances in a pattern similar to that seen in contrast enhanced CT

Hepatic adenoma; they are rare tumors associated with long term contraceptive use and glycogen storage diseases. Hepatocytes within the tumor contain abundant fat which is detectable on imaging studies. The lesion appears hyperechoic US and hypodense on CT. Calcification following necrosis or haemorhage may be seen. Post IV contrast there is intense enhancement during the arterial phase that becomes isodense on delayed scans. They are hyperintense on TIWIs because of fat or haemorhage.

Fibrolamellar carcinoma: this is a hepatocellular malignancy which presents typically as a large mass in a young adult (mean age 23).Imaging shows a large lobulated well defined mass with a characteristic central scar. On US the mass has mixed echogenicity and the central scar is echogenic. On CT the mass is hypodense with strong heterogenous enhancement during arterial and veinous phases. Maximal enhancement of the scar is seen on delayed scans.

Fibrolammellar carcinomais usually hypointense on TIWI s images but sometimes it may be isointense

Hepatocellular carcinoma: is a primary liver malignancy that is associated with chronic hepatitis, cirrhosis and carcinogens such as aflatoxins and sex hormones On imaging, it may be diffuse, solitary or multinodular .The diffuse pattern is very difficult to detect imaging studies. Calcification may be present with the mass and it may be surrounded by a fibrous capsules. On US these lesions appear hyperechoic,

colour Doppler studies may show intratumoral vessels and arteriovenous shunting. HCC are usually hypodense and enhance during the early arterial phase, appearing hypertense to the liver. If present, maximal enhancement of the tumor capsule is seen in the delayed images. CT, like US, also helps to detect vascular extension of tumor, biliary obstruction and regional lymph nodes.

Benign cysts: are frequent incidental findings on liver imaging. On ultrasound they are rounded, smooth walled echo-free structures with distal enhancement. The presence of internal echoes should raise the suspicion that the lesion is not a simple cyst. Cysts are seen as sharply marginated homogenous areas with HU near that of water and they do not enhance after IV contrast medium injection

Pyogenic abscess: early abscess appears as a focal hypoechoic area on ultrasound which later liquefies to produce the typical cavitating lesion.On CT, the mass is hypodense with peripheral rim enhancement post contrast injection. Intra-lesional gas may be present. Amoebic abscess may be indistinguishable from pyogenic abscess. Both can be treated with percutaneous aspiration or catheter drainage under imaging guidance

Hydatid cysts: They present as single or multiple cystic masses with well defined margins on imaging studies, daughter cysts may be visualized within the parent cyst.

Diagnostic aspiration has a risk a anaphylactic reaction.

Interventional radiology

Technological advances have made it possible to use imaging techniques to treat diseases. In some cases interventional radiology can replace surgical methods whereas in others they are a useful adjunct to surgery.

- **Percutaneous liver biopsy under imaging guidance** (US or CT) can be carried out in focal or diffuse liver masses with very low morbidity. In patient with normal coagulation.

Transjugular liver biopsy is performed through the hepatic vein in order to avoid external bleeding. The procedure is performed under fluoroscopy.

- **Embolization or transcatheter vascular occlusion therapy** usually under fluoroscopy guidance is indicated in the treatment of abdominal trauma, malignant or benign tumors and inflammatory diseases. It may have a curative role in intractable bleeding following trauma or in vascular malformation. Pre existing occlusion of the portal vein is a contraindication to embolization of the main hepatic artery

Malignant lesions are treated with selective chemoperfusion with cis- platinum, epirubicin or Iodine 131 which is often combined with Lipiodol as a CT contrast.

- **Percutaneous liver tumor ablation** This may be categorized into three major groups namely
  - injection of the materials such as ethanol acetic acid and hot saline
  - heating which is introduction of radiofrequency electrodes or laser fiber into the tumor under US , CT or MRI guidance. They generate intralesional heat which causes almost immediate coagulation necrosis (at temperature of 60C or greater) and a preferable cyto toxic effect on tumor cells at temperature between 41 and 45^{o}C
  - Other techniques include high intensity focus ultrasound electrocautery**,** Freezing (cryotherapy).
- **Transjugular intrahepatic portosystemic shunt (TIPS)** is the creation of a communication between the portal and hepatic venous system for the relief of the portal hypertension. The shunts are passed through the right internal jugular vein into the appropriate hepatic vein (usually right hepatic) and then through the hepatic parenchyma into the portal vein. When the portal vein is entered the catheter tract is dilated and a flexible TIPS stent is positioned between the hepatic and portal veins thus decompressing the portal venous system thereby allowing flow into the systemic circulation.

CONCLUSION

The optimal care of patients with liver diseases require a close cooperation between the referring clinician and the radiologist, first of all to select the appropriate imaging technique for each patient and to exploit imaging techniques for palliative or definitive treatment. Though CT is globally accepted as the initial diagnostic test, in a resource poor setting ultrasound is versatile, available, relative cheap and it can answer most of the diagnostic questions and it can also be used in imaging guided therapy.

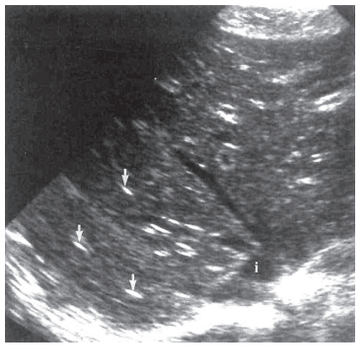

Fig 1: Ultrasound: Starry night appearance of acute hepatitis

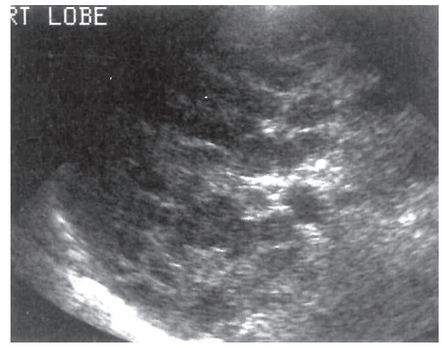

Fig 2: Ultrasound: Hypoecoic regenerating nodules in hepatic cirrhosis

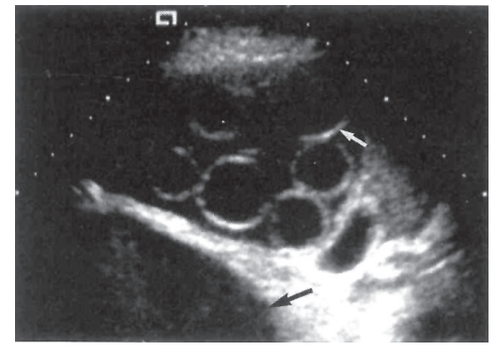

Fig 3: Ultrasound: Hydatid cyst with daughter cysts

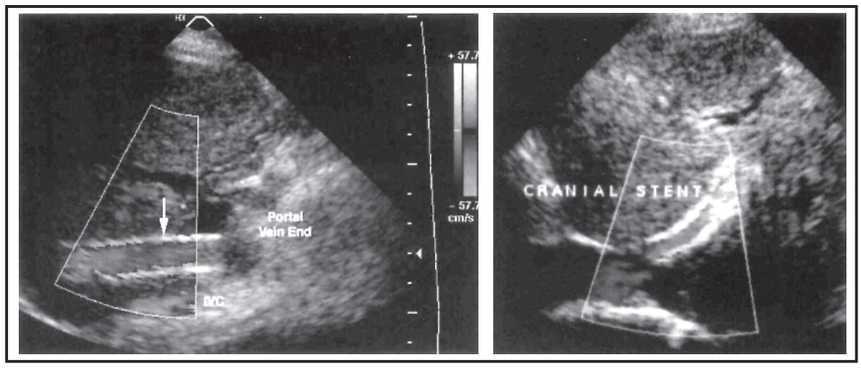

Fig 4: Ultrasound: TIPS Stent

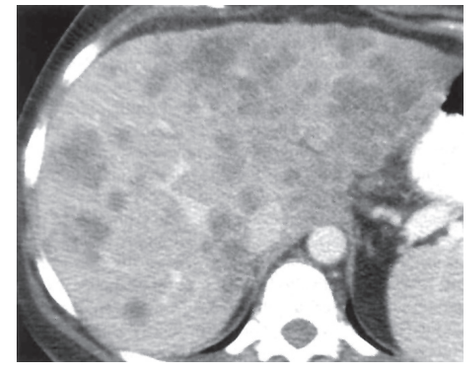

Fig 5: Enhanced CT: Multiple hypodense metastases

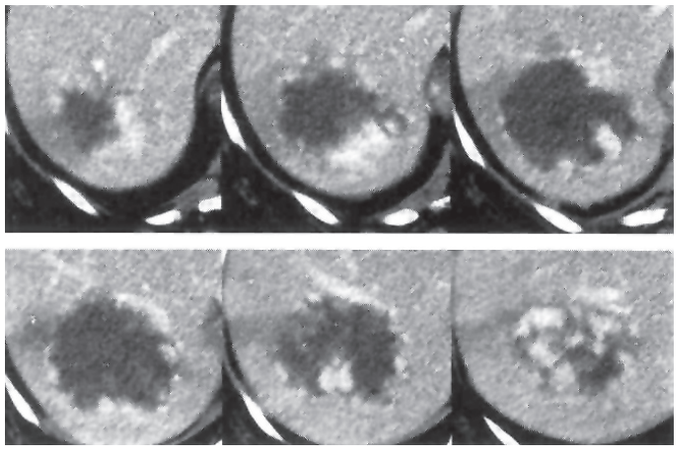

Fig 6: Contrast Enhanced CT: Haemangioma, hypodense lesion filling with contrast from the periphery on delayed views

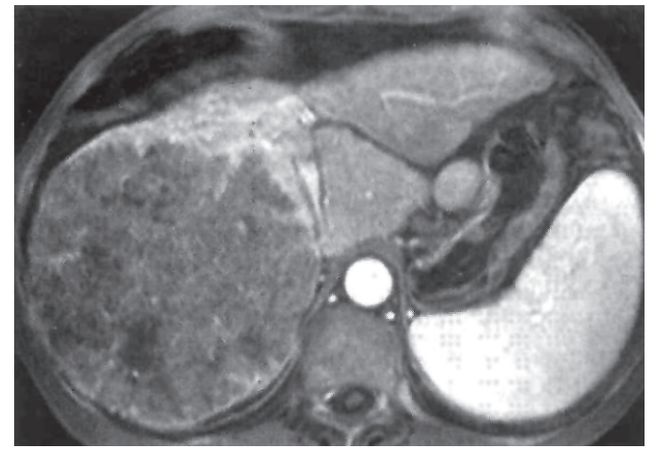

Fig 7: MRI: Hepatocellular carcinoma

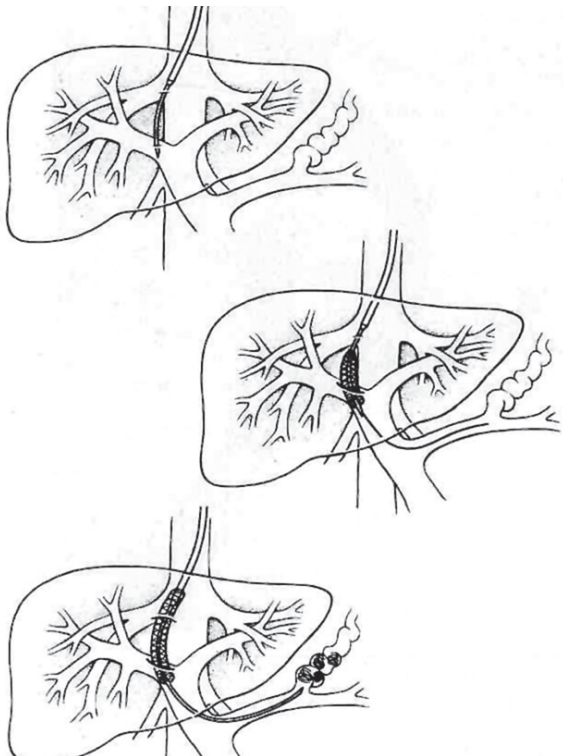

Fig 8: Transjugular Intrahepatic Portosystemic Shunt TIPS (Schematic diagram)

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