Malignant liver tumours

Michael J Hughes

Ewen M Harrison

Abstract

The liver is commonly affected by malignant tumours, both primary and secondary. The majority of liver tumours are diagnosed radiologically and MRI and CT scan are accurate at detecting even small tumours. Hepatocellular carcinoma (HCC) is the most common primary tumour and often presents on the background of liver cirrhosis. The curative options for HCC are liver resection and transplant. However non-curative management such as radiofrequency ablation (RFA) and trans-arterial chemoembolization (TACE) can prolong survival in patients not suited to curative management. Cholangiocarcinoma is a less common malignancy but unfortunately has poorer outcomes. It affects the bile ducts and treatment relies on resection of the affected liver and biliary tree, requiring reconstruction of the biliary drainage system. Postoperative morbidity is high and long term survival is often short. Colorectal liver metastases (CLM) are the most common liver tumours. With improvements in preoperative chemotherapy and surgical techniques such as portal vein embolization (PVE) and two stage resections, curative resection with good long term outcomes are often achieved.

Keywords Chemotherapy; cholangiocarcinoma; colorectal liver metastases; hepatocellular carcinoma; radiofrequency ablation (RFA); resection; trans-arterial chemoembolization (TACE)

Introduction

The liver is commonly affected by malignancy and represents 5.7% of all cancer cases.[1] Both primary and secondary tumours can affect the liver. The most common primary liver tumours are hepatocellular carcinoma and cholangiocarcinoma. The most common secondary tumour is a metastasis from colorectal cancer. This review will summarize the salient issues pertaining to the most common liver malignancies.

Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the most common primary liver tumour and one of the most common tumours worldwide representing 7.9% of all malignancies.[2] In northern Europe the incidence is <5 per 100,000 people. In areas of high incidence such as China and South East Asia HCC is reported in 20 per 100,000 people. Its incidence is increasing in the Western world but decreasing in areas with traditionally high levels of HCC.[2]

Michael J Hughes *MBChB MRCS is a Research Fellow at the Department of Clinical Surgery, University of Edinburgh, UK. Conflicts of interest: none declared.*

Ewen M Harrison *PhD FRCS is a Senior Lecturer in General Surgery and Transplant and HPB Surgeon at the Department of Clinical Surgery, University of Edinburgh, UK. Conflicts of interest: none declared.*

Presentation

The majority of HCCs are picked up incidentally with no symptoms being evident. Symptoms include right upper quadrant pain or fatigue or weight loss. Most often symptoms are related to underlying liver disease, as HCC commonly presents on a background of cirrhosis. As symptoms are often mild or absent, presentation is often late and patients are often unresectable at the time of presentation.[3] As a result of this, ultrasound surveillance programmes are recommended for patients who are at risk of developing HCC, namely cirrhotic patients or chronic hepatitis B or C carriers.[3]

Risk factors for HCC

HCC presents on the background of underlying chronic liver disease in around 80% of cases.[3] It is important to establish the cause of the underlying liver disease as this can have implications for outcome and definitive management.

Chronic viral liver disease is an important precursor to HCC, namely hepatitis C virus (HCV) and hepatitis B virus (HBV), which together are present in 70% of all HCC cases.[3] Hereditary heamochromatosis, alcoholic liver disease and autoimmune disease are also significant risk factors.[3]

The presence of cirrhosis from any cause is a risk factor for developing HCC with an annual risk of 1–6%.[3] However, patients with HCV and HBV related cirrhosis are more at risk of developing HCC than other aetiologies.[3]

Diagnosis

Routine modalities for diagnosis and assessment of surgical approach are ultrasound, CT scanning and MRI scanning. Alpha-fetoprotein is often raised in HCC, has a sensitivity of 41–65% and a specificity of 80–94%[4] and is used as a tumour marker to aid diagnosis and monitor disease progression.

Often imaging is the only method of diagnosis and certain criteria are applied to contrast studies to help confirm the diagnosis. CT scanning that employs an arterial and venous phase of the scan of the intravascular contrast is important. This is because HCCs are only supplied by arteries whereas the liver receives blood supply from both the arterial system and the portal venous system. This anatomical distinction allows for radiological characterization.

When contrast is shown up in the arterial system the tumour will be brighter than the surrounding liver because the blood in the portal venous system will not show up with contrast. In the venous phase, the contrast will be in the portal venous system, enhancing the liver parenchyma and not the arteries supplying the tumour. This phase, known as the 'washout' phase, will show the tumour to be less bright than the surrounding tissue and is diagnostic for HCC.[5] MRI employing contrast that is taken up by hepatocytes and excreted via the biliary system allows for accurate assessment of pathology with rate of uptake indicative of cell involvement. This has allowed for a reduction in biopsy related diagnoses.

CT and MRI scanning have high sensitivities for diagnosing HCC. However, the specificity is not as high so there are instances of false positives. Because of this, particularly for small tumours both CT and MRI should be performed to provide the best chance of correctly diagnosing the lesion.[4]

Obtaining a biopsy of the tumour to confirm diagnosis prior to treatment is not normally indicated due to the ability to diagnose HCCs with CT and MRI scanning in the majority of cases. If these modalities are not diagnostic and there is a specific concern regarding the diagnosis, a biopsy may be performed. The concern with this approach is seeding of tumour during the procedure although reported instances of this occurring are low.

Treatment

The curative options for treatment of HCC are liver resection or liver transplantation. Radiofrequency ablation (RFA) or microwave ablation involve burning the HCC and may be curative if the lesion is very small, though for many patients with background liver cirrhosis there is a high chance of further lesions developing elsewhere within the abnormal liver. Trans-arterial chemoembolization (TACE) involves delivering chemotherapy directly to the tumour but does not result in cure. The choice of treatment depends on several factors, most notably the size and number of tumours, progression of disease, underlying liver disease, patient comorbidity and functional status as reported by the Barcelona Clinic Liver Cancer classification system (Figure 1).

Liver resection: surgical resection is indicated in patients with good liver function. Tumours must be positioned within the liver to allow curative resection while leaving a remnant liver of sufficient size. In patients without cirrhosis, liver resection for HCC results in a 5-year survival rate of 50%;[6] 50% of patients with non-cirrhotic liver will recur within 2 years.[6] Re-resection is often indicated in these patients with similar long-term outcomes to primarily resected patients.[6]

The majority of HCCs develop on the background of cirrhosis.[4] When assessing treatment options grading of the Child-Pugh score is important (Table 1) to quantify the underlying degree of hepatic compensation. Further assessment should be made to exclude portal venous hypertension, including detailed CT scanning to determine splenomegaly and ascites and oesophagogastroscopy to exclude oesophageal varices.[4] Portal hypertension is considered a contraindication for hepatic resection in patients with cirrhosis.[4]

The regenerative capacity of patients with higher Child-Pugh scores is compromised resulting in higher rates of liver failure and postoperative mortality. The 5-year survival rates for patients with cirrhosis who undergo resection for HCC is 45%; however, the recurrence rates have been reported as high as 80%.

In non-cirrhotic patients resection of up to 75% of the liver can be performed and an expected future liver remnant (FLR) of 25% would be expected to function adequately and regeneration would be expected to satisfactorily replace the resected liver.[7]

Should the FLR be anticipated to be less than 25% the options to permit surgical resection include portal vein embolization. This involves occlusion of the portal vein branch supplying the affected hemiliver in order to induce ischaemia and therefore atrophy to the affected segments and hypertrophy of the disease free segments in anticipation of resection of the atrophied portion of liver. In patients who are cirrhotic an FLR of up to 40% is required.[7]

Liver transplantation: is considered for HCC when the underlying liver disease is more advanced and the HCC size and number are more. The Milan criteria for liver transplant for HCC were developed to aid identification of patients are suitable for transplantation. These criteria stipulate that on imaging, the tumour should be either single and <5 cm in diameter or up to three nodules all <3 cm and without vascular invasion.[8] Pathological analysis of the explanted liver from those who have undergone transplantation can show if an individual was actually beyond the Milan criteria. That these individuals often have good long-term

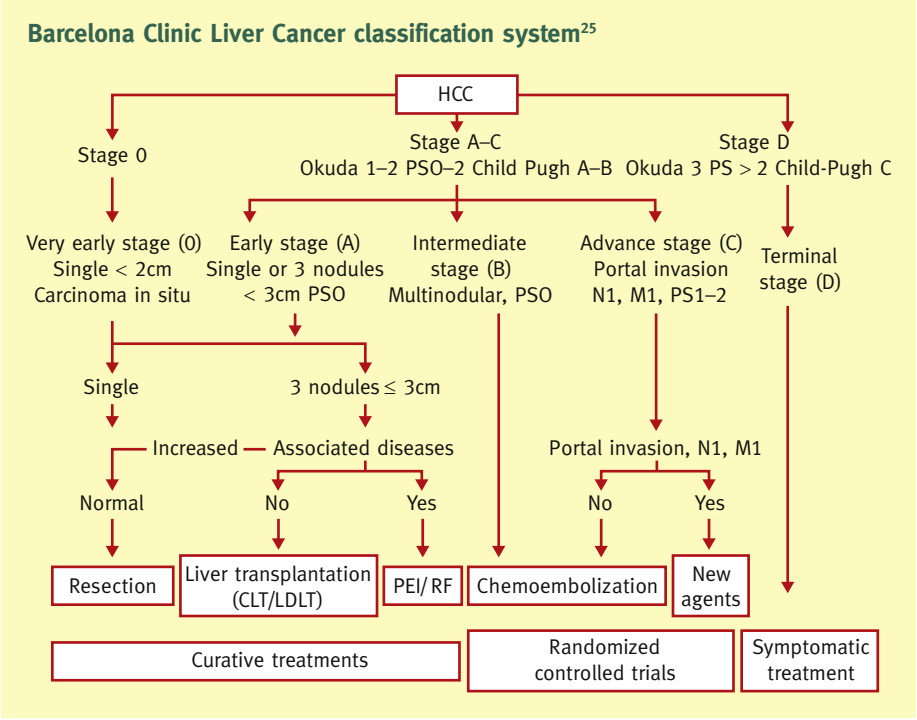

Figure 1