**Hepatocellular carcinoma**

 Incidentally diagnosed at screening/follow up of chronic liver disease

 Right upper Quadrant pain/mass, Jaundice, Nausea, weight loss, symptoms related to metastasis

Triphasic CECT Abdomen and pelvis

Gadolinium enhanced MRI scan abdomen (in cirrhotics and suspected cirrhotic patients)

CBC , Liver function tests, PT/INR HBSAg *HBV Total Core Ab*, HCV

Child and HKLC/BCLC scoring, Alfa feto protein, *PIVKA*

Endoscopy for varices, *HVPG*

Metastatic workup if curative treatment : CT Scan chest,

 If Surgical management -Measurement of FLR (functional Liver Remnant) for major resections

US / CT guided Biopsy only LIRADS 4 and AFP< 400ng/mL

Nutritional evaluation and supportive care for liver disease

If HbsAg +ve screen family and treat/vaccinate

**Good Liver Function(Childs A/ B)**

**Poor liver function (Child C)**

- Liver transplant for tumors within Standard criteria if no metastatic disease and no PVT

Best supportive care

**Resectable tumour (adequate FLR)**

**No main trunk venous thrombosis**

**No extra hepatic disease**

**Limited co-morbidity**

**Curative treatment options**

Liver Resection if Child score is A or early B / HKLC I or II , no or mild portal hypertension.

Liver transplantation if Child score is B or C or if moderate to severe portal hypertension is present. (fitting LT criteria for HCC)

RFA may be used as an alternative for tumors up to 3 cm in poor risk patients

TACE can be considered to downstage tumours to fit in size criteria for transplant / facilitate resection.

**Multiple/ bilobar tumours, Inadequate FLR, No extra hepatic disease**

**Limited co-morbidity**

**Good liver function(Child A,B)**

Transarterial chemo-embolization (TACE) if no portal venous thrombosis

Multiple sessions of TACE can be given at 3 monthly intervals for control.

Can reassess for curative resection with or without augmentation of FLR by PVE

 OR

add Sorafenib/Lenvatinib

 **Extra hepatic disease**

**Irrespective of PVT, or no and size of the tumors and good liver function (Child A or early B)**

Palliative therapy with targeted agents with Sorafenib/ Lenvatinib

**Surveillance**

Patients must be followed up for liver failure and recurrence every 3 months with LFT, AFP and contrast MRI / CECT Scan,abdomen and pelvis + CT chest

Local recurrence with good liver function would necessitate complete work up for potentially curable salvage treatments

**KEY – Normal font- Essential, Underlined -desirable, italics- optional**

 NOTES:

1. Screening is suggested for all cirrhotics with good functional status (who would be eligible for treatment if a lesion is found), and those who are HBsAg+ve. A 6 monthly ultrasonography and AFP is recommended by the APASL. A new nodule or growing nodule to be investigated by cross sectional imaging.
2. For diagnosis of lesions > 2cm a triple phase CECT abdomen is appropriate. For smaller lesions a dynamic multiphase contrast MRI may be added.The LIRADS score should be followed. For LR-3 lesions, repeat imaging at 3 months is effective unless immediate decision making is required eg transplant suitability assesment. Contrast US is an effective tool for problem solving especially for patients with raised creatinine.*18 FDG PET CT has no role in routine evaluation or follow up of HCC (except borderline renal function and for transpalnt evaluation). 11C Choline PET may be useful for troubleshooting.*
3. Patients with Hepatitis B and C will need evaluation and treatment for the virus in addition and all cirrhotics need management in conjunction with gastroenterologists.
4. Liver resection for non cirrhotic patients is ideal with FLR > 30% but in selected cases with excellent liver function even FLR 20% may be tolerated. In cirrhotic patients, ideal candidates are those with Childs A status, platelet counts > 100,000 and no varices or HVPG < 10 mmHg wherein FLR 40% may be accepted. For those with bilirubin 1-2 mg/dL and portal hypertension, segmental resections may be considered in selected cases and is ideally predicted by ICG resection <15%
5. Liver transplantation is ideally reserved for patients within Milan criteria (Single tumour < 5cm or not > 3 tumours each < 3cm in diameter) wherein the mortality is similar to patients not having a tumour . *With additional increase in size and number the risk of tumour recurrence post transplant increases proportionately (The Metro Ticket concept). The decision to transplant is best taken as a decision between the transplant team and the patient and family understanding the risks involved.* Extrahepatic metastasis and tumour thrombus in the portal vein is an absolute contraindication. *In very selected cases segmental portal vein thrombosis patients may be transplanted under a study protocol.* AFP > 1000 ng/mL is usually a contraindication for transplant.
6. In tumours less than 3 cm RFA may give similar results to resection. It is particularly useful in deeper tumours, wherin a large resection may be spared or in unfit patients. The decision should be taken by a multidisciplinary team. RFA should not be considered in tumours > 5cm in size. TACE + ablation may be performed in tumours 3-5cm in size and proximity to vessels to overcome the heat sink effect.*Microwave ablation gives similar results to RFA.*
7. *Transarterial radioembolisation (TARE) has no proven benefit over TACE or sorafenib. Anecdotal cases of resolution of portal vein tumour involvement with TARE facilitating transplant exist.*
8. *SBRT is under evaluation for tumours where ablation or embolization has failed or is contraindicated especially in presence of portal vein thrombosis and size < 5cm.*
9. Targeted agents such as Sorafenib / Lenvatinib may improve survival in metastatic disease but there is no evidence of improvement of quality of life. These are currently not cost effective in India. The recommended dose is 400mg bd but often lesser doses need to be given to improve tolerability. There is no evidence to support use of these drugs in conjunction with other treatment modalities. Nivolumab may be considered for initial responders to sorafenib but now progressing.

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