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Malignant Hepatic Lesions: Ct, Biochemical and Pathologic Findings in Northeast India

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Abstract: *Hepatic Space Occupying Lesions (SOLs) are increasingly being detected due to the widespread use of imaging modalities.It is important to label the lesion as benign or malignant.It is also essential to categorise the malignant lesion as primary or secondary.Knowledge of the underlying key pathologic features with biochemical indices and imaging findings of liver masses on MDCT(MultidetectorComputed Tomography) allows characterization in most cases. Some masses, however, may exhibit overlapping and nonspecific radiologic features, and in such cases percutaneous image-guided biopsy may become necessary. This study was performed to review the CT characteristics of malignant hepatic lesions with biochemical and pathological correlation.61patients who underwent contrast CT with a 128-slice CT scanner were included. The precontrast,late arterial,portal venous phase and equilibrium phase were evaluated with biochemical and histopathological correlation.22 patients belonged to non-tribal population while 39 were tribals from Northeast India.The age ranged from 16-80 years and 22 patients were females.31 patients had hepatic metastases from various primaries,27 patients had Hepatocellular carcinoma,2 patients had primary hepatic neuroendocrine cancer(PHNEC) and one had desmoplastic round cell tumour.*

The imaging characteristics on multiphase contrast-enhanced CT in combination with clinical and biochemical correlation allows noninvasive characterization of most liver lesions comparable to MRI. It also has an added advantage of detecting primary extrahepatic tumor and allows proper staging.

Keywords: *128-sliceMDCT,common malignant hepatic lesions,PHNEC,desmoplastic round cell tumour*

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I. Introduction

Liver masses are increasingly being identified due to the widespread use of imaging modalities. Metastatic disease should always be considered in the differential for a mass that does not meet imaging criteria for a simple cyst in a patient with known extrahepatic malignancy undergoing imaging surveillance. In patients with chronic liver disease or cirrhosis, hepatocellular carcinoma (HCC) is the leading differential (1).Presently MDCT(Multidetector Computed Tomography) is widely used for further characterizing suspicious lesions in the liver. CT is also useful in detecting primary abdominal malignancy and evaluating lymph node status and distant metastasis which are all critical prognostic factors . While US(Ultrasound) and MRI(Magnetic Resonance Imaging) also have similar accuracy, CT is preferred because it out-performs US and MRI in evaluating the non-hepatic abdominal structures. Other benefits of CT are easy access due to wide availability, and patient-friendly protocols allowing even a chest–abdomen–pelvis CT examination in a less than 20-second breath-hold using multidetector CT technology (2). While some single-center comparative studies have shown slightly better performance of dynamic MR imaging using extracellular contrast agents than multiphasic CT for evaluation of HCC, the differences are small. The per-lesion sensitivity of MR imaging for nodular HCC of all sizes is 77%–100%, while that of CT is 68%–91%. The per-lesion sensitivities, stratified by size, are 100% for both modalities for nodular HCCs larger than 2 cm, 44%–47% (MR imaging) and 40%–44% (CT) for 1–2-cm HCCs and 29%–43% (MR imaging) and 10%–33% (CT) for HCCs smaller than 1 cm . Thus, both modalities provide excellent sensitivity for nodular HCCs larger than 2 cm, modest sensitivity for 1–2-cm HCCs, and poor sensitivity for HCCs smaller than 1 cm, and it is not yet clear which modality is superior. Disadvantages of CT include radiation exposure and relatively low soft-tissue contrast(3).The Northeast Region of India has higher incidence of cancer as compared to the rest of the country, with the dubious distinction of having the highest incidence of several gastrointestinal cancers, including HCC.The cancer registries indicate that the incidence of

HCC in age standardized population is highest in North-eastern states(4).This study was undertaken to review the CT characteristic of malignant hepatic lesions presented to a tertiary hospital in North East India with biochemical and pathological correlation where applicable.

II. Materials and Methods

Study design: This retrospective study was conducted at a public sector tertiary hospital in Northeast India by the Department of Radiology in collaboration with Departments of Surgical Oncology,Medicine and Pathology, over a period of one year 8 months (September' 2016 – May' 2018).

CT Procedure methodology:

Patients were kept nil per oral for 3 hours prior to the study. It was ensured that the serum creatinine and blood urea were within normal limits. All patients were scanned with a 128 Slice MDCT scanner (SOMATOM Definition AS+**,** Siemens, Erlangen, Germany).Collimation 0.6mm x 128 with a reconstruction interval of 1 mm, pitch was 1.2 and gantry rotation was 0.5 seconds.

80-100 ml of nonionic contrast(Ultravist) with concentration of 350mgI/ml was used. A saline chaser of 40 ml was used. Rate of injection was 4- 5 ml per second for both the contrast and chaser with power injector (IMAXEON, Sydney, Australia). We use automated bolus tracking trigger software for starting the scan.CT abdomen was performed by taking plain scan initially followed by late arterial(8seconds after a threshold of 175 HU),portal venous(50 seconds after start of arterial phase) and equilibrium phase(150 seconds after start of arterial phase)in the region of the liver . Image interpretation was performed on a dedicated 3D workstation (Syngo.via) by two experienced radiologists.

Images were analysed for number of lesions,size of the lesion or size of the largest lesion when there are multiple lesions,presence of calcification in plain scan,arterial hyperenhancement,portalwashout,presence of portal vein and IVC thrombosis,presence of chronic liver disease(CLD),presence of lymphnodes,pulmonary nodules in visualized lungs,adrenal gland nodule/mass, and any other abnormal findings in the rest of the abdomen (stomach,bowel,peritoneum, mesentery,adnexae,ascites). All patients were discussed by a Multidisciplinary Team consisting of Surgical/Medical/Radiation Oncologists and pathologist, along with the radiologists. The data was entered into Microsoft Excel and analysed.

III. Result

We included 61patients.Two patients suspected of HCC on CT were excluded due to lack of biochemical/histopathological confirmation.All patients with hepatic metastases had pathological confirmation of the primary malignancy except for two patients with unknown primary. 9(29%) patients underwent biopsy/FNAC from the hepatic lesions.Of the HCC patients, biopsy was performed in 8 patients,1 patient underwent FNAC from bone metastasis.Both patients with Primary Hepatic Neuroendocrine Cancer(PHNEC) and another with desmoplastic round cell tumour were also biopsied.

Table no 1: Types of malignantLiver lesions

Metastasis 31(50%)	HCC 27(43.5%)	PHNEC 2(3.2%)	Desmoplastic round cell tumour 1(1.6%)

Table no 2: Prevalence of different biochemical and imaging parameters in malignant hepatic lesions

	Number	Cal	HbsAg	AFP	CLD	Lymph nodes	PVT	IVCT	Pul nod	Bone mets
Metastasis Ca lung 8(25.8%)	8 multiple								3	2
Ca colorectal 7(22.5%)	1 single 6multiple	1							3	
	2 single 4 multiple		1						3	

Ca Breast 6(19.3%) Ca stomach 4(12.9%) CUP[x] 2(6.4%) Ca Esophagus 1(3.2%) Ca prostate 1(3.2) Ca larynx 1(3.2%) Ca GB 1(3.2%)	4 multiple									
	2 multiple									1
	1 multiple						1		1	1
	1 multiple								1	
	1 single									
	1 multiple									
HCC	12(44.4%) single 15(55.5%) multiple	4(14.8%)	+ 13(48.1%)	0.72-2lakhs	14 (51.8%)	2(7.4%)	9(33.3%)	3(11.1%)	4(14.8%)	1
PHNEC	2, both single	nil	-	wnl	nil	1	nil	nil	nil	1
Desmoplastic round cell tumour	1,multiple	nil	-	wnl	nil	nil	nil	nil	nil	nil

x-Carcinoma of unknown primary
cal-calcification
HbsAg-Hepatitis B surface antigen
AFP-Alpha fetoprotein
PVT-Portal vein thrombosis
IVCT-Inferior venecava thrombosis
Pul nod-Pulmonary nodules
Bone mets-Bone metastasis
wnl-within normal limits

Patients included 39 men and 22 women aged 16–80 years (mean age, 48years) .Thirty nine(63.9%) belong to the tribal communities of different Northeastern States of India with no definite preponderance of any particular cancer in any specific community.

Secondary Metastases were the most common malignant hepatic lesion(50%) with Cancers of the lung,colorectum and breast being the most common primary.Twenty seven(87.1%) patients had multiple lesions with four(12.9%) patients having solitary lesion.Lesion sizes ranged from 0.8-5.5 cm.Calcification was seen in only one(14.3%) patient with sigmoid colon adenocarcinoma primary. All these lesions were hypovascular. We detected fifteen(48%) primary lesions in our study. Disseminated metastases in lungs or bones were detected in eleven(35.5%) patients.None of the patients had features suggesting chronic liver disease(CLD), while one patient with unknown primary had bland portal vein thrombosis.One patient of Cancer breast had Hepatitis B Surface Antigen(HbsAg) positivity.

In patients with HCC,serologic evidence of hepatitis B was found in thirteen(48.1%)patients and AFP ranged from 0.72-2lakh ng/ml. While eighteen(66.6%) patients had AFP>400,in2(7.4%) patients the AFP was within normal limits. Fourteen(51.8%)patients had CLD features of which six patients had HbsAg positivity.Lesion size ranged from 2.9-23.8cm. Single lesions were found in 12(44.4%) patients, predominantly involving the right lobe.Four(14.8%) patients had patchy calcification within.

In twenty six(96.3%)patients, lesions were hyperenhancing in the arterial phase with washout in the portal venous and equilibrium phase.One(3.7%)patient had a solitary 10cm hypovascular lesion which was better visualized in the portal venous phase.We detected small (<1cm) periportal lymphnodes in two(7.4%) patients.Nine9(33.3%) patients had malignant portal vein thrombosis.All these patients had multiple/solitary large lesions(>10cm).All three(11.1%) patients with IVC thrombosis had concurrent portal vein thrombosis.Four(14.8%) had pulmonary nodules, with three of them having concurrent portal vein thrombosis.One patient(3.7%) with a left adrenal nodule also had portal vein thrombosis.

Two(3.2%) middle-aged female patients with large solitary hepatic mass were diagnosed as PHNEC on histology.HbsAg was negative with very lowAFP(2.6-3ng/ml).

One(1.6%) male patient, 19 years of age presented with multiple hepatic SOLs,with the biopsy revealing desmoplastic round cell tumour.HbsAg was negative and AFP was within normal limits.

Figure 1:Hepatic metastases in a patient with Ca lung:Axial CT scan obtained during the portal venous phase demonstrates solid(arrow) and peripherally enhancing(block arrow) lesions of varying sizes.

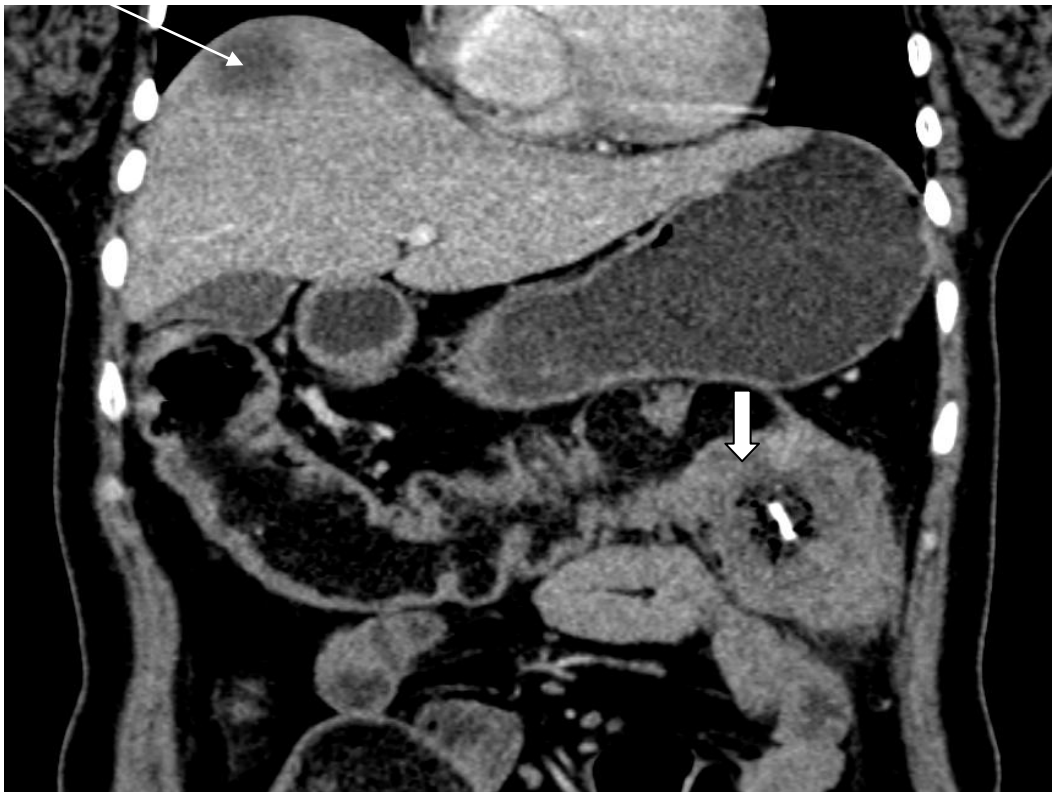

Figure 2:Hepatic metastasis in a patient with Ca Colon:Coronal reformation CT in the portal venous phase reveal a mass in the splenic flexure (block arrow) with a hypodense hepatic lesion (line arrow).

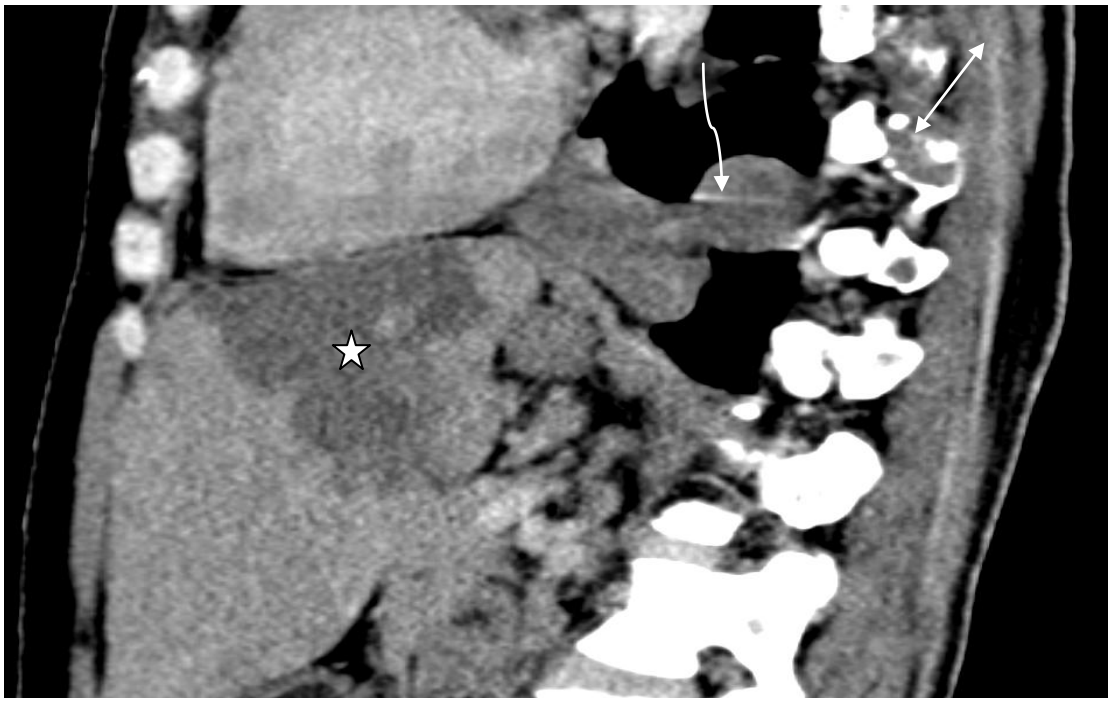

Figure 3: Hepatic metastasis in a patient with Ca breast:Sagittal reformation CT demonstrates hepatic lesion (star), pulmonary nodules (curve arrow) and rib metastasis (double arrow) in the visualized lung.

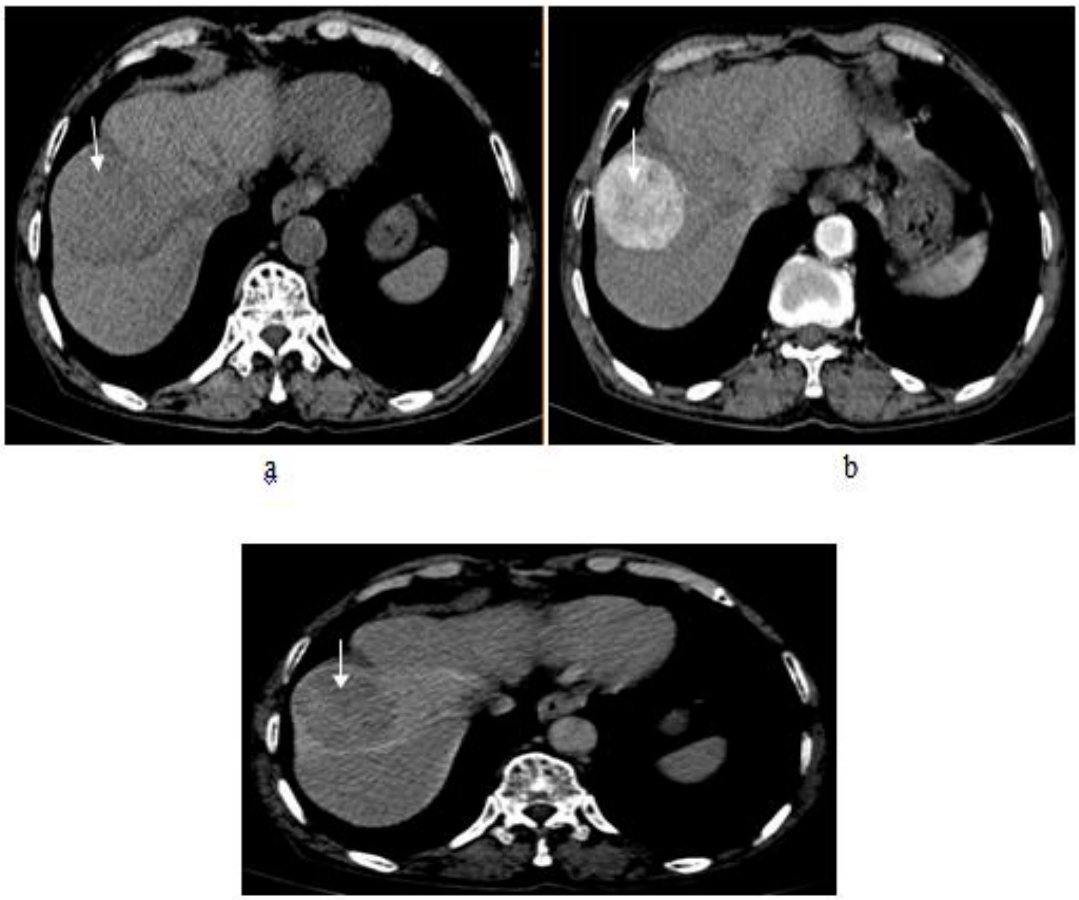

Figure 4:Solitary HCC in a 75 year old male:(a)Axial nonenhanced CT scan shows a mass (arrow) in the right lobe that is hypoattenuating to the liver. (b) Axial CT scan obtained during the hepatic arterial phase after bolus injection of contrast material demonstrates heterogeneous enhancement of the tumor with well defined margins. (c) Axial CT scan obtained during the portal venous phase demonstrates contrast wash out by the tumor.

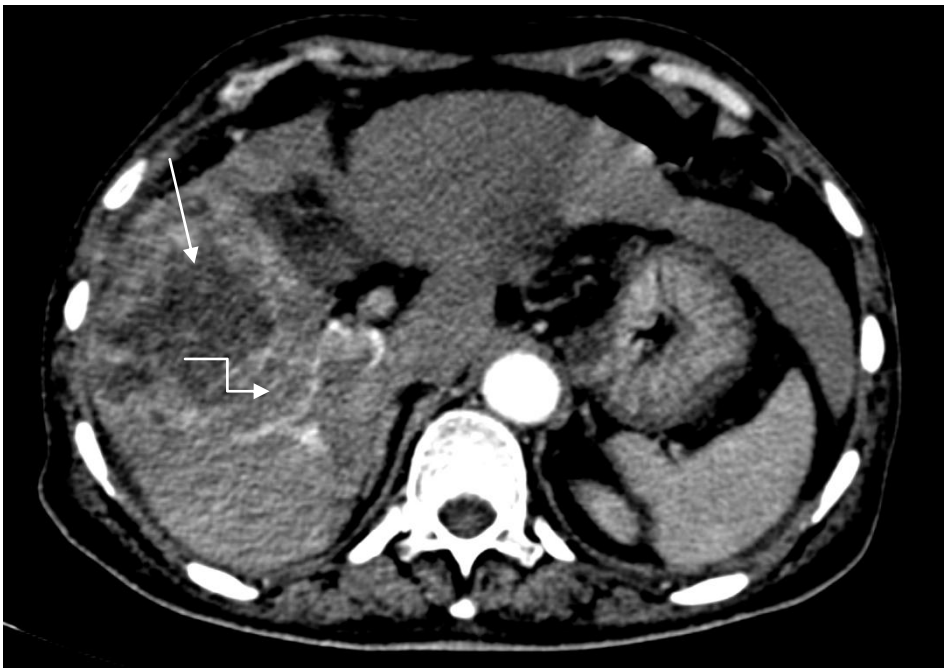

Figure 5 : Multifocal HCC in a 66 year old male:Axial CT scan obtained during the hepatic arterial phase demonstrate a hypervascular mass (arrow) in the right lobe of liver with thrombosis of the right portal vein (curve arrow).

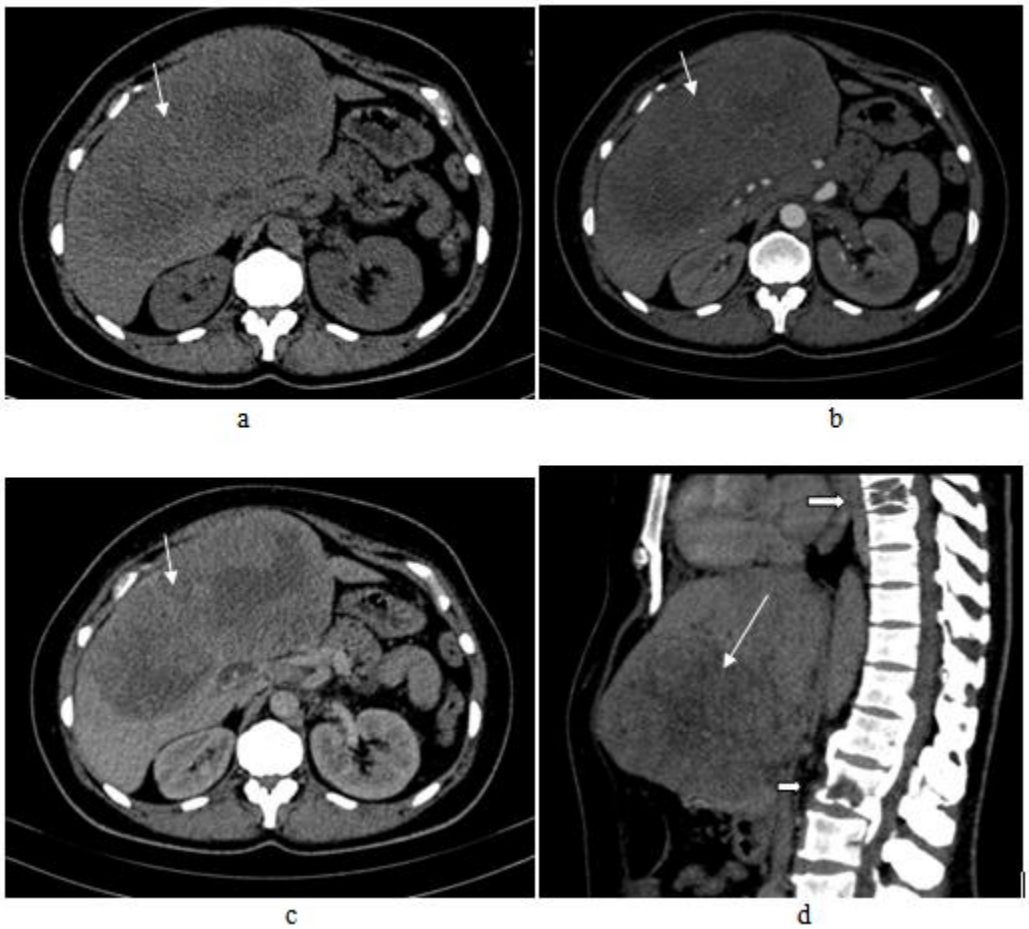

Figure 6:PHNEC in a 43 year old female:Axial nonenhanced CT scan shows a large mass (arrow) occupying both lobes of the liver that is hypoattenuating to the liver. **(b)** Axial CT scan obtained during the hepatic arterial phase after bolus injection of contrast material demonstrates mild enhancement of the tumor. **(c)** Axial CT scan

obtained during the portal venous phase demonstrates more enhancement of the tumor with fairly well defined margins.(d)Sagittal reformation of the same patient reveal the hepatic mass (arrow) and bony metastases (block arrow) in the visualized vertebrae.

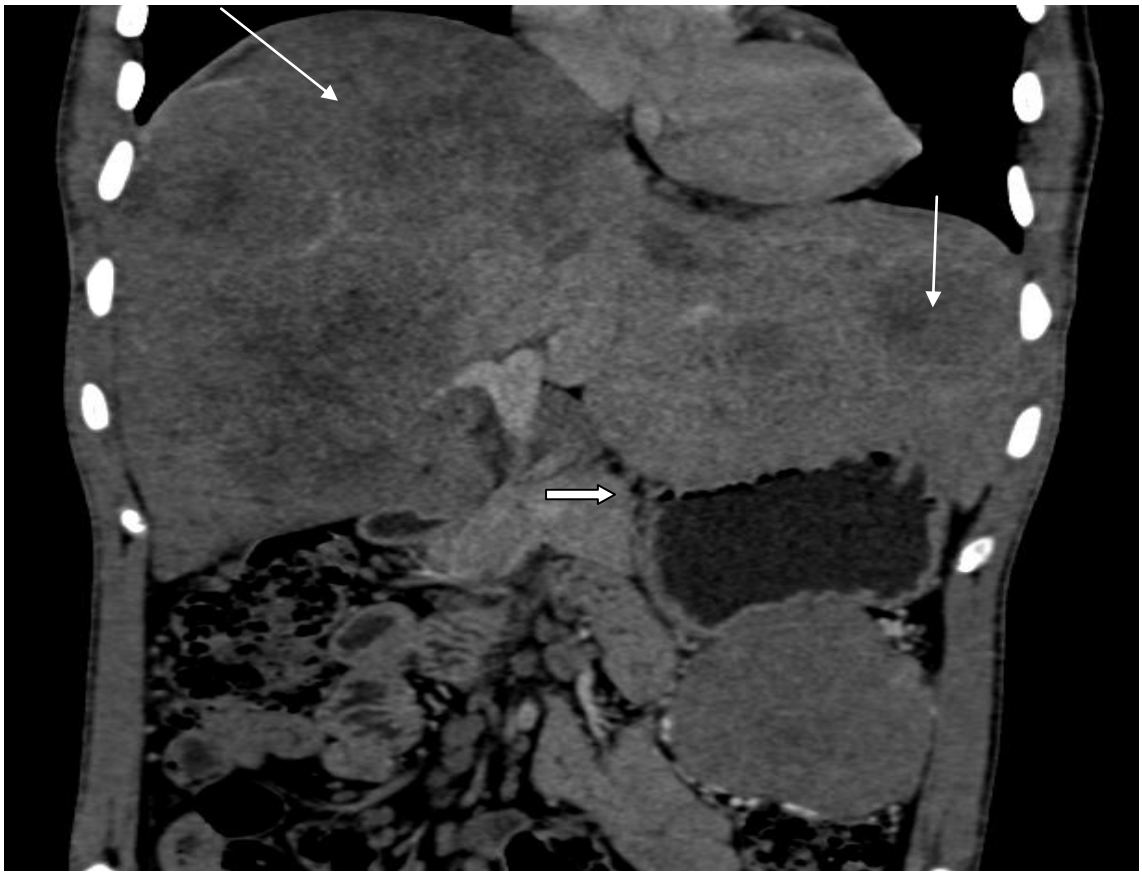

Figure 7: Desmoplastic round cell tumour in a 19 year old male:Coronal reformation CT scan obtained during the portal venous phase demonstrates multiple large enhancing lesions (arrow) in both lobes of liver with central non enhancing areas.Awell defined similar density lesion (block arrow) is also present in the mesentery.

IV. Discussion

Our study found metastasis as the most common malignant hepatic lesion(50%),followed by HCC(43.5%),two cases of PHNEC and one Desmoplastic round cell tumour.

Cholangiocarcinoma(CCA)was not detected in any of our patients during the study period.According to Bergquist et al, CCA is the second most common primary liver tumour and accounts for approximately 10-15% of all hepatobiliary malignancies(5).

According to Lamba et al,metastasis is by far the most common malignancy of the liver with colon, stomach, pancreas, breast, and lung being the most common primary sites(1).However the most common primary from this region was Cancer lung followed by colorectal and breast cancers.It is also noted that head and neck cancers and oesophageal cancers, which have a high incidence in this part of the country has less propensity for hepatic metastasis.We encountered only one laryngeal cancer and one oesophageal cancer which metastasized to the liver.

Only nine(29%) of our patients labeled as hepatic metastasis underwent biopsy/FNAC from the hepatic lesions which included four patients with solitary lesions,two patients with unknown primary and three patients with multiple lesions.According to Assy et al, if a patient is known to have a primary malignancy and the lesion was found at tumor staging or follow up, histology is required only when the nature of the liver lesion is doubtful(6).

All these lesions were hypovascular since none of our patients had primary malignancy which are known to produce hypervascular hepatic metastasis.These lesions were better depicted in the portal phase showing solid or peripheral enhancement. According to Tsao et al,approximately 90% of hepatic metastases are partially or completely hypovascular(7).Soyer et al also showed that portal-dominant phase imaging depicted significantly more hypovascular hepatic metastases than did unenhanced (P > .001) or arterial-dominant (P >.01) phase imaging(8).

Calcification is seen in only one(14.3%) patient with sigmoid colon adenocarcinoma.According to Scatarige et al, fifteen of eighty two patients (18.3%) with liver metastases from colorectal carcinoma showed calcific deposits(9).

Twenty seven(87.1%) patients had multiple lesions with four(12.9%) patients having solitary lesion.Lu et al found 21% solitary lesions in his study which is much higher as compared to our study.

We could detect fifteen(48%) primary lesions in our study which is comparable to a study done by Lu et al(50%)(10). In the United States, CT is the most widely used imaging modality for screening the abdomen and pelvis for metastatic disease. In addition to evaluating the liver, extrahepatic metastases can be evaluated during the same examination(1).

HCC accounts for 43.5% of hepatic lesions in the current study which supports the cancer registries that the incidence of HCC in population at large is highest in north-eastern state(4).Size range from 2.9-23.8cm,single lesion are twelve(44.4%) in number predominantly involving the right lobe.According to Yaqoob et al, unifocal lesions constitute 32.5% and size range from 0.8 to 14 cm(11).

In four(14.8%) patients who had patchy calcification,lesions were large(>10cm),solitary and located in the right lobe.According to Scatarige et al,calcific deposits were noted in nine of fiftynine patients (15.3%) with hepatocellular carcinoma (HCC) but it offers no beneficial clue to the diagnosis(9).

CLD features were seen in fourteen4(51.8%) patients, of which six patients had HbsAg positivity.Reports from tertiary care centers in India on HCC indicate that 70–97% of patients with HCC at the time of diagnosis had underlying cirrhosis of liver(4).A study by Koea et al revealed four of the five patients with HCC had radiological signs of cirrhosis(12).

According to Assy et al,AFP values >400 ng/ml are indicative of HCC and 30% of patients with HCC < 2 cm have normal AFP(6).Our two patients with normal AFP however had lesion >6cm in size.Biopsy was not done in patients with AFP>400 showing classic arterial hypervascularity and portal washout according to AALSD(The American Association for the study of liver disease)(1).

While HbsAntigen was positive in thirteen(48.1%) patients,all three with AFP<20 were negative for HbsAg.According toMurakami et al, the annual carcinogenesis rates for liver cirrhosis related to hepatitis B is 2.5%–3% and carcinogenesis can be observed early after infection and in young patients(13).In our study, only three patients were below 40 years of age and the age group of patients with hepatitis B positivity was 29-75 years.

In twentysix(96.3%) patients, lesions showed hyperenhancement in the arterial phase with washout in the portal venous and equilibrium phase.One(3.7%)patient had a solitary 10cm hypovascular lesion which was better visualized in the portal venous phase.Biopsy from the mass revealed HCC in the background of cirrhosis.His AFP level was >7000 and HbsAg was negative.Several studies have demonstrated that 27%–34% of small HCCs are hypovascular (9).

Nine (33.3%) patients had portal vein thrombosis**.** Incidence of malignant portal vein thrombosis in association with HCC has been reported to range from 5% to44%(1).All these patients had multiple/large lesions(>10cm).All three(11.1%) patients with IVC thrombosis had concurrent portal vein thrombosis.Four(14.8%) had pulmonary nodules, while three of them also had concurrent portal vein thrombosis. According to Lee et al, 2.7% of pulmonary nodules represented HCC metastases(14).

In the two patients diagnosed as PHNEC,CT revealed large, solitary lesions located predominantly in the right lobe measuring 13-16cm in sizes.None had calcification.HbsAg were negative with very low AFP(2.6-3ng/ml).The lesions were well-encapsulated,showed mild enhancement in the arterial phase which persisted in the portal venous phase with central areas of necrosis.One of them had periportal lymphnodes and bone metastases, with none showing portal vein thrombosis.In a study by Yang et al, ten of the eleven patients exhibited two or more lesions, and one patient exhibited a single lesion. Abdominal CT of 8 cases revealed multiple round or oval-shaped masses with well-defined borders, which were heterogeneous and hypodense on precontrast CT images. Significant diffuse heterogeneous enhancement was observed during the arterial phase in 8 cases and continued enhancement in the portal venous phase(15).Zhoa et al reported two cases of PHNEC, wherein one of the cases presented with a large tumor in the right liver lobe and the other presented with tumors in both liver lobes, invasion into the left branch of hepatic portal vein, and metastasis in the hepatic hilar lymph node(16).

There was one patient 19 years of age suspected of having lymphoma but biopsy from the liver lesion showed desmoplastic round cell tumour.There were multiple large hypovascular hepatic lesions with mild heterogeneous enhancement on portal phase.No calcification present.A well-defined similar density mass lesion was also present in the mesentery.No retroperitoneal lymphnodes were seen.In a study by Chen et al comprising of 4 patients with intraabdominal desmoplastic round cell tumour, CT revealed multiple large slightly or moderately heterogeneous enhancement abdominopelvic lesions. Other observations from these patients included calcification (n=2), peritoneal seeding (n=3), hepatic metastasis (n=3), retroperitoneal lymphadenopathy (n=3) and ascites (n=2)(17).A study by Chouli et al of 13 cases(12men,mean age 24.8 years)

found peritoneal involvement as the most common finding and liver metastases in 5 patients(18).In a study by Pichardt et al of 14 patients,lobulated peritoneal masses is the hallmark imaging feature and hepatic metastasis is a less common associated finding(19).

As with all retrospective studies, ours has limitations. Specifically, we did not study the imaging characteristics of other benign hepatic lesions or compare our findings with MRI,which is a more established imaging modality for hepatic SOLs.Besides, we could not include those patients with malignant hepatic lesions who presented to us with imaging done from other centres.

V.Conclusion

Metastases,the hypovascular variety, remain the commonest hepatic malignancy in Northeast India followed closely by HCC. The size of HCC lesions are bigger compared to other population groups. The imaging characteristics on multiphase contrast-enhanced CT in combination with clinical and biochemical correlation allows non-invasive characterization of most liver lesions comparable to MRI.Although the findings are non-specific,we can also suggest diagnoses of uncommon malignant hepatic lesions which do not fit with established imaging findings of metastasis and HCC.

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