Original Research Article

Magnetic Resonance Imaging in Focal Liver Lesions with Diffusion Weighted Imaging (DWI) and Pathological Correlation

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Abstract

Background: Magnetic resonance signal intensity of focal liver lesions is affected by numerous pathologic factors. Lesion histologic features, such as cellularity, vascularity, stromal component, and intratumoral necrosis or hemorrhage, strongly affect T1 and T2 relaxation times.

Aim and objectives: To assess the lesion characterization potential of MRI by evaluating unenhanced and dynamic gadolinium enhanced sequences, Histopathological correlation of the lesions to explain the major MRI findings and Assessment of the lesions by diffusion weighted imaging and investigating the role of b value in differentiating malignant and benign lesions

Materials and methods: The study was done on 42 patients where contrast was given in 38 members. Focal liver lesions were analyzed based on clinical findings, laboratory investigations and MR imaging. Sonographically detected focal lesions were included in the study. Tissue diagnosis (FNAC/ Biopsy), surgery were done in feasible cases. In other cases, where surgery/ tissue diagnosis is not possible, follow up was done (range 3 months - 12 months, average 7.2 months).

Results: MRI features of forty two patients with focal liver lesions were studied and morphological features and signal intensities of the masses were described. Contrast study was done in 39 cases. Of the 42 cases, 24 lesions were benign and 18 lesions were malignant. The mean age group ranged from 18 to 74 years with majority between 40 to 60 years. 61% of the lesions were located in right lobe of the liver. Contrast enhancement was done in 39 cases. Contrast enhancement was able to better delineate the cases. Specific pattern of contrast enhancement was typical of certain lesions as

homogenous early arterial phase enhancement for hepatocellular carcinoma and ring enhancement in arterial phase for metastases. Delayed enhancement was specific for cholangiocarcinoma. Hemangiomas showed peripheral puddling and delayed central enhancement. Diffusion weighted imaging can be used as an additional tool in differentiating benign and malignant focal liver lesions. ADC value using a cut-off of 1.43 X 10^{-3} sec/ mm^2 was a useful adjunct for determining benign cystic lesions and hemangiomas from malignant lesions.

Conclusion: MRI was able to predict diagnosis in 38 of the 42 tumors. It could suggest the nature of all lesions in benign cysts, hemangiomas, focal nodular hyperplasia and metastases. But it was not possible to achieve a specific diagnosis in two early abscesses, one multifocal hepatocellular carcinoma and one case of regenerative nodules. This accounted for a detection rate of 90%. Thus MR imaging is a powerful tool for the evaluation of focal liver lesions. Pre contrast T1 weighted gradient echo images, T2 weighted images, in phase and out phase imaging, EPI – DWI and gadolinium enhanced T1 weighted images provide accurate characterization of the lesions.

Key words

Liver focal lesions, MR imaging, DWI values, Hemangioma, HCC, FNH, Hepatic adenoma, Simple cysts, Abscess, Hydatid cysts, Biliary cystadenoma, Regenerative nodules.

Introduction

Magnetic resonance signal intensity of focal liver lesions is affected by numerous pathologic factors. Lesion histologic features, such as cellularity, vascularity, stromal component, and intratumoral necrosis or hemorrhage, strongly affect T1 and T2 relaxation times. Additionally, intracellular content of certain substances, such as glycogen, fat, melanin, iron, and copper, may also have a substantial role in determining MR signal behavior.

The exact prevalence of benign liver masses is unknown but some studies suggest that they may be found in more than 20% of the general population [1].

With the application of multi-row detector CT and thin collimation, it is likely that more liver lesions will be detected that will need additional imaging for characterization, most likely with MR imaging. It is also important to distinguish benign and malignant liver lesions. Several malignancies, such as breast, pancreas and colorectal tumors metastasize to liver.

The survival rate following the resection of isolated metastasis especially in colorectal malignancies can be as high as 38% [2]. MRI is particularly well-suited to the evaluation of liver pathology due to an ability to generate contrast by a variety of mechanisms. This allows specific evaluation of important diffuse processes such as abnormal fat, as may be seen in non-alcoholic steatohepatitis, or iron accumulation as seen in hemochromatosis.

The use of intravenous gadolinium-based contrast agents allows evaluation of the vascular supply to benign and malignant tumors, yielding important diagnostic information. MRI can be very useful for confirming the diagnosis of hemangioma, focal nodular hyperplasia, complex cyst, etc. without the need for biopsy, surgery, or multiple follow-up examinations.

Coexisting benign lesions such as hemangiomas and cysts were also noted. The anatomical proximities of the lesions to the inferior vena cava or hepatic veins, hepatic hilum and to the main portal branches were assessed. For this purpose, a scale for the lesion's proximity of less than 1 cm or more than 1 cm was used.

Benign or suspected malignant lymph nodes were scrutinized and the possibility of other extrahepatic involvement such as infiltration

through the hepatic capsule or peritoneal metastases was considered.

Intravenous gadolinium contrast agents provide additional opportunities for the characterization of the lesions. Diffusion weighted imaging enables qualitative and quantitative assessment of tissue diffusivity (apparent diffusion coefficient) without the use of gadolinium chelates, which makes it a highly attractive technique, particularly in patients with severe renal dysfunction at risk for nephrogenic systemic fibrosis [3].

Our study was done to assess the lesion characterization potential of MRI by evaluating unenhanced and dynamic gadolinium enhanced sequences.

Materials and methods

A total of 42 consecutive patients who were referred to the department of Radiodiagnosis, NRI General Hospital and were diagnosed by sonography as having focal liver lesions were included in the study after informed consent. In all studies MR imaging was performed with a clinical 1.5 T system (General electrical medical systems). A dedicated phased-array body coil was used.

Sequences

Pre contrast: Axial T2-weighted SSFSE, Axial 2D FIEST and Axial in phase and opposed phase 2D FSPGR sequences.

Post contrast: Dynamic Gd-enhanced MR imaging using the fat-suppressed Multiphase LAVA performed in the arterial, portal venous phases and equilibrium phases. (Magnavist, Bayer pharmaceuticals, 0.1 mmol/kg body weight; injection rate 2 ml/s. Liver-specific contrast agents were not used in our study).

Diffusion-weighted respiratory-triggered single shot spin echo echoplanar imaging (SS SE-EPI) sequence using b-values 600 s mm-2.

Evaluation of images:

On the basis of signal characteristics, enhancement patterns and morphology, the lesions were characterized. The size and number of liver lesions as well as the hepatic segments involved were recorded for the solid lesions. Couinaud's anatomical description of eight liver segments for lesion localization was used. Coexisting benign lesions such as hemangiomas and cysts were also noted.

Benign or suspected malignant lymph nodes were scrutinized and the possibility of other extrahepatic involvement such as infiltration through the hepatic capsule or peritoneal metastases was considered.

Tissue diagnosis (Fine needle aspiration cytology/ trucut biopsy) was obtained in feasible cases.

In patients with hemangiomas and simple cysts either follow-up (range 3 months- 12 months, average 7.2 months) or post-surgical histopathology had been considered.

Results

MRI features of forty two patients with focal liver lesions were studied and morphological features and signal intensities of the masses were described. Sex distribution was as per **Table – 1**.

Contrast study was done in 39 cases. Of the 42 cases, 24 lesions were benign and 18 lesions were malignant. The mean age group ranged from 18 to 74 years with majority between 40 to 60 years (**Table – 2**). 61% of the lesions were located in right lobe of the liver (**Table – 3**). Enhancement patterns on gadolinium enhanced MRI was as per Table – 4. Incidence of benign and malignant lesions was as per **Table – 5**.

Table – 1: Sex distribution.

Sex	Number of cases	Percentage
Male	29	68%
Female	13	32%

Characterization of the lesions as benign and malignant by various sequences was as per **Graph – 1**.

The mean ADC value of benign lesions was 2.092 X 10^{-3} sec/ mm^2 and that of malignant lesions was 1.241 X 10^{-3} sec/ mm^2. The difference in mean ADC values in both the groups was significant ($p<0.0001$). The threshold ADC values to distinguish the above two groups was determined to be 1.43 X 10^{-3} sec/ mm^2 by ROC analysis. The area under the curve was 0.922 and the standard error was 0.066 (**Graph – 2**).

Correlation between radiological and histopathological diagnosis of benign entity was as per **Table – 6**. Correlation between radiological and histopathological diagnosis of malignant entity was as per **Graph – 3**.

Table – 2: Age distribution.

Age	No. of Patients
10 – 20 years	0
20 – 30 years	4
30 – 40 years	12
40 - 50 years	9
50- 60 years	15
60 – 70 years	2
>70years	0

Table – 3: Location of the lesions.

Location	Number of lesions
Right lobe	26
Left lobe	7
Both lobes	9

Discussion

The study was done on 42 patients of whom contrast was given in 36 members. Focal liver lesions were analyzed based on clinical findings, laboratory investigations and MR imaging.

Sonographically detected focal lesions were included in the study. Tissue diagnosis (FNAC/ Biopsy), surgery were done in feasible cases. In other cases, where surgery/ tissue diagnosis is not possible, follow up was done (range 3 months - 12 months, average 7.2 months)

MR imaging

We considered multiple lesions of similar morphology in a single patient as a single lesion. Metastasis is the most common malignant lesion and abscesses are the most common benign lesions. The size of the lesions varied from 0.7 cm to 14 cm with an average of 6.3 cm for malignant lesions and 5.5 cm for benign lesions. The size of the lesions is not predictive of the malignant character of the lesion.

Lesion detection

Of the total Lesions detected by contrast enhanced sequences, 90% were detected on T2 WI and 97% were detected on diffusion weighted images. Diffusion weighted images were able to detect small metastatic lesions which were inconspicuous on T2 weighted images. These small lesions were also identified on gadolinium enhanced scans. According to Parikh, et al. [4] the malignant focal liver lesions detected by DW imaging (86.4%) was significantly greater than that detected with T2-weighted imaging (62.9%).

Table – 4: Enhancement patterns on gadolinium enhanced MRI.

Arterial phase enhancement patterns	HCC	Metastasis	Hemangiomas	FNH
Homogenous	4			1
Inhomogenous	1			
Complete ring		8	1	
Incomplete ring		1		
Peripheral puddles			3	

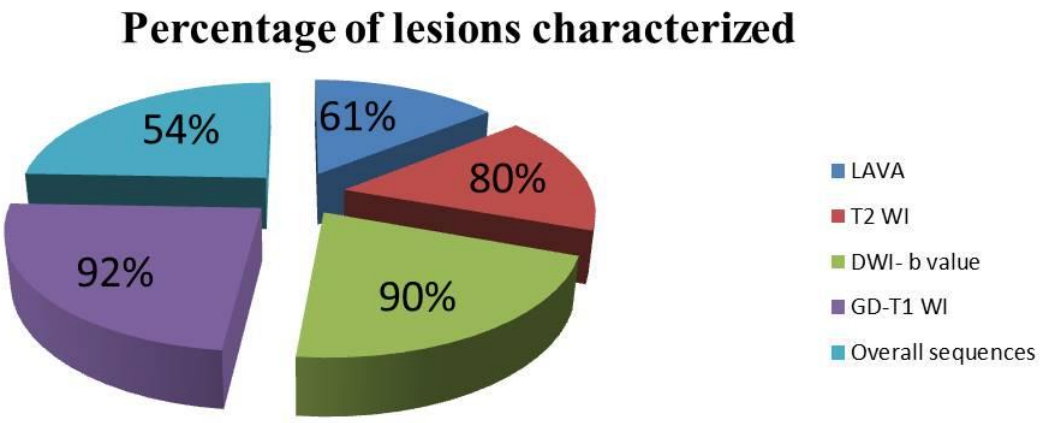
Table – 5: Incidence of benign and malignant lesions.

Lesions	Nature of the lesions	
	Benign	Malignant
Simple cysts	4	
Abscess	7	
Hydatid cysts	4	
Hemangiomas	4	
Focal fat sparing	2	
Biliary cystadenoma	1	
Focal nodular hyperplasia	1	
Metastasis		9
Hepatocellular carcinoma		5
cholangiocarcinoma		4
Regenerative nodules	1	
Total	24	18

Table – 6: Correlation between radiological and histopathological diagnosis of benign entity.

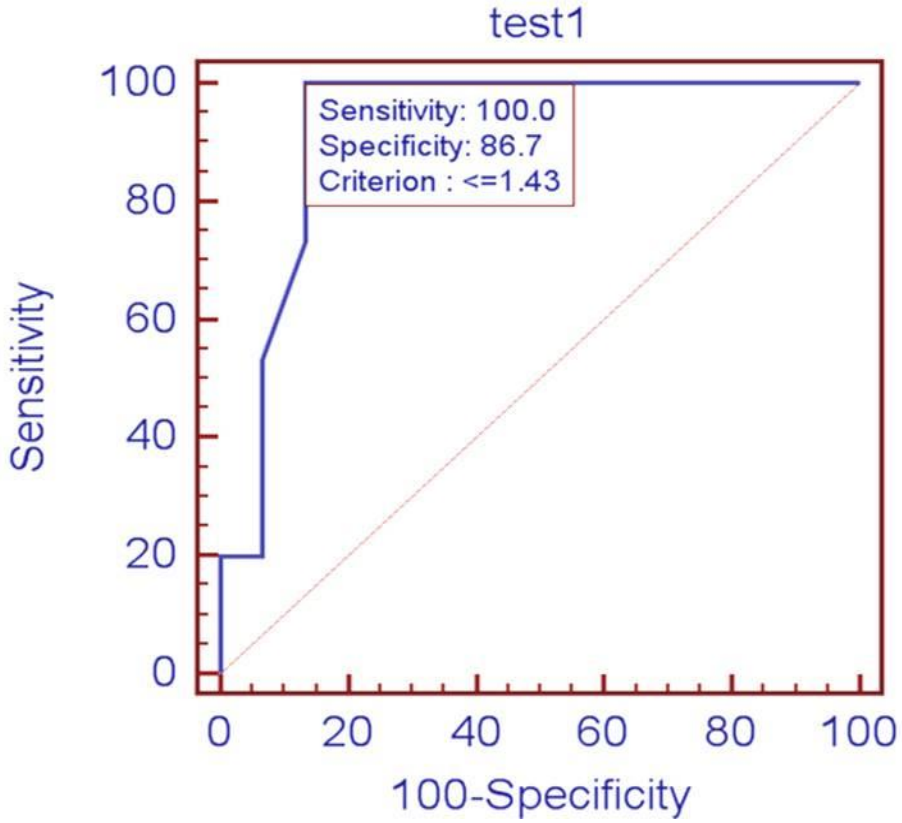
Benign lesion	Radiologically diagnosed cases	Confirmed by HPE / Follow-up	%
Simple cyst	4	4	100%
Abscess	5	5	100%
Hydatid cyst	4	4	100%
Hemangiomas	5	5	100%
Focal fat sparing	2	2	100%
Biliary Cystadenoma	1	1	100%
FNH	1	1	100%

Graph – 1: Characterization of the lesions as benign and malignant by various sequences.

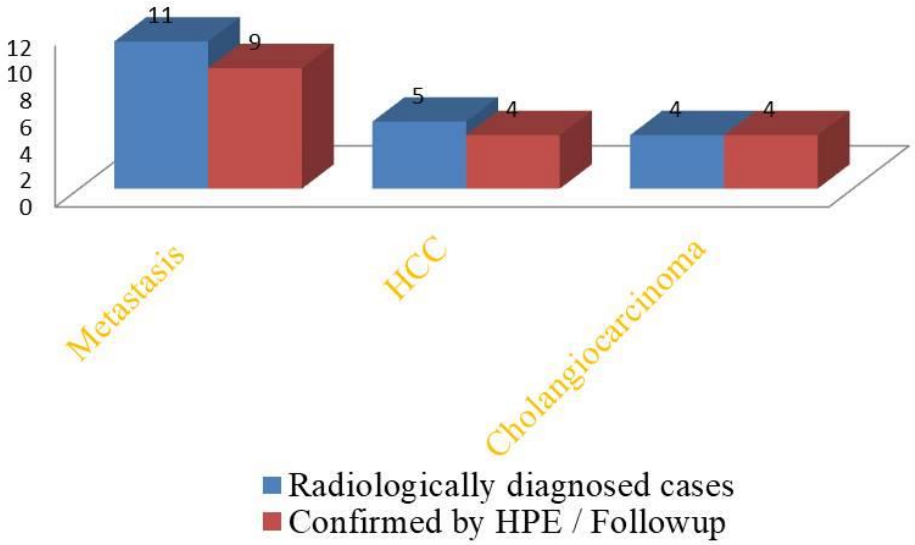


When assessed for image quality, the T2 weighted images have the best quality and less number of artifacts. The cystic lesions were more conspicuous on T2 weighted images whereas metastases were conspicuous on DW imaging. This is in accordance with other studies which highlights SE-EPI DWI as a promising technique for detecting small (<10 mm) focal malignant liver lesions.

Graph – 2: ROC curve analysis for ADC values of benign and malignant liver lesions.



Graph – 3: Correlation between radiological and histopathological diagnosis of malignant entity.



The reason for a high detection rate of focal hepatic lesions on DWI is attributed to the better contrast-to-noise ratio and better lesion conspicuity by suppression of background vessels. Furthermore, the solid tumors tend to appear larger on DWI than on T2 weighted images. This phenomenon may contribute to the high detection rate of small solid tumors on DWI [5].

Although the use of T2 weighted images is helpful for the detection of the focal hepatic lesions, lesion detectability is suppressed by low

lesion-to-liver contrast and the interfering high signal intensity from intrahepatic vessels [6].

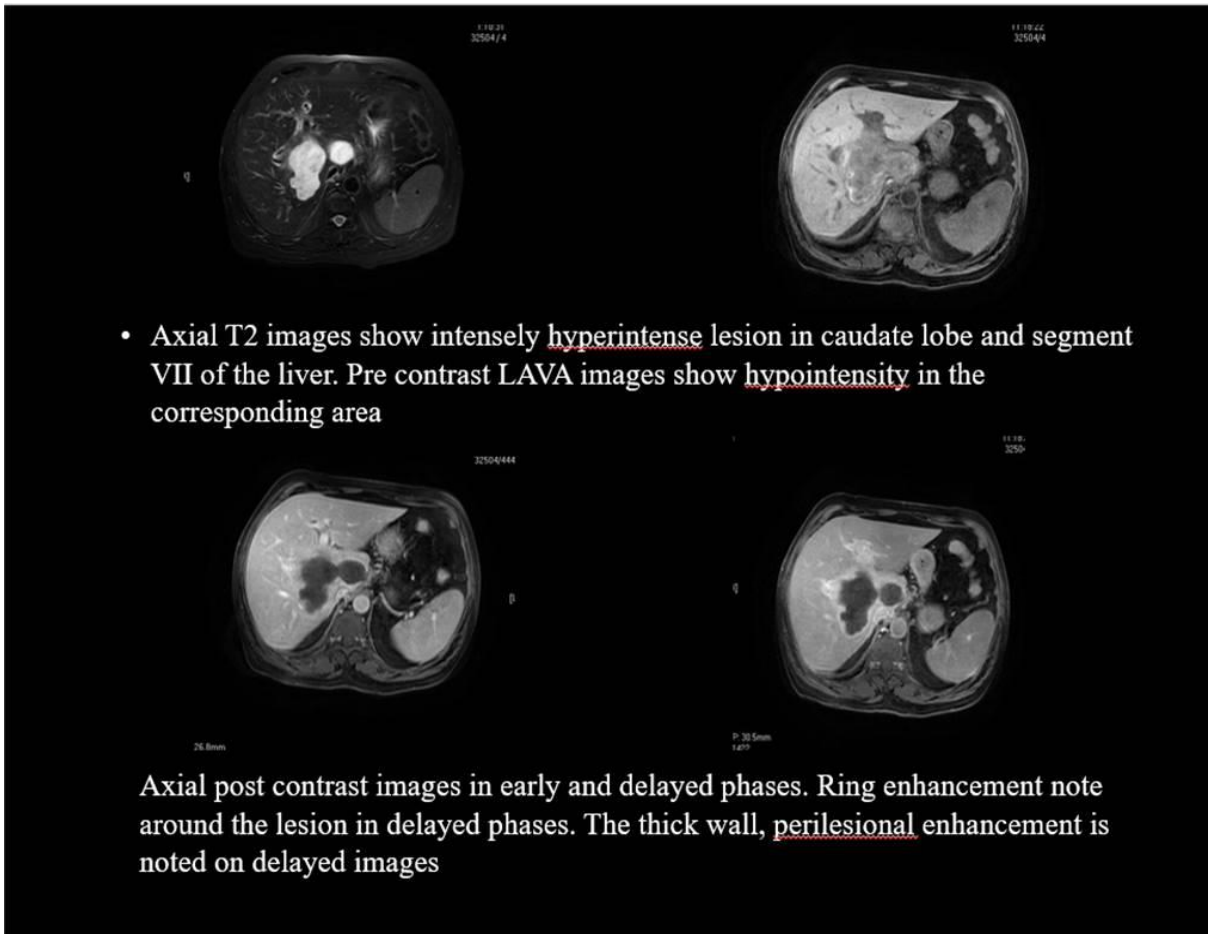
Lesion characterization

The results show that the classification into malignant and benign liver lesions and the assessment of specific diagnosis were most reliably achieved when all sequences were collectively evaluated. Several previous investigations also advocate the use of a combination of sequences in liver diagnostics. Coulam, et al. [7] reported a sensitivity of 97% and a specificity of 95% in revealing clinically relevant focal liver lesions using a Tl- weighted multiphase contrast-enhanced 3D sequence. Similar results are encountered in the present study.

According to the present results, the best individual sequence in distinguishing between malignant and benign liver lesions is the dynamic Gd-enhanced Tl-weighted sequence. This sequence also demonstrated the highest success in the assessment of specific diagnosis, with a 90% rate of correct diagnosis. Several previous studies support this result as Gd-enhancement particularly when used in a dynamic fashion in different phases of enhancement, has been considered to be highly important in liver tumor characterization [8].

In our study out of 5 hemangiomas (**Figure - 2**) T2 WI was able to characterize three of them. All the three hemangiomas had high signal intensity on T2 WI and heavily weighted T2 sequences. But as some of the hyper vascular metastasis can have longer T2 relaxation times, contrast examination was done in all these cases.

Figure - 1: 51 yrs. / M alcoholic, complains of the right hypochondric pain associated with fever, since 1 week, MR images followed by USG, revealed abscess. Diffusion weighted imaging: Bright on diffusion weighted imaging. ADC value: 1.68 x 10^{-3}



One patient with carcinoid metastasis had the metastatic lesion with longer T2 relaxation times. The fourth patient with hemangioma had a large lesion and had varied appearance on T2 WI. Contrast enhancement was diagnostic in that patient Overall T2 WI has a detection rate of 92% in our study [9].

Benign lesions were seen in 24 patients. Of these there were four simple cysts. These cysts were detected incidentally in one patient with pancreatitis and other with bladder malignancy. These cystic lesions showed well defined thin wall with intense hypointense signal on T1 WI and intense hyper intense signal on T2 WI which increased on heavy T2 sequences. These lesions showed no enhancement on contrast administration.

These lesions were followed up with sonography which showed no increase in size and number of the lesions. One patient had polycystic liver disease with multiple well defined cystic lesions without any communication with biliary system. All the cysts were intensely hypointense on T1 WI without any evidence of hemorrhage. All the cystic lesions were mild to moderately hyper intense on DWI.

To differentiate simple cysts, abscess (**Figure - 1**) and hydatid cysts with diffusion weighted imaging, the ADC value has been calculated. The mean ADC value of simple cysts and hydatid cysts (2.4. x 10 ~ 3) was significantly higher than the mean ADC value of the abscesses (1.2 x 10-3) in our study. These results were in accordance with the studies by Nagihan, et al. [10].

Biliary cystadenoma, seen in a one patient, is multiseptated lesions with hypointense signal on T1WI and hyperintensity on T2 WI. On contrast admiration there is enhancement of the capsule and internal septations. Differentiation from hydatid cyst is difficult, but enhancement of the internal septae with no evidence of daughter cysts and with vascularity noted within the internal septations on color Doppler is diagnostic [11].

There is delayed enhancement of the scar tissue noted in post contrast images. Ultrasound guided Fine needle aspiration biopsy showed dense fibrous septum with vascular structures and adjacent hepatic parenchyma showed increased cell plate thickening. The dense cellularity is responsible for the hypointense signal intensity on T2 WI and the vascularity for the intense arterial phase enhancement (**Figure – 3**).

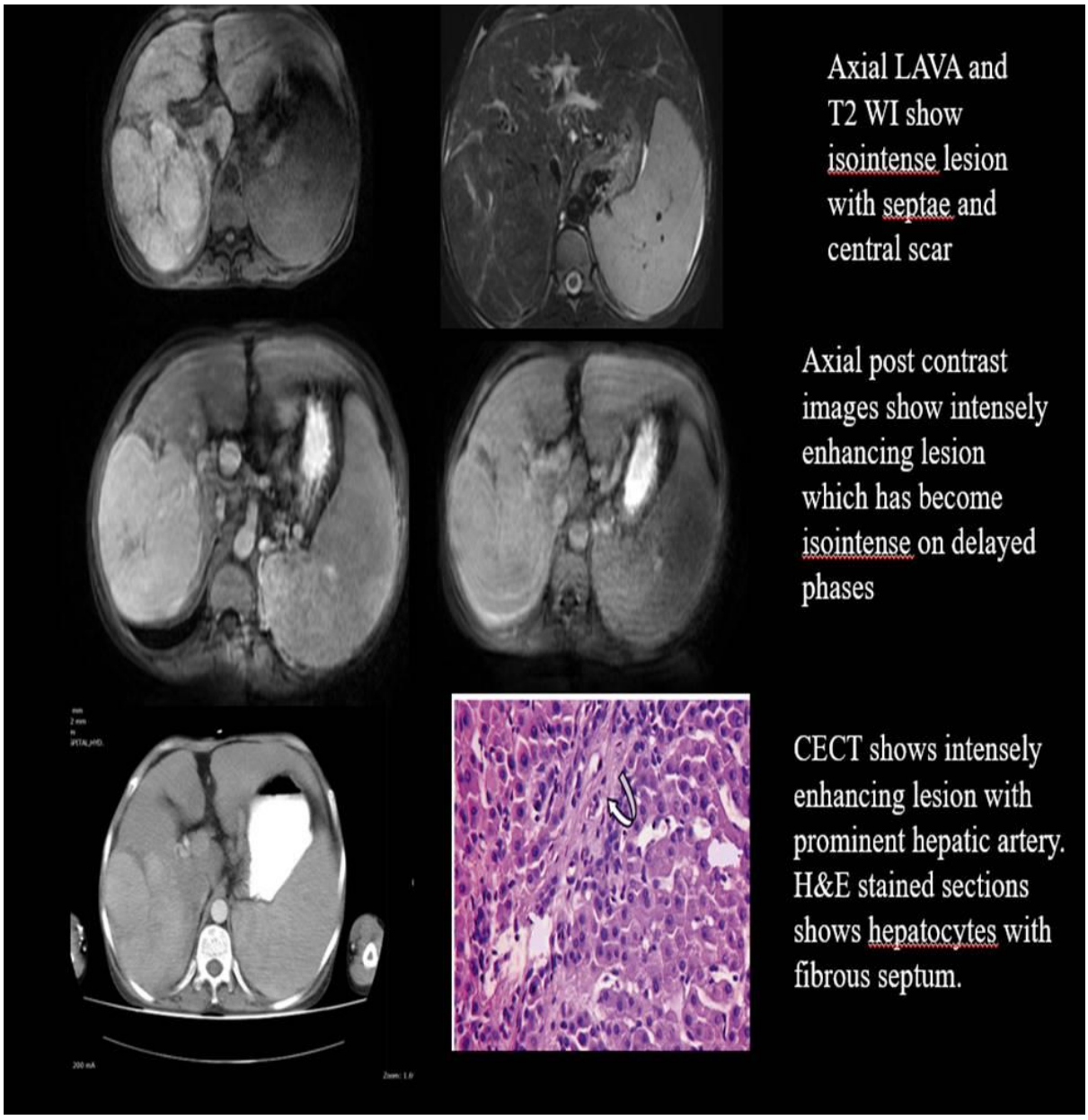
Of the 42 cases imaged, 18 patients harbored malignant lesions. Hepatocellular carcinoma was seen in 5 cases (**Figure - 5**). 3 cases showed solitary lesions whereas multiple nodules were noted in two cases. All the cases were hypointense on T1 WI and hyperintense on T2 WI. Three of the lesions showed central hyperintensity which corresponded with necrotic areas on pathology. These areas were non enhancing on contrast administration. Hypointense areas on T2 WI were noted in two of the cases which corresponded with fibrotic areas.

Tumor capsule was noted in four of the cases (80%). This is a characteristic sign of large HCCs. The capsule is seen normally in 60-82% of the cases. In one study, 56 of the 72 HCCs showed a capsule at histology and 75% of the lesions with a capsule were larger than 2 cm .The tumor capsule becomes thicker with increasing tumor size. It is hypointense on T1 and T2 weighted images. Contrast enhancement was either homogenous or variegated arterial phase enhancement. The variegated appearance noted is due to abnormal internal vessels in the lesion [12].

In our study 4 patients showed homogenous enhancement and one patients showed variegated appearance which are in consistent with the study by Matilde, et al. [13].

Portal vein encasement is seen in one case. Portal vein involvement is seen more often in infiltrative type of HCCs.

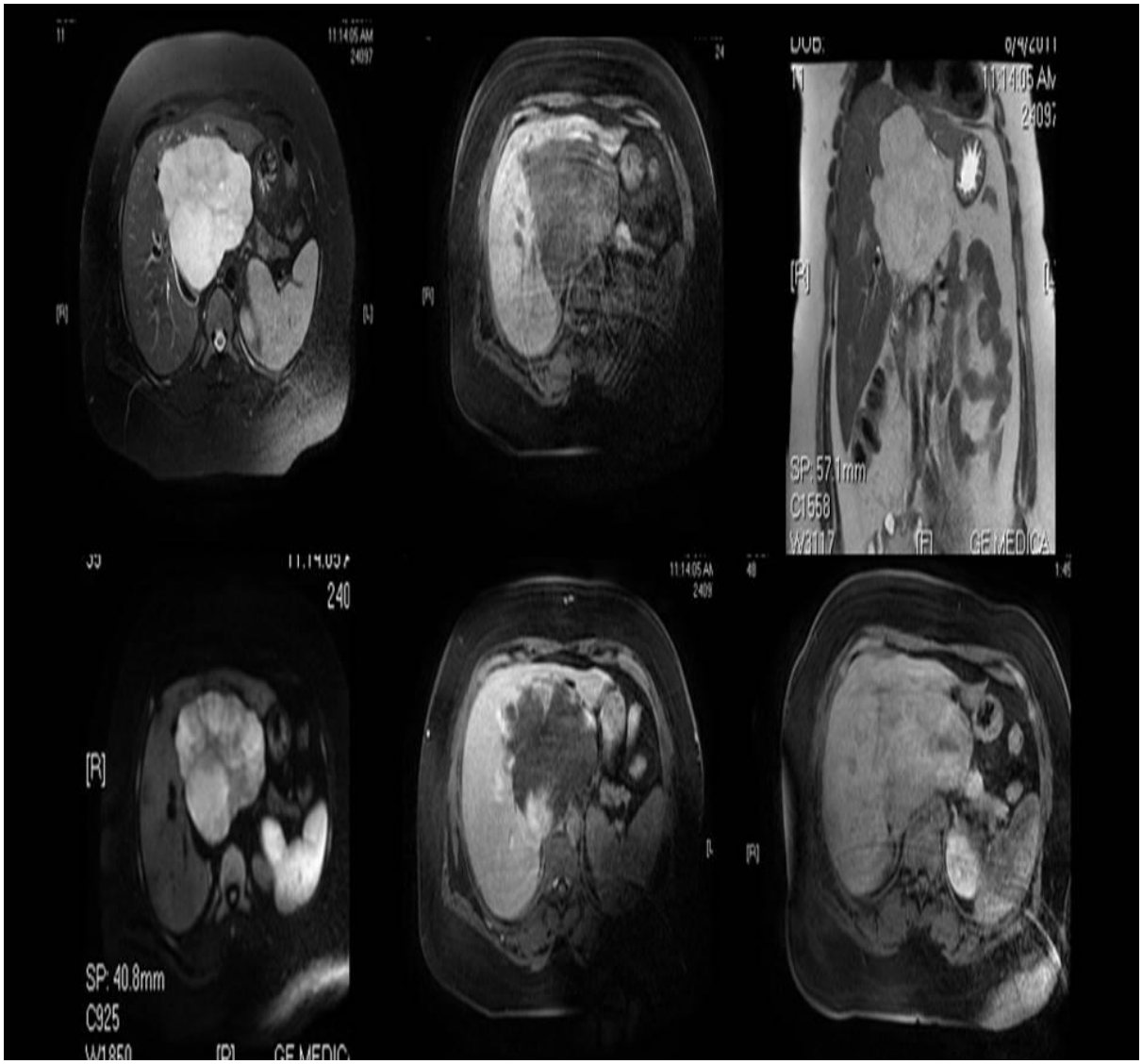
Figure - 2: Hemagioma: A 41 yrs. /F came for health check-up, on ultrasound there was large lesion noted in the segment IV of right lobe of the liver, MRI showed Axial pre contrast T2 WI and LAVA sequences showed large lesion which was intensely hyperintense on T2 WI and hypointense on T1 WI. Coronal T2 WI and DWI. The T2 WI showed bright lesion and the DWI image also showed bright lesion (due to the T2 shine effect.). Contrast LAVA sequences which showed peripheral puddling in early phase and delayed centripetal enhancement.The average ADC value of the lesion was 1.8 X 10^{-3}



Of the 9 metastases (**Figure - 4**), two were from pancreatic adenocarcinoma, one metastases was from gallbladder malignancy, two are from gastric neoplasms (one GIST and one gastric carcinoma), one is Adenocarcinomatous deposit from unknown origin, one metastases is from carcinoid bowel, two are from colon malignancy.

The metastases from bowel are having typical target like appearance on T2 weighted images. All the metastases were having intermediate to high signal intensity on T2 weighted images. These lesions are not as bright as cysts and hemangiomas.

Figure - 3: A 35 yrs. / F c/o dyspnoea, pain abdomen. Known case of idiopathic pulmonary hypertension. Sonography showed mild Hepatomegaly with evidence of large isoechoic mass noted in right lobe of liver with mass effect in the form of displacement of adjacent vessels. MRI and histopathology revealed it as FNH with Diffusion weighted imaging: bright: ADC value: 1.1 x 10^{-3}



Of the 4 cases with intrahepatic cholangiocarcinoma hypointense area is noted on T2 weighted images in two of the cases corresponding with central fibrosis. MR imaging showed irregular T1 hypointense, T2 hyperintense lesion with central radiating hypointensities inT2 W images. On post contrast images the lesion show peripheral enhancement in the arterial phase and gradual centripetal filling in the equilibrium and delayed phases. The central hypointensities in the T2 W images were unenhancing suggesting central fibrosis. Our findings were correlating with the study done by Yoji Maetani, et al. [14] which showed similar findings on contrast enhanced MRI.

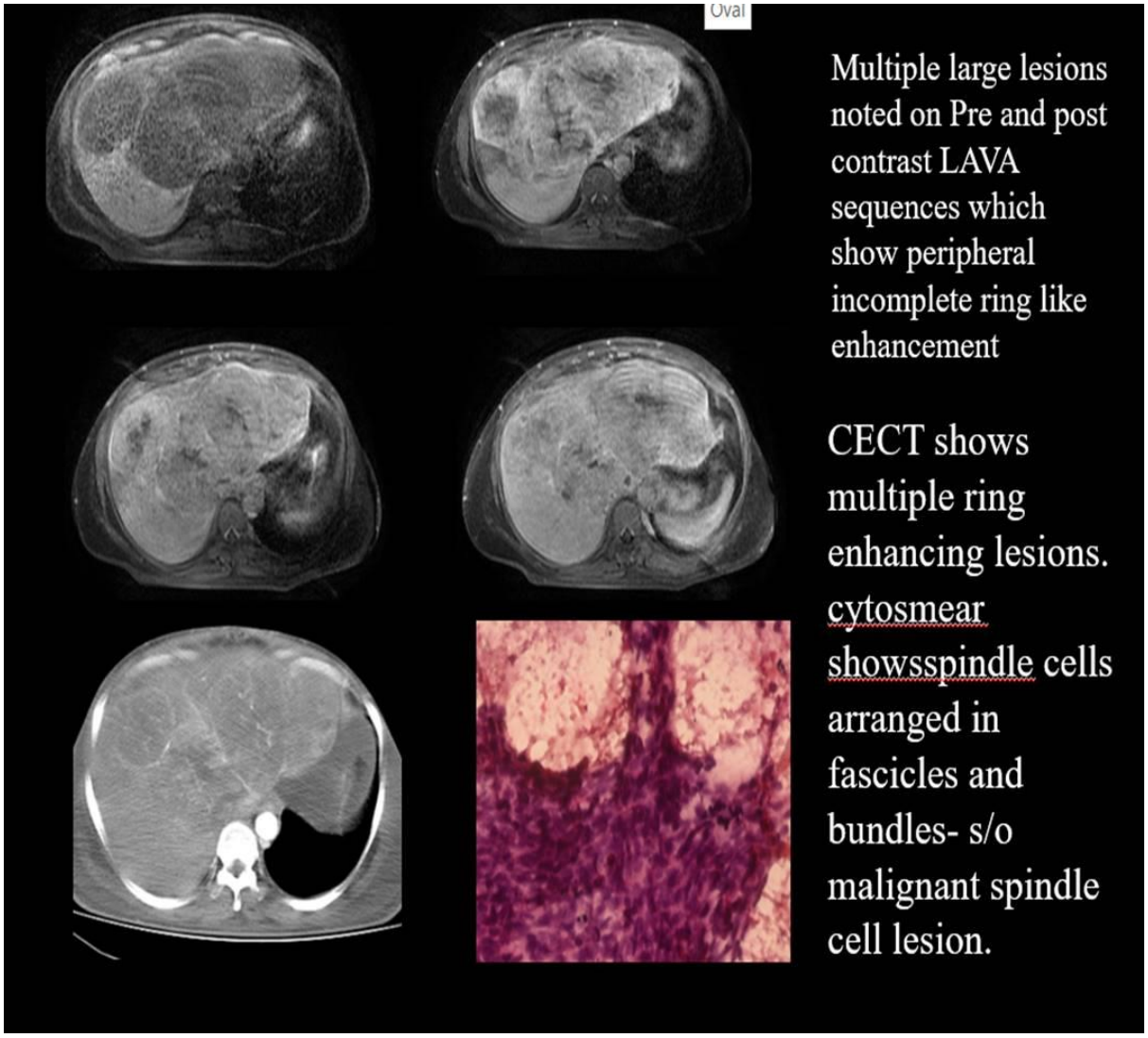
Out of 5 hepatocellular carcinomas, correct diagnosis was made in four cases. One case of multifocal HCC, in view of intense arterial enhancement and multiple lesions of varying sizes, hypervascular metastases was considered.

One lesion thought to be metastases, in patient with adenocarcinoma in head of pancreas showing ring enhancement and intermediate signal intensity on T2 weighted images, turned out to be early abscess. The ADC value of the

lesion is $1.2x10^{-3}$. Fine needle aspiration and cytology reveled neutrophils and debris. Follow up studies showed it to be an abscess.

One patient had Budd Chiari syndrome with multiple nodules which are hypointense on T1 WI and of intermediate signal intensity on T2 WI, showing delayed enhancement on T2 WI. These nodules were indeterminate on MRI as benign regenerative nodules almost never show increased signal intensity on T2 weighted imaging and hepatocellular carcinoma/ dysplastic nodules show intense arterial enhancement.

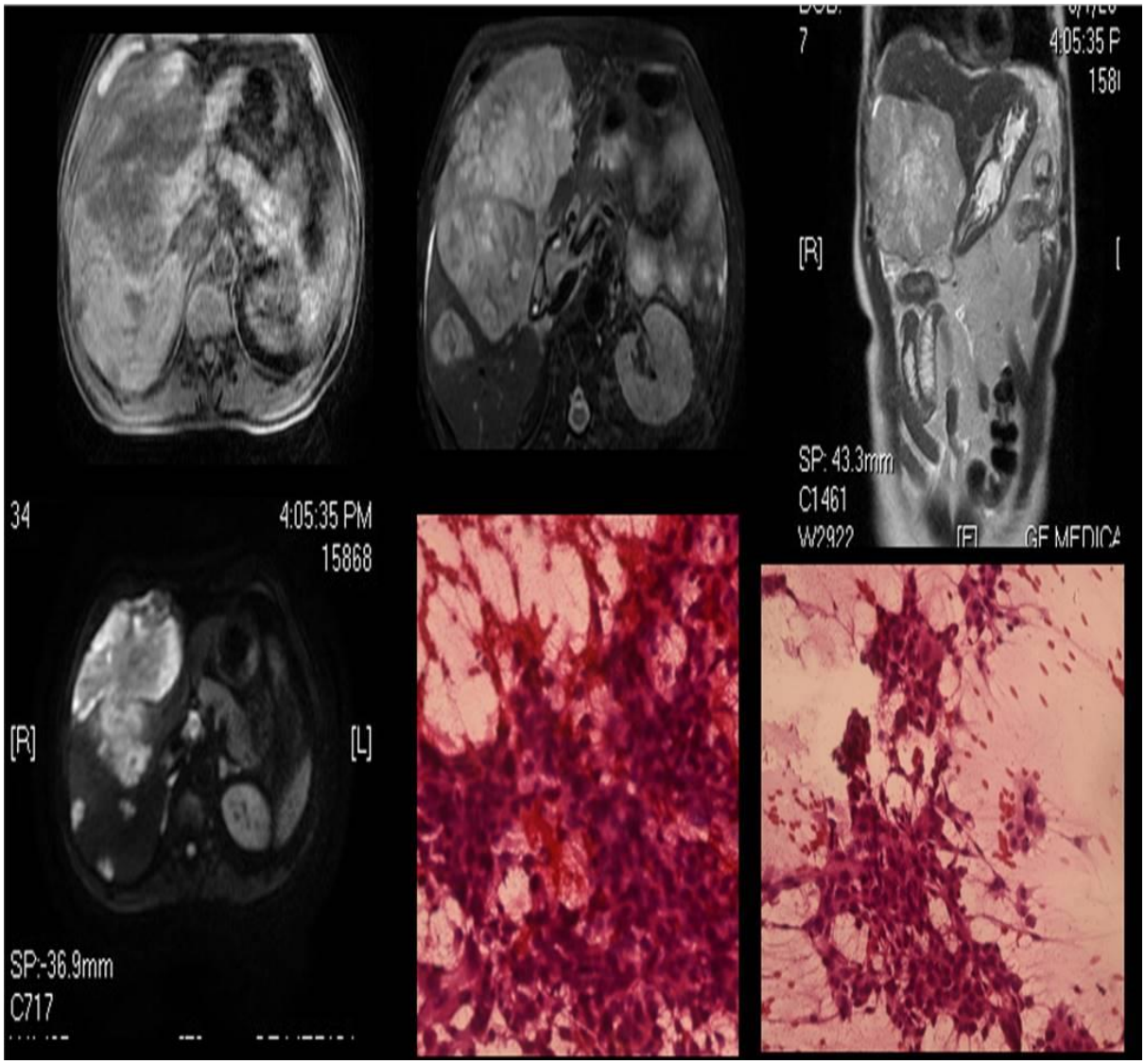
Figure - 4: A 40 yrs. /M known case of gastric GIST. Status: post partial gastrectomy. Presented with right hypochondrial mass. sonography: Multiple large hypoechoic lesions noted in both lobes of liver. MRI shows multiple lesion with delayed enhancement – s/o Metastases. HPE as spindle cell deposit. Diffusion weighted imaging: bright on DWI. ADC value:$1.30x\ 10^{-3}$



Tissue diagnosis showed that these nodules are benign regenerative nodules. Review of literature showed that benign nodules in Budd Chiari syndrome can show increased T2 signal intensity [6]. Central area altered signal intensity which is hypointense on T1 weighted images and hyperintense on T2 weighted images is noted in many nodules in the patient. This corresponded with central scarring. In a study by Maetani, et al. [14] of 15 lesions larger than 1 cm in diameter, a central scar was found with either CT or MR imaging in six nodules.

In the delayed phase of contrast-enhanced imaging, the central scar showed high signal intensity. They concluded that central scar is a characteristic finding of benign hepatic nodules larger than 1 cm in Budd-Chiari syndrome.

Figure - 5: A 59 yrs./M Pain and mass right hypochodrium, sonography: Multiple hypoechoic lesions noted in both lobes predominantly in left lobe of liver. Internal vascularity noted Axial LAVA, T2, coronal T2 and DWI. The lesion is hypointense on LAVA, hyperintense on T2 WI, bright on diffusion weighted images. Cytosmear shows tumor tissue arranged in sheets, clusters with round to oval cells and moderate to scanty cytoplasm- s/o poorly differentiated Hepatocellular carcinoma. DIFFUSION WEIGHTED IMAGING: Bright on DWI.ADC value: $1.23x10^{-3}$



Conclusion

MRI was able to predict diagnosis in 38 of the 42 tumors. It could suggest the nature of all lesions in benign cysts, hemangiomas, focal nodular hyperplasia and metastases. But it was not possible to achieve a specific diagnosis in two early abscess, one multifocal hepatocellular carcinoma and one case of regenerative nodules. This accounted for a detection rate of 90%.

Thus MR imaging is a powerful tool for the evaluation of focal liver lesions. Pre contrast T1 weighted gradient echo images, T2 weighted images, in phase and out phase imaging, EPI - DWI and gadolinium enhanced T1 weighted

images provide accurate characterization of the lesions. The varied appearances of the lesions on these sequences are the result of the dominant histological composition of the lesions.

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