Journal of Pathology of Nepal (2020) Vol. **10**, 1718 - 1721

Journal of
**PATHOLOGY**
of Nepal

www.acpnepal.com

Original Article

# Profile of uncommon primary adult hepatic malignancies at a tertiary care centre

Eliz Thomas[1], A Venkatasubramanian[1]

[1]*Department of Pathology, PSG Institute of Medical Sciences & Research, Coimbatore, India*

**Keywords:**

Hepatopathology;
Liver cancer;
Non-hepatocellular liver malignancy;

## ABSTRACT

**Background:** Hepatocellular carcinoma has been the most common primary malignancy of the liver in adults, followed by cholangiocarcinoma. The less common malignancies are those arising from the vascular endothelial cells, neuroendocrine cells, hematolymphoid tissues, and mesenchymal tissues. Imaging studies alone may pose a diagnostic challenge, due to the variable appearances. Histological review of the tissue specimen along with immunohistochemical stains are imperative for diagnosis. However, a multidisciplinary approach is necessary to make an accurate diagnosis and help in management.

**Materials and Methods:** The unusual adult primary hepatic malignancies were studied in 2 years period with clinic-radiological and biochemical correlation and also the age and sex distribution were determined. Ethical approval was obtained. Statistical analysis used: SPSS version 23.0.

**Results:** A total of 24 liver malignancies were encountered. Metastatic tumors and tumor-like lesions were excluded. The patient's clinico-radiological findings and laboratory investigations were noted. A total of 6 unusual non-hepatocellular malignancies were seen and identified based on morphology and special stains. Out of 6 non-hepatocellular malignancies, 3 were neuroendocrine carcinomas, 2 were leiomyosarcomas and 1 was a hematolymphoid malignancy. Radiologic impression and biochemical parameters helped arrive at a definitive opinion as the lesions were not typical of this location. A high index of suspicion along with the immunohistochemical profile finally facilitated the diagnosis.

**Conclusion:** The cases of primary non-hepatocellular malignancies are unexpected. A multidisciplinary approach is mandatory.

**Correspondence:**

*Dr. Eliz Thomas*
*Department of Pathology*
*PSG Institute of Medical Sciences & Research, Coimbatore, India*
*ORCID ID: 0000-0002-1247-8592*
*Email: elshaddai4eliz@gmail.com*

**Received** : July 9th 2020 ; **Accepted** : September 30th 2020

**Citation**: Thomas E, Venkatasubramanian A. Profile of uncommon primary adult hepatic malignancies at a tertiary care centre. J Pathol Nep 2020;10: 1718-21. DOI: 10.3126/jpn.v10i2.29933

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## INTRODUCTION

Primary liver cancers are rare. Because the liver is made up of several different types of cells, several types of tumors can originate from there. Hepatocellular carcinoma has been the most common primary malignancy of the liver in adults, followed by cholangiocarcinoma. The less common are those arising from the vascular endothelial cells, neuroendocrine cells, hematolymphoid tissues, and mesenchymal tissues.[1]

Many times, imaging studies alone may pose a diagnostic challenge due to the variable appearances of the tumors. Histological review of the tissue specimen, along with immunohistochemical stains is imperative for definitive

diagnosis. A multi-disciplinary approach is necessary for accurate diagnosis and management.

## MATERIALS AND METHODS

This is a retrospective study for 2 years which was conducted in a tertiary care center. The study included the collection of data from the patients' record sheets available in the Medical Records Department. Information pertaining to the cases was recorded and tabulated.

All investigated cases of primary non-hepatocellular hepatic malignancies of 2 years were included in the study. Metastatic tumors and tumor-like lesions were excluded. Approval from the Institutional Human Ethics Committee was obtained (Approval number – 19/137). All the data were analyzed using SPSS version 23.0 (Armonk, NY: IBM Corp.). It is represented as proportions and percentages.

## RESULTS

We encountered a total of six unusual cases of primary non-hepatocellular hepatic malignancies which included three neuroendocrine carcinomas, two leiomyosarcomas, and one hematolymphoid malignancy. All of these cases were biopsies. The mean age at presentation for the patients was 56 years, of which the majority of them were males. No cases were reported in childhood or adolescence.

There were varied symptoms at presentation, ranging from abdominal pain to asymptomatic presentation. The most common presenting symptoms were abdominal pain and loss of appetite. Other presentations include yellowish discoloration of eyes, tiredness, and nausea. Almost all the cases had a palpable mass in the right hypochondrium. Liver enzymes were deranged in all the cases. Imaging studies done were ultrasound, computed tomography (CT) scan, or both. Diagnosis of malignancy was established for all the cases with most favoring a hepatocellular carcinoma. Of the 6 non-hepatocellular primary hepatic malignancies, three were neuroendocrine carcinomas (fig.1A-D), two were leiomyosarcomas (fig. 2A-D) and one was a hematolymphoid malignancy (fig.3A-F). Search for primary origin elsewhere was negative, and metastasis was ruled out. The diagnosis was established with the help of immunohistochemical markers.

## DISCUSSION

A variety of hepatic lesions can present as hepatic masses. Amongst the malignant neoplastic lesions, primary hepatocellular carcinoma and cholangiocarcinoma are the most common. Primary non-hepatocellular hepatic malignancies although rare, are known to occur.[2,3] Prior to pathological examination for primary hepatic malignancies, misdiagnosis was frequent due to similar presentation and imaging findings in both hepatocellular and non-hepatocellular malignancies.[4,5]

Approximately 50- 90% of all neuroendocrine tumors cases are known to arise from the gastrointestinal tract and their occurrence as primary hepatic tumors is rare (0.3%).[6]

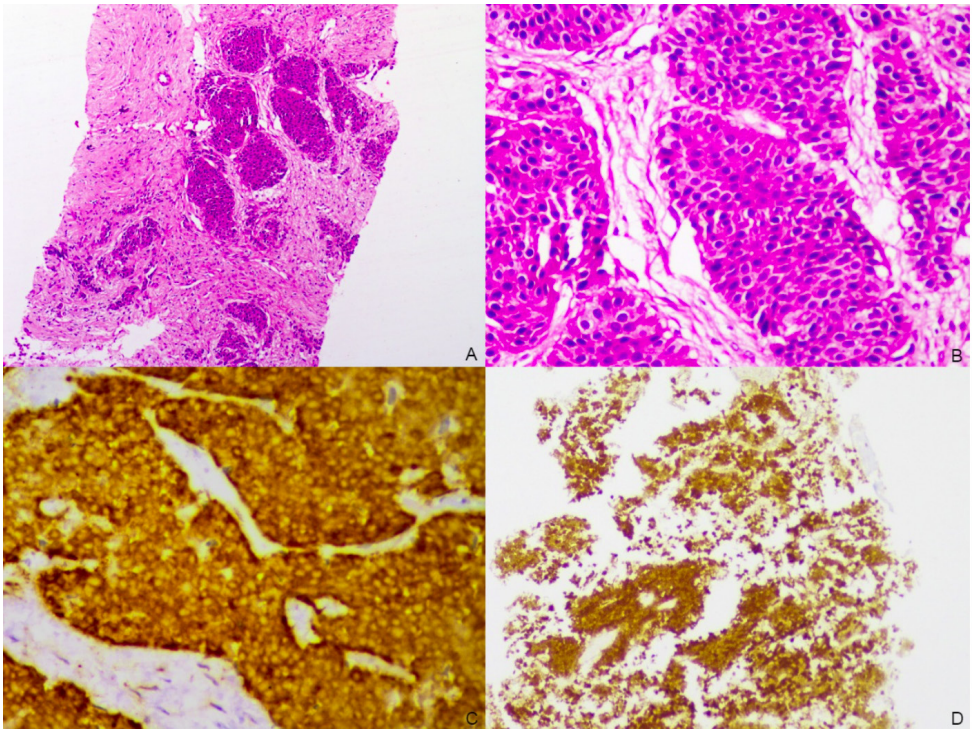


***Figure 1:*** *Neuroendocrine tumour. A) Photomicrograph showing infiltration by tumour cells arranged in nests and cords (HE stain; X100) The cells are small to medium with eosinophilic finely granular cytoplasm, round nuclei with finely stippled chromatin (HE stain; X400). The tumour cells show immunopositivity with synaptophysin (C) and chromogranin (D).*

*DOI : 10.3126/jpn.v10i2.29933*

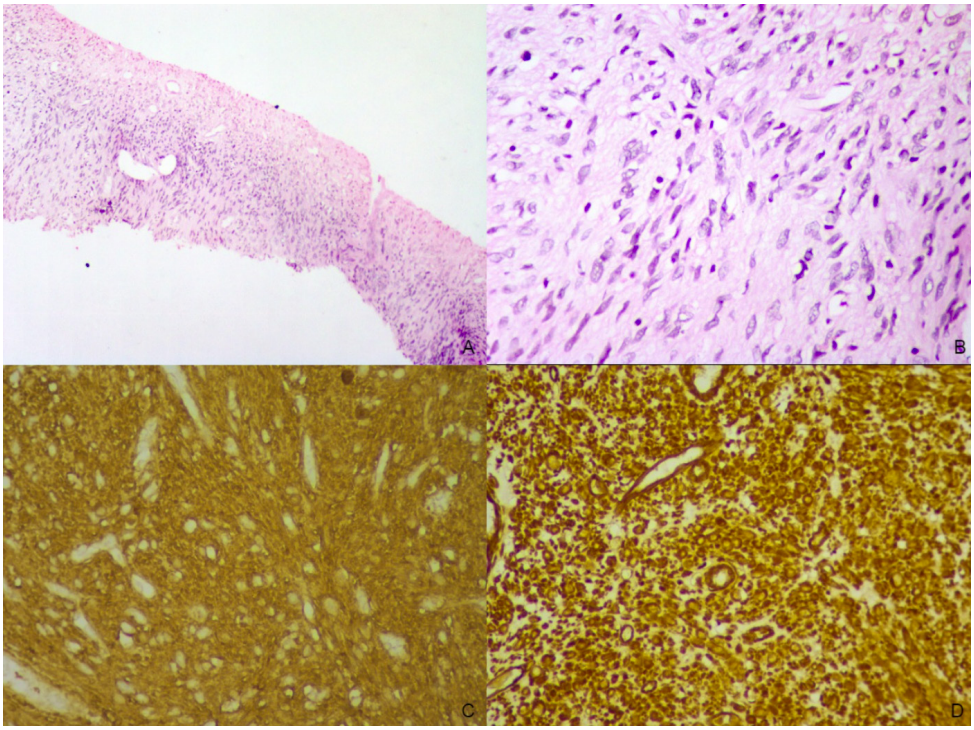


***Figure 2:*** *Leiomyosarcoma. Histopathological examination on H&E stain showing hepatic parenchyma infiltrated by pleomorphic spindle cells arranged in palisading pattern (A: X100, B: X400). The tumour cells are positive for smooth muscle actin (C) and vimentin (D) by immunohistochemistry (100X)*

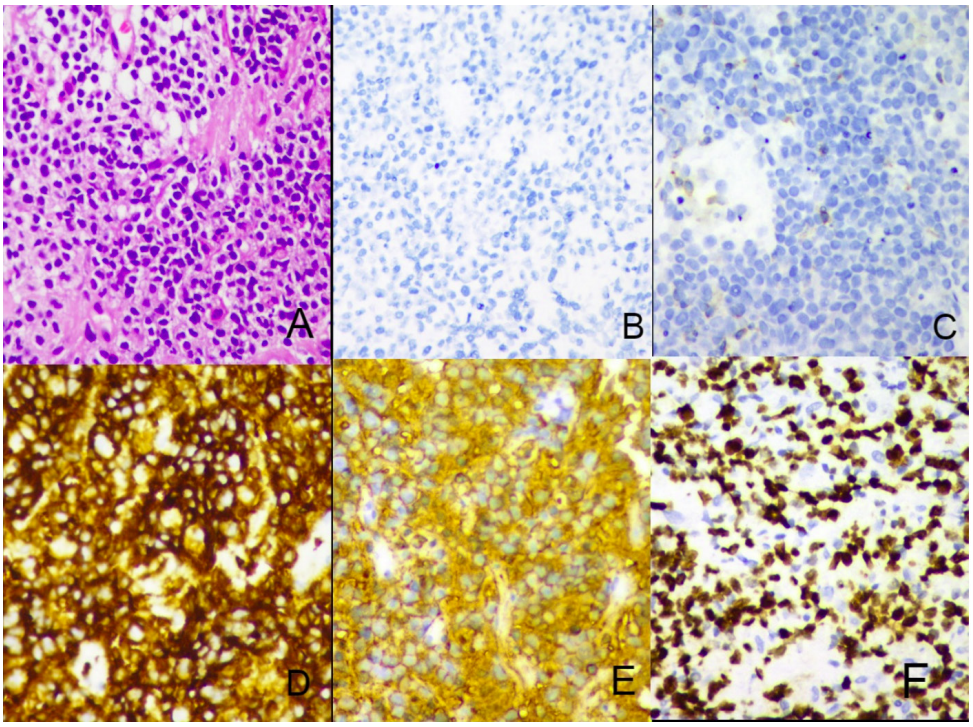


***Figure 3:*** *B-cell non-Hodgkin lymphoma. A: The tumour cells are intermediate to large and show diffuse infiltrating pattern (HE stain; X400). The tumour cells are negative for Heppar-1 (B) and CD 3 (C). They are strongly positive for LCA (D) and CD 20 (E). The Ki-67 proliferation index (F) is >80%.*

A definitive diagnosis of primary neuroendocrine carcinoma is possible only after hepatic biopsy and the use of ancillary tools like special stains and immunohistochemistry. Therefore, it can be established that biopsy and pathological examination are the gold standards for diagnosis.[2]

On histopathological examination, neuroendocrine tumors (NET) are composed of uniform round to polygonal cells with pale eosinophilic granulated cytoplasm, monotonous, round, centrally located finely stippled nuclei, and small inconspicuous nucleoli. Mitosis and necrosis are infrequent.

The tumor cells show immunoreactivity with synaptophysin and chromogranin and are negative for Heppar-1. This staining pattern was seen in all our cases reported as NET (fig. 1).

Mesenchymal tumors are also rarely encountered in adults.[7] Amongst the primary malignant mesenchymal tumors, hepatic angiosarcomas are most common. Primary hepatic leiomyosarcoma are again rare tumors and not many cases have been reported in the literature.[8,9] It is often associated with immunodeficiency or viral infections (HCV, EBV, etc).[10] The cases in our study were not associated with any such underlying condition.

Histomorphology of leiomyosarcoma shows a spindle cell lesion with features of anaplasia which has to to be distinguished from other spindle cell lesions of this region.

Our cases were confirmed to be primary, by ruling out metastases from other origins. Immunohistochemical markers helped in confirming the diagnosis (fig.2)

Hematolymphoid malignancies with hepatic involvement are a relatively common presentation of the extranodal disease. Rarely, lymphomas can involve the liver exclusively (primary hepatic lymphomas). As defined by previous studies, primary hepatic lymphoma is to be considered when the patient gives a negative history of prior or subsequent lymphoma diagnosis, no biopsy-proven hematolymphoid neoplasm at a nonhepatic location, and no other reason for clinical concern for hematolymphoid malignancy elsewhere in the body.[11,12] Most common primary hepatic lymphoma reported so far, is diffuse large B-cell lymphoma (DLBCL) which is closely associated with HCV infection and immunocompromised states, including HIV infection.[13,14] Our case was diagnosed as primary non-Hodgkin lymphoma of B-cell type and further typing could not be done as the tissue was insufficient (fig. 3). The patient was immunocompetent.

## CONCLUSIONS

The correlation of clinical, serological, radiological, and histopathological findings is helpful in the early detection, diagnosis, and management of hepatic masses. Imaging studies are a reliable tool to detect hepatic malignancy. However, histological examination with immunohistochemistry remains the gold standard for diagnosis and confirmation of different types of malignancies arising from the liver.

**Conflict of interest:** None

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