Case report

Primary hepatic carcinoid tumour: a clinicopathlogical correlation and review of literature

Shiv Pankaj Khanna, MD[α], Rigvardhan, MD[β], Prabal Deb, MD[#]

[α]Associate Professor, Dept of Pathology, Command Hospital, Lucknow

[β] Associate professor, Dept of Pathology, Saraswati Medical College, Unnao

[#]Professor, Department of Pathology, Army Hospital (Referral & Research), Delhi

Institute : Army Hospital, Research & Referral, Delhi-10

Communicating author: Dr (Lt Col) Rigvardhan , Associate Professor , Department of Pathology, Saraswati Medical college , Unnao- 209859

Abstract:

Primary hepatic carcinoid tumor is rare and poses a challenge for diagnosis and management. To the best of our knowledge, there is the no case in literature where primary neuroendocrine tumour in the liver was truly proved by an autopsy without involvement of other organs. We present a 54 year old male patient, who was incidentally detected to have a tumour in the left lobe of liver. It was opined as hepatocellular carcinoma on imaging. Patient died intra-operatively due to extensive bleeding. Subsequently, he was detected to have a primary neuroendocrine tumour of the liver on autopsy.

Keywords: Primary hepatic carcinoid tumor; autopsy

INTRODUCTION:

There are reports in literature of primary neuroendocrine tumors (NET) of the liver, excluding involvement of any other organ by endoscopy, follow up etc [1]. However, primary hepatic carcinoid tumor (PHCT) is very rare and the first case was documented by Edmondson in 1958. This rarity makes it difficult for clinicians to diagnose it precisely before biopsy, resection of tumor, or autopsy. Large-sized tumors are common presentations when they are diagnosed [2]. With less than 100 reports in the literature, little is known of PHCT. They often present as large centrally situated liver masses. Data is scarce on the outcome of surgical treatment but these tumors seem to be associated with a favorable prognosis, justifying an aggressive surgical approach [3]. The diagnosis of primary hepatic etiology requires an extensive work up and continued survey to exclude a missed primary. Meticulous investigation and follow up is required to rule out an occult extrahepatic malignancy with hepatic metastasis to confirm the primary nature of PHCT [2, 3].

CASE REPORT:

The deceased a 54 year old male, a known case of diabetes mellitus and hypertension was transferred from primary health care unit because of incidentally detected hepatic tumour visualized during a laparotomy which he underwent due to duodenal perforation. On admission at our centre he had vague complaints of abdominal pain, dyspepsia and progressive weight loss. Per abdominal examination revealed 13x12 cms lump in right hypochondrium and epigastrium in continuation with liver. Other systems were unremarkable. The patient underwent a complete laboratory and radiological work up involving all the systems. CT scan suggested hepatocellular carcinoma of left lobe of liver ? fibrolamellar variant. Tumour markers including AFP, CEA

and CA19-9 were within normal limits. CT scan of chest, upper and lower GI endoscopy for further work up for a primary tumour or metastatic site were negative. The decision was made to resect the tumour and subsequent liver transplantation was planned. He underwent hepatectomy in view of hepatocellular carcinoma of left lobe of liver. On gross inspection it was found that the left lobe of liver was completely replaced by a highly vascular tumour of approximately 19 x13 cms with infiltrative borders (Fig 1a-b). Intraoperatively, patient bled extensively which could not be controlled and died. Postmortem examination was performed. No gross lesion was seen in other visceral organs including lung, brain, kidney, bladder, pancreas and gastrointestinal tract. Histological evaluation of hepatectomy specimen revealed that the tumour was organised in cords, trabeculae, and in nodular architecture in a vascularized and hyalinised stroma and tumour cells were composed of monomorphic cells containing small, round nuclei, stippled chromatin and scant cytoplasm (Fig 2a-b). Immunohistochemistry (IHC) revealed the tumour cells to be positive for synaptophysin, chromogranin (Fig 2c) and NSE and were negative for Hep-par (Fig 2d), CDX2, CK20, MUC- 2 and MUC-6, CA19.9 and TTF-1. Ki-67 index was low, 25%. *The histomorphological features coupled with IHC results supported the diagnosis of PHCT as it was conclusively proven that no other organ is involved.*

Additional findings in autopsy were atherosclerosis of aorta (Fig 3a), granulomas in left hilar lymph nodes (Fig 3b) which were negative for acid fast bacilli and endomyocardial fibrosis (Fig3c-d).

Cause of death ascertained on autopsy examination was massive intra-operative bleeding occurring in a case of PHCT.

DISCUSSION

Carcinoid tumors are defined as neuroendocrine tumor. The origin of primary hepatic carcinoid tumors is not well known but they may arise from scattered neuroendocrine cells in the intrahepatic biliary epithelium. It is also postulated that chronic inflammation in biliary system may initiate intestinal metaplasia, which in turn predisposes to the development of neuroendocrine tumors. Another possibility is that they originate from ectopic pancreatic or adrenal tissues found within the liver [1]**.**

Fifty-four percent of carcinoids occur within the gastrointestinal tract, mostly in the appendix (16.7%), small bowel (44.7%), rectum (19.6%), colon (10.6%), and stomach (7.2%). Carcinoids also occur in the lung (30.1%), pancreas (2.3%), genitals (1.2%), biliary tract (1.1%), and head and neck (0.4%) [3, 4]**.**

The 2010 World Health Organization carcinoid and pancreatic neuroendocrine tumor grading system takes into consideration the number of mitoses per 10 high power microscopic fields or the percentage of tumor cells that are immunolabelled positively for Ki-67 antigen. These measures reflect the rate of proliferation and prognosis. Carcinoids are classified into three types: (1) well-differentiated tumors of low grade malignancy (2) moderately differentiated or intermediate grade neoplasms, and (3) poorly differentiated or high grade epithelial neoplasms that carry a poor prognosis [3].

PHCT occur mainly in middle age and is slightly more frequent in females (58.5%). The symptoms of PHCT are non-specific, such as abdominal pain, abdominal mass, fatigue, and weight loss. More than 10% cases are asymptomatic. Only a small percent of patients present the typical carcinoid syndrome (skin flushing, abdominal pain and diarrhea) [5]. Our case was 54-year-old male who suffered with right upper quadrant abdominal pain along with symptoms as described.

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Concerning CT findings in PHCT, in most cases non-contrast images show low-density masses, and some have cystic component. Dynamic contrast CT shows enhanced masses in the early phase and low density masses in the late phase [6].

To ascertain that a carcinoid liver tumor is a primary rather than a secondary deposit is challenging. A single large centrally situated tumor is suggestive of a primary tumor whereas neuroendocrine liver metastases present typically as multiple diffuse liver masses [1, 6]. Index case presented with a large solitary mass in the liver.

Although pancreas is the most common primary site (35%) of neuroendocrine liver metastases, in 11–14% of patients with liver carcinoids no primary tumor is found. Thorough investigations are required before concluding PHCT including CT scan, magnetic resonance, PET scan, upper and lower gastrointestinal endoscopy, bronchoscopy, video capsule endoscopy or balloon enteroscopy, and operative exploration. In patients having previously undergone appendectomy the pathology report should be reviewed to exclude a primary tumor [3].

The diagnosis of hepatic carcinoid tumor is mainly based on histological and IHC examination [1]. In our case, histological examination of the autopsy specimen of liver revealed that the tumor cells were neuroendocrine in origin which was confirmed by IHC. *However, the differentiation between primary and secondary hepatic carcinoid tumor is impossible to be identified by histology alone.* As the patient had undergone autopsy, it was conclusively proven that no other organ is involved and thus this was a case of PHCT.

Functional carcinoid tumours secrete bioactive mediators, especially serotonin, which results in the manifestations of carcinoid syndrome. These are characterized by flushing, diarrhea, bronchoconstriction, and palpitations. Excess serotonin appears to be the major contributor to cardiac damage notably endomyocardial fibrosis which was seen in our case, tricuspid insufficiency, and pulmonary valvular disease [7].

Surgical resection is the preferred treatment for PHCT and has provided favorable outcomes. One study showed that postoperative 1-, 5-, and 10-year survival rates were 88%, 80% and 68%, respectively [8]. Liver transplantation has been reported in a small number of unresectable patients. Studies showed that liver transplantation is a feasible and affordable option in patients with unresectable PHCT that gives good long-term results for disease-free survival [1]. Transcatheter arterial chemoembolization has been reported to achieve good palliation in some unresectable patients [9].

Conclusion:

PHCT are rare therefore classifying them as primary in nature requires extensive work up and prolonged follow up. All neuroendocrine tumours have inherent malignant potential that has to be recognized. As less than 100 cases of PHCT have been reported in literature, we present a case which was misdiagnosed as hepatocellular carcinoma clinically and radiologically and turned out to be PHCT on autopsy. Therefore we want to emphasize that as the incidence of PHCT is increasing, this entity should also be kept in mind. Diagnosis should always be supplemented with histological examination and IHC confirmation, as PHCT can mimic hepatocellular carcinoma as was seen in our case.

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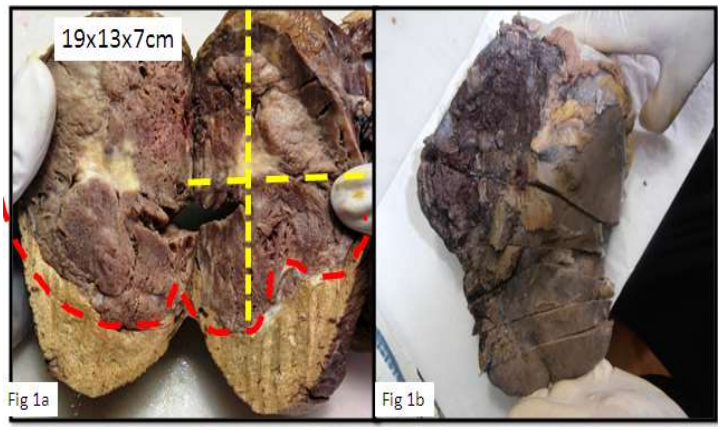

Fig 1. (a) shows a large vascular tumour (b) tumour replacing the entire left lobe of liver

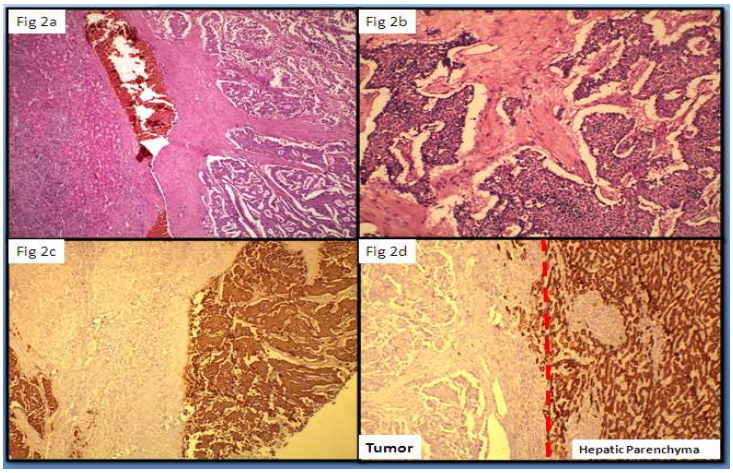

Fig 2 (a & b) tumour cells were composed of monomorphic cells containing small, round nuclei, stippled chromatin and scant cytoplasm.
Tumour cells were positive for chromogranin (c) and negative for Hep-par (d).

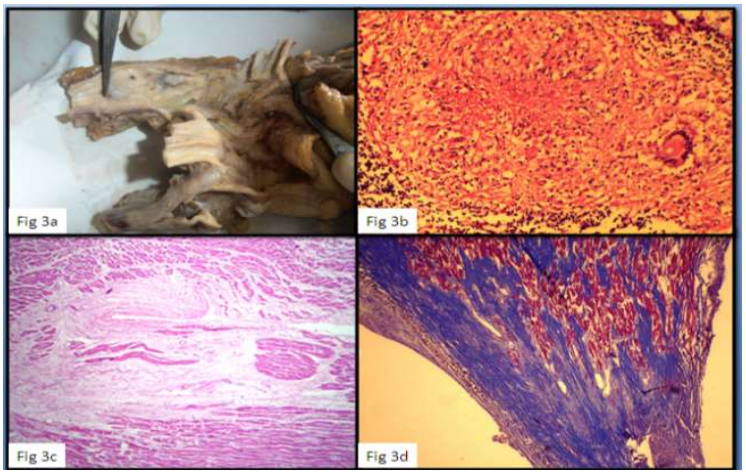

Fig 3 showing atherosclerosis of aorta (a), granulomas in hilar lymph node (b). Endomyocardial fibrosis seen in H&E stain (c) and Masson Trichome stain (d)

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