

# Case Report



## Primary Liver Small Cell Carcinoma Masquerading as Cholangiocarcinoma - A Rare Case Report

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### Abstract

Primary liver small cell carcinoma is a rare malignancy with poor prognosis. Our patient, 44 years old male presented with the symptoms of abdominal pain, decreased appetite & black colored watery stool since one month. On PET -CT he had multiple rounded lesions in liver which were thought to be cholangiocarcinoma initially. Biopsy & immunohistochemistry were performed & it was found to be small cell carcinoma. Patient was managed with chemotherapy. Being rare, it is necessary to do proper typing of such tumor so that patient gets benefited by specific treatment. Further, it also helps to know the prognosis.

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### Keywords:

*Extra-pulmonary small cell carcinoma, liver, immunohistochemistry*

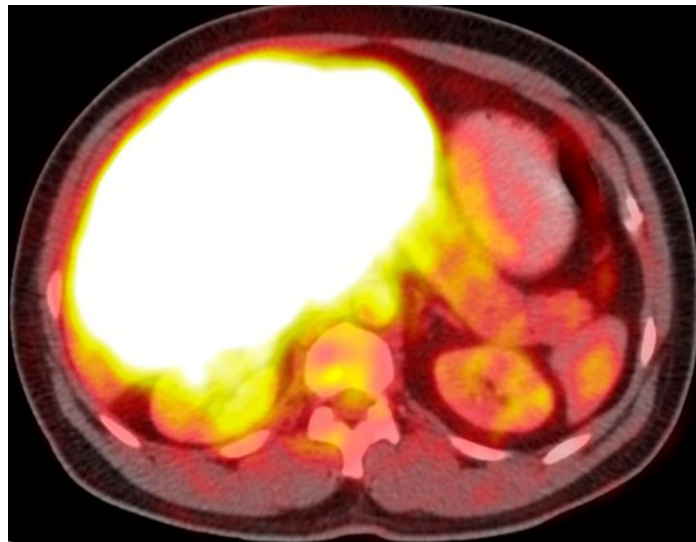
## Introduction

Pulmonary small cell carcinoma is a very well-known entity. Extrapulmonary small cell carcinoma is unusual & accounts for 2.5-4% of malignancies. [1, 2] It is a fatal disease with poor prognosis. It is essential to diagnose extrapulmonary small cell carcinoma on histopathology as these tumors are relatively chemosensitive. The diagnostic criteria include histological features of small cell carcinoma & absence of disease in the lung. Several common sites of extrapulmonary small cell carcinoma include esophagus, larynx, prostate, breast, small intestine & pancreas. Very few cases of primary liver small cell carcinoma were reported in the literature. Here, we report a rare case of small cell carcinoma of liver.

## Case Report

A 44 years old male presented with the complaints of abdominal pain, loss of appetite & passing black colored watery stool since one month. He was a chronic smoker and non-alcoholic. On physical examination, he was moderately built with mildly distended abdomen and tender right hypochondriac region. His laboratory investigations were done. Hemoglobin was slightly reduced (8 gms/dl) whereas total, direct & indirect bilirubin were within normal range. Serum AFP was normal, serum CA19.9 was mildly elevated (44.3U/ml, reference range-0-37U/ml). Coagulation tests were normal. Patient underwent endoscopy to evaluate the gastrointestinal tract & it was found to be within normal limits.

Further, his Contrast Enhanced Computed Tomography (CECT) abdomen & chest were done. It showed multifocal lesions in liver. Chest appeared normal. His PET-CT scan showed multiple FDG avid discrete & confluent heterogeneously enhancing rounded lesions involving both the liver lobes. Largest one was measuring 10.8cm with SUV max of 46.7 (Fig- 1). Background liver was non-cirrhotic. Based on the clinical & radiological picture, initial diagnosis of cholangiocarcinoma was made.

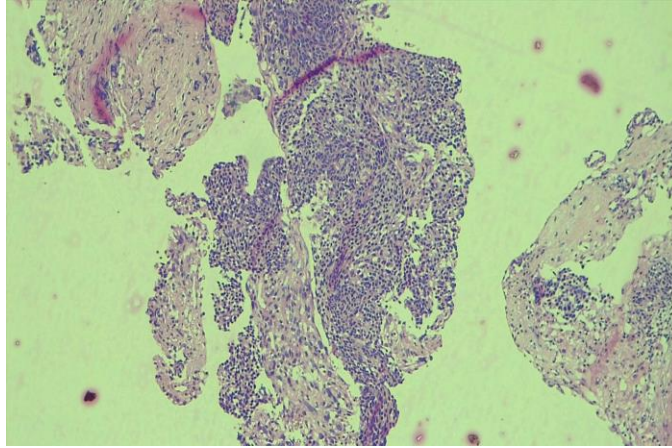


*Figure 1: showing FDG avid lesions involving both the liver lobes with SUV value of 46.7*

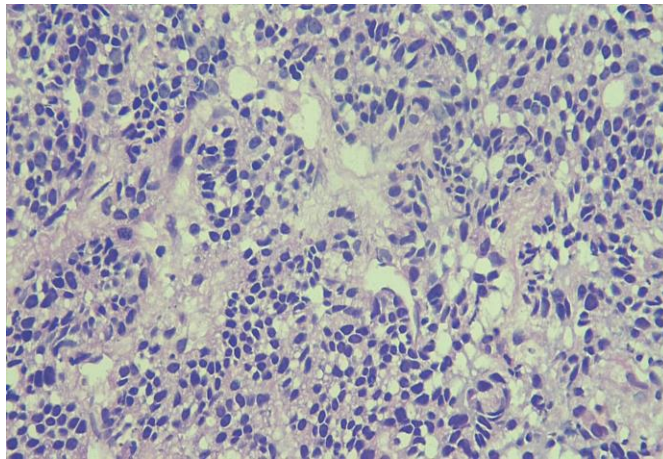
Biopsy from the largest lesion was done. On histology, it showed blue looking tumor cells arranged in the nested pattern and in irregularly infiltrating sheets (Fig- 2). Ill-defined rosette formation was seen. Tumor cells had hyperchromatic nuclei & scanty cytoplasm (Fig- 3). Mitotic count was 4-5/10hpf. Area of necrosis were seen. Immunohistochemistry (IHC) was run to confirm the diagnosis. Tumor was strongly positive for synaptophysin (Fig- 4), CK showed peri-nuclear dot like staining. Ki67 was high-80%. Tumor was negative for TTF1 (thyroid transcription factor), CD45, CK7, 19, 20 & Hepar1. Taking into consideration all these findings, diagnosis of small cell carcinoma was made. Patient had unresectable disease. Hence, chemotherapy was started. Patient responded well to chemotherapy.

## Discussion

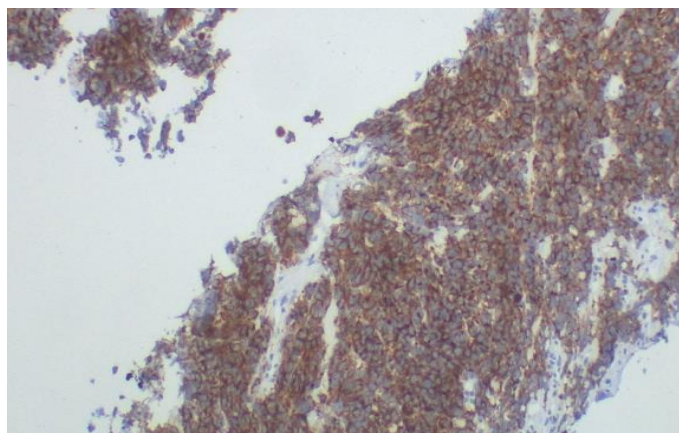
Extra-pulmonary small cell carcinoma is a very uncommon tumor. It accounts for 2.5-4% of all the malignancies.[1, 2] Few studies have reported small cell carcinoma involving gall bladder,[3] pancreas[4] & ampulla of vater.[5] However primary small cell carcinoma involving liver is extremely rare. As small cell carcinoma commonly involves lung, it is important to rule out lung primary. Histology of small cell carcinoma involving any organ will be similar. Also, immunohistochemistry profiles are same.



*Figure 2: Low power showing blue looking tumor cells with scanty cytoplasm arranged in the nested pattern and in irregularly infiltrating sheets.*



*Figure 3: High power showing tumor cells arranged in nested pattern with hyperchromatic nuclei & scanty cytoplasm. Moderate nuclear atypia noted. Ill-defined rosettes formation seen.*



*Figure 4: On IHC Synaptophysin shows diffuse & strong cytoplasmic staining*

So, proper radiological evaluation is very important such cases. In our patient, CECT chest was normal. Further his PET- CT showed uptake in liver only, and no active disease elsewhere in the body. PET-CT has good sensitivity to detect lung small cell carcinoma.[6, 7]

Embryonal neural crest cells are present in pulmonary & gastrointestinal system during developmental period. Hence this cancer occur more frequently in lung & gastrointestinal system & is uncommon in liver due to absence of these cells.[1, 8] The clinical presentation and immunohistochemistry profile may vary in extra-pulmonary small cell carcinoma as reported in literature but most commonly synaptophysin, CD56 and chromogranin markers are used to confirm the diagnosis on IHC.[9-12] (Table -1)

**Table 1: showing clinical features and immunohistochemistry pattern seen in extra-pulmonary small cell carcinoma in literature**

	Clinical features	Lab investigations	Cirrhosis	Immunohistochemistry	Treatment
Choi et al <sup>[9]</sup>	Abdominal discomfort	Within normal limits except HbsAb-positive	Absent	Synaptophysin, chromogranin, CD56, NSE, TTF1-positive. CK7, 19, 20-negative	Surgery
Jo et al <sup>[10]</sup>	Chest pain, Jaundice	Raised total, direct and indirect bilirubin	Absent	Synaptophysin, CD56-positive. TTF1-Negative	Chemotherapy
Morikawa et al <sup>[11]</sup>	Fatigue, breathlessness	Raised SGPT, SGOT, LDH, NSE	Absent	AE1/AE3, CK7, CK19, CK20-Positive. NSE, Vimentin-Negative	Chemotherapy
Dravid et al <sup>[12]</sup>	Fatigue, Anorexia, Vomiting	Raised indirect bilirubin	Absent	Synaptophysin, CD56-Positive. Chromogranin, Hepar1- Negative	Chemotherapy
Zanconati et al <sup>[13]</sup>	Abdominal discomfort	AFP->200 ng/ml	Absent	AE1/AE3, CK8,18,19, NSE, AFP-Positive. S100, CEA-Negative	Partial hepatectomy
Zanconati et al <sup>[13]</sup>	Weight loss		Absent	AE1/AE3, CK8,18,19, NSE, AFP-Positive. S100, CEA-Negative	No
Zanconati et al <sup>[13]</sup>	Jaundice	AFP-150 ng/ml	Absent	AE1/AE3, CK8,18,19, NSE, AFP-Positive. S100, CEA-Negative	
Kim et al <sup>[14]</sup>	Palpable mass	HBsAg & HBsAb-Negative	Absent	Synaptophysin, CD56, Ckit-Positive. CK, CEA, AFP-Negative	Surgery + Chemotherapy
Our case	Abdominal pain, black coloured stool	CA19.9-Mildly increased, Bilirubin, AFP-Normal	Absent	Synaptophysin, AE1/AE3-Positive. CK7,19,20,45, Hepar1, TTF1-Negative	Chemotherapy

Most of the pulmonary small cell carcinoma are positive for TTF1, whereas extrapulmonary small cell carcinoma shows variable expression of the same. One case of extra pulmonary small cell carcinoma reported by Kim et al was positive for TTF1. [13] Our case shows negative expression of TTF1.

Cytokeratin expression have been studied in small cell carcinoma of liver. Cases described by Morikawa et al & Zanconati et al showed positive staining for CK7, CK20, CK 8, CK18 and CK 19.[11, 14] Whereas cases studied by Suk Jin Choi et al and Kim et al showed negative expression of CK7, CK19 & CK 20 in agreement with our case.[9, 13] Synaptophysin & CD56 markers were uniformly positive in all the cases described in the literature. Background liver is normal in all the cases, no association with cirrhosis is noted yet.

## Conclusion

It is essential to diagnose & differentiate extrapulmonary small cell carcinoma accurately on morphology as it is relatively chemosensitive & has poor prognosis. Though extra-pulmonary small cell carcinoma is rare, one must keep this diagnosis in mind when we see small round blue cell tumor on histopathology. Being rare, it is necessary to study these cases thoroughly to know its exact clinical course & survival rate.

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## References

1. Levenson RM, Ihde DC, Matthews MJ, et al. Small cell carcinoma presenting as an extrapulmonary neoplasm: sites of origin and response to chemotherapy. *J Natl Cancer Inst.* 1981 Sep;67(3):607-12
2. Remick SC, Ruckdeschel JC. Extrapulmonary and pulmonary small-cell carcinoma: tumor biology, therapy, and outcome. *Med Pediatr Oncol.* 1992;20(2):89-99
3. Eriguchi N, Aoyagi S, Noritomi T, et al. Adeno-endocrine cell carcinoma of the gallbladder. *J Hepatobiliary Pancreat Surg.* 2000;7(1):97-101
4. Nakamura Y, Tajiri T, Uchida E, et al. Changes to levels of serum neuron-specific enolase in a patient with small cell carcinoma of the pancreas. *J Hepatobiliary Pancreat Surg.* 2005;12(1):93-8
5. Sugawara G, Yamaguchi A, Isogai M, Watanabe Y, Kaneoka Y, Suzuki M. Small cell neuroendocrine carcinoma of the ampulla of Vater with foci of squamous differentiation: a case report. *J Hepatobiliary Pancreat Surg.* 2004;11(1):56-60
6. Walenkamp AM, Sonke GS, Sleijfer DT. Clinical and therapeutic aspects of extrapulmonary small cell carcinoma. *Cancer Treat Rev.* 2009 May;35(3):228-36
7. Fischer BM, Mortensen J, Langer SW, et al. A prospective study of PET/CT in initial staging of small-cell lung cancer: comparison with CT, bone scintigraphy and bone marrow analysis. *Ann Oncol.* 2007 Feb;18(2):338-45
8. Cho SB, Park SY, Joo YE. Small cell carcinoma of extrahepatic bile duct presenting with hemobilia. *Korean J Gastroenterol.* 2009 Sep;54(3):186-90
9. Choi SJ, Kim JM, Han JY, et al. Extrapulmonary small cell carcinoma of the liver: clinicopathological and immunohistochemical findings. *Yonsei Med J.* 2007 Dec 31;48(6):1066-71
10. Jo JM, Cho YK, Hyun CL, et al. Small cell carcinoma of the liver and biliary tract without jaundice. *World J Gastroenterol* 2013; 19(44): 8146-8150
11. Morikawa H, Nakayama Y, Maeda T, et al. A case of primary small cell carcinoma liver that was treated with chemotherapy. *Hepatol Int* 2,500-504(2008)
12. Dravid A, Natarajan K, Medisetty M, et al. (2017) Primary small cell carcinoma of liver in a HIV/Hepatitis B co-infected patient on virologically suppressive antiretroviral therapy: case report & literature review. *Oncol cancer case Rep*3:137.
13. Kim YH, Kwon R, Jung GJ, Roh MH, Han SY, Kwon HC, Jeong JS, Shin TB, Oh JY, Lee KN. Extrapulmonary small cell carcinoma of the liver. *Journal of Hepato - Biliary - Pancreatic Surgery.* 2004 Oct;11(5):333-7.
14. Zanconati F, Falconieri G, Lamovec J, Zidar A. Small cell carcinoma of the liver: a hitherto unreported variant of hepatocellular carcinoma. *Histopathology.* 1996 Nov;29(5):449-53.