

# Small Cell Carcinoma of Gallbladder: A Rare Case Report

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### ABSTRACT

A small cell carcinoma of the gallbladder is being reported from a young lady of 31 years of age, for the first time from Jammu and Kashmir state. The SCC, also called Neuroendocrine carcinoma of gallbladder are comparatively very rare and are reported usually from elderly ladies but in the present case the lady was very young. The patient presented with clear cut symptoms of cholecystitis and was thus diagnosed at early stage of life, which however is not true with most of the cases, which depict symptoms very late at older age leading to their low survival rate after diagnosis.

The present report is a case of pure SCC without any association with any other disease. The patient had multiple gallstones, a mass each in fundus and neck of gallbladder. The left hepatic duct was partially blocked and dilated. Microscopy of stained sections of gallbladder showed tumour cells, with hyperchromatic nuclei and high N:C ratio, arranged in nests, cords and trabeculae extending up to serosa (or features suggestive of SCC). The diagnosis of SCC was also confirmed immunohistochemically. Cholecystectomy along with removal of portahepatic lymphnodes was done. The patient is undergoing chemotherapy and is showing signs of improvement.

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## Introduction

In this paper, small cell carcinoma (SCC), of the gallbladder, is being reported from a 31 year old female. On perusal of the available literature, this seems to be the first report of SCC from Jammu region of Jammu and Kashmir State. This is a neoplasm, referred to as, carcinoid tumor or endocrine cell carcinoma but the more preferred term for this is small cell carcinoma (SCC).

This tumor was first reported and described by Albores Saavedra *et al.* in 1981<sup>[1]</sup>. The most important characteristics of SCC include, its clinicopathological distinctness from other tumours, its rarity, highly aggressive nature, that tends to metastasize early, its poor prognosis and being more prevalent in elderly ladies.<sup>[2]</sup> However, a few cases have been reported in elderly males also.<sup>[3]</sup> Sometimes, it also shows association with endocrine manifestations and chemosensitivity.<sup>[2]</sup> All these clinicopathological features have been recognized to make it a distinct and separate neoplasm from other ordinary gall bladder carcinomas.<sup>[4]</sup> This carcinoma is reported to be having high malignant potential leading to its low survival rate. The other reason being very late presentation of symptoms.<sup>[5]</sup>

The present case of neuroendocrine carcinoma of gallbladder is peculiar in that it was diagnosed and resected in a comparatively a very young lady with cholelithiasis.

## Case Report

A 31 year old female presented to the OPD, in the Department of Surgery with chief complaints of loss of appetite, abdominal fullness and right upper quadrant abdominal pain for 3 months. On per abdominal examination, a palpable mass was felt over the lower border of liver along the mid-clavicular line.

Serum total bilirubin was 4.1mg/dl, direct 3.8mg/dl, SGOT 211 U/L, SGPT 225 U/L and Alkaline phosphatase 659 U/L.

An ultrasound revealed multiple stones (Average, 8-10mm) in the lumen of gallbladder, a mass measuring 42 x 33 mm at the gallbladder fundus and, another mass measuring 33 x 25 mm at the neck of gallbladder, partially blocking the left hepatic duct, which was dilated (8mm). There were multiple enlarged lymph nodes at porta. A CT guided FNAC was done which revealed few clusters of cells with round and dense nuclei. (Fig- 1)

Open cholecystectomy was carried out. The gallbladder along with stones, and three porta hepatic lymphnodes were resected out. Liver biopsy was also done. All the three specimens were thoroughly examined in the Department of Pathology. On gross examination, gallbladder measuring -13x4x3cm with growth at fundus and neck measuring

-5x3.5 cm and 3x2cm was seen.(Fig -2) Microscopy revealed intact mucosa, with tumor cells arranged in nests, cords and trabeculae extending up to serosa.(Fig- 3,5). The tumour cells were round to oval, with hyperchromatic nuclei, high N:C ratio, indistinct nucleoli, scanty cytoplasm and nuclear moulding, in desmoplastic stroma. (Fig- 4) There were foci of necrosis, however, peritoneal surface was free of tumour and there was no invasion to liver and no vascular invasion. There was metastasis to lymph node with total replacement of lymph node tissue by tumour but there was no pericapsular invasion. Hence diagnosis of Small cell Carcinoma was made which was later

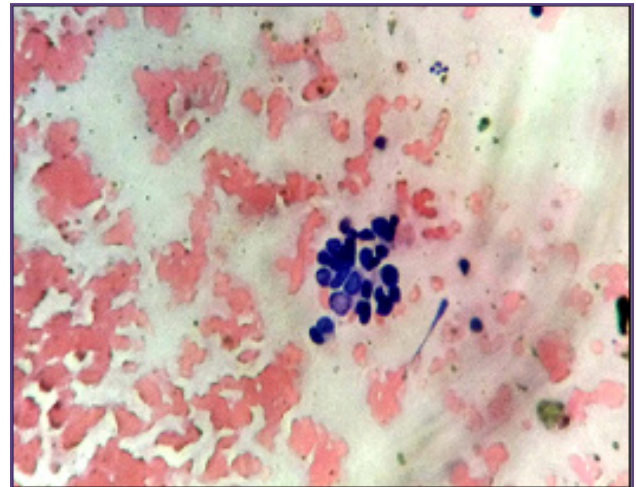


Fig. 1: CT guided FNAC showing cells with round and dense nuclei ,40X Giemsa.

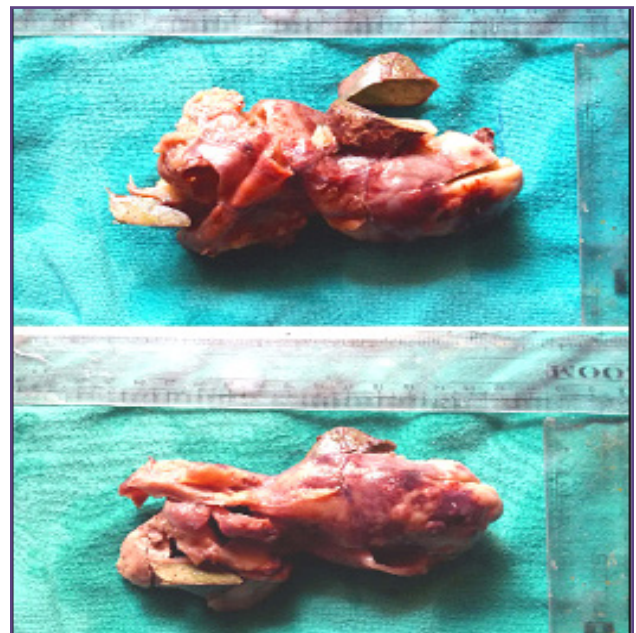


Fig. 2: Gross images.

confirmed by Immunohistochemically, the tumour cells were positive for NSE (neuron specific enolase). (Fig- 6) The diagnosis was revised to be small cell neuroendocrine carcinoma of gallbladder. Currently, the patient is receiving chemotherapy and is doing well.

### Discussion

Although gallbladder carcinomas are fifth most common gastrointestinal malignancies, with seven thousand new cases being reported every year in the United States of America,<sup>[6]</sup> yet the small cell carcinomas or neuroendocrine carcinomas of gallbladder are exceedingly rare, comprising 0.2% of all the gastrointestinal carcinomas.<sup>[7]</sup> But according to Henson, 1992,<sup>[8]</sup> it was 0.5% of all the gallbladder carcinomas. According to Peter Nau et al, 2010<sup>[9]</sup> and Amit Mahipal, 2011,<sup>[10]</sup> 40 and 73 cases only were respectively, reported in English medical journals. However, Moskal et al, 1999,<sup>[11]</sup> have reported a higher incidence of these carcinomas being of 3.5%. The reasons for its rarity can be two-fold. Firstly, that this tumour is discovered very late when the disease process

has advanced and affected the adjacent organ systems including the obstruction of biliary system leading to poor prognosis. Secondly, the survival rates of this carcinoma are very low than other gallbladder malignancies, causing death before they are properly diagnosed.

As per the available literature, small cell carcinoma of gallbladder affects elderly ladies from whom it has been mostly reported,<sup>[11]</sup> but exceptions are there, where it has been reported from elderly males also<sup>[3, 10]</sup>. According to Amit Mahipal et al, (2011), the age of these ladies ranges from 25-86 years with median age of 67years. The present case is peculiar in that the patient belonged to a very younger age group, who was 31 yrs of age. The simple reason is that she was, exceptionally, presenting well defined symptoms and was thus diagnosed at an early stage, that is why she is surviving and doing well after cholecystectomy and is presently undergoing chemotherapy. One important feature of small cell carcinoma is that it is usually associated with cholelithiasis, reported to be 68%<sup>[10]</sup> which has been confirmed in the present case also.

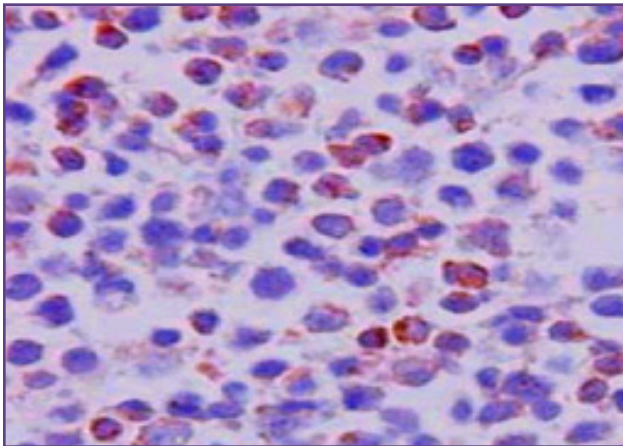


Fig. 3: Cells showing positivity for Neuron Specific enolase, 40X

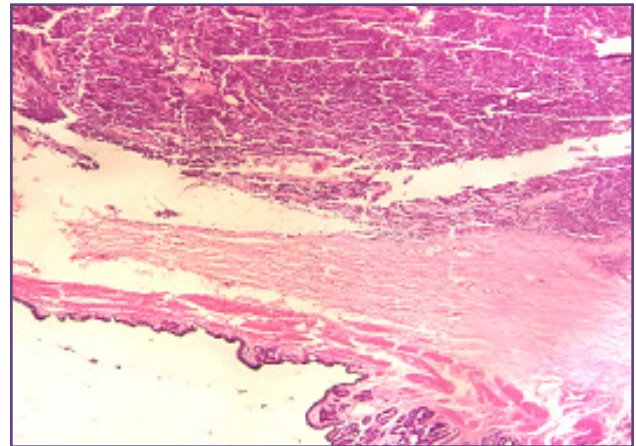


Fig. 4: Small cell carcinoma, low power view, 10X, H&E

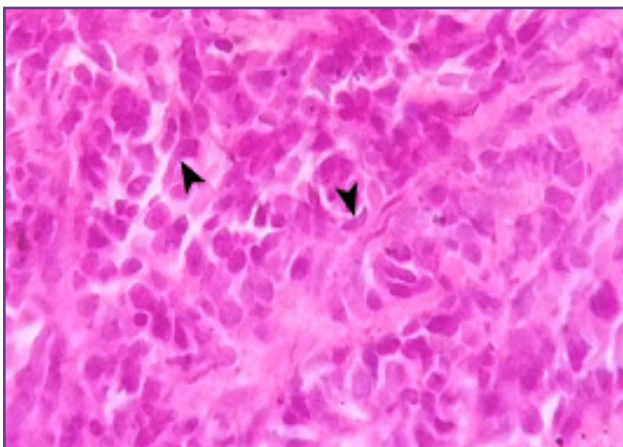


Fig. 5: small, Hyperchromatic cells with molding, 40 X, H&E

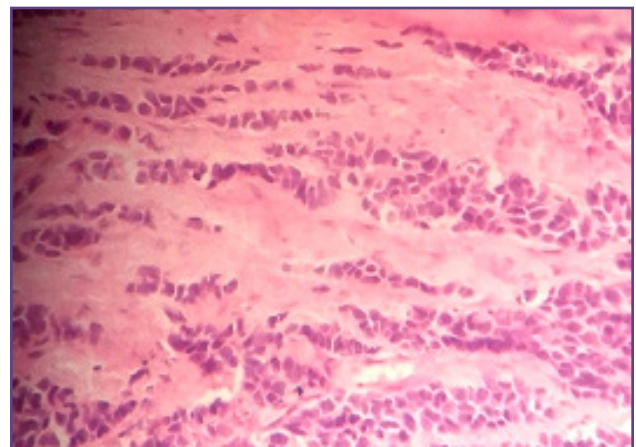


Fig. 6: Tumor cells infiltrating upto serosa, 40X, H&E, 40X.

In some cases, Small cell carcinoma has been reported in combination with adenocarcinoma of gallbladder with transitions between the two types of carcinomas,<sup>[10]</sup> however, in present case such combination and transitions were not observed. 28% cases are reported as combined small cell carcinoma and adenocarcinoma or squamous cell carcinoma, whereas, pure Small cell carcinoma is reported in 72%.<sup>[10]</sup> The present case was pure Small cell carcinoma without any association with other carcinomas.

In some cases, Small cell carcinoma has been found associated with AIDS<sup>[10]</sup> but in present case, the patient did not suffer from any other ailments except Small cell carcinoma. Such combined cases are thought to be incidental findings and has no clinically significant association.<sup>[10]</sup>

66% cases have been diagnosed at stage IV and the remaining at stage I –stage III.<sup>[10]</sup> The present case was at stage II B according to TNM.

In the present study, the metastasis had taken place only to porta hepatis lymph nodes where as, metastasis has been reported maximum (70%) in lymph node, liver (64%), lungs (10%) by Amit Mahipal et al, 2010.<sup>[10]</sup>

The median survival has been given as nine months, ranging from 1-18 months.<sup>[10]</sup> However, the patient in present study is surviving since last six months, and is on regular observation.

Regarding the origin of SCC the accepted view is that it arises from metaplastic epithelium of gallbladder wall.<sup>[12]</sup> This concept is based on the fact that no neuroectodermal cells are found in the gallbladder mucosa.<sup>[13]</sup> This has been confirmed by work of some investigators who have reported metaplasia in the gallbladder with chronic cholecystitis. However, in the present study although chronic cholecystitis with cholelithiasis was confirmed but no metaplasia or dysplasia was observed in the gallbladder mucosa. This confirms the views of Shih Sung<sup>[3]</sup> who support a common endodermal, multipotent stem cell origin of Small cell carcinoma, which was also advocated by Nash.<sup>[3, 10]</sup>

The diagnosis of SCC is difficult and cannot be relied upon a single criterion like radiological findings. Immunohistochemistry along with histological studies are necessary to confirm the diagnosis.

## Conclusion

Gallbladder neuroendocrine carcinomas remain an exceptionally rare malignancy with a strikingly poor prognosis. Early diagnosis with prompt surgical intervention provides the patient with the best long term outcome.

Clinicians and especially pathologists must be aware of this entity to avoid misdiagnosis and erroneous treatment.

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## Competing Interests

None Declared

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