

A Rare Presentation of Gall Bladder (GB) Mass in the Form of Mixed Adenoneuroendocrine Carcinoma (MANEC): A Case Report

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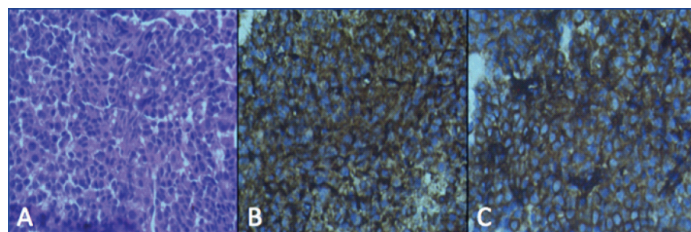
ABSTRACT

Primary Neuroendocrine Carcinoma (NEC) of gall bladder is extremely rare. The diagnosis is incidental in most cases. Here, we present a case of Mixed Adenoneuroendocrine tumour (MANEC) in a 48-year-old female who presented with pain in abdomen, nausea and loss of appetite and diffuse non-tender lump in right hypochondrium. CECT abdomen showed distended Gall Bladder (GB) with intraluminal polypoidal mass, with multiple liver and retroperitoneal metastasis. Histopathological and immunohistochemistry study revealed MANEC in GB with NEC metastasis in liver. This case highlights the rarity of the disorder and role of immunohistochemical studies and therefore MANEC should be considered as a differential to GB carcinoma.

Keywords: Gall bladder, Immunohistochemistry, Malignant

CASE REPORT

A 48-year-old female with complaints of pain in abdomen, on and off nausea and loss of appetite since one month presented to the department. Laboratory investigation revealed elevated SGOT (511 U/L), SGPT (93 U/L), ALP (1350 U/L), direct serum bilirubin (2.11 mg/dL), total serum bilirubin (2.91 md/dL) with normal HbsAg and Anti HCV. On clinical examination an approximately 11×10 cm, diffuse non-tender lump was noted in right hypochondrium, which extended to the epigastrium and umbilical region and was moving with respiration. Chest X-Ray was normal. Ultrasound (USG) showed multiple hypoechoic lesions in liver. Triple phase CECT abdomen was done which showed distended GB with intraluminal polypoidal mass, with multiple liver Space Occupying Lesions (SOL) and retroperitoneal enlarged nodes [Table/Fig-1]. Patient was admitted with provisional diagnosis as carcinoma GB with liver and nodal metastasis. Guided TRU cut biopsy from liver lesions and FNAC from polypoidal mass of GB lumen was done. Histopathological examination of liver biopsy showed tumour arranged in sheets, perivascular rosetting and focal organoid pattern. The individual tumour cells showed hyperchromatic nuclei, increased nucleus to cytoplasmic ratio (N:C) and moderate amount of eosinophilic cytoplasm. IHC study showed diffuse strong positive in tumour cells for cytokeratin, synaptophysin, chromogranin A, CD56 and CDX-2, 65% for Ki-67 and negative for CK7 and CK20 suggesting neuroendocrine carcinoma [Table/Fig-2]. FNAC from GB mass showed atypical cells arranged in papillary clusters sheets, gland formation and singly scattered. The cells showed moderate nuclear pleomorphism, high N:C ratio, suggestive of adenocarcinoma with focal neuroendocrine features.



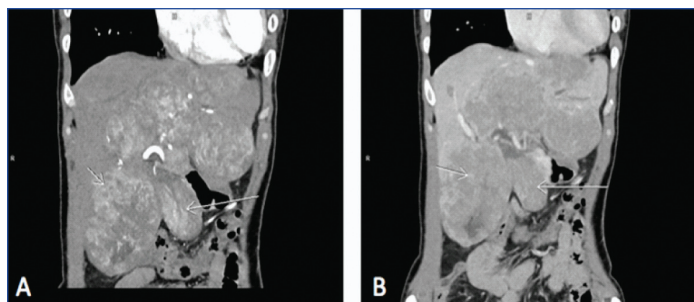
[Table/Fig-2]: Tumour cells stain positive for cytokeratin (a), chromogranin (b) and synaptophysin (c).

DISCUSSION

Neuroendocrine Tumours (NETs) previously known as carcinoid tumours are neoplasm of enterochromaffin/neuroendocrine cell origin, with neurosecretory capacity [1,2]. Neuroendocrine neoplasms are classified according to the WHO Classification of Tumours of the Digestive System in 2010 as well-differentiated, low-grade (G1); well-differentiated, intermediate-grade (G2); and poorly differentiated, high-grade (G3) [3]. Carcinoid tumours are quite unusual endocrine tumours arising mainly in the gastrointestinal tract. The site for primary carcinoid is appendix, jejunum and rectum in most of the cases. Primary GB carcinoid are extremely rare, till date only 278 cases of GB NETs are reported in the Surveillance, Epidemiology, and End Results (SEER) database. The age of presentation ranges from 38 to 81 years with marked higher incidence in women and it corroborates with our case [4]. NETs of GB probably originate from a multipotent stem cell or from endocrine cells induced by intestinal metaplasia of the body and fundus as well as from pre-existing endocrine cells in the neck of the GB, which occurs following cholelithiasis and/or chronic inflammation [1].

Neuroendocrine carcinoma is frequently combined with other tumours such as adenocarcinoma or squamous cell carcinoma. MANEC is diagnosed only when both tumour types are more than 30% in the pathological examination [5].

The imaging modalities like USG, CT and MRI, cannot distinguish GB-NEC from other gall bladder carcinomas. The radiological findings are similar to presentations of any other GB tumour. MRI is the modality of choice in staging GB tumours and when combined with MRCP, gives full overview of biliary radicles invasion. Sensitivities are as high as 100% and 92% for direct hepatic invasion and lymph nodes invasion on MRI respectively [6]. Diagnosis is generally made on pathological and immune histochemical examinations.



[Table/Fig-1]: CECT of abdomen, Coronal sections, (a) shows distended GB with intraluminal polypoidal mass (large arrow) and multiple well-defined lobulated intrahepatic masses (small arrow) of varying sizes with moderate heterogeneous enhancement on arterial phase and washout on venous phase (b).

NEC also invades the adjacent liver parenchyma and cause biliary obstruction, thus making it difficult to diagnose at an early stage. Due to the nature of NECs, patients are often diagnosed at an advanced stage with lymph node metastasis or liver infiltration, and have a poor prognosis [3,7]. Since there is no characteristic imaging finding to suspect this tumour and it is almost impossible to differentiate it from other subtypes of gall bladder tumour, only postoperative diagnosis was done previously. But now-a-days, TRU cut biopsy from lesion is rampantly done under ultrasound guidance and preoperative diagnosis is possible and it helps in better management of the cases. GB NETs treatment comprises of multidisciplinary approach including surgery, chemotherapy and radiotherapy. In patients in advanced stages without distal metastasis, radical cholecystectomy and lymphadenectomy combined with hepatic resection are done [3]. Systemic chemotherapy is the treatment of choice in case of unresectable tumours.

CONCLUSION

The findings of NEC are similar to presentations of any other GB tumour. So its specific diagnosis on imaging is difficult. USG is the initial modality of choice in diagnosis GB tumours. Multiphasic CECT, MRI, and PET-CT are imaging which helps in further characterising

and staging of tumours. Radical surgery with adjuvant chemotherapy is the main line of treatment in patients without metastatic disease. This case highlights the rarity of the disorder and role of preoperative USG guided TRU cut biopsy and immunohistochemical studies in diagnosis of MANEC.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Nov 19, 2018**
Date of Peer Review: **Dec 11, 2018**
Date of Acceptance: **Feb 25, 2019**
Date of Publishing: **Apr 01, 2019**