



Gallbladder Mixed Neuroendocrine-Non-Neuroendocrine Neoplasms: A Case Report

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Abstract

The gallbladder Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN) are extremely rare. The association of at least two components including one neuroendocrine tumor, and a non-neuroendocrine one defines MiNEN.

We are reporting a case of 50-year-old woman referred to our department for management of a gallbladder tumor suspected on imaging. She undergone a cholecystectomy enlarged to the vesicular bed according to Gleen and hepatoduodenal lymphadenectomy.

The histological examination conclude on MiNEN of the gallbladder; and the patient received adjuvant chemotherapy and she shows no sign of recurrence at 6 months.

Keywords: *Gallbladder, MiNEN, Neuroendocrine tumors, Adenocarcinoma.*

Introduction

The gallbladder Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN) are extremely rare; only few cases have been reported in the literature and are accounting for less than 0.5% of all gallbladder neoplasms.

We are reporting a case of gallbladder Minen for the extreme rarity of the diagnosis as a small contribution in order of a better understanding of its clinical aspect.

Case presentation

A 50-year-old woman, with no medical record, was referred to our department for management of a gallbladder tumor suspected on ultrasound. She suffered intermittent pain in the right upper abdominal quadrant, for the past 2 months, with no other digestive signs, fever or jaundice. There was no significant family medical history and her general physical examination was normal.

Abdominal ultrasound showed a heterogeneous intra-luminal mass of gallbladder measuring 24x23 mm. there was no evidence of biliary tree dilation, of pathological findings of the liver and ascites.



Figure 1: Ultrasound image showing the gallbladder tumor. The gallbladder is stone free.

Laboratory findings including tests for tumor markers were normal.

The CT scan and MRI showed an intra-luminal process of the gallbladder and multiple hepatoduodenal nodes; with no evidence of hepatic invasion (Figure 2 and 3).

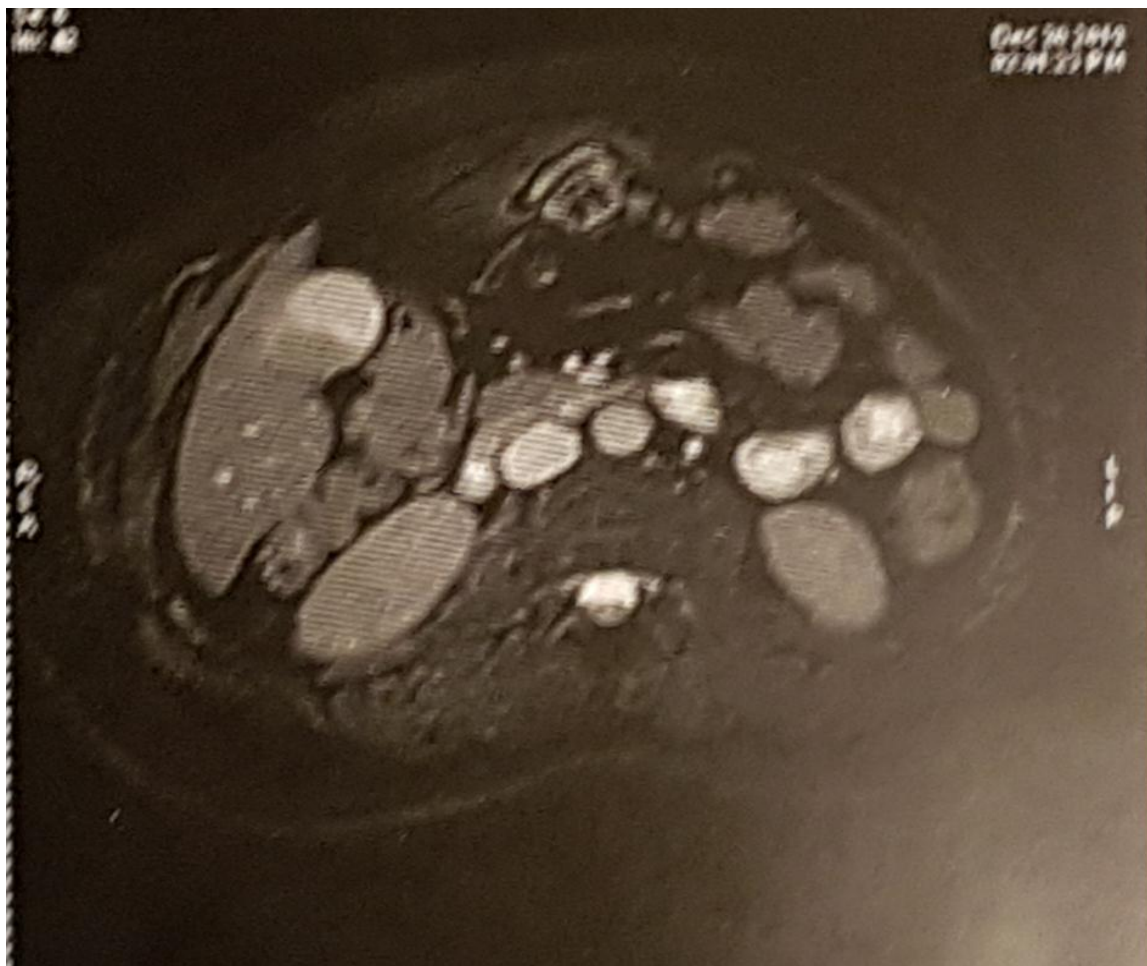


Figure 2: Computed tomography images show a 1.6 × 3.2 cm mass located on the body of gallbladder

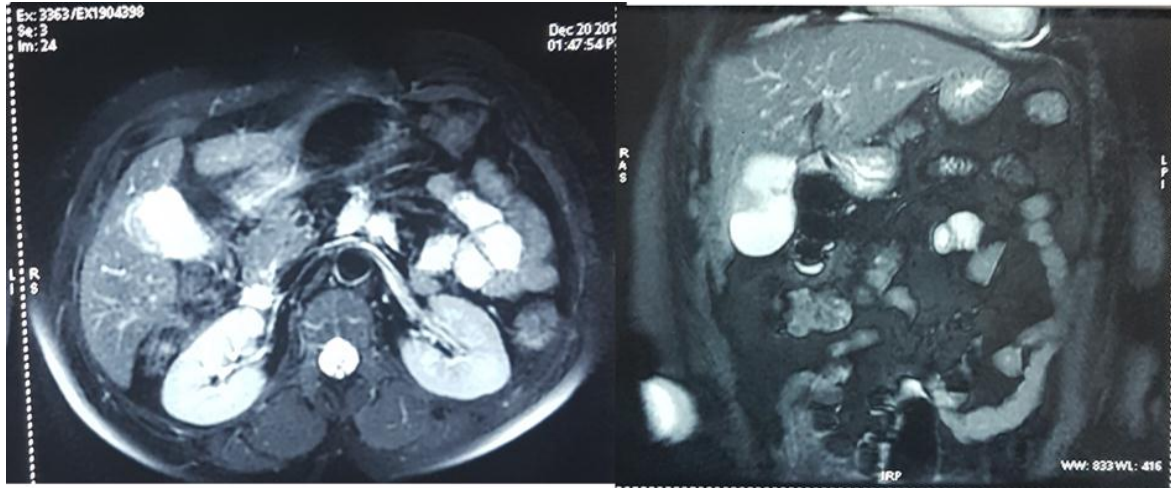


Figure 3: MRI images showing the gallbladder tumor and no invasion of the adjacent liver or structures.

Given the resectable character of the tumor according to preoperative imaging, the patient benefited by laparotomy from a cholecystectomy enlarged to the vesicular bed according to Gleen and hepatoduodenal lymphadenectomy.

Post operative courses were uneventful and the patient was discharged on postoperative day 4.

The histological examination shows a tumor proliferation with double component: the first one is adenocarcinomatous made essentially of tube and spans of cells of intestinal differentiation to

the nuclei endowed with marked atypia with abundant eosinophilic cytoplasm. The tumor stroma is fibro-inflammatory. (Figure4a)

The second one is neuroendocrine in appearance, made up of spans and cords of cells with finely granular cytoplasm and nuclei with chromatin in plover and salts separated by a fibro-vascular stroma.

At the immunohistochemical study, the neuroendocrine cells exhibited the strong expression of the neuroendocrine markers chromogranin A (Figure4b) and synaptophysin (Figure 4c).

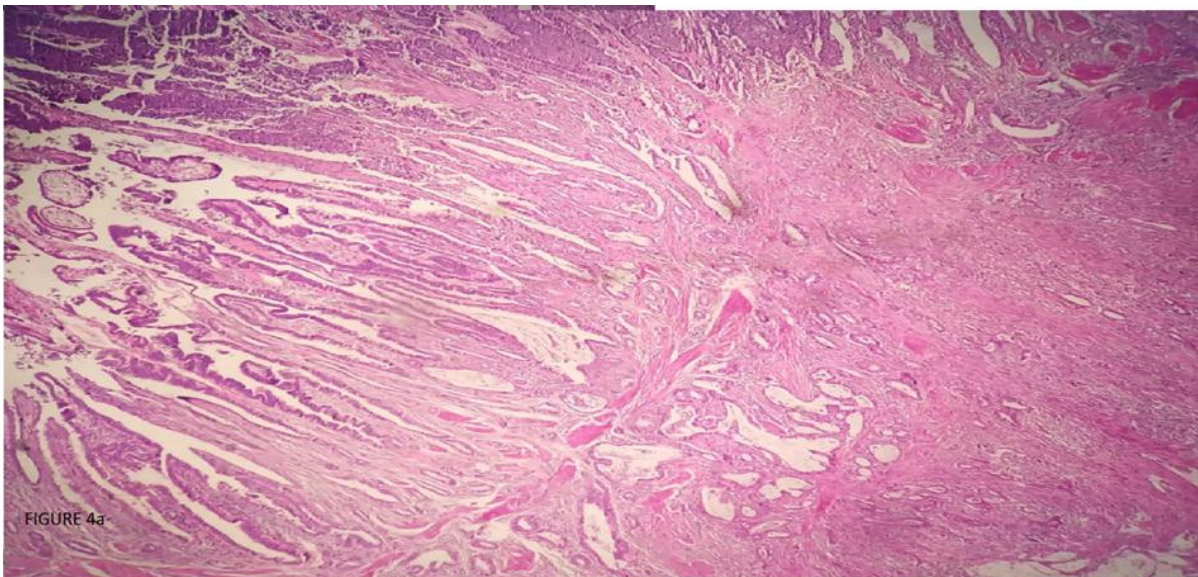


FIGURE 4a

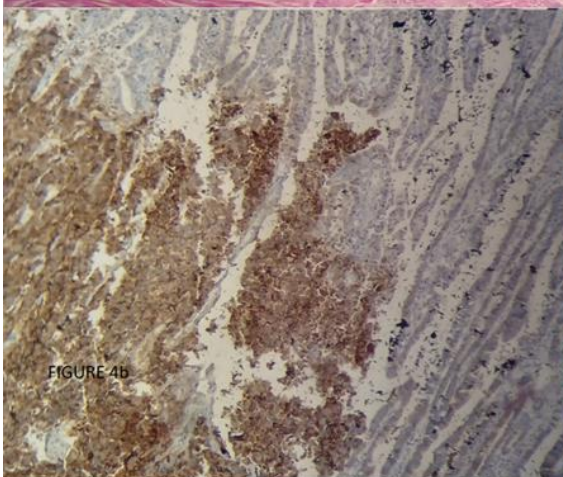


FIGURE 4b

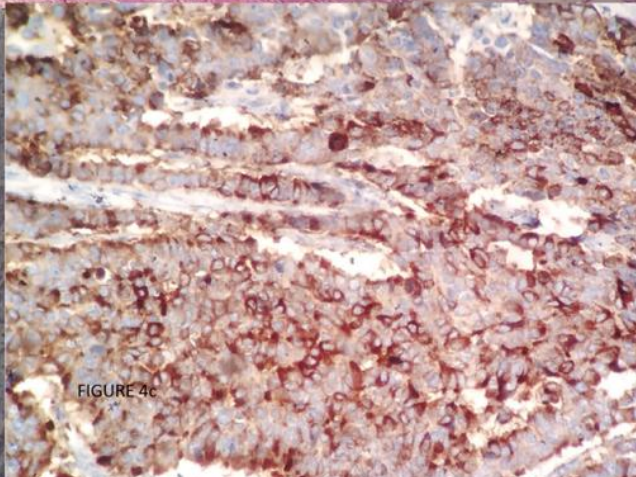


FIGURE 4c

Figure 4a: Tumor proliferation with two components: adenocarcinomatous and neuroendocrine.

Figure 4b: Immunohistochemical study: positive labeling of neuroendocrine tumor cells by chromogranin.

Figure 4c: Immunohistochemical study: positive labeling of neuroendocrine tumor cells by synaptophysin.

The morphological aspect and immunohistochemical profile confirmed a mixed adeno-neuroendocrine carcinoma (MINEN) infiltrating the walls up to the serosa, with vascular embolism and perineural sheaths. One of the six lymph nodes removed was invaded. Thus, this lesion was assigned a final classification of pT3N1M0, according to the Union Internationale Contre le Cancer guidelines.

Adjuvant chemotherapy was started 3 weeks of the intervention, as her clinical control was satisfying. Currently she shows no sign of recurrence at 6 months.

Discussion

The gallbladder cancer is rare; adenocarcinoma represent the most common tumor, although neuroendocrine tumors are reported. Mixed neuroendocrine-non-neuroendocrine neoplasms (MiNEN) are defined by the association of at least two components including one neuroendocrine tumor (NET G1, NET G2, NEC), and one non-neuroendocrine component generally adenocarcinoma.

MiNEN of the gallbladder are extremely rare; only few cases have been reported in the literature and are accounting for less than 0.5% of all gallbladder neoplasms.

The origin of these rare gallbladder malignancies remain hard to determine as normal gallbladder mucosa contains no neuroendocrine cells.^[1]

However, the most accepted hypothesis at this day is that both component are arising from a common, multipotent stem or progenitor cell^[2] persisting in the biliary tree^[3].

The clinical presentation of these aggressive tumors as well as other gallbladder tumors; is not specific; and usually mimic a biliary colic ,symptoms that our patient presented; weight loss and jaundice are often associated with more advanced disease. Carcinoid syndrome and paraneoplastic syndromes are exceptional.

Pre-operatively, imaging can only detect solid masses of gallbladder and are unable to distinguish MINEN from common adenocarcinoma. Computed Tomography (CT) remains the basic imaging technique and could show polyps or local wall thickening of the gallbladder initially; or a mass replacing the gallbladder and further infiltrating the liver parenchyma in more advanced stages. It could also show suspected metastatic site and lymph nodes, and remains helpful for the TNM staging and surgery plan. In our case, the diagnosis of gallbladder cancer was first evoked on ultrasonography and seriously suspected on CT scan.

Other imaging techniques correctly indicated, such as MRI and FDG PET scan can provide the specificity and sensitivity of diagnosis of malignant process of almost 90%^[4-5].

On the other hand, the confirmative diagnosis of gallbladder MINEN is obtained on pathology which according to the definition should morphologically recognize at least two components including one neuroendocrine tumor and one non-neuroendocrine component; and that each cell component must account for more than 30% of the neoplasm^[6-7],

Also by immunostaining for markers such as chromogranin A or synaptophysin for the neuroendocrine component^[8]. The neuroendocrine component account for almost 40 % of the neoplasm we are describing.

Surgery is the only potentially curative treatment. For in situ and T1N0M0 tumors, cholecystectomy could be enough.

However, the standard procedure in early-stage disease is an [en bloc] resection of the gallbladder and the hepatic parenchyma surrounding, with hepatoduodenal lymphadenectomy. Hepatectomy should be considered in a locally advanced disease.

For patients with distant metastasis, surgical treatment remains controversial. In general, a local liver invasion requires early and radical dissection to improve life quality and decrease tumor-induced complications.

Actually, neuro endocrine tumors are known to be insensitive to the traditional radiotherapy; therefore, its role in the management of gallbladder MINEN is unclear. In general, Systemic therapy can be used in the neoadjuvant and adjuvant setting and targets the most aggressive component to prolong the few months survival^[9].

In our case the patient undergo a cisplatin with etoposide association as a First line treatment which represent one of the standard regimens employed for the treatment of small cell lung cancer^[10].

Conclusion

MINEN of the gallbladder is extremely rare. Clinical features and management modalities are comparable to the more common adenocarcinoma of the gallbladder. The patient prognosis is poor overall, but early detection with complete resection may result in a relatively good prognosis.

Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper. Authors' Contributions
All authors participated in the care of the patient and the writing of the manuscript. All authors have read and approved the final version of the manuscript.

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