

# Neuro Endocrine Tumor of the Gall Bladder: A Case Report

Eddy Oleko Ekuke<sup>1\*</sup>, Yassine Kdhissi<sup>1</sup>, Fatoumata Djouldé Smith Diallo<sup>2</sup>, Pierlesky Elion Ossibi<sup>1</sup>, Hicham El Bouhadoutti<sup>1</sup>, El Bachir Benjelloun<sup>1</sup>, Ouadii Mouaqit<sup>1</sup>, Benajah Dafr-Allah<sup>2</sup>, Abdelmalek Ousadden<sup>1</sup>, Khalid Mazaz<sup>1</sup>, Khalid Ait Taleb<sup>1</sup>

<sup>1</sup>Department of Visceral Surgery, Hassan II University Hospital, Fez, Morocco

<sup>2</sup>Department of Gastroenterology and Hepatology, Hassan II University Hospital, Fez, Morocco

Email: \*olekoekuke20121982@gmail.com

**How to cite this paper:** Ekuke, E.O., Kdhissi, Y., Diallo, F.D.S., Ossibi, P.E., El Bouhadoutti, H., Benjelloun, E.B., Mouaqit, O., Dafr-Allah, B., Ousadden, A., Mazaz, K. and Ait Taleb, K. (2017) Neuro Endocrine Tumor of the Gall Bladder: A Case Report. *Surgical Science*, 8, 422-427.

<https://doi.org/10.4236/ss.2017.89046>

**Received:** July 3, 2017

**Accepted:** September 26, 2017

**Published:** September 29, 2017

Copyright © 2017 by authors and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

## Abstract

Neuroendocrine tumors (NET) of the gallbladder are a rare entity with only 0.2% of all NET located in the gall bladder. Well-differentiated NETs occur at a relatively lower age group unlike other gallbladder tumors, whereas neuroendocrine carcinoma (NEC) occurs in an older category of patients. The aim of our study is to discuss the current level of evidence regarding this pathological entity by means of a rare case report on a neuroendocrine carcinoma of the gall bladder in a 63-year-old patient with a history of diabetes. Patient underwent cholecystectomy for acute cholecystitis. Pathology findings on surgical specimen came back for neuroendocrine tumour.

## Keywords

Neuroendocrine Tumors, Endocrine Carcinoma, Gall Bladder

## 1. Introduction

Primary NET can occur throughout the entire gastro-intestinal tract (from the esophagus down to the anus), the pancreas and exceptionally in the liver or the gall bladder.

Gallbladder NET are uncommon, due to their extremely rare epidemiological character and their circumstances of discovery, mostly fortuitous. Only 0.2% of all neuroendocrine tumors are located in the gallbladder [1]. Clinical setting points to one of acute cholecystitis, but definite diagnosis is only made on the pathology examination of surgical specimen. We hereby report a case of gallbladder NET, discovered on pathology examination of cholecystectomy specimen in a 63-year-old male with a history of diabetes.

## 2. Case

Patient, 63-year-old diabetic male on insulin, presented with a three-month history of biliary colic with associating intermittent fever relieved by over the counter analgesics and antispasmodic drugs.

Symptoms worsened a week prior to his admission by the exacerbation of right upper quadrant pain and fever prompting his consultation at our department.

Physical examination found a conscious patient, stable vitals, HR 100 beats/minute, 39°C febrile with right upper quadrant guarding on abdominal examination.

Lab test came back with leukocytosis 22000/mm<sup>3</sup>; CRP level at 212 mg/l and 236 mg/l blood sugar. The rest of the lab results notably urea and electrolytes as well calcitonin levels were unremarkable.

Abdominal ultrasound revealed a large gallbladder with a thickened wall, 12 mm thick, containing several gallstones and a perivesicular effusion.

After initial fluid resuscitation patient was admitted for surgery, with peroperative discovery of a distended gall bladder with pseudomembranes (**Figure 1**) and a slightly purulent perivesicular abscess about 5 cc, which was aspirated. Macroscopically, the surrounding liver tissue was normal with no palpable mass. Retrograde cholecystectomy was performed.

Immediate postoperative recovery was marked by surgical wound infection, which responded favorably to adequate antibiotics and dressing for up to 10 days post operatively.

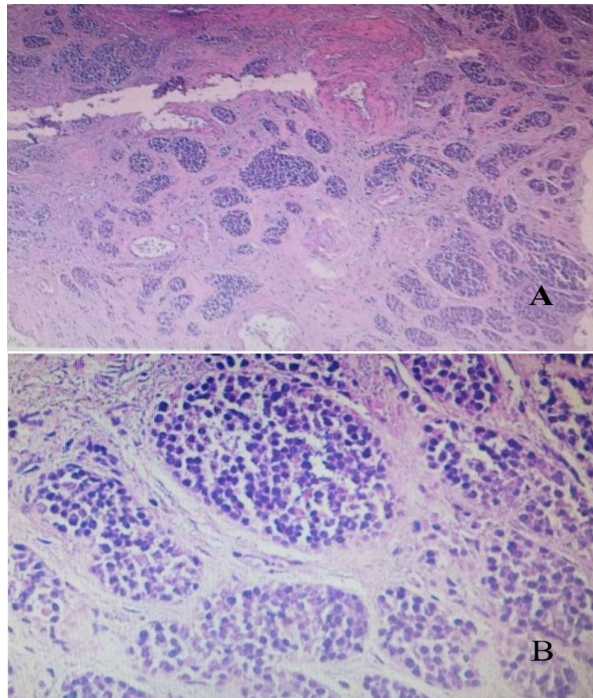
Pathology examination with immune histochemical marking of surgical specimen came back for a stage 3 (WHO 2010, ENETS 2006) large cell neuroendocrine carcinoma (**Figure 2**). There were no vascular emboli nor were perineural invasion and resection margins were clean. The tumor was staged pT2Nx.

The case was discussed at a multidisciplinary cancerology meeting where thoracic-abdomino-pelvic CT was recommended.

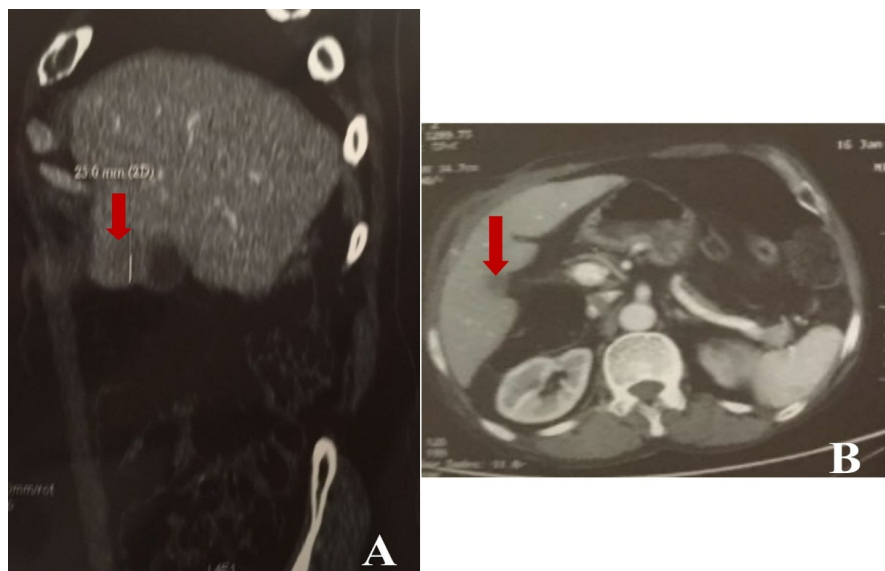
Thoracic-abdomino-pelvic CT revealed a metastatic lesion of segment V of the liver (**Figure 3**).



**Figure 1.** Peroperative image of distended gallbladder.



**Figure 2.** (A) Tumor proliferation infiltrating gall bladder wall, arranged in islets (HES  $\times$  5); (B) Monomorphic tumor cells with irregular nuclei containing small nucleolus and abundant eosinophilic cytoplasm (HES  $\times$  40).



**Figure 3.** (A) Sagittal CT scan showing a metastatic lesion in segment V of the liver; (B) Axial CT showing metastatic lesion located in segment V of the liver.

The case was reviewed with the findings of CT at the multidisciplinary oncology meeting where chemotherapy was indicated. Patient was referred to the oncology department for chemotherapy sessions and subsequent follow up. Patient underwent 3 cycles of chemotherapy, CDDP (cisplatin) protocol with Etoposide, with no signs of local recurrence until date.

### 3. Discussion

Primary NETs, all locations combined, are rare with 2 to 5 new cases per year per 100,000 inhabitants.

Primary NETs can occur throughout the GI tract (from the esophagus down to the anus), the pancreas, rarely the liver, and the gall bladder. Globally, its incidence is considerably low, about 0.5 - 5/100,000, with an estimated 70% of cases affecting the digestive system, with only 0.2% located in the gall bladder.

Generally two broad spectrum can be identified: functional tumors (eliciting characteristic clinical symptoms pertaining to tumor secretion of peptides or amino acids) requiring specific anti-secretory treatment and non-functional tumors (not eliciting symptoms). The rarity and heterogeneity of NETs explain the low number of randomized studies and apparent lack of evidence. Their incidence and localizations varies with sex: men tend to have more NETs in the esophagus and stomach, whereas cases of hepatobiliary and colorectal PNETs involve women.

Neuroendocrine tumors in general are rare, accounting for only 0.5% of all gallbladder tumors and 0.2% of all neuroendocrine digestive neoplasms. Well-differentiated NET presents itself at a lower age compared to other gallbladder tumors [1], whereas NEC occurs mostly in an older category of patients [1]. Neuroendocrine tumors of the gall bladder are common in women (68%) with ages ranging between 25 - 85 years [2].

Circumstances of discovery are extremely variably: as symptoms may relate to the local mass effect in the event of NF-NETs; right upper quadrant (RUQ) pain; jaundice, RUQ mass pointing to a large distended gall bladder. They could also be discovered fortuitously on cholecystectomy specimen in cases of non-complicated cholecystitis [3] [4]. Due to rapid growth of these tumors, metastases, mainly hepatic, may be revelatory in some cases (39.8%).

Ultrasound came back for a distended gall bladder with thickened wall and containing several gallstones. This finding was not of a great diagnostic relevance. "If a gall bladder tumor presents as a large hepatic mass and/or lymphadenopathy at the time of diagnosis, a NEC should be considered. However, other neoplasms such as hepatocellular carcinoma, cholangiocarcinoma, hepatic metastases involving the gall bladder region, and gallbladder adenocarcinoma may have similar clinical presentations. Ultrasound is the first-line imaging tool in the presence of biliary colic as it allows preoperative diagnosis of gallbladder tumor. However, its sensitivity in the preoperative diagnosis of gall bladder cancer is low (44%) [5]. Abdominopelvic CT represents the second line examination after ultrasound. No significant differences have been reported in literature regarding the role of CT scan in differentiating between small cell neuroendocrine and large cell gallbladder carcinomas. Doppler coding ultrasound seems to be more specific for BDC [3]. Magnetic resonance imaging is more sensitive than CT. Laparoscopy allows the detection of small peritoneal metastases and secondary liver lesions not seen on preoperative imaging. It also allows biopsies to

be performed for pathology examination. It is also useful in identifying unresectable tumors thereby reducing the number of unnecessary laparotomies. 1 out of 3 of BDC patients are often considered operable after the radiological staging [6].

In principle, symptomatic gall bladder NETs are difficult to distinguish from other cancers of the gall bladder. Precise diagnoses are only made on pathology examination. Pathology findings not only confirm the diagnosis of NETs they also determine histo-prognostic factors. NETs are characterized by the presence of chromatin clumps (granulations with hyper dense material). The peculiar phenotype of these cells contribute to precise diagnosis immune histochemical marking. In fact, the following markers are expressed in varying degrees of specificity in neuroendocrine tumors: synaptophysin, NSE, chromogranin A. The presence of at least two of these markers allows the precise diagnosis of neuroendocrine carcinoma [7].

Treatment of NETs of the gallbladder should take into account the histological type and tumor staging. Surgery is the sole curative treatment, especially for carcinoid tumors with a poorer prognosis for poorly differentiated carcinomas that are aggressive and are rapidly metastatic at the time of diagnosis. Five-year survival rate varies from 0.0 to 8.3% [2]. The vast majority of gallbladder cancers require multi-visceral surgery or sometimes regional surgery. With the progress of anesthesia and intensive care coupled with a marked improvement in knowledge of liver anatomy and surgery, multiple attempts at an aggressive surgical approach by certain teams have reported interesting survival at three and five years even in patients with advanced stage NEC [5]. Surgery for non-metastatic vesicular cancer remains rather less encouraging with an overall survival at five years not exceeding 5% even after complete resection. Surgery remains the sole curative treatment. Indications depend mainly on tumor staging. Consideration has to be given to patients' age, general condition and associated co-morbidities. In general, about 20% of patients are inoperable at the time of diagnosis. The role of radiotherapy and chemotherapy in the treatment of non resectable NETs is not clear as recent studies generally suggest NEC are not sensitive to conventional radiotherapy.

#### **4. Conclusion**

Gallbladder NETs constitutes a rare pathological entity. These tumors are often discovered fortuitously postoperatively on pathology findings of surgical specimen. Pathology examination should be carried out systematically on all cholecystectomy specimens as this remains the only way to confirm the precise diagnosis of neuroendocrine tumor of the gallbladder, determine histo-prognosis and guide management.

#### **References**

- [1] Zimmermann, A. (2016) Neuroendocrine Tumors of the Gallbladder. *Tumors and*

*Tumor-Like Lesions of the Hepatobiliary Tract*, **27**, 1-15.

- [2] Buscemi, S., *et al.* (2016) "Pure" Large Cell Neuroendocrine Carcinoma of the Gallbladder: Report of a Case and Review of the Literature. *International Journal of Surgery*, **28**, S128-S132. <https://doi.org/10.1016/j.ijisu.2015.12.045>
- [3] Komatsuda, T., Ishida, H., Konno, K., *et al.* (2000) Gallbladder Carcinoma: Color Doppler Sonography. *Abdominal Imaging*, **25**, 194-197. <https://doi.org/10.1007/s002619910044>  
<https://doi.org/10.1007/s12157-011-0239-5>
- [4] Jacob, J., Chargari, C., Helissey, C., Ferrand, F.-R., Ceccaldi, B., Le Moulec, S., Bauduceau, O., Fayolle, M. and Védrine, L. (2013) Neuroendocrine Carcinoma of the Digestive Tract: A Literature Review. *La Revue de Médecine Interne*, **34**, 700-705. <https://doi.org/10.1016/j.revmed.2013.02.013>
- [5] El Fattach, H., Guerrache, Y., Eveno, C., Pocard, M., Kaci, R., Shaar-Chneker, C., Dautry, R., Boudiaf, M., Dohan, A. and Soyer, P. (2015) Primary Neuroendocrine Tumors of the Gallbladder: Ultrasonographic and MDCT Features with Pathologic Correlation. *Diagnostic and Interventional Imaging*, **96**, 499-502. <https://doi.org/10.1016/j.diii.2014.11.027>
- [6] Gourgiotis, S., Kocher, H.M. *et al.* (2008) Gallbladder Cancer. *The American Journal of Surgery*, **196**, 252-264. <https://doi.org/10.1016/j.amjsurg.2007.11.011>
- [7] El Mernissi, H., Benzoubeire, N., Salihoune, M., Errabih, I., Krami, H.E., Jahid, A., Ouazzani, L., Mahassini, N. and Ouazzani, H. (2011) Neuroendocrine Tumours of the Gallbladder with Pulmonary and Liver Metastasis: A Report on One Case. *Journal Africain d'Hépatogastroentérologie*, **5**, 133-136. <https://doi.org/10.1007/s12157-011-0239-5>



**Submit or recommend next manuscript to SCIRP and we will provide best service for you:**

Accepting pre-submission inquiries through Email, Facebook, LinkedIn, Twitter, etc.  
A wide selection of journals (inclusive of 9 subjects, more than 200 journals)  
Providing 24-hour high-quality service  
User-friendly online submission system  
Fair and swift peer-review system  
Efficient typesetting and proofreading procedure  
Display of the result of downloads and visits, as well as the number of cited articles  
Maximum dissemination of your research work

Submit your manuscript at: <http://papersubmission.scirp.org/>

Or contact [ss@scirp.org](mailto:ss@scirp.org)