

A Rare Case of Small Cell Neuroendocrine Carcinoma of the Ampulla: Case Report and Literature Review

Sabin Yadav¹, Rui Xin Lin^{*}, Qiao Shi Xing^{*}, Shu Li Yang²

¹Medical Department of General Surgery, the Second Hospital of Jilin University, No. 218 of Ziqiang St., Changchun, Jilin Province, 130041, China.

^{*}Department of Hepatobiliary and Pancreatic Surgery, the Second Hospital of Jilin University, No. 218 of Ziqiang St., Changchun, Jilin Province, 130041, China.

²Department of Obstetrics and Gynecology, the Second Hospital of Jilin University, No. 218 of Ziqiang St., Changchun, Jilin Province, 130041, China.

Abstract: Neuroendocrine carcinoma (NEC) of the ampulla of vater is rare and highly aggressive malignancy. The patient was 40-years-male presented with complains of jaundice and pruritus. Laboratory investigations showed elevated levels of direct bilirubin, total bilirubin, alanine aminotransferase, urine amylase, lipase, and carbohydrate antigen 19-9. Imaging studies revealed a mass of 1 cm × 1.5 cm in the distal portion of common bile duct, dilation of intrahepatic ducts, common bile duct as well as pancreatic duct. Laparoscopic pancreaticoduodenectomy was performed. Resected specimen revealed a mass of 2 cm × 1.5 cm in the distal common bile duct and ampulla. Histologically, the tumor cells were located in the ampulla; had small, round, hyperchromatic nuclei with scanty cytoplasm and were poorly differentiated. Mitotic activities were found in 15 cells per 10 high power fields. The tumor cells were positive for synaptophysin, CD 56 and CK 7. Ki-67 index was found to be 95%. The diagnosis of small cell neuroendocrine carcinoma was made. The patient was discharged on 15th post-operative day. Follow up computed tomography revealed solitary liver metastasis. He refused further surgery and is taking chemotherapy in the form of cisplatin and etoposide since last 6 month. Though rare, NEC must be in mind as a differential diagnosis. To the best of my knowledge, this is the rare case of small cell NEC of the ampulla managed by laparoscopic pancreaticoduodenectomy.

Keywords: Ampulla, laparoscopic pancreaticoduodenectomy, neuroendocrine carcinoma, small cell.

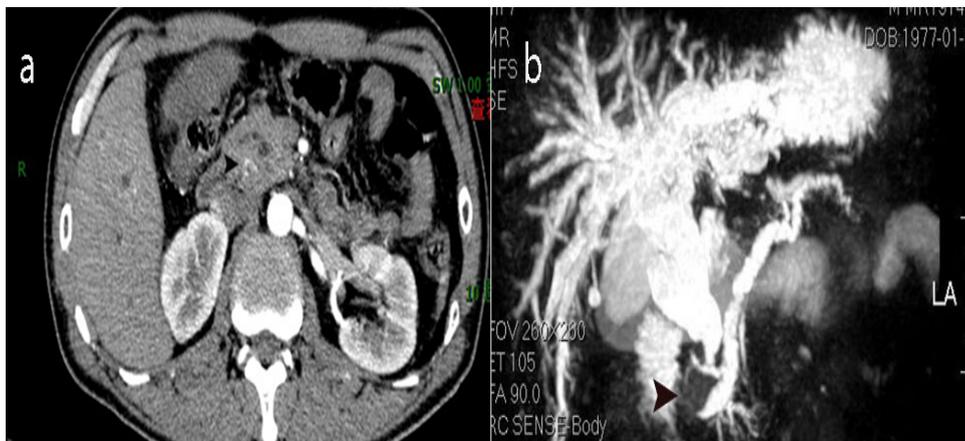
1. INTRODUCTION

Neuroendocrine Carcinoma (NEC) of the ampulla of vater is a rare and highly aggressive malignancy. It accounts for 0.2-0.3% of gastrointestinal tumors and about 6% of periampullary tumors [1-3]. About half of the ampullary neuroendocrine carcinomas originate from intestinal type adenomas [4]. The incidence of NEC is increasing possibly due to improvement in diagnostic procedures and accurate pathological classification [5,6]. We conducted PubMed search with keywords: “small cell carcinoma,” “ampulla,” and “neuroendocrine carcinoma” and found only 10 cases of pure small cell NEC of ampulla. Here, we present another rare case of small cell NEC of the ampulla which was managed laparoscopically.

2. CASE REPORT

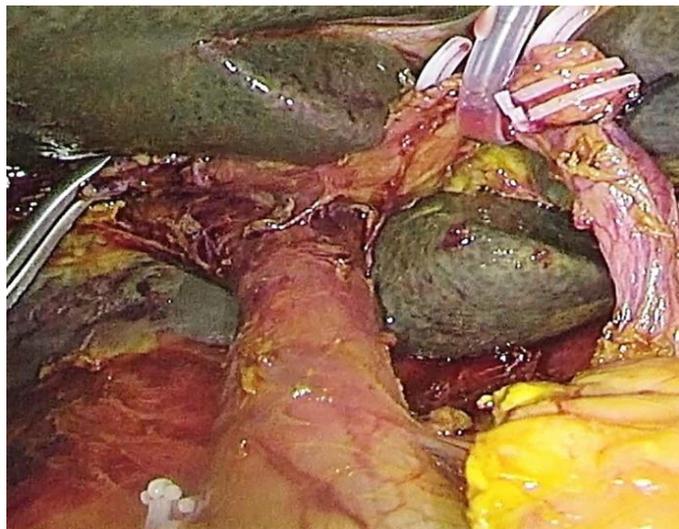
In February 2017, a 40-year-old Chinese male presented to our department with 20 days' history of jaundice and pruritus. The patient had no abdominal pain, nausea and vomiting. His medical history included recently diagnosed diabetes

mellitus and was not on medication. The patient denied any family history of cancer. On examination, the patient was icteric and gall bladder was palpable 2 finger breadth below right sub-costal margin with no tenderness. Laboratory data showed abnormally elevated levels of direct bilirubin, 132.3 $\mu\text{mol/L}$; total bilirubin, 153.2 $\mu\text{mol/L}$; alanine aminotransferase, 131 U/L; urine amylase, 3132 U/L; lipase, 2268 U/L; and carbohydrate antigen 19-9, 389.8 U/mL. Ultrasound (USG) examination revealed distended gall bladder (GB), dilated common bile duct (CBD), intrahepatic ducts as well as pancreatic duct. Abdominal computed tomography (CT) and magnetic resonance imaging (MRI) scan confirmed a mass of 1 cm \times 1.5 cm in the distal portion of CBD with enhancement on contrast phase, dilatation of CBD, intrahepatic ducts as well as pancreatic duct (Figure 1(a) & (b)). On the basis of these findings, a presumed diagnosis of distal CBD carcinoma was made. USG and chest X-ray did not reveal any signs of metastasis. Therefore, laparoscopic pancreaticoduodenectomy (LPD) was performed (Figure 2). The intraoperative frozen specimen of resected margin was microscopically negative for tumor.



“Fig 1. (a)

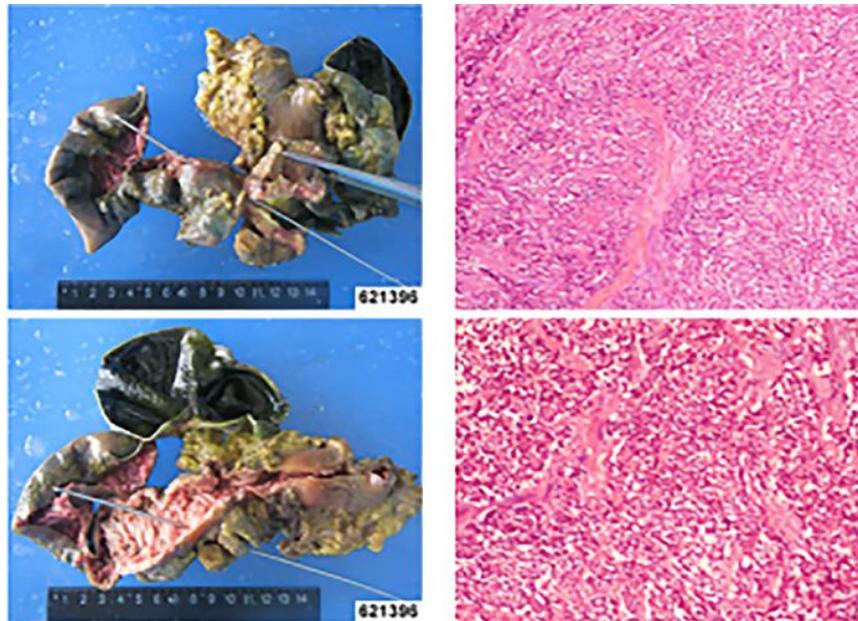
Abdominal computed tomography (CT) scan showing an enhanced mass (black arrowhead) in distal portion of common bile duct, and (b) magnetic resonance imaging (MRI) scan showing a mass in the distal portion of CBD (black arrowhead), dilatation of CBD, intrahepatic ducts as well as pancreatic duct”.



“Fig 2. Intraoperative view of laparoscopic pancreaticoduodenectomy”

In the resected specimen, the tumor measured 2 cm \times 1.5 cm and was confined to distal CBD and ampulla. Microscopically, the tumor cells were located in the ampulla; had small, round, hyperchromatic nuclei with scanty cytoplasm and were poorly differentiated. Mitotic activities were found in 15 cells per 10 high power fields.

Immunohistochemically, the tumor cells were positive for synaptophysin, CD 56 and CK 7. Ki-67 index was found to be 95% (Figure 3). Based on these findings, a diagnosis of small cell NEC of ampulla was confirmed.



“Fig 3. Resected specimen with microscopy showing small, round, hyperchromatic nuclei with scanty cytoplasm and poorly differentiated tumor cells.”

The patient's post-operative period was uneventful. CT scan of the abdomen 7 days after the operation was normal and he was discharged on the 15th post-operative day. Follow up CT scan after 4 months of surgery revealed solitary liver metastasis. The patient refused to undergo liver resection and currently he is receiving combination chemotherapy in the form of cisplatin and etoposide since last 6 months.

3. DISCUSSION

Neuroendocrine neoplasms arise from neuroendocrine cells that are found in numerous locations in the body[5,7]. Based on WHO classification of 2010, neuroendocrine neoplasms are classified into NET (Grade 1 and 2) and NEC (Grade 3). NEC is a poorly differentiated, highly aggressive neuroendocrine neoplasm with marked nuclear atypia, multifocal necrosis and high mitotic count of > 20 per 10 HPF and/or Ki-67 index $>20\%$. Histologically, NEC is of small cell or large cell type. Lung is the most common site for NEC but extrapulmonary NEC occurs most commonly in the gastrointestinal tract [3,6]. Literature reports along with surveillance, epidemiology and end result (SEER) shows that NEC is most common in men and most are in their six decades of life[3,4,8].

Most of the NEC does not show any feature as they are non-functional. Recent literature shows that those who are symptomatic, the presenting symptom is obstructive jaundice. Jonathan et al. reported obstructive jaundice in 54% of cases whereas Mayank et al. reported it in 53% of cases[1,8]. Few cases present with pain abdomen, pancreatitis and upper gastrointestinal bleeding. Constitutional symptoms in the form of anorexia, back pain, weight loss and fatigue are common in case of advanced disease. Symptoms related to the overproduction of hormones are rare in NEC[1-3,8].

It is difficult to diagnose NEC. NEC can secrete some peptides, like chromogranin A, neuron-specific enolase and synaptophysin which can be used as tumor markers. Many patients in advanced staged NEC have increased chromogranin A level. It can also be used as an immunohistochemical marker in NETs[3,6,9,10]. So, when a patient is suspected of having NEC based on clinical findings, and tumor marker, confirmation should be done by further imaging modalities such as endoscopy, endoscopic ultrasonography, ERCP, CT and MRI[2,3,11].

There are very few reported cases and data regarding the treatment options for ampullary NEC. For localized disease, curative surgical resection in the form of open pancreaticoduodenectomy (OPD) is the standard surgical method[3,8,12-14]. Surgery alone is not curative in most of the cases as many patients have a nodal disease or distant metastasis at the

time of presentation and many patients develop recurrence at a distant site[6]. Radical resection with lymphadenectomy along with platinum-based chemotherapy in the form of cisplatin and etoposide should be considered as a main therapy [3,6,12]. In those with advanced inoperable carcinoma with normal organ function, systemic chemotherapy should be considered. Radiotherapy can be considered in cases of localized metastasis [3].

Localized disease has a median survival of about 34-38 month, regional disease has a median survival of 14 month and distant disease has a median survival of about 5 month[3,6,7]. The main prognostic factors for survival are types of tumor (large vs small cell), age of the patient and distant metastasis[6,8].

Our patient was managed successively with laparoscopic pancreaticoduodenectomy (LPD). In this report, we would like to emphasize LPD as an emerging alternative to OPD for the treatment of localized ampullary NEC. The number of LPD in the last 5 year has grown dramatically, possibly due to improvement in surgeon's experience, passion for the procedure along with innovative technologies[12,15,16]. Of the 47 patients with ampullary neoplasms, Brandon et al. found decrease median blood loss (300 vs 500 ml), shorter median operative times (314 vs 359 minutes), lower rate of intraabdominal abscess (0 vs 16%) and lower rate of wound infection (9.1 vs 28%) in LPD compared to OPD[12]. Meta-analysis performed by Han et al. found shorter length of hospital stay, decreased blood loss, decreased wound complications in minimally invasive pancreaticoduodenectomy compared to OPD [17]. Both studies did not find any difference in pancreatic fistulas and oncological outcomes between LPD and OPD[12,17]. Another meta-analysis performed by Akira et al. also found shorter length of hospital stay and less intraoperative blood loss in LPD but the rate of pancreatic fistulas and oncological outcomes were similar in both LPD and OPD[16].

In summary, we reported a rare case of small cell NEC of the ampulla. There are very few treatment options available and surgery in the form of OPD is the only hope for cure in localized disease. Number of laparoscopic procedures are increasing now a day due to improving surgeons experience along with innovative technologies. Laparoscopic procedure has fewer complications compared to open procedures but the oncologic outcomes are similar. More LPD should be performed in well-established centers which will help to collect and analyze data regarding oncologic outcomes.

ACKNOWLEDGEMENT

The authors were thankful to the patient and the ethical committee for the successful completion of the project. The authors also thank Anisha Maharjan (anishamaharjan24@gmail.com) for the English language polishing.

FUNDING

This work was supported in part by a grant from Natural Science Foundation of Jilin Province, China (Grant No. 20150101162JC)

CONFLICT OF INTEREST

None

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International Journal of Novel Research in Healthcare and Nursing

 Vol. 5, Issue 1, pp: (195-199), Month: January - April 2018, Available at: www.noveltyjournals.com

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