

Unexplained ascites, a sign for neuroendocrine carcinoma

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SUMMARY

Neuroendocrine neoplasm is an epithelial neoplasm with predominant neuroendocrine differentiation that can arise from many organs in the body. We reported a rare case of gastric neuroendocrine carcinoma which accounts for less than 1% of all gastric tumours that is associated with poor prognosis. The recognition of this rare tumour in early stage is challenging and high suspicious into it might bring to early detection and so forth might improve the prognostication.

INTRODUCTION

The first two cases of gastric neuroendocrine tumour (NET) were described by Askanazy in 1923 and in 1961. Subsequently, Christodouloupoulos and Klotz (1961) published 79 cases in the literature, noting that their diagnosis was usually delayed due to the late presentation and diagnosis is often made during autopsy. This late presentation is due to slow growing tumour and asymptomatic except if it is hormone secreting tumor or compressive effect of the tumor. NETs of the stomach comprise less than 1% of gastric neoplasms. In the pre-endoscopy era, they comprised 1.9% of all carcinoids, but in more recent studies, 10% to 30% of all carcinoids are reported in the stomach.¹ According to the most recent World Health Organization (WHO) classification, NETs that involve the stomach are generally divided into well-differentiated NETs, well differentiated neuroendocrine carcinomas (NECs), and poorly differentiated NECs.²

CASE REPORT

We report a case of a 47-year-old man, an active smoker presented with 3 months history of abdominal distension, loss of appetite and weight loss. He has no significant personal and family history of malignancy and chronic liver disease. Physical examination revealed a gross ascites, bilateral pitting oedema and bilateral pleural effusion. He has no stigmata of chronic liver disease and lymphadenopathy.

Initial laboratory investigations showed normal haemoglobin level, total white blood cells count, platelet count, renal and liver profiles with serum albumin of 34g/L. Serum amylase, lactate dehydrogenase, immunoglobulins, tumour markers; alpha fetoprotein, carcinoembryonic antigen and CA19.9 were within normal range. Hepatitis B,

C and HIV serology were negative. Peritoneal fluid analysis revealed serum ascites albumin gradient was 5g/L with no evidence of malignant cells and the cultures for bacteria and mycobacterium were negative. Subsequently, abdominal ultrasound demonstrated a 'hidden' epigastric mass. Computed tomography of the abdomen (figure 1A) revealed a 'hidden' mass in the posterior wall of the gastric antrum measuring 2.1 x 4.5cm with numerous intra-abdominal lymph nodes involving perigastric area, greater omentum, peritoneum, mesenteric and rectovesical pouch. PET scan was not performed in view of extensive disease. Endoscopically, gastric mucosa and submucosa were normal and endoscopic ultrasound (figure 1B) was performed with fine needle aspiration cytology and biopsy of gastric mass was taken. Histologically, the biopsy revealed a poorly differentiated NEC with high index of proliferation of malignant cells of grade 3 (figure 2A-D). Chromogranin A level was not raised, at less than 36.7 ng/ml. Surgical treatment was not indicated for this patient as he had distant metastasis and poorest prognosis (poorly differentiated carcinoma). Chemotherapy was initiated which comprised of cisplatin and etoposide as the chemotherapy is standard management for patients with advanced disease. However, the patient developed life-threatening post-chemotherapy neutropenic sepsis and with the background of this aggressive disease, the oncology team had decided for palliation.

DISCUSSION

Gastric neuroendocrine carcinoma (NEC) is an uncommon tumor, usually associated with highly malignant biological behavior with extremely poor prognosis. NEC is composed of uniform small round cells with salt and pepper chromatin along with specific immunohistochemical staining that required to confirm the diagnosis.

Gastric NET is classified into pathological grading and clinical staging. In the 2010, based on the WHO pathological grading criteria, NETs of the stomach are defined as neoplasms with neuroendocrine differentiation, including neuroendocrine tumors (NETs) and NECs either well or poorly differentiated carcinoma arising from the stomach.² American Joint Committee on Cancer (AJCC) endorsed staging neuroendocrine neoplasm using specified TNM-based system. Recent study has demonstrated that malignant disease, defined by direct invasion of adjacent organs by tumor, lymph node metastases, or distant organ spread, may

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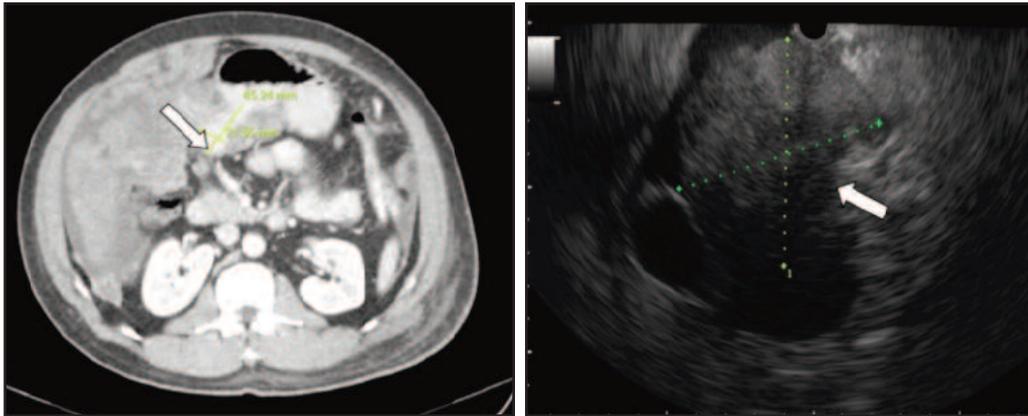


Fig. 1: A) Contrast-enhanced computed tomography of the abdomen showed a mass in the posterior wall of the stomach measuring 2.1 x 4.5 cm (Arrow). B) Endoscopic ultrasound showed a heterogeneous mass measuring 69 mm x 71mm near antrum (Arrow).

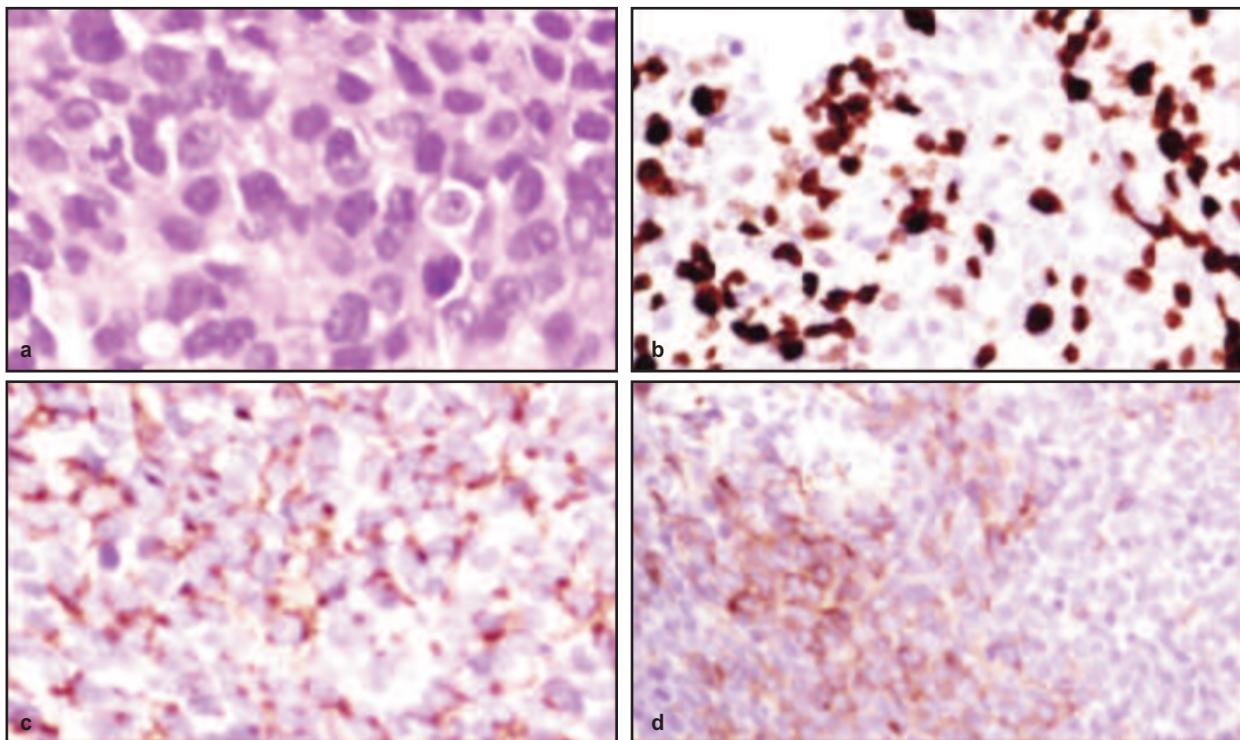


Fig. 2: A) Histopathological examination of the tissue from the stomach (HE stain with magnification 400x) showed high grade of mitotic cells; B) Ki-67 preparation showed high index of proliferation of the malignant cells; C) CK AE1/AE3 preparations and D) NSE preparation showed positive results.

have 5-year survival rates as high as 77% to 95% when treated aggressively with resection of primary tumor and adjunctive therapy.³

NETs are commonly divided according to the primary site; foregut (lung, bronchus, stomach or duodenum), midgut (jejunum, ileum, appendix or proximal colon) and hindgut (distal colon or rectum). Recently, the WHO proposed a new diagnostic criteria mainly depend on the rate of cellular proliferation and the proliferative rate of the tumor is assessed based on number of mitoses/10 high power field or the percentage of neoplastic cells immunolabelling for Ki-67, a proliferative marker.²

In our case, histologically the tumour was infiltrated by malignant cells and had high mitotic activity with Ki-67 proliferation index of 80%. These malignant cells were positive to NSE and CD56 that confirmed the diagnosis of gastric NEC. Combination of debulking surgery and chemotherapy is recommended. However, the role of surgery is not clear in patient with high-grade poorly differentiated NEC. In view of rapid progressive nature of disease, palliative chemotherapy is generally favoured as in our patient. Cisplatin-based regimens are preferred chemotherapy in advanced NEC⁴ due to a superior response that can lead to a decrease in tumour size and our patient is currently receiving a combination of cisplatin and etoposide chemotherapy.

Unlike our case, somatostatin analogues therapy is beneficial in patients with functioning NEC and G1/G2 small intestine.⁵

CONCLUSION

This case illustrates that the diagnosis of NEC is challenging and can be missed in early stage of the disease due to a slow growing tumour and not typical carcinoid syndrome manifestation. We hope that highly suspicious of this rare tumour will lead to early recognition and might improve the prognostication of the patient.

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