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CASE REPORT

A neuroendocrine cause for refractory symptoms in coeliac disease

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Abstract

Neuroendocrine tumours while rare, need to be considered in patients with chronic diarrhoea. Reported herein is a case of vasoactive intestinal peptideoma in a patient with refractory diarrhoea following a diagnosis of coeliac disease.

Introduction

VIPoma is a rare pancreatic NET with an incidence of 1 in 10 million individuals per year.[1] This tumor is often associated with large-volume secretory diarrhea and hypokalemia. Serum VIP levels are elevated and levels greater than 10 times normal are considered near diagnostic.[1] About 90% of all VIPomas occur in the body or tail of the pancreas.[2] EUS can often help localize pancreatic VIPomas and FNA allow cytological confirmation.[3] More than half of patients have established liver metastases at the time of diagnosis.[4]

Case Report

A 49-year-old, previously well woman, presented with a four-week history of large-volume diarrhea (up to 10 times per day). Additional symptoms included urgency, abdominal bloating, and discomfort.

Her physical examination was unremarkable. Full blood count and serum biochemistry were normal. Transglutaminase antibody (tTG-IgA) was raised (18 U/mL [normal < 7]) with a positive endomysial IgA antibody. Stool microscopy and culture (M&C) and clostridium difficile toxin polymerase chain reaction were negative. Fecal calprotectin level was 9 μg/g (normal < 50).

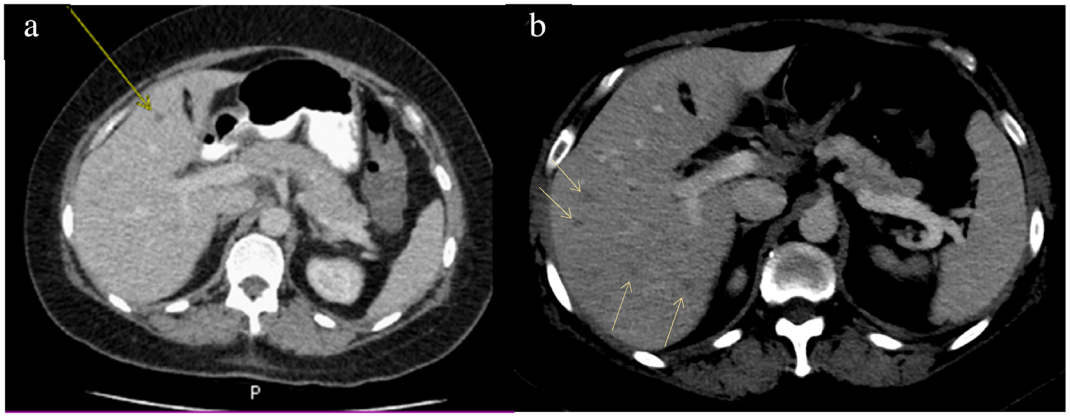

Figure 1 Initial computed tomography (CT) (a) with a nonspecific 5 mm low-density liver lesion. Subsequent CT (b) showing numerous small low-density liver lesions suspicious for a metastatic disease in the liver.

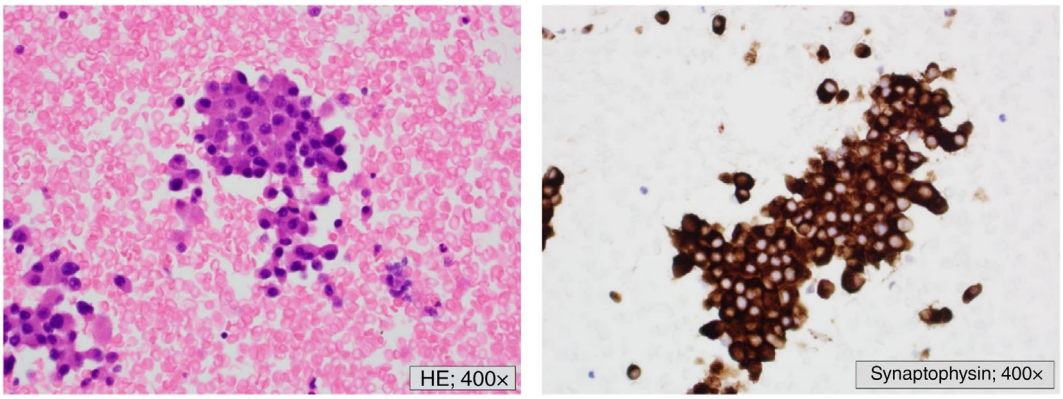

Figure 2 Fine needle aspirate of the liver lesion consistent with a metastatic pancreatic neuroendocrine tumor. Immunohistochemistry showing atypical cells that express chromogranin, synaptophysin, and CD 56 with a Ki-67 less than 3%.

Gastroscopy and colonoscopy showed no macroscopic abnormality. Colonic biopsies were normal, however, multiple duodenal biopsies from the second part of the duodenum revealed intraepithelial lymphocytosis without villous atrophy.

Although her histological changes were subtle, given the positive serology and investigations excluding other common causes of diarrhea, coeliac disease was considered the most likely diagnosis and she was advised to commence a gluten-free diet (GFD). Despite strict GFD adherence, her diarrhea worsened with reported daily bowel motions up to 20 times a day. Diarrhea persisted during times of fasting. The patient requiring inpatient admission for management of debilitating symptoms.

Inpatient investigations demonstrated persistent hypokalemia, with a nadir of 2.9 mmol/L (normal 3.5–5.2). She developed new mildly deranged liver function tests. Repeat fecal M&C was negative. Computed tomography (CT) imaging of the abdomen and pelvis demonstrated a normal pancreas. A low-density liver lesion, measuring 5 mm was noted but too small to formally characterize (Fig. 1). Testing for neuroendocrine tumors (NET), including calcitonin, 24-h urine 5-hydroxyindole acetic acid, serum chromogranin A, and gastrin were unremarkable.[1]

Initiation of intravenous hydrocortisone, 100 mg qid, was associated with a significant reduction in the frequency of diarrhea and symptomatic improvement. She was discharged with weaning doses of oral dexamethasone since prednisolone tablets contain gluten.

Following her hospital discharge, the result of a serum vasoactive intestinal peptide (VIP) level sent during her admission became available and was elevated to more than 10 times the normal value at 336.4 pmol/L (normal < 30). Repeat testing returned a value of 463.0 pmol/L.

Repeat abdominal CT scan performed 3 months after her initial scan demonstrated numerous subtle diffuse low-density foci within the liver measuring up to 10 mm, consistent with liver metastases (Fig. 1). Endoscopic ultrasound (EUS) of her pancreas revealed a 15 mm pancreatic tail mass. Fine needle aspirate (FNA) confirmed a well-differentiated low-grade pancreatic neuroendocrine VIPoma (Fig. 2). She was commenced on lanreotide, a somatostatin analog, with good effect. Three months after commencing a strict GFD, her coeliac antibodies returned to normal.

Discussion

While coeliac disease has a high prevalence and is a common cause of chronic diarrhea, the severity of clinical presentations correlates poorly with the degree of villous atrophy.[5] However, in those who fail to improve with a strict GFD, it is essential to consider alternative causes including rare disorders such as VIPoma.[6]

References

1 Jensen R, Norton J. Endocrine tumors of the pancreas and gastrointestinal tract. In: Feldman M, Friedman LS, Brandt LJ (eds). *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. Philadelphia, PA: Elsevier; 2016; 518–19.
2 Sokoll LJ, Chan DW. Chapter 12 - Malignancy-associated endocrine disorders. In: Winter WE, Holmquist B, Sokoll LJ, Bertholf RL (eds). *Handbook of Diagnostic Endocrinology*, 3rd edn. Cambridge, Massachusetts: Academic Press, 2021; 449–75.
3 Ghaferi AA, Chojnacki KA, Long WD, Cameron JL, Yeo CJ. Pancreatic VIPomas: subject review and one institutional experience. *J. Gastrointest. Surg.* 2008; **12**: 382–93.
4 Peng SY, Li JT, Liu YB *et al*. Diagnosis and treatment of VIPoma in China: (Case report and 31 cases review) Diagnosis and treatment of VIPoma. *Pancreas*. 2004; **28**: 93–7.
5 Brar P, Kwon GY, Egbuna II *et al*. Lack of correlation of degree of villous atrophy with severity of clinical presentation of coeliac disease. *Dig. Liver Dis*. 2007; **39**: 26–9.
6 Downey L, Houten R, Murch S, Longson D. Recognition, assessment, and management of coeliac disease: summary of updated NICE guidance. *BMJ*. 2015; **2**: h4513.