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Case Report

Emergency hepatic metastasectomy for symptomatic control of metastatic VIPoma

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ABSTRACT

Vasoactive intestinal peptide-secreting tumours (VIPoma) are a rare subset of functioning pancreatic neuroendocrine tumours (pNET) which can lead to severe electrolyte derangement due to high volume secretory diarrhoea. Whilst surgery remains the mainstay in the management of non-metastatic disease, the role of debulking and surgical resection in metastatic disease is unclear, particularly with the proliferation of systemic therapy options. We outline a case of a male in his 80s presenting with severe metabolic derangements secondary to symptomatic metastatic VIPoma with hepatic metastases. He underwent a successful non-anatomical hepatic metastasectomy after initially failure of multiple lines of systemic medical therapy. The surgery was technically successful, and he recovered remarkably well in the post-operative period with almost immediate cessation of his symptoms.

Keywords: Metastatectomy, VIPoma, Tumour debulking, Liver resection

INTRODUCTION

Vasoactive intestinal peptide-secreting tumours (VIPoma) are a rare subset of functioning pancreatic neuroendocrine tumours (pNET).[1,2] VIPomas can cause high-volume secretory diarrhoea and resultant severe metabolic derangements.[3] Surgery remains the mainstay of treatment for localised pancreatic neuroendocrine tumours but in the setting of metastatic disease, management options include medical therapy, liver directed therapies, surgical resection and debulking.[4,5] The role of metastasectomy for functional pancreatic neuroendocrine tumours (VIPoma) is unclear owing to the rare nature of VIPoma's. In the setting of severe symptoms refractory to medical therapy, tumour debulking through metastasectomy can be an effective method of reducing tumour burden with resultant rapid improvement of symptoms.[4-6] We present a case where hepatic metastasectomy was successfully performed on a patient with metastatic pancreatic VIPoma who presented with severe metabolic derangements due to uncontrollable diarrhoea despite best medical therapy.

CASE REPORT

A male in his 80s presented with profuse watery diarrhoea with resultant acute kidney injury, severe hypokalaemia and non-anion gap metabolic acidosis requiring ICU admission. This was on a background of a previous distal pancreatectomy and splenectomy performed four years earlier for a well-differentiated neuroendocrine tumour (pT3, N1 (1/5), M0, Ki67 5%).

There was interval development of hepatic metastases three years post-pancreatectomy that was being managed medically with Lanreotide, a somatostatin analogue. In the 4 months leading up to this admission, he started developing worsening diarrhoea and attempts were made to optimise symptom burden by up-titrating medical management with high dose Octreotide, anti-diarrhoeal medications and was even trialled on systemic chemotherapy which he did not tolerate. At this stage, a DOTATATE PET scan demonstrated several DOTATATE avid metastatic liver lesions (Figure 1) and serum VIP levels were >120 pmol/l (NR <30 pmol/l).

Given the severity of his metabolic derangements from the metastatic VIPoma despite multiple lines of medical therapy, a multidisciplinary team meeting was undertaken, and a consensus was reached for surgical debulking for urgent control of symptoms and reduction of tumour burden. He underwent an emergency open hepatic metastasectomy, with resection of all palpable lesions in addition to those identified on intraoperative ultrasound.

The resection was performed in a non-anatomical fashion (segments III, IV, V, VI X2, VII and VIII) with macroscopic clearance of all lesions. Within 24 hours, the patient had an immediate improvement in symptoms with no further diarrhoea, resolution of all metabolic derangements and normalization of VIP level (13.5 pmol/l post-operatively). Histopathology demonstrated 7 hepatic lesions consistent with a well-differentiated neuroendocrine tumour (Mitosis rate~7 U/mm2, Ki 67 10%). He was discharged home on maintenance Lanreotide therapy following an uncomplicated post-operative recovery.

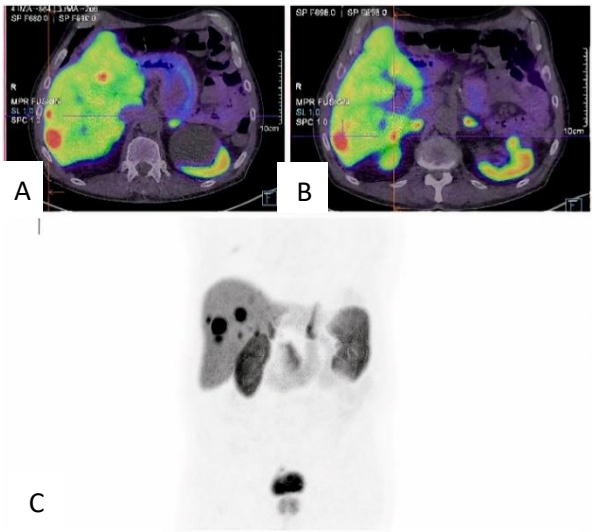

Figure 1 (A-C): Pre-operative DOTATATE PET/CT imaging demonstrating PET avid metastatic hepatic deposits seen on axial and coronal imaging.

DISCUSSION

Vasoactive intestinal peptide (VIP) is gastrointestinal peptide hormone produced in the duodenum and delta-2 pancreatic islet cells responsible for mediation in predominantly the gastrointestinal system, with additional cardiac, neuronal and respiratory mediation.[2,4] VIPomas are a rare subset of a functional NET with an estimated incidence of 0.05-2% predominantly originating from the pancreas, although there have been reports of primary lesions originating from the colon, bronchus, adrenals, liver and sympathetic ganglion.[3,7] VIPoma's are characterised by a clinical syndrome of watery diarrhoea, hypokalaemia, achlorhydria due to excessive circulating VIP often known as WDHA, 'pancreatic cholera' or Verner-Morrison Syndrome.[4,6,7] Isolated primary pancreatic disease is often asymptomatic, with most patients having metastatic disease on initial diagnosis, presenting with the clinical syndrome outlined.[4] Diagnosis is established by noting elevated circulating serum VIP levels, and imaging with CT, MRI and Dotatate PET is key in determining the location and burden of disease.[1,3,8]

Surgery is the only definitive treatment available for VIPoma and is the recommended treatment for patients with isolated primary pancreatic disease.[1,7,9] Contrastingly, there are no clear guidelines on the management of metastatic VIPoma owing to the scarcity of diagnosis and available data on its management. Whilst metastasectomy has been proven to be efficacious and confer survival benefit in certain malignancies, the evidence remains unclear and there is no consensus on the role of metastasectomy for metastatic VIPoma.[10,11]

The 2023 European Neuroendocrine Tumour Society (ENETS) consensus guidelines for small bowel and pancreatic NET suggest that cytoreductive resection in pNET should be considered as an option for treatment where 70-90% of macroscopic disease can be safely resected.[9] This varies with the 2017 guidelines which suggested metastasectomy should only be performed if complete macroscopic reduction was achievable in the heterogenous functional NET group.[12] Additionally, the role of surgery is further unclear with the development of multiple lines of systemic therapy and the availability of targeted liver directed treatment.[3,4]

Somatostatin analogues such as Octreotide and Lanreotide are now the foundation of systemic treatment.[8] Sunitinib, Everolimus, Cetuximab, and Rituximab are chemotherapy agents used as systemic therapy options, with some combination regimes with Lanreotide and Capecitabine also demonstrating benefits as systemic therapy options.[4,9]

In the setting of severe symptoms refractory to multiple lines of medical therapy, tumour debulking through metastasectomy is considered for symptomatic relief. Small multi-centre case series and limited case studies have demonstrated a successful improvement in symptomatic relief post-metastasectomy in addition to survival benefit.[13-15] Ultimately, the scarcity of evidence means that decision making on suitability of metastasectomy remains unclear and should be decided on a case-by-case basis in a multidisciplinary team setting.

CONCLUSION

We describe a successful case of hepatic metastasectomy for a rare case of metastatic VIPoma resulting in immediate resolution of clinical symptoms, biochemical levels and associated metabolic derangements. The patient was discharged once they were well, allowing for

maintenance therapy on anti-NET treatment and return to functional baseline. Surgical debulking should be a key consideration for all patients presenting with metastatic VIPoma.

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