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## Metastatic VIPoma presenting as an ovarian mass



Jaron Mark<sup>a</sup>, Stephen Bush<sup>b</sup>, Evan Glazer<sup>b</sup>, Jonathan Strosberg<sup>b</sup>, Ozlen Saglam<sup>b</sup>, Sachin M. Apte<sup>b,\*</sup>

<sup>a</sup> University of South Florida, 12901 Bruce B. Downs Blvd, Tampa, FL, USA

<sup>b</sup> H. Lee Moffitt Cancer Center, 12902 Magnolia Drive, Tampa, FL 33612, USA

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## ABSTRACT

**INTRODUCTION:** Pancreatic VIPomas are exceedingly rare, with an annual incidence of less than 1 per million. Most VIPomas are metastatic at diagnosis, with the liver being the most common site of spread. **PRESENTATION OF CASE:** We describe a highly unusual case of a metastatic pancreatic VIPoma to an ovary in a 54 year-old patient. She was ten years out from her initial diagnosis when routine CT scan showed an enlarging left adnexal mass. After having both ovaries removed laparoscopically the final pathology was consistent with her pancreatic primary. To our knowledge, there has been only one other such case described in the literature.

**DISCUSSION:** In this case, pathology revealed metastatic neuroendocrine tumor involving both the left and right ovaries despite only the right ovary apparently enlarging. In our literature search, only two other cases of metastatic PNET to the ovaries have been reported. One case was a glucagonoma and the other a VIPoma. We recommend that clinicians consider referral of patients with metastatic NET and ovarian metastases to gynecologic surgery for consideration of surgical resection.

**CONCLUSION:** In conclusion, this case proves that although uncommon, PNET can show metastases in both ovaries even a decade after initial diagnosis.

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## 1. Introduction

Pancreatic neuroendocrine tumors (PNET) are rare neoplasms, representing approximately 3–5% of all pancreatic malignancies. They are often classified as functional (hormone producing) or nonfunctional. Examples of functional PNETs include gastrinomas, insulinomas, glucagonomas, somatostatinomas, or vasoactive intestinal peptide tumors (VIPomas) [2,3]. VIPomas are exceedingly rare, with an annual incidence of less than 1 per million. They are characterized by severe watery diarrhea, often associated with electrolyte abnormalities such as hypokalemia and achlorhydria. Most VIPomas are metastatic at diagnosis, with the liver being the most common site of spread. In this case report, we describe a highly unusual case of an isolated metastatic pancreatic VIPoma to an ovary. To our knowledge, there has been only one other such case described in the literature. This case demonstrates the importance of pre-operative consideration of metastatic NET to the ovary.

## 2. Presentation of case

A 54 year old female with no significant past medical history presented with 18 month history of diarrhea in August of 2004 and was found to have profound dehydration with hypokalemia requiring multiple hospital admissions. She had a markedly elevated VIP level of 1299 pg/ml and was placed on octreotide 500 micrograms twice daily with symptom resolution. Pancreas protocol CT demonstrated a mass in the tail of the pancreas with suspected liver metastases. In October of 2004, she underwent distal pancreatectomy, splenectomy, and radiofrequency ablation of multiple liver metastases. Final pathology revealed well differentiated neuroendocrine tumor, with a proliferative index of 2–3%. She remained on octreotide monotherapy until May of 2011 when imaging showed increasing size of liver metastases. She was placed on capecitabine and temozolomide achieving stable disease as best response after 9 cycles. She continued to be clinically stable on octreotide until July 2014 when CT scans revealed progressive liver metastases and a new left sided pelvic mass. The ovaries were further imaged via pelvic US (Fig. 1). Somatostatin receptor scintigraphy revealed somatostatin receptor expression in the liver and left ovary. She was started on everolimus, but tolerated the drug poorly and discontinued it after one week and subsequently underwent two additional bland hepatic artery embolizations. Due to enlarging left ovarian metastasis as the only known site of viable disease, the

\* Corresponding author.

E-mail address: [Sachin.Apte@moffitt.org](mailto:Sachin.Apte@moffitt.org) (S.M. Apte).



Fig. 1. Transvaginal ultrasound showing left sided adnexal mass.

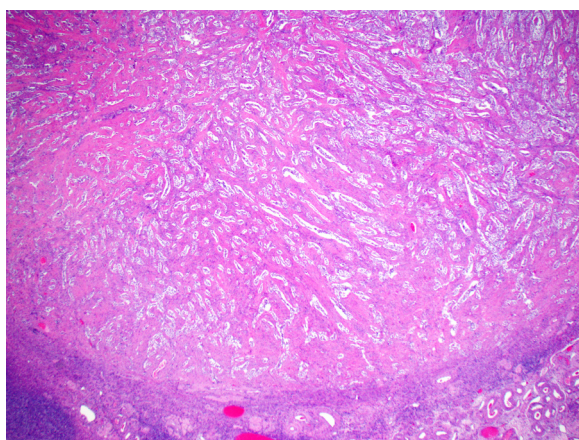


Fig 2. Well-circumscribed nodular lesion with H&E at 20x magnification.

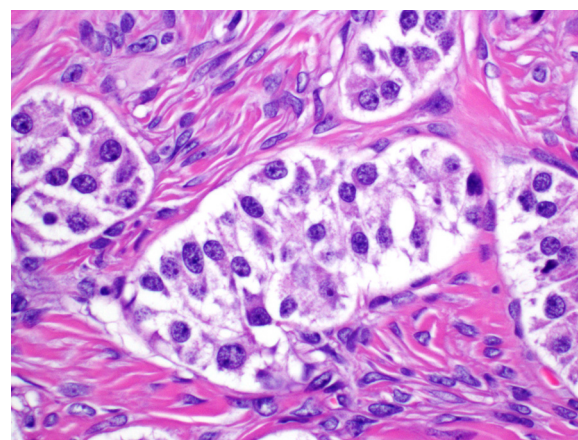


Fig 4. Tumor cells with salt and pepper chromatic H&E at 200x magnification.

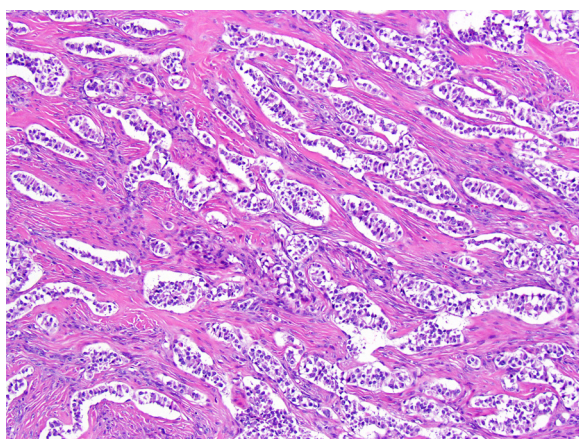


Fig. 3. Tumor cell formation with H&E at 200x magnification.

patient underwent a laparoscopic bilateral salpingoophorectomy in February of 2015 (Figs. 2 & 3 ).

**3. Discussion**

Metastatic neuroendocrine tumors (NET) from the pancreas to the ovary are extremely rare. We identified two cases of PNET metastatic to the ovary in the literature. The first case involved a

patient who presented with a right ovarian mass five years after resection of a glucagonoma involving the body and tail of the pancreas [1]. The second case was a VIPoma in the body of the pancreas along with somatostatin receptor scintigraphy revealing a 1.8 cm right ovarian mass. This particular patient was treated with the somatostatin analogue octreotide only [4]. Although systemic options for treatment of PNETs are expanding, surgical cytoreduction remains an important treatment modality [5]. It should also be mentioned that neuroendocrine tumors arising in different anatomic sites share similar morphology and short-term outcomes [5] as long as their grades are the same. Ovarian metastases from neuroendocrine tumors can often enlarge even in the setting of otherwise stable systemic disease (Fig. 4). The presence of bilateral tumors and well-circumscribed nodular lesions (especially when they are multiple) are in favor of metastatic disease in the ovaries. In this case, pathology revealed metastatic neuroendocrine tumor involving both the left and right ovaries consistent with the patients known pancreatic primary NET despite only the right ovary apparently enlarging. Consequently, we recommend that clinicians consider referral of patients with metastatic NET and ovarian metastases to gynecologic surgery for consideration of surgical resection (Fig. 5). Removal of both ovaries is critical since metastases are typically bilateral [6].

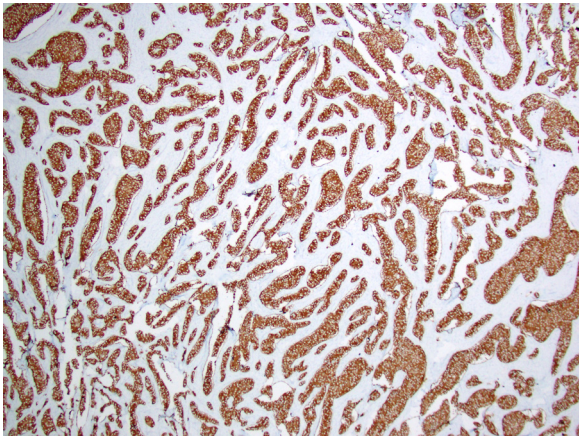


Fig. 5. Tumor with immunostain for synaptophysin positive at 100x magnification.

#### 4. Conclusion

The above case highlights that physicians should consider metastatic NET in females with a pelvic mass or enlarging adnexa and a history of primary NET. NETs in general, and VIPomas in particular, do not require as an aggressive surgical approach as primary ovarian malignancies. Standard debulking, in the form of metastatectomy such as oophorectomy, would likely render patients as no evidence of disease without a lymphadenectomy required of a debulking operation for primary ovarian cancer. As such, we cannot stress the importance of considering the diagnosis pre-operatively to allow for the best intraoperative decision pathway and informed consent.

#### Conflicts of interest

The authors declare that there are not conflicts of interest.

#### Funding

None.

#### Ethical approval

Approval has been given by our Scientific Review Committee.

#### Consent

Written informed consent has been obtained and is available on request.

#### Author contributions

Jaron Mark- Writing the paper.

Stephen Bush- Writing the paper, literature review.

Evan Glazer- Writing the paper and literature review.

Jonathan Strosberg- Writing the paper and literature review.

Ozlen Saglam- Provided histology slides and assisted in writing paper.

Sachin M. Apte- Writing the paper.

#### Guarantor

Jaron Mark.

Sachin M. Apte.

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