International Surgery Journal
Ayyamperumal JA et al. Int Surg J. 2024 Aug;11(8):1380-1384
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20242139

Case Report

Unusual neuroendocrine tumor in unusual site: a case report and review of literature

Jeya Anand Ayyamperumal*, Amudhan Anbalagan, Satish Devakumar Murugesan, Selvaraj Thangasamy, Jeswanth Satyanesan

Institute of Surgical Gastroenterology and Liver Transplantation, Stanley Medical College, Chennai, Tamil Nadu, India

Received: 02 June 2024
Revised: 10 July 2024
Accepted: 16 July 2024

***Correspondence:**
Dr. Jeya Anand Ayyamperumal,
E-mail: jattzzz@gmail.com

ABSTRACT

Paragangliomas (PGL) are uncommon tumors that develop in the extra-adrenal chromaffin cells of the autonomic nervous system. They are usually found in the retroperitoneum along the abdominal para-aortic region. PGL arising near the pancreas are extremely rare. These tumors can be difficult to diagnose as they can resemble more common pancreatic tumors, making it challenging for clinicians, radiologists, and pathologists alike. In this report, we describe a case of PGL that originated in the pancreaticoduodenal groove, which was initially diagnosed as a neuroendocrine tumor arising from the second part of the duodenum. The patient underwent pancreas-preserving surgery to remove the tumour.

Keywords: Paraganglioma, Peripancreatic, Pancreaticoduodenal groove, Neuroendocrine tumor

INTRODUCTION

The paraganglia are clusters of neuroendocrine cells associated with the sympathetic and parasympathetic nervous system. Neoplasms arising in the paraganglia of the adrenal medulla are traditionally termed pheochromocytomas, whereas tumors arising in extra-adrenal paraganglia are designated paragangliomas (PGL). The origin of these neoplasms is usually from paraganglia within the ganglia of the sympathetic trunk and of the coeliac, renal, suprarenal, aortic, and hypogastric plexuses.[1] But these tumors can also arise from unusual locations, which makes it difficult to diagnose preoperatively.

CASE REPORT

A 57-year-old female presented with vague abdominal pain for 6 months and had an ultrasonogram done which showed a 7.9×5.4 cm hyper to mixed echoic lesion inferior to the liver and anterior to the right kidney. Her blood investigations were within normal limits. She was a known case of hypothyroidism and was on thyroxine replacement therapy. Contrast enhanced computed tomography (CECT) abdomen showed a well-defined lobulated enhancing lesion measuring 5.6×7.4×6.4 cm arising from the second part of the duodenum (Figure 1b and d). The lesion was supplied by a branch from the superior pancreaticoduodenal artery. Multiple well-defined tiny enhancing lesions without washout in the venous phase were noted in segments V, VI, II with the largest measuring 11×4.6 mm noted in segment II of the liver. A possibility of gastrointestinal stromal tumor (GIST) or neuro endocrine tumour (NET) arising from the second part of the duodenum was suggested by the radiologists. In magnetic resonance imaging (MRI), the lesion was T1 isointense T2 hyperintense with positive diffusion restriction. The well-defined enhancing lesion was

DOTANOC avid (Figure 1a and c), and the liver lesions were reported as flash haemangiomas with no significant DOTANOC uptake. Serum chromogranin was elevated (249 ng/ml). Upper GI endoscopy was done, and the visualized duodenal mucosa and ampulla were normal.

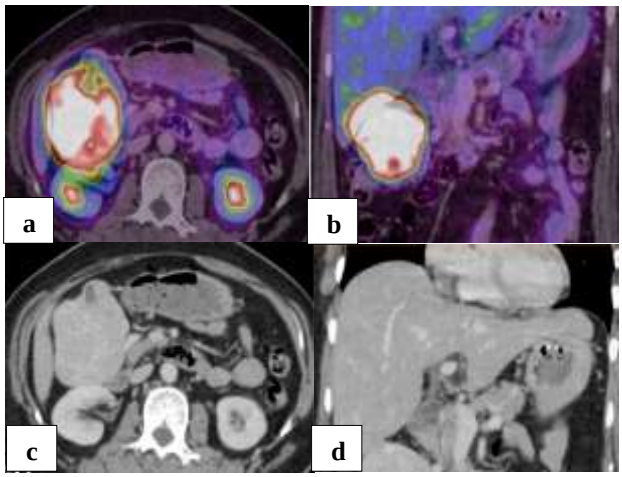

Figure 1: (a) Axial images of 68Ga DOTANOC avid heterogeneously enhancing lobulated soft tissue mass lesion; (b) axial images of CECT abdomen showing an well-defined enhancing lesion with cystic/necrosis; (c) coronal images of 68Ga DOTANOC avid heterogeneously enhancing lobulated soft tissue mass lesion; and (d) coronal images of CECT abdomen showing the lesion located in the right subhepatic region closely abutting the second part of duodenum.

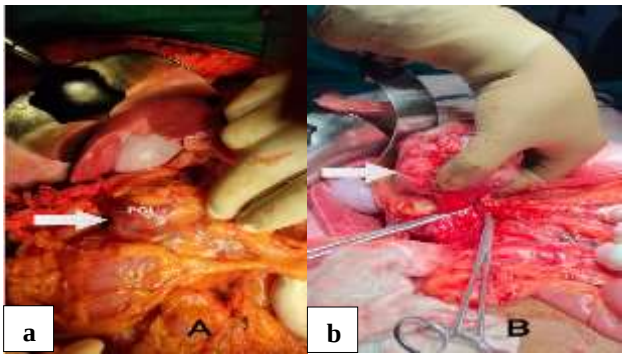

Figure 2: (a) Intra operative picture showing the tumor inferior to the liver; and (b) intra operative picture showing the well circumscribed tumor arising from the PDG by a thin stalk.

PGL – Paraganglioma, PDG – pancreaticoduodenal groove, arrow mark pointing the PGL.

With all the investigations pointing to a diagnosis of NET arising from the second part of the duodenum, she was posted for a Whipple's surgery. Intraoperatively, we found a well-circumscribed, highly vascular and soft tumor of size 8×7 cm (Figure 2a) arising from the pancreaticoduodenal groove (PDG) with a thin stalk (Figure 2b). It was flimsily adherent to the duodenum, transverse mesocolon and greater omentum. The liver was found to be normal and there was no associated lymphadenopathy. We did a complete excision of the tumor (Figure 3a) and deferred a Whipple's procedure. Histopathological examination (HPE) was reported as paraganglioma (Figure 3b) and the immunohistochemical markers (IHC) markers were positive for S-100 and chromogranin. The patient recovered well and was discharged uneventfully. A surveillance DOTANOC PET CT was done at 12 months postoperatively and there were no DOTANOC avid lesions either in the surgical bed or elsewhere in the body.

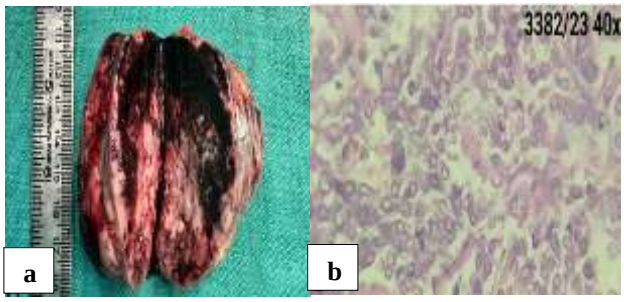

Figure 3: (a) Post-operative specimen showing a 8×7×3 cm well circumscribed lobular soft tissue mass with hemorrhagic areas on cut section; and (b) HPE 40x microscopy – circumscribed lesion separated by fibrous septate and the cells are round to oval with eosinophilic cytoplasm.

DISCUSSION

After an exhaustive search through the literature, only 16 cases of peripancreatic PGL and 19 cases of primary pancreatic PGL have been reported.[2-4] These are limited to mostly clinical and radiologic case reports, as these lesions usually cause a diagnostic dilemma for both clinicians and radiologists. Sometimes these lesions are observed to be challenging for the experienced pathologists also.[5] Our case is the 17th case of peripancreatic PGL, reported in the literature.

Location

PGL is confined mostly to retroperitoneal location, mainly in the abdominal para-aortic region, including the Zuckerkandl body, but they can be found ubiquitously in any site with paraganglia. Neural crest cells get dispersed throughout the body and aggregate to form paraganglia. It is unclear whether the origin represents a true visceral origin with derivation from ectopic paraganglia or an extension from a retroperitoneal tumor.[1] In our patient, the tumor was seen arising from the PDG.

The PDG is a confined space between the head of the pancreas and the C-loop of the duodenum. Various lesions of benign and malignant etiology can arise in the vicinity of this space. The differential diagnosis for a solid mass centered in the PDG is like that of primary retroperitoneal tumors, including lesions arising from mesoderm, neurogenic, or lymphoid origin.[6]

Clinical features

PGL may manifest sporadically or in conjunction with genetic syndromes, such as neurofibromatosis type 1, Von Hippel-Lindau syndrome, multiple endocrine neoplasia type 2, and Carney-Stratakis syndrome.

Pancreatic PGL are typically non-functional, distinguishing them from PGL arising in other sites where functional activity is more commonly observed.

The functional activity of these tumors can manifest with hypertension, headache, palpitations, and sweating. This can be attributed to the secretion of catecholamines in 30-60% of cases. Abdominal pain, palpable mass, or incidental discovery during radiological imaging may indicate non-secretory tumors. Hence, they are more important to be aware of, as they can produce symptoms very late only after causing compressing symptoms or metastasis.[7]

Our patient's imaging revealed a mass on evaluating her abdominal pain, which was diagnosed as a non-functioning pancreatic neuroendocrine tumor (PNET) preoperatively and as PGL after histopathological examination, post operatively.

Diagnosis

Imaging-wise on CT scan, PGL are highly vascular well-defined tumors with avid enhancement, punctate calcification, hemorrhage, and areas of cystic degeneration and necrosis. Since these features are also seen in other types of PNET, differentiating between these two entities could be challenging. In contrast, pancreatic adenocarcinoma are usually hypo-enhancing lesions.[8] The identification of a fat plane between the mass and the adjacent pancreas may indicate PGL.[9]

MRI should be the next imaging investigation of choice as CT scans cannot differentiate PNET from other hypervascular tumors, like metastases or pancreatic cystadenoma. Metastatic renal cell carcinoma (RCC) is one of the important differential diagnoses to be considered as they share a lot of similarities in imaging as well as histology. An IHC panel might be needed in difficult cases to differentiate these diagnoses as metastatic RCCs express CD10 and renal-cell carcinoma markers but are negative for S-100 protein and neuroendocrine markers.[10]

Lanke et al reported, in their compilation of pancreatic and peripancreatic PGL, correct preoperative diagnosis was possible only in 17% of the cases and the majority (62%) were misdiagnosed as PNET or pancreatic neoplasms, and cysts.[11]

The majority of PGL are benign, but it's important to note that 10% of PGL can be malignant.[12] However, this is highly variable in various studies. Singhi et al claimed that one-third of the patients presented with metastases within five years of their surgery and two of them expired due to their disease, in his study.[5] Interestingly, Tsukada et al reported that none out of 6 peripancreatic PGL developed metastases with follow-up data ranging from two to six years, in his study.[4] Burnichon et al in their study, reported that PGL arising from the thorax, abdomen, and pelvis were found to exhibit a fivefold increase in the likelihood of developing metastatic disease when compared to those arising from the head and neck.[13]

Unfortunately, predicting malignancy is challenging due to the lack of reliable markers. This emphasizes the fact that these patients ultimately will require long-term follow-up as metastatic disease can appear even years after diagnosis.

The clinical diagnosis of PGL relies on the accurate correlation of the tumor's specific location with the symptoms of hyperadrenalism. Unfortunately, it is challenging in instances of unusual locations, such as the one we describe here, which involves the peripancreatic chromaffin cells.[14] Most patients with pancreatic PGL typically have negative results for serum tumor markers, such as CA 19-9, CA 12-5, and CEA.[15]

Fine needle aspiration cytology, when attempted through Endoscopic ultrasonogram (EUS), is usually either inaccurate or non-diagnostic. Biopsy should usually be avoided, as PGL are hypervascular tumors and can cause significant bleeding.[15] When performed, the retrieval of tumor cells or tissue from a lesion is not always guaranteed with biopsies. The complexity of this issue further complicates the diagnostic process. The conclusive diagnosis of PGL, established through postoperative histopathological and immunohistochemical examinations, is significantly more reliable.

Grossly, these lesions are highly vascularized tumors, typically adjacent to neurovascular structures. Immunohistochemical positivity for neuron-specific enolase (NSE), synaptophysin, and chromogranin, along with no staining for cytokeratin, is indicative of PGL.[16] Metastasis is usually the primary indicator of malignancy.

Treatment

There is no therapeutic consensus, yet for pancreatic PGL and the majority of case reports recommend surgical resection as the primary treatment option. The rationale of surgical excision can be explained by two reasons. The main reason being the need for a definitive diagnosis when preoperative diagnosis is not possible. Secondly, the tumors may undergo malignant transformation, and this can only be definitively diagnosed when metastases develop.[17]

The right approach depends on where the tumor is located in the pancreas. The recommended surgical approach for lesions located in the pancreatic head is

pancreaticoduodenectomy, while lesions in the pancreatic body and tail are best addressed through distal pancreatectomy. Parenchyma preserving pancreatic resection such as central pancreatectomy is also an option when the tumor is small and confined to the body.

For peripancreatic PGL, excision of the lesion and preserving the pancreas is usually sufficient as these show the retroperitoneal extension of a PGL into the pancreas rather than a true pancreatic neoplasm. In relation to surgical treatment, the prognosis is equally good for simple excision of the tumor and radical surgery such as pancreaticoduodenectomy.[18]

It has been reported in the literature that the period of post-surgery follow-up spans from three months to six years. In all cases, the patients had a favorable prognosis and were free of tumors at the time of follow-up.[19] Currently, our patient is tumor-free one year after follow-up. None of the studies that we reviewed proposed an adjuvant therapy post operatively.

CONCLUSION

Pancreatic and peri pancreatic PGL are rare tumors. These are mostly benign, but metastasis can occur, which is often difficult to diagnose pre-operatively. An awareness of these tumors is essential to the surgeons as they can broaden the differential diagnosis and appropriate surgical management can be planned. Pancreas preserving excision can be a simpler approach to a benign peri pancreatic PGL as these represent the retroperitoneal origin of these tumors rather than a true pancreatic neoplasm.

ACKNOWLEDGEMENTS

Authors would like to thank Dr. P. Arunalatha, MD, and Dr. K. Valarmathi, MD, Department of Pathology for their crucial role in diagnosing this rare entity.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Borgohain M, Gogoi G, Das D, Biswas M: Pancreatic paraganglioma: An extremely rare entity and crucial role of immunohistochemistry for diagnosis. Indian J Endocrine Metabo. 2013;17:917-9.
2. Gong Y, DeFrias DV, Nayar R. Pitfalls in Fine Needle Aspiration Cytology of Extraadrenal Paraganglioma: A Report of 2 cases. Acta Cytologica. 2003;47:1082-6.
3. Inzani F, Rindi G, Tamborrino E, Cobelli R, Bordi C. Extra-adrenal composite paraganglioma with ganglioneuroma component presenting as a pancreatic mass. Endocrine Pathol. 2009;20:191-5.
4. Tsukada A, Ishizaki Y, Nobukawa B, Kawasaki S. Paraganglioma of the pancreas: a case report and review of the literature. Pancreas. 2008;36:214-6.
5. Singhi AD, Hruban RH, Fabre M, Imura J, Schulick R, Wolfgang C, et al. Peripancreatic Paraganglioma: A Potential Diagnostic Challenge in Cytopathology and Surgical Pathology. Am J Surg Pathol. 2011;35:1498-504.
6. Bello HR, Sekhar A, Ross W. Filice, Radmard AR, Davarpanah AH. Pancreaticoduodenal Groove: Spectrum of Disease and Imaging Features. RadioGraphics. 2022;42:1062-80.
7. Shah S, Mortele KJ. Semin: Uncommon Solid Pancreatic Neoplasms: Ultrasound, Computed Tomography, and Magnetic Resonance Imaging features. Semin Ultrasound CT MRI. 2007;28:357-70.
8. Elsayes KM, Narra VR, Leyendecker JR, Francis IR, Lewis JS Jr, Brown JJ. MRI of adrenal and extraadrenal pheochromocytoma. Am J Roentgenol. 2005;2005:860-7.
9. Raman SP, Hruban RH, Cameron JL, Wolfgang CL, Fishman EK. Pancreatic Imaging Mimics: Part 2, Pancreatic Neuroendocrine Tumors and their Mimics. Am J Roentgenol. 2012;199:309-18.
10. Renshaw AA, Lee KR, Madge R. Accuracy of Fine Needle Aspiration in Distinguishing subtypes of Renal Cell Carcinoma. Acta Cytologica. 1997;41:987-94.
11. Lanke G, Stewart JM, Lee JH. Pancreatic paraganglioma diagnosed by endoscopic ultrasound-guided fine needle aspiration: A case report and review of literature. World J Gastroenterol. 2021;27:6322-31.
12. Fliedner SM, Lehnert H, Pacak K. Metastatic paraganglioma. Semin Oncol. 2010;37:627-37.
13. Burnichon N, Rohmer V, Amar L, Herman P, Leboulleux S, Darrouzet V, et al. The succinate dehydrogenase genetic testing in a large prospective series of patients with paragangliomas. J Clin Endocrinol Metab. 2009;94(8):2817-27.
14. Ginesu GC, Barmina M, Paliogiannis P, Trombetta M, Cossu ML, Feo CF, et al. Nonfunctional paraganglioma of the head of the pancreas: A rare case report. Int J Surg Case Rep. 2016;28:81-4.
15. Liew SH, Leong AS, Tang HM. Tracheal paraganglioma: a case report with review of the literature. Cancer. 1981;47:1387-93.
16. Ginesu GC, Puledda M, Feo CF, Cossu ML, Fancellu A, Addis F, et al. Abdominal wall schwannoma. Gastrointest Surg. 2016;20(10):1781-3.
17. Manning MA, Paal EE, Srivastava A, Mortele KJ. Radiographics: Nonepithelial neoplasms of the pancreas, part 2: malignant tumors and tumors of uncertain malignant potential from the radiologic pathology archives. Radiographics. 2018;38:1047-72.
18. Meng L, Wang J, Fang SH. Primary pancreatic paraganglioma: A report of two cases and literature review. World J Gastroenterol. 2015;21:1036-9.

19. Jiang CN, Cheng X, Shan J, Yang M, Xiao YQ. Primary pancreatic paraganglioma harboring lymph node metastasis: A case report. World J Clin Cases. 2021;9(27):8071-81.

Cite this article as: Ayyamperumal JA, Anbalagan A, Murugasen SD, Thangasamy S, Satyanesan J. Unusual neuroendocrine tumor in unusual site: a case report and review of literature. Int Surg J 2024;11:1380-4.