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CASE REPORT

Mesenteric paraganglioma mimicking nodal metastasis of an occult small intestinal neuroendocrine tumor

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Summary

Paragangliomas (PGLs) are rare neuroendocrine neoplasms of neural-crest origin, with primary mesenteric localization representing an exceptionally uncommon entity that is rarely considered in the preoperative differential diagnosis of mesenteric masses. We report the case of a 51-year-old woman who was referred to our institute following the incidental detection of a 12 × 9 mm hypervascular nodule within the pelvic small bowel mesentery on contrast-enhanced computed tomography (CT). Subsequent ^{68}Ga-DOTATOC positron emission tomography/CT showed intense somatostatin receptor uptake confined to the mesenteric nodule, with no other lesions. Dedicated pan-colonoscopy was unremarkable and 24-h urinary 5-hydroxyindoleacetic acid was within normal limits. Preoperative diagnosis of nodal metastasis from an occult ileal neuroendocrine tumor was made, and laparoscopic surgery was undertaken. Meticulous bimanual palpation of the small bowel with transillumination did not reveal any primary lesions, while a 1 cm mesenteric mass was identified and excised. Histology revealed a solid tumor with Zellballen architecture with tumor cells positive for chromogranin A and GATA3, and negative stains for cytokeratin, CDX2, and serotonin, establishing the diagnosis of paraganglioma. This case highlights the importance of recognizing paraganglioma as a potential diagnostic mimic in solitary somatostatin receptor-avid mesenteric nodules to prevent unnecessary investigations and guide appropriate surgical management.

Keywords: neuroendocrine tumors; paraganglioma; SI-NET; nodal metastases

Learning points

- Primary mesenteric paragangliomas should be considered in the differential diagnosis of solitary, hypervascularized mesenteric masses.
- A solitary SSTR-avid mesenteric nodule in an asymptomatic, biochemically silent patient does not necessarily imply nodal metastasis from an occult small intestinal neuroendocrine tumor.
- Considering alternative diagnoses may avoid unnecessary endoscopic, radiological, and surgical investigations for an intestinal primary lesion.

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- Definitive diagnosis and risk stratification rely on histopathology and immunohistochemistry, including epithelial markers, GATA3, and SDHB.
- Awareness of mesenteric paraganglioma as a diagnostic mimic can prevent overtreatment and guide appropriate surgical management.

Background

Pheochromocytomas and paragangliomas (PPGLs) are rare, non-epithelial neuroendocrine neoplasms of neural-crest origin that arise from sympathetic or parasympathetic paraganglia distributed along the autonomic chain. Pheochromocytomas arise from the adrenal medulla and account for 80–85% of all PPGLs, whereas paragangliomas (PGLs) originate from extra-adrenal paraganglia and represent the remaining 15–20% (1). PGLs may occur in the head and neck (parasympathetic) or along the sympathetic chain in the thoracoabdominal region (2, 3). Among PGLs, head and neck tumors account for approximately 3–5%, while the majority are located in the abdomen (80–85%), followed by the thorax (12%) and pelvis (<5%). Primary mesenteric PGLs represent an exceptionally rare subset, with only isolated cases reported in the literature. Because of their rarity, mesenteric PGLs are seldom considered in the differential diagnosis of mesenteric masses, and the diagnosis is usually established only after surgical excision. Their marked hypervascularity and avidity for somatostatin receptor (SSTR)-based tracers may closely mimic nodal metastases from epithelial neuroendocrine tumors (NETs) (2, 4). Herein, we report a rare case of mesenteric PGL that was preoperatively diagnosed as a nodal metastasis from an occult ileal NET, leading to extensive but ultimately unnecessary investigations. This case underscores the importance of including PGLs in the differential diagnosis of solitary SSTR-avid mesenteric lesions.

Case presentation

A 51-year-old asymptomatic woman, with no relevant personal and family medical history, underwent a routine check-up. Contrast-enhanced computer tomography (CE-CT) revealed a 12 × 9 mm hypervascular, well-defined lesion, located in the pelvic cavity at the S1–S2 vertebral level, within the ileal mesentery (Fig. 1).

Investigation

The differential diagnosis included mesenteric lymph node metastasis and small mesenteric arterial aneurysm. A multidisciplinary review involving vascular surgery specialists and detailed re-evaluation of imaging findings excluded the aneurysmal hypothesis. Functional imaging with ^{68}Ga-DOTATOC positron emission tomography (PET)/CT demonstrated an intensely SSTR-avid, round focus in the right hemipelvis corresponding to the CT finding, with no other sites of abnormal uptake (Fig. 2). Under the working hypothesis of nodal metastasis from an occult NET of the small intestine, additional investigations were performed. Entero-CT confirmed a hyper-enhancing nodal-like lesion anterior to the aortic bifurcation (16 × 9 mm), closely related to terminal branches of the superior mesenteric artery, but no discrete small bowel

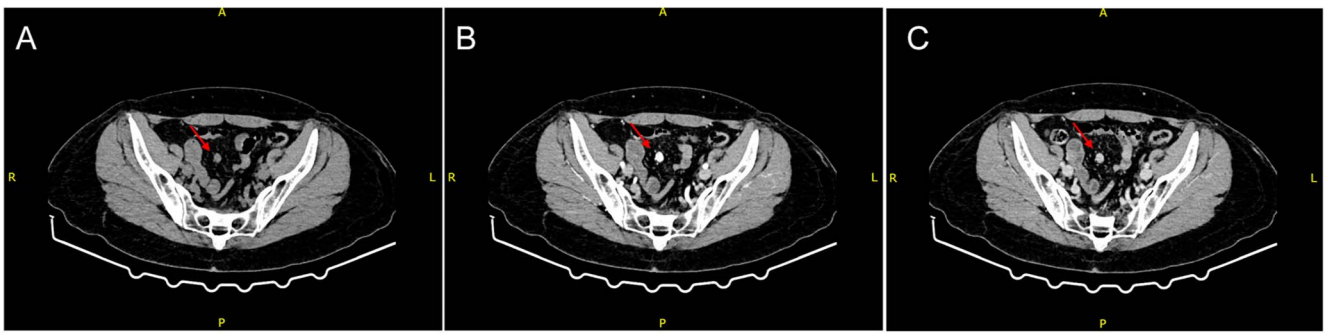

Figure 1

Contrast-enhanced (CE) computed tomography (CT): axial CT images in basal (A), arterial (B), and venous (C) phases showing a well-defined hypervascular nodule with arterial enhancement, located in the pelvic cavity at the level of the S1–S2 vertebrae, within the ileal mesentery (red arrows).

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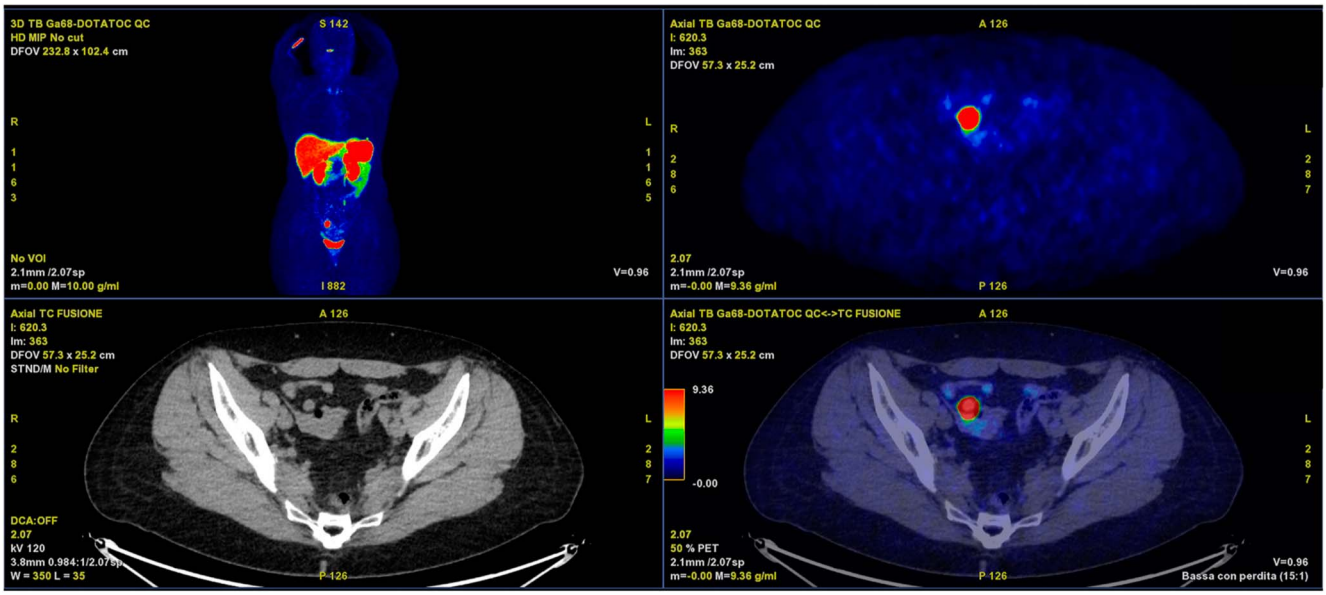

Figure 2

^{68}Ga-DOTATOC PET/CT showing intense radiotracer uptake in a rounded lesion in the right hemipelvis, located within the ileal mesentery.

mass was identified. Colonoscopy with ileal intubation was unremarkable chromogranin A (CgA) plasma levels, and 24 h urinary 5-hydroxyindoleacetic acid (5-HIAA) levels were within normal limits (CgA: 57.6 ng/mL; reference: <100 ng/mL; 5-HIAA: 2 mg/24 h; reference: 0.7–8.2 mg/24 h).

Treatment

Given the persistent diagnostic ambiguity, the suspicion of a mesenteric lymph node metastasis from an occult ileal NET, and the technical feasibility of resection, surgical exploration was performed. At laparoscopy, a firm, 1 cm nodule was identified within the mid-ileal mesenteric fat at the level of terminal mesenteric branches, matching the PET/CT focus, and was excised. A systematic bimanual palpation of the entire small intestine (4), combined with transillumination, was carried out, revealing no main small intestinal (SI) primary. Of note, a 1 mm serosal micro-prominence on a distant segment of small bowel, remote from the drainage of the mesenteric nodule, was identified and excised. The patient remained hemodynamically stable throughout the procedure.

Outcome and follow-up

Histological examination of the surgical specimens demonstrated that the small bowel serosal prominence consisted solely of smooth muscle and vascular tissue, with no evidence of tumor, thereby excluding the possibility of a minute intestinal primary. Definitive histopathological analysis of the mesenteric nodule demonstrated nests of tumor cells arranged in an irregular Zellballen pattern, exhibiting diffuse and strong immunoreactivity for chromogranin A and GATA3. Immunostains for cytokeratin 8/18, CDX2, PDX1, gastrin, serotonin, and somatostatin were negative. The S100-positive sustentacular network was not preserved (Fig. 3). These findings were consistent with a diagnosis of mesenteric PGL (5). The Ki-67 index was approximately 1–2%. Succinate dehydrogenase complex iron sulfur subunit B (SDHB) immunostaining showed preserved granular cytoplasmic positivity, and alpha-thalassemia/mental retardation X-linked (ATRX) and death domain-associated protein (DAXX) nuclear expressions were also retained. No necrosis, vascular invasion, or capsular invasion was identified. The lesion scored 3 according to the grading of adrenal pheochromocytoma and paraganglioma (GAPP) system (1). The postoperative course was uneventful. At six months after surgery, 24-h urinary fractionated metanephrine levels were evaluated and were within the reference range (urinary metanephrine 58 μg/24 h, reference 52–341 μg/24 h; urinary normetanephrine 120 μg/24 h, reference 88–444 μg/24 h). At two-year follow-up, the patient remains disease-free.

Discussion

PPGLs are rare neuroendocrine neoplasms, with an annual incidence below 1 per 100,000 person-years (3). They are non-epithelial tumors arising from neural-crest-derived chromaffin cells of the sympathetic and parasympathetic paraganglia. PPGLs

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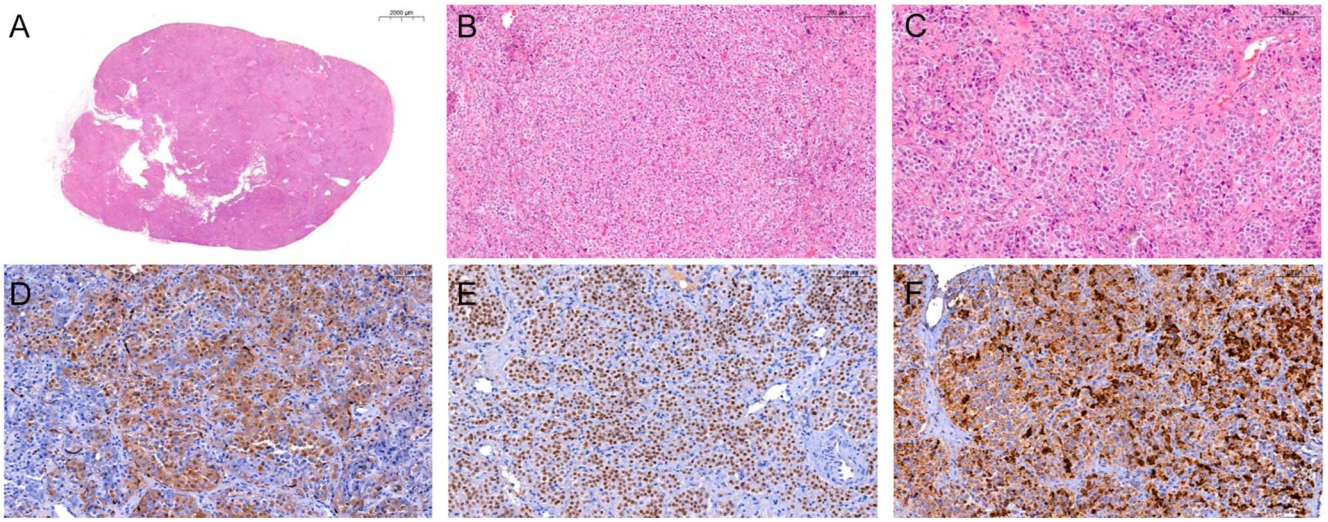

Figure 3

Histological and immunohistochemical findings in the excised mesenteric nodule. (A, B, C) Hematoxylin and eosin stainings showing an irregular Zellballen pattern of tumor nests separated by delicate fibrovascular stroma. (D) Immunohistochemistry for S100 showing a disrupted sustentacular cell network. (E) Nuclear GATA3 positivity. (F) Preserved granular cytoplasmic SDHB expression.

are classified as functioning, producing catecholamines that cause hypertension, palpitations, or diaphoresis, or non-functioning, presenting as incidental or mass-related lesions. Approximately 80–85% of PPGLs are pheochromocytomas, while the remaining 15-20% occurs at extra-adrenal sites as PGLs (1). Parasympathetic PGLs occur predominantly in the head and neck region (carotid body, vagal, jugulotympanic, and laryngeal) and are almost always non-functioning. In contrast, sympathetic PGLs arise along the thoracic, abdominal, and pelvic sympathetic chains (2). Among these, primary mesenteric PGLs represent an exceptionally rare subset, typically non-functioning, with only a few dozen cases reported since their first description by Areán *et al.* (6, 7).

Most mesenteric PGLs are discovered incidentally during imaging screening for unrelated conditions (8), although some present with a palpable abdominal mass or vague abdominal pain (7). Owing to their low incidence and nonspecific clinical and radiological features, preoperative diagnosis remains challenging and is rarely achieved.

Radiologically, mesenteric PGLs are frequently misinterpreted as more common intra-abdominal lesions such as gastrointestinal stromal tumors, desmoid-type fibromatosis, or ovarian and colonic neoplasms (9). In recent years, however, a new diagnostic pitfall has emerged with the widespread adoption of ^{68}Ga-DOTA-labeled PET imaging. Indeed, solitary somatostatin receptor (SSTR)-avid mesenteric nodules are often presumed to represent nodal metastases from small intestinal neuroendocrine tumors (SI-NET), prompting exhaustive endoscopic, radiologic, and surgical investigations in search for primary lesion (4). However, mesenteric PGLs may display identical imaging characteristics: well-differentiated morphology, intense vascularity at cross-sectional imaging, and strong SSTR expression (2). This overlap can lead to diagnostic misclassification and unnecessary radiological and surgical exploration for a non-existent ileal primary, as exemplified in our case. Indeed, the patient underwent two CE-CT scans, colonoscopy with ileal intubation, and extensive intraoperative bimanual exploration with transillumination in search of the primary lesion, procedures that ultimately proved unwarranted.

In addition to imaging studies, the diagnostic work-up of suspected PGLs includes biochemical quantification of plasma-free or urinary catecholamines and their O-methylated metabolites, metanephrines. However, these analytes often remain within physiological ranges in sporadic or biochemically silent forms, therefore reducing their diagnostic sensitivity and clinical utility (2). Further complicating the differential diagnosis, small SI-NETs may exhibit urinary 5-HIAA levels within normal limits (10), resulting in overlapping biochemical profiles with mesenteric PGLs.

Consequently, histopathology remains the cornerstone of PGLs diagnosis (5). Mesenteric PGLs typically display the characteristic Zellballen architecture composed of nests of chief and sustentacular cells. Immunohistochemically, they show diffuse positivity for chromogranin A and GATA3, with S100 highlighting the sustentacular framework. Moreover, PGLs consistently lack epithelial markers such as cytokeratin, EMA, and CDX2. In contrast, SI-NETs are keratin+, CDX2+, and serotonin-positive but

GATA3-negative (4). In our case, the combination of chromogranin A and GATA3 positivity with cytokeratin and CDX2 negativity established the diagnosis of mesenteric PGL.

Although up to 30–40% of PGLs harbor germline variants (3), most commonly within the SDHx gene complex, such alterations have never been reported in small, sporadic, mesenteric non-functional tumors (7). Nonetheless, SDHB immunohistochemistry is recommended in all cases of PGLs, as loss of expression identifies patients at higher risk of metastatic behavior who may benefit from genetic counseling and long-term surveillance (2, 3). Assessment of malignant potential can be further refined using the GAPP system (1), which integrates histological, proliferative, and biochemical parameters. In the present case, a GAPP score of 3 was calculated, based on an irregular Zellballen pattern (+1), moderate cellularity (+1), absence of vascular invasion and comedonecrosis (0), and a Ki-67 index of 1–2% (+1), placing the tumor within the low-to-intermediate risk category. When considered alongside preserved SDHB expression and small tumor size, these findings collectively supported an indolent biological behavior of the lesion.

Complete surgical excision remains the treatment of choice for localized mesenteric PGLs, with minimally invasive approaches being suitable for small, well-circumscribed lesions (2). Preoperative α-adrenergic blockade is required for functional PGLs to prevent catecholamine crises (3), whereas non-functional lesions, as per our case, can be safely resected without pharmacological preparation. Prognosis following complete resection is excellent, with disease-free survival approaching 100%. Nevertheless, given the inherent malignant potential of all paragangliomas and the extra-adrenal location, current guidelines recommend long-term surveillance ranging from at least 10 years to lifelong follow-up (2, 3). Further studies are required to better define the optimal duration and intensity of surveillance and to establish whether follow-up strategies may be safely de-escalated in carefully selected, low-risk patients.

In conclusion, the present case emphasizes the importance of including mesenteric PGL within the differential diagnosis of solitary, SSTR-avid mesenteric lesions in asymptomatic, biochemically silent patients. Early recognition of this entity may prevent unnecessary diagnostic work-up, optimizing surgical strategy, and ensuring appropriate patient management.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the work reported.

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Author contribution statement

AB wrote the original draft and contributed to review; editing; conceptualization; investigation; and data curation. MSL contributed to writing, review, and editing; data curation; and material support. VA helped in writing, review, editing, and data curation; SP contributed to writing of the original draft and helped in review and editing, conceptualization, investigation, and data curation. MF contributed to writing, review, and editing; conceptualization; and data curation.

Patient consent

Written informed consent has been obtained from the patient for publication of the submitted article and accompanying images.

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