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CASE REPORT

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When thoracic trauma does more good than harm: About an incidental finding of a gangliocytic paraganglioma of the ampulla of Vater

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Key Clinical Message

Gangliocytic paragangliomas are benign neuro-endocrine tumors of the ampulla of Vater. Their preoperative diagnosis is hampered by the low yield of biopsies and non-specific imaging. Their management relies then on resection. But the type of resection is controversial. Radical resection is indicated in case of lymph node involvement.

KEYWORDS

ampulla of Vater, duodenopancreatectomy, gangliocytic paraganglioma, lymphovascular invasion

1 | INTRODUCTION

Gangliocytic paragangliomas (GP) represent a little-known pathological group, due to their rarity. Their management relies on surgical resection to confirm the diagnosis and exclude malignancy. But the type of resection is controversial. This dilemma is further triggered with the demonstration of lymph nodes metastasis. We report such a case, diagnosed incidentally in the assessment of thoracic trauma, which required duodenopancreatectomy. And through a literature review, we ought to highlight its distinctive features, to spread awareness of this entity and to make the appropriate therapeutic decisions. Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

2 | CASE HISTORY/EXAMINATION

A 66-year-old man was admitted to our department for thoracic trauma following a traffic accident, leading to pulmonary contusion, which responded well to medical treatment. He was put on analgesics combining paracetamol and tramadol along with respiratory physiotherapy. The whole-body CT-scan revealed a thickened tissue centred on the ampullary region, with eccentric endoluminal development, extending to the D3 with heterogeneous enhancement, 27 mm thick and 60 mm wide (Figure 1) The latter was responsible for dilatation of the intra- and extrahepatic bile ducts and pancreatic ducts, and was associated with two pre- and latero-caval adenomegalia measuring 12 and 11 mm. Physical examination was unremarkable. He was discharged on 4th day of trauma because required 3 days of surveillance and medical conditioning.

3 | INVESTIGATIONS AND TREATMENT

After passing the acute stage, he was assessed by upper gastrointestinal endoscopy showing a hemi-circumferential ulcero-budding ampullary lesion

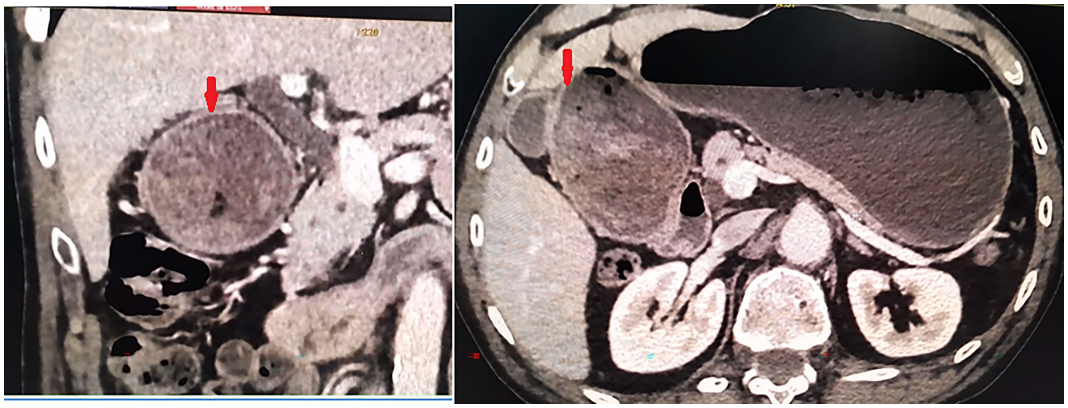

FIGURE 1 CT slices of the ampullary lesion (red arrow).

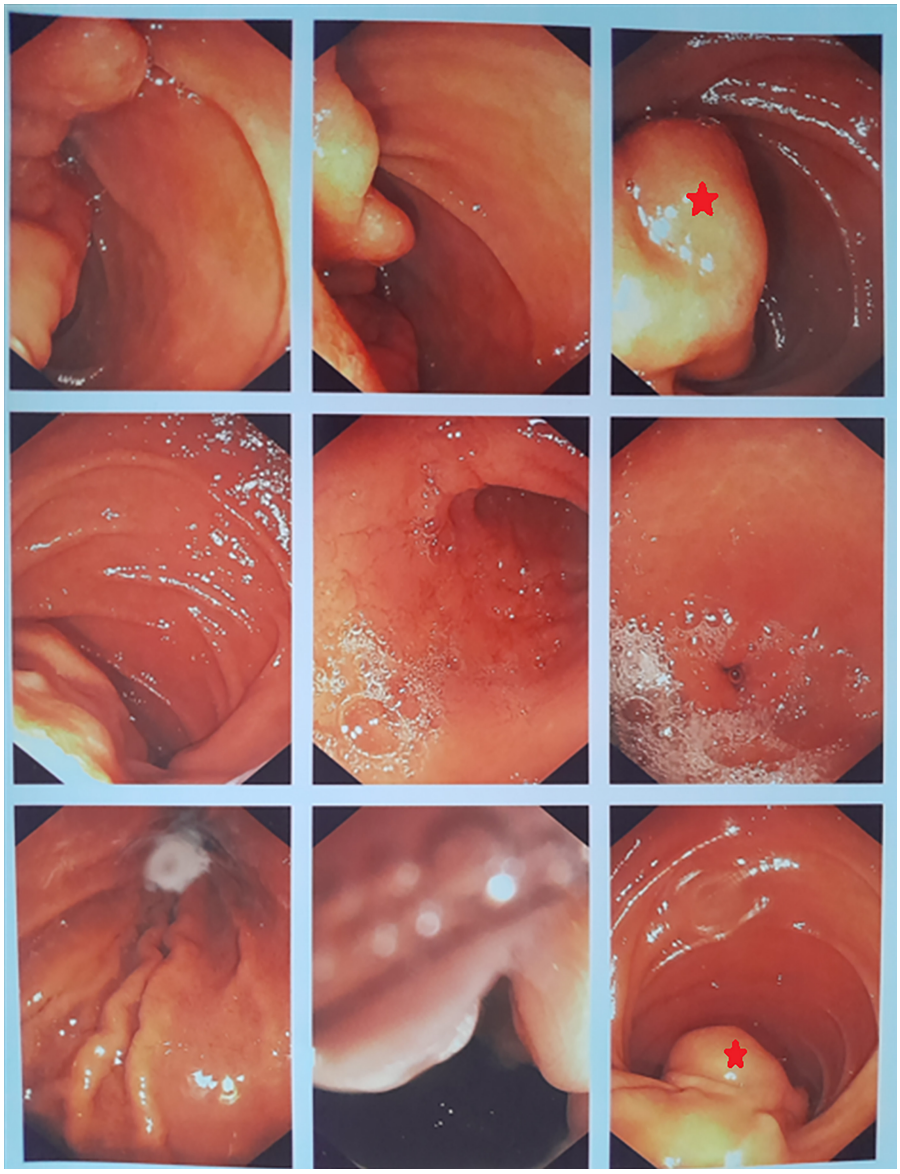

FIGURE 2 Upper GI endoscopy displaying the tumor developing the ampulla of Vater and bulging into the duodenal lumen (red star).

(Figure 2). Histological examination revealed a mixture of large mature spindle Schwann cells and neuroganglion cells associated (Figure 3) with a mild polymorphic inflammatory infiltrate of lymphocytes and eosinophilic polynuclears (Figure 4). S-100 protein labeled Schwann cells and synaptophysin labeled neuroganglion cells.

These cells were negative for pancytokeratin, GFAP and CD1a. There were also no signs of malignancy. As the distant extension workup (thoraco-abdomino-pelvic CT) was negative and due to lymph node involvement, he was scheduled for surgery. Intraoperative exploration revealed a 3 cm tumor, bulging into the lumen of the second duodenum and causing biliary retro-dilation with the main biliary tract measuring 20 mm. No retropancreatic nor retroportal lymph nodes were found. The surgical procedure included a cephalic duodenopancreatectomy with anastomosis according to the Child model.

4 | OUTCOME AND FOLLOW-UP

The postoperative course was favorable: no pancreatic fistula was observed and he resumed eating on third POD. Histological exam found a tumoral proliferation limited to the submucosa, made up of monomorphic epitheliode cells with abundant esoinophilic nucleolated cytoplasm, grouped in loubles, dissociated by bundles of schwannian spindle cells, ganglion cells and mononucleated inflammatory cells. The immunohistochemical study reported positive staining of tumor cells: epithelial cells expressed diffusely synaptophysin, focally chromogranin and progesterone. PS100 stained spindle and ganglion cells. Histological features were consistent with a gangliocystic paraganglioma with lymph node metastases, staged T3N1. He was kept on the radar regularly.

5 | DISCUSSION

The aim of this study was to investigate GP: their epidemioclinical manifestations, their bio-radiological behavior, the difficulties encountered in preoperative diagnosis and our reasoning to call for oncological surgery.

Neuro-endocrine tumors occur rarely in the ampulla of Vater. In a study enrolling neuro-endocrine tumors of the ampulla in a timelapse of 17 years, from 1989 to 2006, only seven cases were enrolled.[1] GP are a rare subtype,[2] but not all of them have a secretory feature.[3] This explains that some were incidentally discovered. They are characterized by its triphasic cellular differentiation (epithelioid neuroendocrine cells, spindle cells with Schwann cell differentiation, ganglion cells) along with characteristic immunoprofiling.[4] Hence, it has the features of a ganglioneuroma, a paraganglioma, and a carcinoid tumor.[5] In spindle-cell predominant tumors, the differential diagnosis includes schwannomas and GIST. If there is a predominance of ganglion cells or epithelioid cells, the differential diagnosis includes ganglioneuromas for the former and well-differentiated neuroendocrine tumors or carcinomas for the latter.[6] They should be distinguishable from paragangliomas even though epithelioid cell component is morphologically and immunohistochemically similar.[7] According to a multi-institutional retrospective japanese study, positive immunoreactivity for progesterone receptor and pancreatic polypeptide can differentiate GP from neuro-endocrine tumors grade 1.[7] Another tool to exclude other diagnosis includes PET scan. In fact, GP exhibit high ^{18}F–FDG uptake, thus differentiate them from NETs.[8]

GP are difficult to diagnose preoperatively. Some tumors remain undetectable despite their striking presentation (recurrent pancreatitis for example[9]). This is explained by their ampullary localization, where overlap two ductal structures enveloped by the muscular cuff. Indeed, one case has been reported of a 1.5 cm ampullary paraganglioma that escaped computer tomography and magnetic resonance imaging despite repeated exploration for recurrent cholangitis.[10] Even histological samples optained via endoscopy lack accuracy. In fact, in a cohort study of 52 patients aiming to compare endoscopic imaging and biopsy results to final diagnose of ampullary lesions, the overall diagnostic accuracy of the initial biopsy was 67.3%.[11] This difficulty may be explained by: encountered lesions are usually covered with normal mucosa overlying the ampulla and inflammatory cells emanating from mucosal attrition caused by the countercurrent passage of food and luminal flora hampering histological study.

The forthcoming difficulty resides in its management. GP were long-advocated to lack malignant potential. Rare instances of recurrence, lymph node involvement, and distant metastases have been previously reported.[12] In fact, low incidence of lymph node metastasis (6.9%) was noticed,[13] even on 5-year follow up.[14] The longest follow-up, free from recurrence, was 8 years after surgery.[5] Laparoscopic transduodenal ampullectomy was suggested from certain teams, as it represent a less extirpative surgery than duodenopancreatectomy considering the usual benign tumoral behavior,[15] and no cases of distant metastasis have been reported in nine gathered cases of GP with lymph nodes metastasis by Ogata and al.[16] But on more extensive data of 25 similar cases, liver and pelvic cavity metastases occurred in a patient after pancreatoduodenectomy,[17] thus suggesting that malignant behavior of these tumors in case of lymphovascular invasion is real. In fact, there are no tumor markers or histologic findings to determine if the tumor has malignant potential.[18] Benign and malignant GP cannot be distinguished by tissue morphology, cancer cell pleomorphism, or deep staining.[3] It is only when tumor cells have widely invaded the capsule or

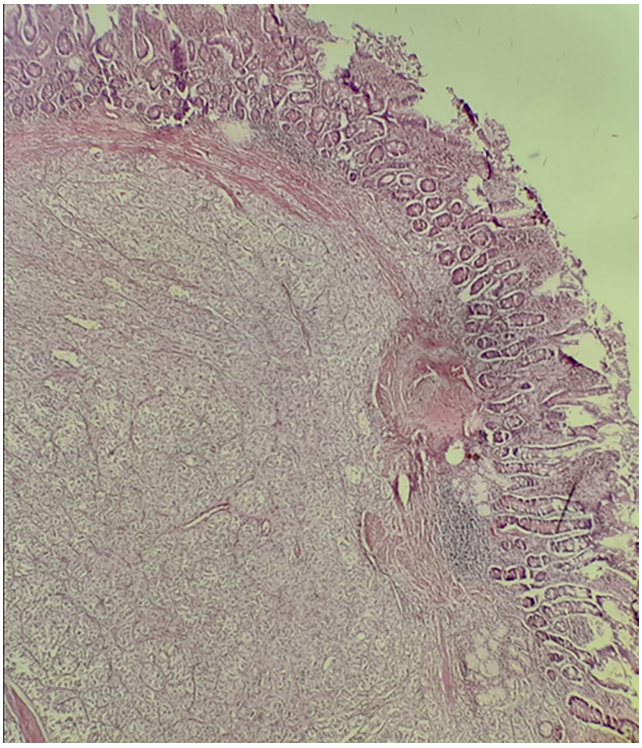

FIGURE 3 Microscopic examination exhibiting submucosal tumor proliferation of ampulla organized into lobules, when stained with hematoxylin and eosin stain ×10.

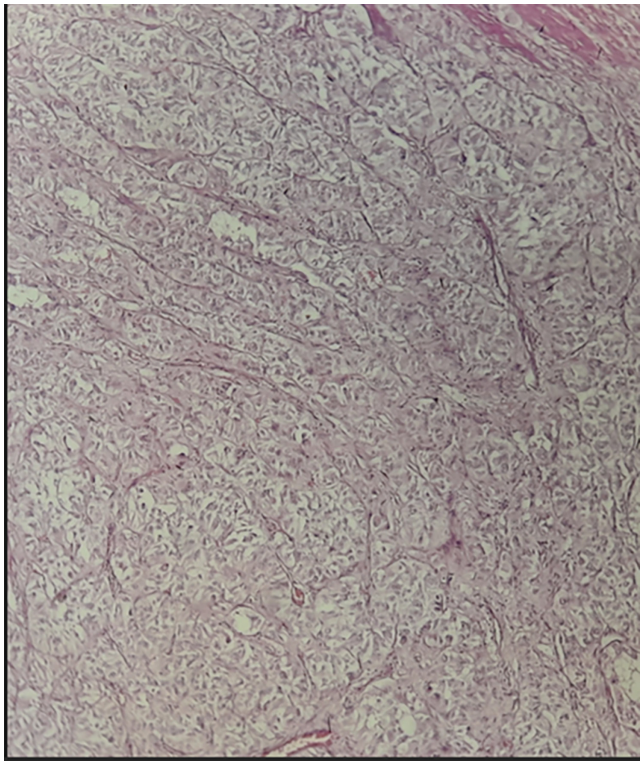

FIGURE 4 Microscopic examination exhibiting epithelioid tumor cells with abundant eosinophilic cytoplasm and ovoid nuclei, when stained with hematoxylin and eosin stain ×20.

tissue and organ metastasis is present, GP is diagnosed as malignant.[3] Even if GP have low malignant potential, of 131 reported duodenal locations, 8 had malignant features accounting for 5%. When considering the ampullary location among the latter, malignant potential rocketed to 33% (7/21).[19] Furthermore, lymph node involvement is uncommon, but can occur, as demonstrated by our case and other reported cases in which this angio-invasion was occult during preoperative exploration.[19,20] Considering the small amount of wordwide cases, this malignant pattern is not really scare and merit the attention of the medical community with a risk abutting 7% of lymph node metastasis.[6] On top, Bucher and al. reported a pancreatic invasion in the setting of this tumor.[19] Guiding ourselves by published data, we advocate duodenopancreatecomty whenever the postoperative journey is predicted to be eventless. Especially when considering that no cases initially treated by pancreaticoduodenectomy showed disease recurrence, despite the presence of simultaneous lymph node metastasis.[19] Therefore, a better outcome seems likely after radical resection. Besides, no histologic features predicting malignant potential has been defined,[12] rendering the "conservative" attitude hazardous. Oncological surgery is emphasized in the case of GP exceeding the submucosal layer. In fact, in this situation, the risk of angio-invasion increase significally from 2.4 to 16.7% ($p=0.03$).[13] On the other side, neither gender nor tumoral size affect the risk of lymph node invasion.[13] But younger patients had a tendancy to develop lymph node metastasis (mean age of 43.5 vs. 53.4 years; $p=0.01$).[13] Moreover, computed tomography scan and endoscopic ultrasound correctly identified lymph node involvement in 64% of cases only.[21] Finally, because these neoplasms dosen't respond to conventional systemic therapy,[22] tumoral resection should as definitive as possible considering the absence of other effective therapeutical means.

6 | CONCLUSION

This report has clinical implications because GP generally has non-specific features, the reported gathered cases raise awareness for this entity and expose different therapeutical pathways. And maintaining high suspicion is now possible. The addition of further cases or the development of a database will enable further study of these tumors.

AUTHOR CONTRIBUTIONS

Guizani Rami: Validation. **Mseddi Mohamed Ali:** Conceptualization; data curation; formal analysis; investigation; writing – original draft; writing – review and editing.

Hsairi Meriem: Resources. **Saad Sarra:** Resources. **Zehani Alia:** Resources. **Ben Slima Mohamed:** Supervision.

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CONFLICT OF INTEREST STATEMENT
All authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

CONSENT
Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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