Rare disease

Totally laparoscopic resection of a rare duodenal tumour

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Summary

A 39-year-old woman presented to the gastroenterology clinic with recurrent right-upper-quadrant pain and elevated liver enzymes. Endoscopy revealed a small submucosal mass at the edge of the major duodenal papilla, which was not amenable to endoscopic resection. The mass was successfully resected by laparoscopy. The papilla was subsequently reconstructed and a cannula inserted in the common bile duct. The postoperative period was uneventful and the patient was discharged on the third postoperative day. Subsequent pathological examination of the excised mass revealed a gangliocytic paraganglioma. Six weeks later, the patient was free of symptoms and the cannula was removed by duodenoscopy.

BACKGROUND

Gangliocytic paraganglioma (GP) is a rare tumour that must be considered in the differential diagnosis of biliary colic. This case report aims to raise awareness on the feasibility and safety of treating endoscopically unresectable duodenal tumours by laparoscopy.

CASE PRESENTATION

A 39-year-old woman presented to the gastroenterology clinic with a few-week-old history of recurrent right-upper-quadrant pain and elevated liver enzymes. The pain occurred after meals but was unrelated to medication and was not associated with nausea or vomiting. She did not smoke or drink alcohol. Her medical history was notable for the presence of a thyroid nodule without thyrotoxicosis and appendectomy for acute appendicitis as a teenager. The patient had no known allergies and was not taking any regular medication. Family and social history were unremarkable. General physical examination revealed a young and otherwise healthy woman with normal body mass index and vital signs, eliciting no abnormal findings.

INVESTIGATIONS

Routine blood tests (full blood count, C-reactive protein, urea and electrolytes, thyroid function tests, liver function tests) were notable for a γ -glutamyltransferase level of 275 U/l (7–36 U/l) and an amylase level of 197 U/l (30–100 U/l). Abdominal ultrasound scan and computed tomography were normal. Oesophagogastroduodenoscopy revealed a small submucosal mass at the edge of the major duodenal papilla, which was not amenable to endoscopic resection. The endoscopic biopsy sample contained normal small intestinal mucosa with fragments of smooth muscle.

DIFFERENTIAL DIAGNOSIS

Although small duodenal tumours are uncommon with an overall prevalence of 0.3–4.6%, their differential diagnosis is relatively broad and can be challenging.¹

Small benign tumours include leiomyomas, adenomas, lipomas and schwannomas, as well as paragangliomas, Brunner's gland hyperplasia, polyps, ectopic gastric or pancreatic mucosa and hamartomas. Malignant tumours on the other hand are usually carcinoids or gastrointestinal stromal tumours (GISTs).^{1 2}

Endoscopic ultrasound can be used to identify the lesions, obtain a fine-needle aspirate, and assess tumour depth and invasion, and to perform lymph-node staging with a reported accuracy of 70–90%. However, the diagnosis is often confirmed by histological examination of preoperative or surgical biopsy. These tumours can also be found incidentally during endoscopy or autopsy.^{1–6}

The biochemical and histological findings relevant to GPs are discussed below.

TREATMENT

Using exploratory laparoscopy under general anaesthesia with the patient in supine position, the ascending colon was dissected and retracted medially, allowing exposure of the duodenum. The duodenum was subsequently dissected using Kocher's manoeuvre (figure 1), and the tumour was localised and transilluminated by duodenoscopy. A transverse duodenotomy was performed at the antimesenteric side in front of the papilla and the mass was identified on the edge of the papilla at the 11-o'clock position (figure 2). A small plastic cannula was passed through the papilla to protect the common bile duct from injury and to prevent postoperative obstruction. The mass was successfully excised with free edges using a Harmonic Scalpel (Ethicon Endo-Surgery, Norderstedt, Germany). The papilla was reconstructed with Vicryl 4-0 sutures, the cannula was left in the common bile duct, and the duodenal incision was closed with Vicryl 3-0 sutures. The procedure was performed under a CO₂ pneumoperitoneum of 14 mm Hg, using three 5 mm trocars and one 10 mm trocar. The operation took 59 min and intraoperative blood loss was negligible.

Figure 1 Dissection of the duodenum from the inferior vena cava.

OUTCOME AND FOLLOW-UP

The postoperative period was uneventful, with the urinary catheter removed and the patient ambulant 6 h after the operation. Fluids and soft food were introduced on the second postoperative day and the patient was discharged on the third postoperative day, returning to work 2 weeks later.

Subsequent pathological examination of the excised mass revealed a 1 cm submucosal GP with free margins and absence of necrosis (figure 3). The morphology was triphasic, consisting of epithelioid cells (synaptophysin and chromogranin positive), spindle cells (S-100 positive) and ganglion cells. The specimen was negative for pankeratin and CD-117, with a Ki-67 proliferative index of less than 1%.

At 6 weeks an abdominal radiograph demonstrated the cannula in situ, which was then removed by duodenoscopy (figure 4). The patient was free of symptoms at follow-up.

DISCUSSION

GP is a rare, typically benign, extra-adrenal neuroendocrine tumour. The term 'paraganglioma' first appeared in the literature in 1908. Five decades later, Dahl *et al* reported GP as

Figure 2 Reflection of the duodenal tumour through the duodenotomy.

Figure 3 Histological appearance of duodenal mucosa with underlying tumour.

'ganglioneuroma', followed by Kepes and Zacharias who coined the term 'gangliocytic paraganglioma' in 1971.^{7–10} A recent literature review by Okubo *et al*¹¹ reported only 192 published cases of GP between 1957 and 2010. The mean age of patients was 52 years (ranging between 15 and 84 years) with a male-to-female ratio of 1.5:1 (114:76).¹¹

Catecholamine-secreting neuroendocrine tumours can arise from chromaffin tissue at various anatomical locations. Intra-adrenal and extra-adrenal tumours are classified as pheochromocytomas and paragangliomas, respectively. As chromaffin tissue is an accessory to the autonomic nervous system, paragangliomas can occur anywhere along the paravertebral and para-aortic axes.¹² The vast majority of GPs is found in the duodenum (90.1%). However, GPs have also

Figure 4 Postoperative abdominal radiograph showing a 10 cm cannula in the common bile duct and an intrauterine device.

been reported at other sites along the gastrointestinal, respiratory and urogenital tracts, as well as in the scalp, vertebral column and mediastinum.^{4 5 11 13 14} Paragangliomas and pheochromocytomas as a collective are attributed to hereditary and germline mutations in at least 30% of cases (mainly due to succinate dehydrogenase gene mutations), with 70% occurring sporadically. They have also been associated with von Hippel-Lindau disease, neurofibromatosis, multiple endocrine neoplasia type 2 and Carney's triad.¹²⁻¹⁵

Most patients (95%) with GP are symptomatic. Given their tendency to arise in the duodenum, GPs most commonly present as gastrointestinal bleeding, abdominal pain and anaemia. Biliary obstruction is considered extremely rare (4.6% of all reported GPs).^{4 11} GPs are usually benign and non-functional. However, patients with functional tumours may present with any of the classic symptoms of catecholamine excess which include hypertension, headaches, palpitations, perspiration, pallor and orthostatic hypertension.¹⁶

If a functional paraganglioma is suspected, biochemical screening for elevated urine and plasma metanephrines should be carried out before a biopsy, in order to avoid a life-threatening hypertensive crisis. Elevated urine and plasma metanephrines are highly sensitive and specific in diagnosing functional paragangliomas. Once a biochemical diagnosis has been made, preoperative biopsies are unnecessary. Approximately 40% of these tumours are confined to the submucosal layer. Forceps biopsies are therefore limited to a diagnostic rate of 11.4%. The presence of multiple paragangliomas can be assessed by CT or MIBG (iodine-131-meta-iodobenzylguanidine) scanning.¹¹⁻¹³

Macroscopically, GPs have a mean maximum diameter of 24.2 mm, ranging from 5.5 to 100 mm. They may appear as a pedunculated or sessile polypoid mass with a smooth or ulcerated surface. Tumour size does not appear to be associated with age, gender or likelihood of metastasis. Lymph node metastasis is uncommon and distant metastases to the liver, lung and bones have been rarely reported. Recent evidence suggests that metastasis is more likely in young patients and in patients with tumours exceeding the submucosal layer.^{4 11 13}

GPs have a characteristic triphasic histological appearance that consists of Schwann-like spindle cells, ganglion cells and neuroendocrine epithelial cells in variable proportions. These tumours are highly positive for various neuroendocrine markers, pancreatic polypeptide and S-100. The histological differential diagnosis depends on which cell population dominates. When spindle cells predominate, the differential diagnosis includes leiomyoma and GIST. In this case, GP can be diagnosed by demonstrating immunoreactivity to chromogranin and synaptophysin. If ganglion cells predominate, the differential diagnosis includes paragangliomas, ganglioneuromas, schwannomas and carcinomas. The histological distinction between benign and malignant disease is limited by tumour rarity, heterogeneity and long latency periods for metastasis. Ki-67 is a marker that correlates with malignancy but cannot exclude it (malignant GPs are currently diagnosed by identifying recurrence or distant metastasis).^{3 4 7 11 12 17} In this case, the biopsy specimen demonstrated a triphasic morphology and was positive for synaptophysin, chromogranin and S-100, with a Ki-67 proliferative index of less than 1%.

The treatment options for duodenal GPs currently include endoscopic resection, local surgical resection or

pancreaticoduodenectomy.⁵ Endoscopic and local surgical resection are preferable for benign lesions, with pancreaticoduodenectomy being reserved for advanced disease because of its complexity and associated morbidity and mortality. Successful surgical excision of distant metastasis and the use of adjuvant external radiotherapy have also been reported. However, the evidence for treating advanced disease with radiotherapy is currently lacking.^{4 5} Preoperative assessment includes a high-quality CT scan to assess surrounding invasion, as well as administration of α -blocking medication in cases of functional paragangliomas.^{5 12}

Although laparoscopy has been widely adopted for the treatment of adrenal tumours, including pheochromocytomas, its use for paragangliomas has been limited. Mitchell *et al*¹² state that this might be attributable to concerns regarding malignancy, multifocality and proximity of major vascular structures, all of which can create difficulty or complications in a laparoscopic approach.

The first report of a purely laparoscopic approach to a duodenal tumour appeared in the literature in 1997. Since then, 30 patient cases have been described where laparoscopy was used on its own or combined with endoscopy (10 cases) and hand assistance (8 cases). In these reports, the mean patient age is 56 years. A variety of duodenal tumours with diameters between 0.6 and 6 mm were resected, mainly from the second part of the duodenum. Duration of operation and length of hospital stay ranged between 90–300 min and 2–12 days, respectively. Complications were only reported on two occasions; namely, an incisional hernia after hand-assisted laparoscopic resection of a carcinoid tumour and gastrointestinal bleeding after laparoscopy-assisted endoscopic resection of a GIST. Endoscopy-assisted laparoscopic resection of a duodenal GP was reported in 2007.^{1 2 18 19}

Following treatment and a definitive diagnosis of paraganglioma, patients should have their family history reviewed for the associated hereditary syndromes mentioned above. If there is evidence of these syndromes, genetic counselling and testing is recommended. In addition, and since malignancy can only be diagnosed by recurrence or metastasis, serum normetanephrines should be periodically measured and followed up with appropriate imaging to locate recurrences or metastases. However, GPs rarely metastasise and thus carry an excellent postoperative prognosis.^{4 12}

In conclusion, this case adds to the existing evidence that laparoscopic approaches to treating duodenal tumours such as GP are feasible and safe, allowing patients to quickly resume their daily activities. Furthermore, it highlights the importance of considering a broad differential diagnosis in patients with biliary colic.

Learning points

- ▶ Totally laparoscopic resection of duodenal tumours is feasible and safe.
- ▶ Consider gangliocytic paraganglioma as a cause of biliary colic.
- ▶ Avoid tumour biopsies in patients with features of catecholamine excess.
- ▶ Clinical follow-up is an important complement to surgical treatment.

Competing interests None.

Patient consent Obtained.

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