Periampullary Gangliocytic Paraganglioma: a Case Report

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This paper reports on a single case of a 62-year-old woman with periampullary GP and discusses potential diagnostic difficulties associated with specific features of this tumour.

Case Report

A 62-year-old woman presented with pain in the hypochondrium that had started several weeks before presentation, followed by intermittent upper intestinal bleeding within the three days prior to presentation. An endoscopy of the duodenum revealed a 2 cm nodular periampullary intestinal wall mass. Because of a clinically suspected gastrointestinal stromal tumour, the patient underwent explorative laparotomy with perioperative biopsy of the lesion.

The frozen section (Figure 1) revealed a tumoural mass within the duodenal submucosa showing several entrapped muscle fibres but sparing the mucosa. Intestinal villi were normally structured and showed no epithelial atypia. Besides the spindle cell component of the tumour, multiple epithelioid islets were found. At higher magnification, many central areas of the latter structures appeared to be necrotic. Histo-pathological findings were suggestive of a neuroendocrine origin of the tumour, however, its origin remained uncertain. The surgery was terminated and the remaining tumoural tissue was fixed in formalin and subsequently embedded in paraffin. Immunohistochemical reactions (Table I) were performed along with haematoxylin-eosin (HE) staining and periodic acid-Schiff reaction.

The tumour presented three distinct components characteristic of a gangliocytic paraganglioma (Figure 2): multifocal islands of carcinoid-like epithelioid cells, spindle cell proliferation and scattered ganglion cells present within both the spindle cell stroma and carcinoid-like portions. Ganglion cells were not pigmented. Several intestinal wall muscle fibres were found entrapped within the tumour. Neither cellular atypia nor tumour necrosis was present in the paraffin-embedded tissue.

Immunohistochemistry (Table II) confirmed the diagnosis of a gangliocytic paraganglioma, which is a benign gastrointestinal neuroendocrine tumour. More specifically, the epithelioid cells displayed strong AE1/AE3 positivity. Furthermore, both the epithelioid cells and some of the...
ganglion cells were immunoreactive for synaptophysin. All
three cell lines were positive for neuron-specific enolase.
Spindle cells were stained strongly with neurofilament.
Interestingly, the epithelioid component displayed moderate
reactivity against somatostatin receptor 2A. To summarise,
the tumour was reported as a benign periampullary
gangliocytic paraganglioma. No other neural tumours were
found. The immediate postoperative course was unremarkable
and the subsequent follow-up of 12 months was uneventful.

Discussion

In the gastrointestinal tract and pancreas, several
neuroendocrine cell types can be distinguished producing
different hormones but all expressing the general
neuroendocrine marker synaptophysin (10). Both their
functional diversity and non-random distribution in the gut
and pancreas are probable reasons for the complexity of
tumours derived from these cell types (11). Gangliocytic
paragangliomas are found mainly in the second
(periampullary) portion of the duodenum, and their size
ranges from 1.5 to 7.0 cm (12-14). These tumours are
composed of three characteristic mature cell types: (a)
epithelial/endocrine cells, arranged in ribbons, solid nests
and/or pseudoglandular structures; (b) S-100-positive neural
spindle cells, which usually represent the major component;
and (c) scattered or aggravated gangliocytic cells (3, 15).
Reports on multifocal lesions of GP are rare (16). Despite
their infiltrative growth, metastasis to the regional lymph
nodes is rarely observed (3, 15, 17). The histological
differential diagnosis of duodenal GP includes conventional
paraganglioma, well-differentiated neuroendocrine carcinoma,
ganglioneuroma, and spindle cell neoplasms (nerve sheath,
smooth muscle, gastrointestinal stromal tumour) (18-20).

In the present case, a perioperative frozen section diagnosis
was performed in order to clarify the origin and dignity of a
periampullary tumoural mass found in the duodenum. Although
cellular atypia was not found on perioperative frozen section
biopsy, both the necrosis-like areas within the lesion and
intralresional entrapped intestinal wall muscle fibres mimicked
malignancy. Thus the lesion was preoperatively reported as a
mesenchymal tumour of uncertain origin. Paraffin embedded
tissue revealed a characteristic admixture of the three cellular
components of GP: epithelioid carcinoid-like islands, spindle
cell background and scattered ganglion cells. It is noteworthy
that the formerly necrotic-appearing areas were reassigned as
artificially loosened groups of both luminal epithelioid cells
within partially trabecular structured epithelioid cells and
ganglion cells. Immunohistochemical findings were typical of
a GP and confirmed the conventional diagnosis. Interestingly,
the epithelioid component showed a moderately positive
reaction for somatostatin receptor 2A antibody. This finding has
a several potential clinical implications. Recent literature has
reported on using somatostatin receptor scintigraphy for
detection and monitoring of head and neck paragangliomas and
carcinoids (21). As with the potential diagnostic usefulness of
somatostatin receptor expression (22), recent literature has also
discussed data on peptide receptor radionuclide therapy with
radiolabelled somatostatin analogues in patients with
somatostatin receptor-positive tumours (23-25). Furthermore,
there is strong evidence, that some mesenchymal tumours with
somatostatin receptor expression may cause systemic oncogenic
osteomalacia (26-29). In the present case of periampullary
gangliocytic paraganglioma, however, possible systemic
endocrine effects of the growing tumour were not observed.

Conclusion

Gangliocytic paraganglioma is a rare benign mesenchymal
gastrointestinal tumour composed of three different cell types
that may present with necrosis-like changes in portions with
artificially loosened ganglion cells and entrapped intestinal wall
muscle fibres during frozen section diagnosis, thus mimicking
a malignancy. When reporting the results of a perioperative
biopsy in cases with similar findings, every precaution should
be taken to avoid possible over-therapy of this benign tumour.

Table I. Immunohistochemical antibodies.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE1/AE3</td>
<td>Dako M3515</td>
<td>1:50</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>Dako M0076</td>
<td>1:20</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Dako M 758</td>
<td>1:20</td>
</tr>
<tr>
<td>Ki-67</td>
<td>Mib-1, Dako M7240</td>
<td>1:400</td>
</tr>
<tr>
<td>NSE</td>
<td>Dako M7305</td>
<td>1:200</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>LK2H10+PHE5, Abcam</td>
<td>1:500</td>
</tr>
<tr>
<td>Somatostatin receptor</td>
<td>SRR2A, Gramsch Lab.</td>
<td>1:1000</td>
</tr>
<tr>
<td>Neurofilament</td>
<td>Dako M0762</td>
<td>1:50</td>
</tr>
<tr>
<td>GFAP</td>
<td>Dako Z334</td>
<td>1:1000</td>
</tr>
<tr>
<td>S-100</td>
<td>NeoMarkers</td>
<td>1:100</td>
</tr>
</tbody>
</table>

Table II. Immunohistochemical analysis of each tumoral component.

<table>
<thead>
<tr>
<th>Primary antibody</th>
<th>Carcinoid-like</th>
<th>Gangliocytic</th>
<th>Spindle cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE1/AE3</td>
<td>+++</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Synaptophysin</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Serotonin</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ki-67</td>
<td>2%</td>
<td>–</td>
<td>2%</td>
</tr>
<tr>
<td>NSE</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>+</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Somatostatin receptor</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Neurofilament</td>
<td>–</td>
<td>–</td>
<td>+++</td>
</tr>
<tr>
<td>GFAP</td>
<td>–</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>S-100</td>
<td>–</td>
<td>++</td>
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References


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