Mucoepidermoid carcinoma of the duodenum: first reported case

To the Editor,

Mucoepidermoid carcinoma (MEC) is a common salivary gland malignancy. It is characterised by a combination of mucus-secreting, squamous-like epithelial and intermediate cell types. However, primary MEC of the digestive tract is rare. The current 2019 World Health Organization classification of digestive system tumours defines MEC as a separate subtype of oesophageal and gastric tumours, and it is not mentioned among intestinal tumours. Here we describe the first report of MEC of the duodenum.

A 67-year-old man was admitted to our hospital because of a 10-day history of epigastric pain. An abdominal computed tomography (CT) scan showed thickening of the intestinal wall in the horizontal part of the duodenum (Fig. 1A). Laboratory tests, which included biochemical examinations and complete blood counts, showed no abnormal findings. The patient underwent duodenotomy. Grossly, the surgically resected specimen revealed an ulcerated tumour of 3.5×2.5×1 cm in the duodenum with a clear margin. The cut surface of the tumour was grey-white, and tumour cells had invaded the whole intestinal wall (Fig. 1B). No pancreatic tissue was found; the tumour was unrelated to the pancreas.

Microscopically, the tumours were composed of cords and sheets of epidermoid, intermediate, and mucin-secreting cells (Fig. 2A,B). The cellular nests were separated by fibrous stroma. No true cell keratinisation or glandular ductal structures were observed. Parts of the glandular epithelium showed a transition to epidermoid cells with atypia (Fig. 2C). Tumour cells had invaded the serosa of the duodenum, venous and nerve invasion were also identified. Alcian blue-periodic acid–Schiff (AB-PAS) staining was only observed in mucin-secreting cells (Fig. 2D). Immunohistochemistry (IHC) showed that all tumour cells were positive for CK19, p63 and CK5/6, and negative for CEA and CK19. The expression showed the presence of Brunner glands and ducts in the intestinal wall in the horizontal part of the duodenum (Fig. 1A). Laboratory tests, which included biochemical examinations and complete blood counts, showed no abnormal findings. The patient underwent duodenotomy. Grossly, the surgically resected specimen revealed an ulcerated tumour of 3.5×2.5×1 cm in the duodenum with a clear margin. The cut surface of the tumour was grey-white, and tumour cells had invaded the whole intestinal wall (Fig. 1B). No pancreatic tissue was found; the tumour was unrelated to the pancreas.

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Primary MEC is the most frequent malignant tumour of the salivary gland. It is also seen in the bronchi, pancreas, liver, oesophagus,5 and stomach.6 However, primary MEC of the intestine is very rare. Until now, globally only two cases of primary MEC have been reported in the colon,7,8 and there has not been a case reported in the literature of MEC in the duodenum (Table 1). MEC was previously considered to arise from excretory ductal epithelial cells with considerable potential for differentiation and metaplasia.1 Hayashi et al. showed that MEC derived from the malignant transformation of a pre-existing ectopic submucosal mucosal gland in the stomach.6 MEC might arise from a stem cell, probably from submucosal glands and ducts, giving rise to biphasic differentiation in the oesophagus.1 The origin and precise histogenesis of this tumour type in the intestine remains unclear. Like the oesophagus, the histological structure of the duodenum showed the presence of Brunner glands and ducts in the submucosa. Therefore, we hypothesised that the malignant mechanism may be the same as in the oesophagus.

Because of the rarity of this tumour type, the pathological diagnoses of MEC is not easy. The possibility of metastatic MEC from salivary glands or other organs should always be considered. This requires careful inquiry about the patient’s detailed clinical history and physical examination.

The differential diagnosis of MEC in histology is primarily separated into adenosquamous carcinoma (ASC) and squamous cell carcinoma (SCC), which is composed of squamous cell differentiation characterised by keratinocyte-type cells with intercellular bridges and/or keratinisation. SCC lacks glandular architecture and stains positive for p63, CK5/6 and negative for CEA and CK19, which could be helpful in distinguishing diagnosis. ASC are composed of a variable combination of squamous and glandular architecture under the microscope. The squamous area stains positive for p63 and CK5/6, and negative for CEA and CK19. The expression of the glandular area is the opposite. Furthermore, MEC lacks an area of genuine pure adenocarcinoma-like glandular tube formation and fully developed squamous differentiation, such as cell keratinisation, which is only individual or focal.

The origin and aetiology of intestinal tract MECs are unclear. Nakano et al. found that 102 cases were positive for CRTC1-MAML2 and eight were positive for CRTC3-MAML2 in a total of 177 salivary MEC cases. MAML2 rearrangement may be associated with better survival and lower histological grade.9 MAML2 rearrangements are found in other tumour types and have recently been identified in MEC of breast10 and metastatic thymoma,11 but were not detected in our case.

At present, MEC is treated with a combination of surgical resection, radiation and chemotherapy. Advanced treatment options such as immunotherapy and targeted therapy have been investigated.12 MEC arising from salivary glands has a favourable outcome compared with MEC of other origins. However, MEC arising from the gastrointestinal tract may have a poor prognosis with a high propensity to metastasise. Sato et al. reported that a patient with MEC of the ascending colon developed liver metastasis and died 10 months after surgery.13 Han et al. also reported a patient who survived for only 7 months after surgery. In our case, the patient received one course of Folfox chemotherapy 2 months following surgery. Unfortunately, he died because of recurrence 12 months post-operatively.

The clinical, morphological, and prognostic factors of MEC in the digestive tract remain poorly understood in contrast to salivary MEC. Additional cases and longer follow-up are necessary to better understand this disease.

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Fig. 1  (A) Computed tomography scan showed thickening of the intestinal wall in the horizontal part of the duodenum (arrows). (B) The surgically resected specimen revealed an ulcerated tumour in the duodenum with a clear margin, the cut surface of the tumour was grey-white, and tumour cells had invaded the whole intestinal wall (arrows).

Fig. 2  (A,B) The tumours were composed of epidermoid, intermediate, and mucin-secreting cells. (C) Glandular epithelium showed a transition to epidermoid cells with atypia. (D) Mucin-secreting cells show AB-PAS positivity. Immunohistochemistry showed diffuse staining for (E) p63 and (F) CK5/6.

Table 1  Reported cases of MEC of the intestine

<table>
<thead>
<tr>
<th>Case no./ reference</th>
<th>1⁹</th>
<th>2⁷</th>
<th>Present case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/sex</td>
<td>71/M</td>
<td>77/F</td>
<td>67/M</td>
</tr>
<tr>
<td>Tumour location</td>
<td>Ascending colon</td>
<td>Transverse colon</td>
<td>Duodenum</td>
</tr>
<tr>
<td>Tumour size, cm</td>
<td>3×3</td>
<td>8×8×7</td>
<td>3.5×2.5×1</td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td>+</td>
<td>NA</td>
<td>+</td>
</tr>
<tr>
<td>Treatment</td>
<td>Radical resection, chemotherapy</td>
<td>Extended resection, chemotherapy</td>
<td>Radical resection, chemotherapy</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Died with systemic failure, 10 months</td>
<td>Died with liver metastases and died of liver failure, 7 months</td>
<td>Died of tumour recurrence, 12 months</td>
</tr>
</tbody>
</table>

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