Unusual presentation of more common disease/injury

Intramural carcinoma of the oesophagogastric junction

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Most oesophageal carcinomas (>70%) are squamous cell carcinomas (SCC) arising from the surface epithelial lining. In the gastro-oesophageal junction (GEJ) adenocarcinomas occur in the setting of Barrett oesophagus (BE). These carcinomas typically present with surface ulceration. The authors report a rare case of a SCC of the GEJ with completely intramural growth underneath intact non-dysplastic oesophageal squamous epithelium and BE without dysplasia. The sharply demarcated tumour was located in the muscularis propria with infiltration of perioesophageal tissue nearly reaching the diaphragm. Intramural squamous carcinomas are very rare with only three reported cases. In this study, the authors discuss this finding and review the relevant literature. Intramural carcinomas are a diagnostic challenge for clinicians and pathologist, since preoperative biopsies mostly fail to establish the diagnosis and surgical explorations must be considered.

BACKGROUND

Most malignant oesophageal tumours are carcinomas arising from the superficial epithelial layer. The two main tumour types are squamous cell carcinoma (SCC) and adenocarcinoma (AC), the latter originating predominantly in the lower third of the oesophagus from columnar ('Barrett') mucosa. According the current TNM-classification¹ carcinomas of the oesophagogastric junction are included in the group of oesophageal carcinomas. The incidence of oesophageal cancer in the UK is 9.6 out of 100000 with a high mortality due to a poor 5-year survival fewer than 10%. The incidence of oesophageal AC in western countries is rising. AC accounts for up to 50% of oesophageal cancers in the West² and exceeded that of SCC,³ whereas SCC remains the primary oesophageal malignancy in the developing world.

Most advanced oesophageal carcinomas present with dysphagia, odynophagia, weight loss, coughing or pain. In other cases, patients just notice a change of eating habits. Since most carcinomas present with obvious mass or ulceration, clinical examination with endoscopic techniques usually allows a straight diagnosis after histological examination of the biopsies. Especially mesenchyme tumours (eg, gastrointestinal stromal tumours, lipomas, leiomyomas) may present underneath intact epithelium. In this case, we present an SCC with entirely intramural growth in the oesophagogastric junction with intact overlying epithelium. Prior cytological evaluation proposed an AC.

CASE PRESENTATION

A 58-year-old man was admitted to our observation with dysphagia. The patient consumed only soft food and lost 5 kg of weight.

The surgical specimen was composed of 2.5 cm lower third oesophagus and a total gastrectomy including the pyloric sphincter. In addition, the specimen included a partial resection of adherent diaphragm measuring 5×2×1 cm, omental tissue and fat tissue of the greater and lesser

curvature. Fat tissue of the compartment II, as well as duodenal resection margins were provided separately. Inspection of the oesophageal surface as well as gastric surface lacked any ulcerations or exophytic tumour masses. The surface of the distal oesophagus appeared velvety red in contrast to the gray appearance of the squamous epithelium. The surface protruded into the lumen (figure 1A). Longitudinal cut sections of the oesophagogastric junction showed a sharply demarcated whitish tumour measuring 7×5×5 cm, located intramural with extension into the adherent perioesophageal adventitial tissue and reaching the muscular tissue of the diaphragm (figure 1B). The tumour did not extend to the surgical specimen margins. Examination of the gastric and duodenal tissue revealed no further tumour mass.

INVESTIGATIONS

Histological examination based on H&E stained sections demonstrated a well-defined malignant epithelial tumour with squamous features lacking gland formation (figure 2A). For immunohistochemistry on formalin-fixed paraffin-embedded tissue samples, 5 µm sections were dewaxed and rehydrated. After antigen retrieval the various sections were stained using an automated staining device (Dako Autostainer, Glostrup, Denmark). Antibody demonstration was performed with the commercially available antimouse IgG detection kit (EnVision, DakoCytomation, Carpinteria, USA). Immunohistochemical investigations revealed a strong immunoreactivity of the majority of tumour cells with antibodies against cytokeratin 5/6 (figure 2B). A subset of tumour cells expressed cytokeratin 7 (figure 2C). A panel of additional immunohistochemical investigations were performed. Tumour tissue expressed p63, a specific marker of squamous differentiation. There was no expression of vimentin, S100, melan-A ruling out mesenchymal or melanocytic differentiation. Negative immunoreactivity with lung specific antibodies TTF-1 excludes a metastatic bronchial carcinoma. Evaluation of

23 lymph-nodes demonstrated one nodal metastasis with infiltration via continuitatem. There was no infiltration of the muscular tissue of the diaphragm and the tumour was completely resected with microscopically free circumferential margins (R0).

Complete clinical examination did not show tumour mass elsewhere, especially CT of the chest lacked any suspicious foci in the lung. Thorough inspection of the head and neck including endoscopy was unremarkable.

OUTCOME AND FOLLOW-UP

The postoperative course and follow-up has been unremarkable for 6 months now. The application of radiochemotherapy was discussed but neglected by the patient. The patient is in fine general condition and receives further surveillance with CT and endoscopy.

DISCUSSION

The present case shows an unusual manifestation of a completely intramural localised carcinoma of the oesophago-gastric junction. The present carcinoma demonstrates an expression both of cytokeratin (5/6) (which typically occurs in SCC) and cytokeratin 7, which generally points towards carcinomas with gland formation (ACs). However, expression of the low molecular CK7 in SCCs of the oesophagus is described in up to 21% of SCCs.⁴ The present carcinoma is best classified as SCC. The typical morphologic features of an adenosquamous carcinoma (gland formation in combination with keratinising squamous tumour cells) were not present. Besides the remarkable anatomical setting the histological pictures differs from that of usual oesophageal SCCs.

Intramural oesophageal SCCs are exceedingly rare with only three cases reported previously. McGregor *et al*⁵ described a case with an exclusively intramurally located SCC. Another case was presented by Kishino *et al*,⁶ showing an intramural, submucosal SCC with gastric metastasis. Previously von Rahden *et al*⁷ presented a 5 cm measuring intramural SCC in the proximal oesophagus. The appearance of the tumour presented in this case differs from those published earlier, since the present SCC forms one solid mass with sharply demarcated margins, imitating a benign lesion such as leiomyoma or gastrointestinal stromal tumour.

The diagnosis of intramural oesophageal SCC requires a carefully clinical investigation in order to rule out metastasis of extra-oesophageal cancers, such as lung cancers or cancers of the head and neck. CT failed to show a tumour outside the oesophagus.

Regarding the pathogenesis of intramural SCC two hypotheses are favoured: 1) The tumour may have originated from a diverticulum or an oesophageal duplication cyst.⁸ However, most cases of congenital oesophageal duplication cyst present in the 1st year of life. They occasionally manifest in adults and mostly remain undetected since they are seldom associated with complications. 2) The second hypothesis is based on the well described presence of submucosal oesophageal glands.⁹ These glands are scattered throughout the entire oesophagus with main location in the upper and lower regions.⁹ These mucinous glands drain into the oesophageal lumen and are lined by cuboidal epithelium, becoming stratified squamous epithelium. SCC may arise from superficial portions of these submucosal glands. In addition, deeper portions of these glands may undergo squamous metaplasia proposing

Figure 1 Macroscopic picture of the surgical specimen. (A) Surgical specimen with protruding tumour beneath intact oesophageal mucosa. (B) The tumour is located beneath the intact squamous epithelium (cross), reaching from the muscularis propria (asterisk) to the para-oesophageal tissue. Right to the squamous epithelium the mucosa is reddish, due to the presence of a Barrett mucosa.

Figure 2 Micrograph showing the tumour at higher magnification (A) (H&E; x200). The tumour grows in a solid pattern without forming gland structures. Strong expression of cytokeratin 5/6 (B) (x200) in most of the tumour cells. Coexpression of cytokeratin 7 (C) (x200).

another origin for SCC. The present case supports the development of SCC in submucosal glands since the overlying squamous epithelium lacks any dysplastic alterations. The Barrett mucosa was devoid of dysplasia and thus does not qualify as a precancerous lesion. The concomitant immunohistochemical expression CK 7 (usually found in gland-forming tumours) supports the hypotheses that the present SCC originated from a metaplastic process of submucosal glands.

In summary, the present case demonstrates the rare setting of an entirely intramural located carcinoma of the oesophagus, best classified as non-keratinising SCC, which represents a challenging diagnostic situation. Clinicians and pathologist have to be aware of this diagnosis, although pretherapeutic biopsies (not in this case) might be negative and endoscopic techniques reveal an unremarkable oesophageal surface.

Learning points

- ▶ Endoscopic techniques often reveal an unremarkable oesophageal surface.
- ▶ Biopsy from mucosal surface may remain false negative.
- ▶ Surgical exploration must be considered to establish a definite diagnosis of intramural carcinoma.

Competing interests None.

Patient consent Obtained.

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