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Pathology in Focus

Gastrointestinal stromal tumour of the pharynx

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Abstract
This documents the case of a 55-year-old female presenting with a solitary polypoidal tumour of the pharynx. Histological examination revealed features consistent with a gastrointestinal stromal tumour. Although well described elsewhere in the gastrointestinal tract, from our literature search, this is the first reported case of such a tumour occurring in the pharynx

Key words: Gastrointestinal Neoplasms; Stromal Cells; Pharynx

Case report

A 55-year-old female presented with a six-month history of intermittent dysphonia. She was otherwise asymptomatic. Nasendoscopic examination of her laryngopharynx showed a sessile polypoidal lesion arising on the left side of her pharynx. It seemed to be crossing the midline and obscuring the airway. It was not visible per-oral examination.

Examination under anaesthesia revealed this to be a mass arising from the left posterior pharyngeal wall at the level of the epiglottis. It was crossing the midline and compressing the epiglottis and aryepiglottic fold. It measured 45 mm × 40 mm × 30 mm in size. This was completely excised. She was discharged well the following day and to date at 11 months has been asymptomatic to follow up.

Histology showed a variably cellular, spindle-cell proliferation with localized interstitial oedema, areas of collagenous and fibrovascular stroma and patchy myxoid ground substance. (Figure 1). The architecture was largely haphazard with no fasciculated or organoid pattern and with no neuroid bodies or skeinoid fibres. There was focal modest nuclear

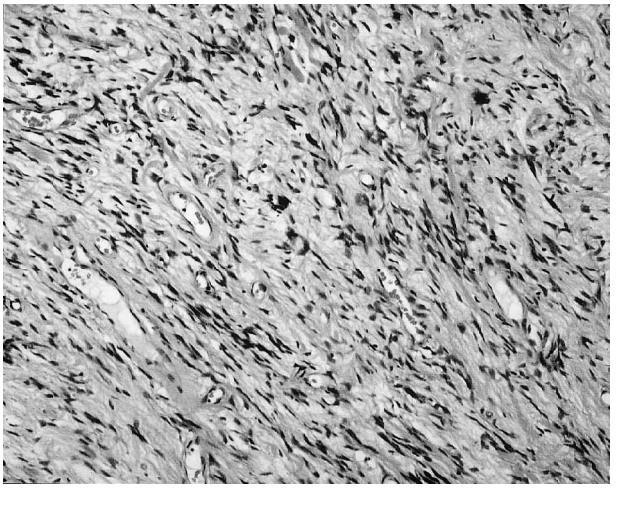

Fig. 1
Low power photomicrograph showing a variably cellular spindle cell proliferation within this tumour (H&E; ×25).

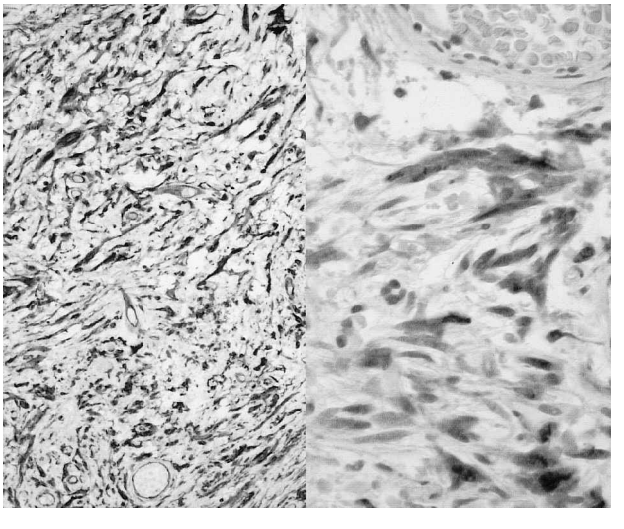

Fig. 2
Composite photomicrograph illustrating uniformly positive staining of the tumour cells for CD34 (left) with both diffuse cytoplasmic and paranuclear dot-like immunoreactively (so-called golgi pattern) for CD117 (right). Left: CD34 immunoperioxidase, ×25; Right: CD117 immunoperoxidase, ×100).

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atypia but mitotic activity was less than 1 per 50 high power fields, and there was no necrosis. On immunohistochemistry the tumour cells co-expressed CD34, CD117 and vimentin, but were negative for smooth muscle actin, desmin, S100 protein, epithelial membrane antigen and high and low molecular weight cytokeratins. (Figure 2)

- **A 55-year-old female presented with a solitary polypoidal tumour of the pharynx**
- **Histological examination was consistent with a gastrointestinal stromal tumour which has not previously been reported in the pharynx**

Discussion

Spindle-cell mesenchymal tumours are relatively uncommon. They have been well described in the gastrointestinal tract. Most gastrointestinal mesenchymal tumours were initially presumed to be of smooth muscle origin, popularly labelled leiomyoma or leiomyosarcoma. However, further studies have demonstrated considerable variability within these mesenchymal tumours at the morphological, immunohistochemical and ultrastructural level. In contrast to typical smooth muscle tumours, the natural behaviour of the majority of these gastro-intestinal tumours cannot always be predicted reliably by the generally accepted morphological criteria of malignancy. Of the numerous acronyms used for these neoplasms, which include STUMP (smooth muscle tumour of uncertain malignant potential), GIST (gastro-intestinal stromal tumour), GANT (gastro-intestinal nerve tumour) and GIPACT (gastro-intestinal pacemaker cell tumour)—GIST has become the most widely used and accepted term. GISTs are the commonest form of mesenchymal tumour of the gastrointestinal tract[1] and appear to originate from stem cells that differentiate toward a pacemaker phenotype.[2] These gastrointestinal pacemaker cells are called interstitial cells of Cajal and consistently express the proto-oncogene *c-kit* (CD117) located on chromosome 4q 11–21.[3] Activation mutations of the *c-kit* gene have been identified in GISTs[4] and GISTs may therefore be defined as mesenchymal tumours of the gastrointestinal tract that express the KIT protein (CD117).[5] Whilst CD117 is a highly sensitive and specific marker in the appropriate context, other tumours such as melanoma, clear cell sarcoma, germ cell tumours and some haematopoietic tumours may also express CD117.

Other mesenchymal tumours of the gastrointestinal tract include classical smooth muscle tumours, schwannomas, neurofibromas and other rare tumours.[6]

Immunohistochemically, antibodies to CD34 and CD117 in particular, although not tumour specific are generally helpful in the differential diagnosis of GISTs from other gastrointestinal tumours as both markers are expressed in most GISTs.[7] CD-117/c-*kit* is especially regarded as a powerful aid in the diagnosis of GISTs. The routine histology supported by the immunohistochemical co-expression of CD34 and CD117 in our case is entirely consistent with GIST.

Predicting the potential biological behaviour of these tumours remains difficult, and there is still a degree of uncertainty and confusion regarding their natural behaviour. Consequently, stringent long-term clinical follow-up is recommended.[7]

Current data indicate that mitotic activity and tumour size may be of some use in predicting biological behaviour. Nevertheless, no individual factor is of unequivocal independent prognostic use and a constellation of parameters is conventionally used to provide some indication of a probable outcome. There are also differences in behaviour depending upon the site – oesophageal tumours as a group have the most favourable long-term survival and small intestinal tumours have the worst.

Until recently, surgery has been the only effective therapy for GIST. However, after discovering a mutation in the c-*kit* proto-oncogene and activation of KIT receptor tyrosine kinase as a central pathogenetic event in most GISTs, imatinib (Gleevec,™ Novaris, Basel, Switzerland) therapy has been hailed as a landmark development in cancer therapy. Imatinib is a small molecule that selectively inhibits the enzymatic activity of a platelet-derived growth factor receptor and KIT tyrosine kinases. It is taken orally, and malignant GIST, usually demonstrated by recurrence or metastasis, that are CD117 immunoreactive, respond dramatically.

The current tumour, which we believe to be the first reported case of GIST of the pharynx in the English literature, has so far behaved in a totally benign fashion, but long-term follow up is still needed to fully assess its behaviour.

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