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Leiomyosarcoma of the larynx

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Abstract
Leiomyosarcoma of the larynx is extremely rare. Histological diagnosis excluding other tumours, in particular fibrosarcoma and spindle cell carcinoma is often difficult. Immunohistochemical studies are helpful in arriving at an unambiguous diagnosis and we present a case characteristically positive for actin and desmin. The difficulties of determining treatment are discussed.

Key words: Leiomyosarcoma; Larynx

Introduction

Leiomyosarcoma is a malignant tumour of smooth muscle cells. It is most usually found in the female genital tract, especially the uterus, retroperitoneum, wall of the gastro-intestinal tract and the subcutaneous tissues (Cottran *et al.*, 1989). These tumours are uncommon and occurrence in the larynx is very rare (Michaels, 1987). They have a wide range of differentiation and low grade tumours may be difficult to differentiate from highly cellular leiomyomas. At the other end of the spectrum, determining the cell of origin of poorly differentiated sarcomas may be difficult. Given the rarity of occurrence of laryngeal leiomyosarcoma and the difficulty of diagnosis we report such a case and discuss the histopathological features including the value of immunohistochemistry.

Case report

An 87-year-old man presented with an eight-year history of dysphonia which had worsened to aphonia in the six weeks prior to consultation. Indirect laryngoscopy revealed a large, red tumour obscuring the right vocal fold and filling the right side of the supraglottis. The left vocal fold moved fully and he had no cervical lymphadenopathy. A chest radiograph demonstrated no focal lesions, full blood count was normal and there were no biochemical markers of abnormal liver function.

Direct, suspension laryngoscopy confirmed a well circumscribed, golf-ball sized tumour which arose from the anterior centimetre of the right vocal fold. It was variegated in appearance from grey to red and also varied from soft to firm on instrument palpation. The remainder of the right vocal fold and the larynx was normal. Removal of the neoplasm was carried out piecemeal and the area of attachment of the vocal fold to the tumour was ablated and diathermied using carbon dioxide laser.

Histology revealed a cellular, pleomorphic spindle cell tumour arranged in interweaving fascicles. Nuclei were vesicular with blunt ends and possessed prominent, sometimes multiple nucleoli (Figures 1 and 2). Cytoplasm was acidophilic. The surface of the lesion was extensively ulcerated and no squamous mucosa was identified. The mitotic rate of the tumour was high with up to 10 mitoses per 10 high power fields (HPF). Occasional morphologically abnormal mitoses were identified. Reticulin preparations showed an intimate pericellular pattern and in phosphotungstic acid haematoxylin (PTAH) preparations many intracytoplasmic, longitudinal filaments were identified (Figure 3).

Immunocytochemical preparations showed strong positive staining against antibodies to actin and desmin and negative staining against antibodies to S100, epithelial membrane antigen and keratin (Figure 4).

In view of the patient's age more extensive surgery was not carried out. He underwent a course of radical radiotherapy and is free of recurrence three months after completion.

Discussion

Leiomyosarcoma is extremely rare in the head and neck. Cases have been reported of tumours arising in the sinonasal tract (Fu and Perzin, 1975; Kuruvilla *et al.*, 1990), oral cavity (Haedicke and Kaban, 1988), trachea (Thedinger *et al.*, 1991), and maxillary sinus (Kanabe *et al.*, 1969). Only seven cases of primary laryngeal tumours have appeared in the English literature (Frank, 1941; Eggston and Wolff, 1947; Wolfowitz and Schaman, 1973; Kleinsasser and Glanz, 1979; Chen *et al.*, 1991). Of these, immunocytochemical studies are present in only one (Chen *et al.*, 1991) and the histological descriptions have been limited.

Kleinsasser and Glanz (1979) and Michaels (1987) have drawn attention to the difficulties of diagnosis in regard to malignant mesodermal tumours. In the first recorded leiomyosarcoma of the larynx (Frank, 1941) there was a divergence of opinion regarding the differential diagnosis with a neurogenic fibroma or neurosarcoma. Undifferentiated sarcomas are usually described according to the shape of the predominant cell such as spindle cell or round cell but this provides little help in determining the primary cell origin. Connective tissue cells of whatever type may also be induced to form different types of matrix (Tighe and Davies, 1984) so further confusing their origin. Distinguishing leiomyosarcoma from fibrosarcoma may be particularly difficult (Michaels, 1987). Both cases reported by Kleinsasser and Glanz (1979) were originally recorded as fibrosarcomas. Furthermore, in the larynx a pedunculated lesion with a malignant, fibroblastic histological appearance growing in the region of the anterior vocal fold is most likely to be a spindle cell carcinoma (Michaels, 1987). These lesions classically have a squamous

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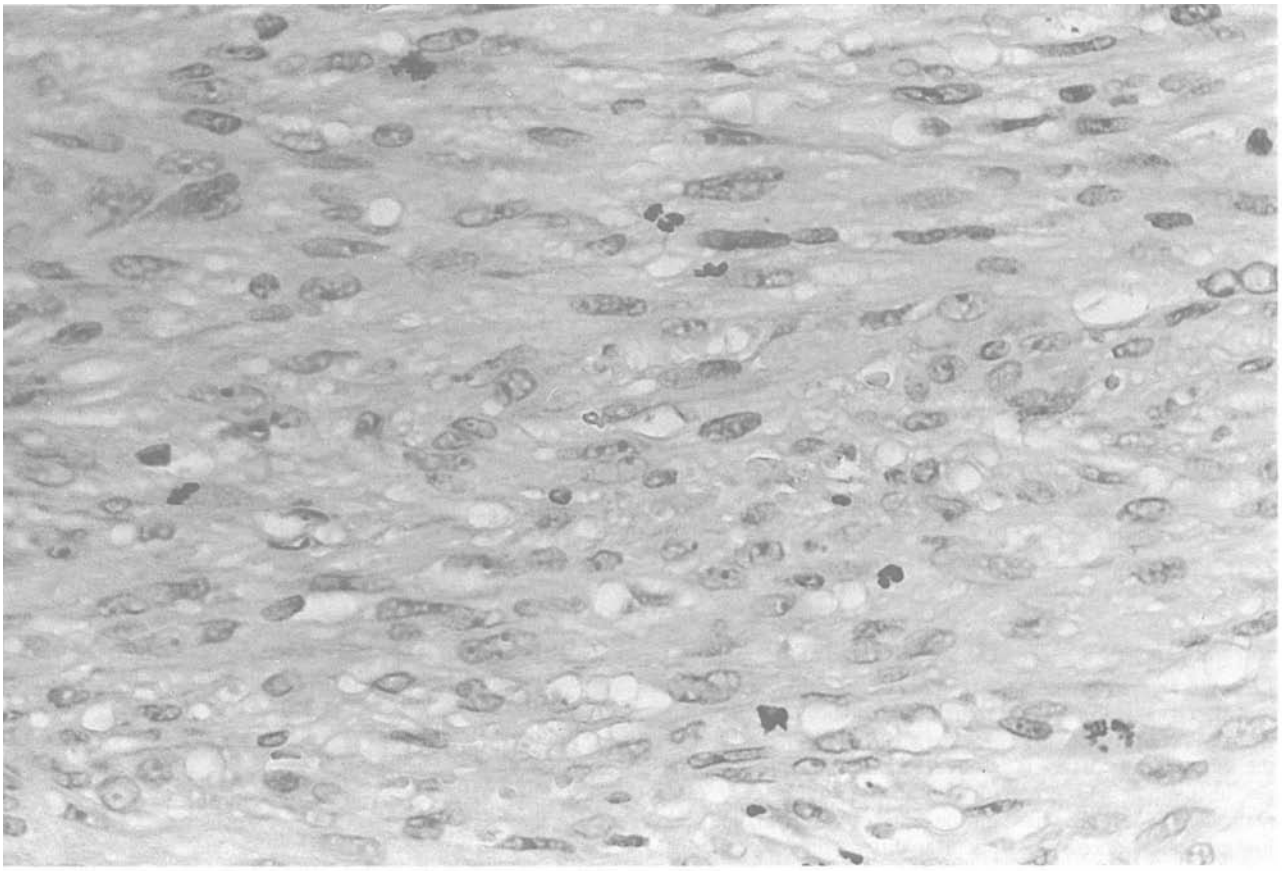

FIG. 1
Fasciculated, pleomorphic spindle cell tumour with blunt-ended nuclei. (H&E; × 720).

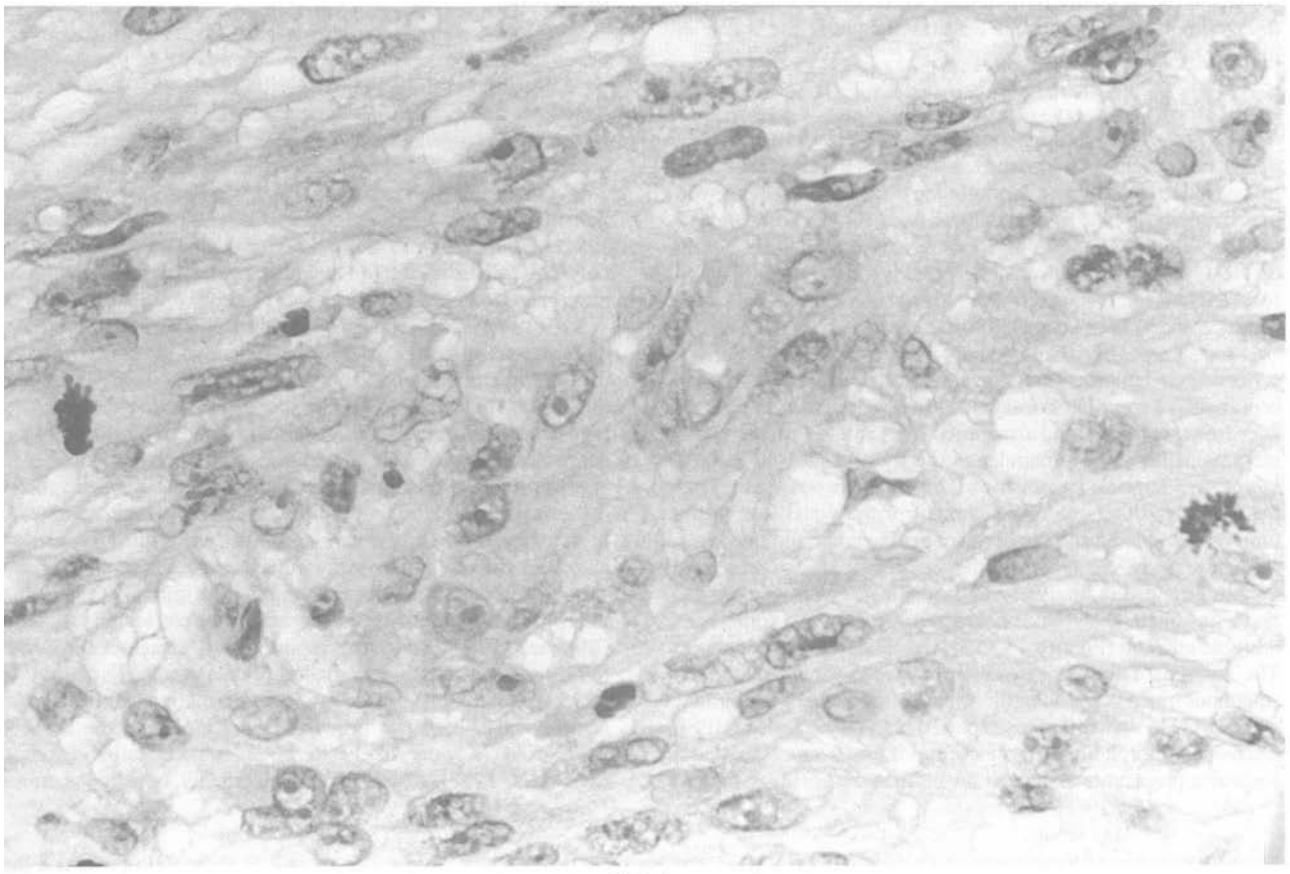

FIG. 2
FIG. 2
High power view to show vesicular nuclei, prominent nucleoli and mitotic activity. (H&E; × 920).

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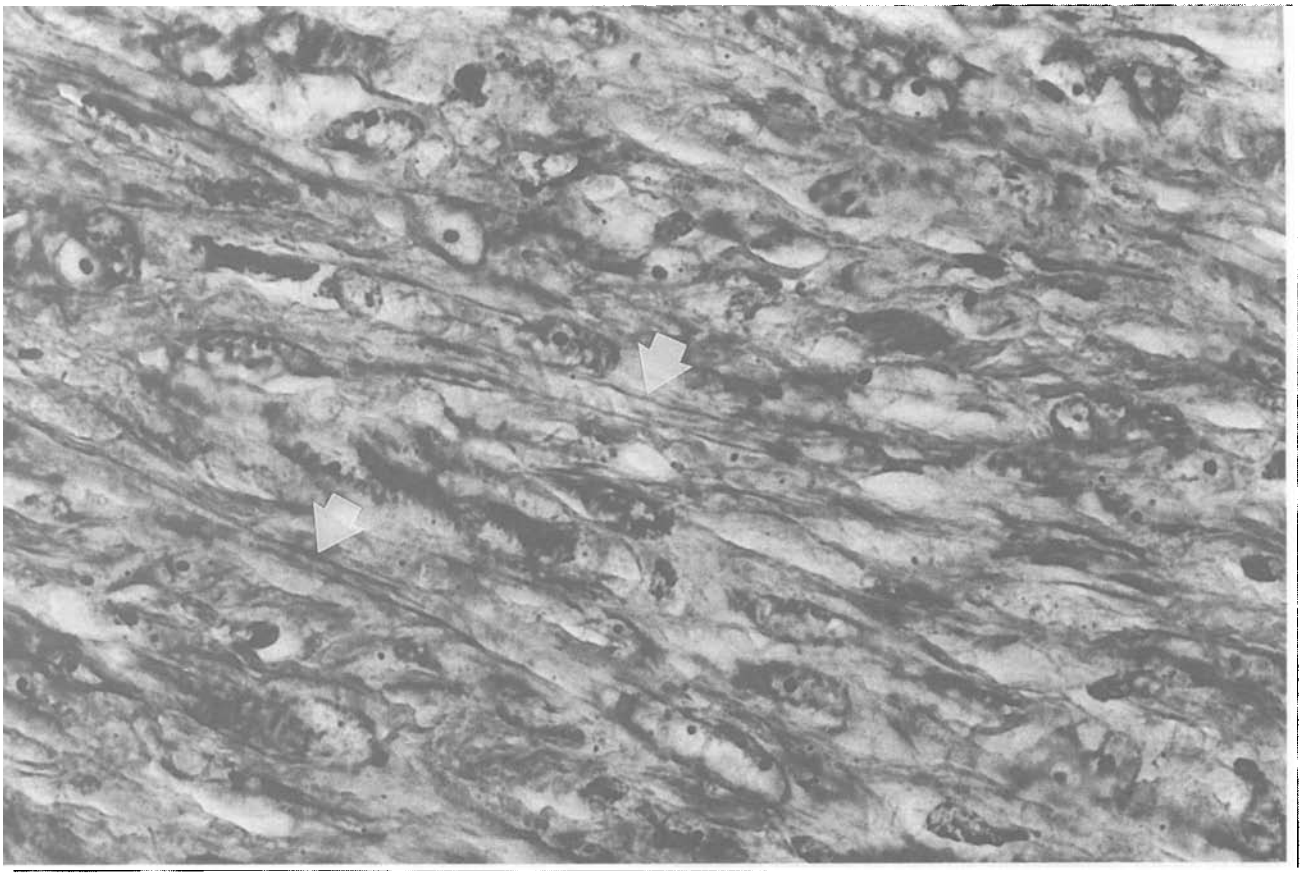

FIG. 3
Intracytoplasmic filaments (arrowheads) demonstrated in phosphotungstic acid haematoxylin preparation. (× 920).

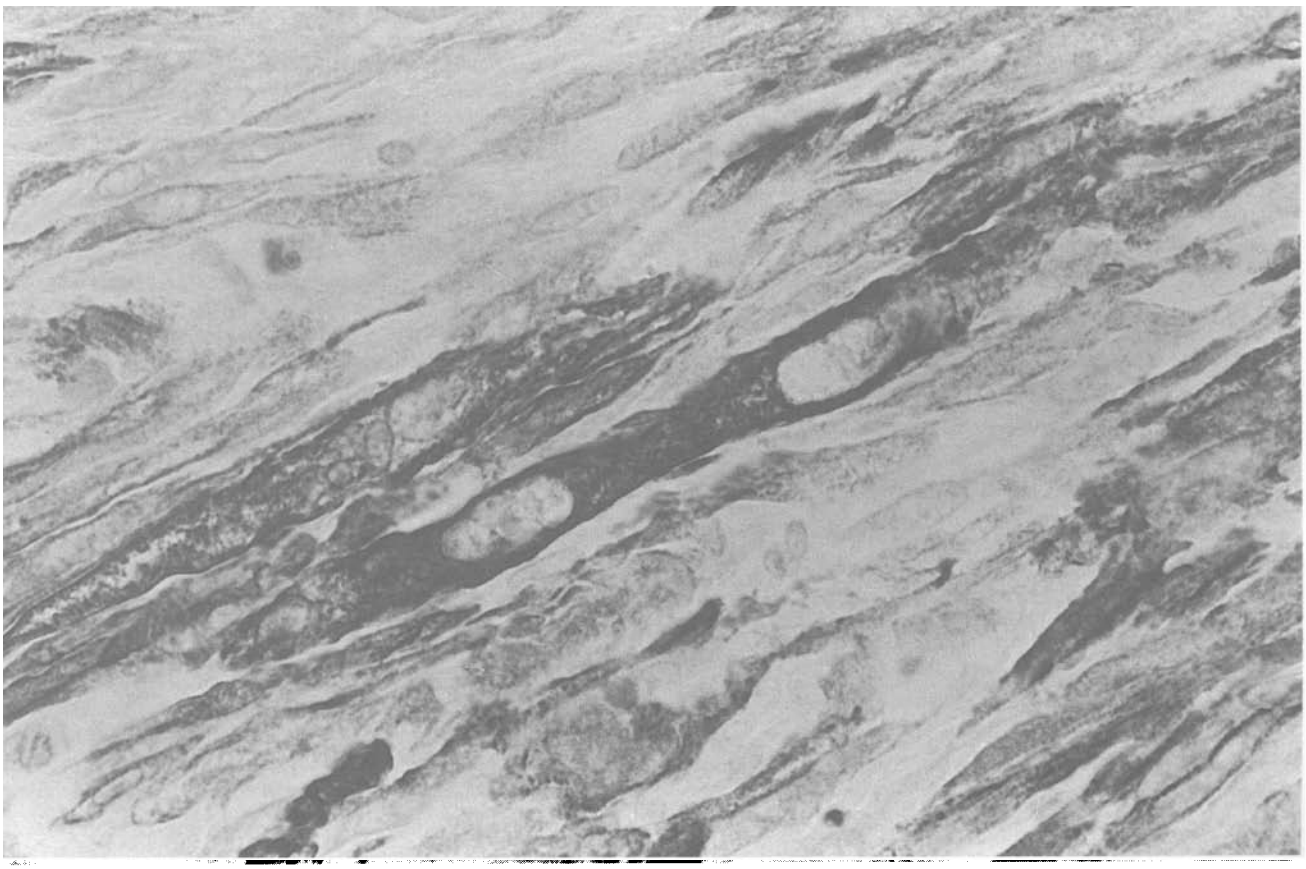

FIG. 4
Strongly positive cytoplasmic staining demonstrated by anti-actin antibody. (× 920).

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carcinomatous component in some part of the lesion, though if this epithelium is of doubtful malignancy, definitive diagnosis is very difficult.

Electron microscopy may help in the recognition of a leiomyosarcoma. The cytoplasm characteristically shows parallel actin filaments with fusiform dense bodies amongst them, which are representative of smooth muscle cells. Immunocytochemical antibody markers however are more readily available and may be directed against the elements of the cytoskeleton found in muscle cells, namely desmin and the muscle specific isoforms of actin (Osborn and Domagala, 1991). A positive result with actin and desmin markers, combined with the histological features in the case described above allows a confident diagnosis of leiomyosarcoma.

In the well differentiated tumour, histologically recognizable as a smooth muscle neoplasm, distinction between leiomyosarcoma and leiomyoma may also be difficult. As with all sarcomas the malignant tumour is more cellular, with less matrix than its benign counterpart. Both tumours may exhibit the characteristic interlacing bundles of spindle cells containing fibrillary cytoplasm and elongated, blunt baton-shaped nuclei. Diagnosis of malignancy is therefore based upon cellularity, cellular and nuclear irregularities and the frequency of mitoses (Friedmann and Piris, 1986). In the more common smooth muscle tumours of the uterus, malignancy is suggested by greater than ten mitoses per ten HPF or between five to ten mitoses per ten HPF with cellular atypia (Cottran *et al.*, 1989). Despite this wide range of differentiation leiomyosarcomas are rare in relation to leiomyomas and are thought to arise de novo rather than from pre-existing leiomyomas. However, given the long history of dysphonia in our case, with a more recent exacerbation, it is possible a slow-growing benign tumour underwent malignant transformation.

Too few cases, especially with an unambiguous diagnosis, exist to predict accurately the outcome of different treatment modalities for leiomyosarcoma of the larynx. In Kleinsasser and Glanz's (1979) review no case was successfully treated with radiotherapy. Prognosis was determined by tumour differentiation. Pleomorphic, 'high grade' forms grew very aggressively and metastasized by blood early. Better differentiated forms were cured by radical surgery. However Chen *et al.* (1992) have had no recurrence at 18 months in a case treated by conservative surgery and post-operative radiation. Outcome though is unpredictable as metastases may appear several years after surgery (Michaels, 1987).

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