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Granular cell tumour of the larynx

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Abstract

Granular cell tumour (GCT) is a benign tumour with abundant eosinophilic cytoplasm filled with granules of varying sizes. These granules are the defining characteristic of the GCT and are believed to represent lysosomes in varying stages of fragmentation. The commonly used term granular cell myoblastoma, found in the older literature, is a misnomer because the tumour is clearly not of muscle origin. Among the major theories of origin, some support the tumour's derivation from neuronal tissue, histiocytes, fibroblast or Schwann cells. In the larynx, pseudoepitheliomatous hyperplasia may predispose to confuse the GCT with squamous cell carcinoma.

The most common region of GCT is in the head and neck, accounting for approximately 30 to 50 per cent of all lesions. The larynx is relatively an uncommon location for these tumours, accounting for approximately three to 10 per cent of the reported cases.

Affected patients typically present with persistent hoarseness, stridor, haemoptysis, dysphagia, and otalgia, but the tumour may be asymptomatic and be discovered only incidentally during a routine examination. Complete excision with an attempt to maintain normal stuctures generally results in cure.

We present the case of a patient with typical features of a GCT of the larynx. The gross appearance, histopathology and brief discussion of the current literature are also presented.

Key words: Larynx; Laryngeal neoplasms; Granuloma, laryngeal

Introduction

The granular cell tumour (GCT) is an uncommon lesion. First described as granular cell myoblastoma, these lesions were originally thought to arise from skeletal muscle cells or their precursors. However, the relationship between granular cells and peripheral nerves has now been identified. As a result, this tumour has been variously termed granular cell neuroma or granular cell neurofibroma. It has also been called granular cell schwannoma based on a Schwann cell derivation; but some authors believe that the tumour arises from undifferentiated mesenchymal cells, histiocytes, or neuroectodermal tissue.

Case report

A 40-year-old African-American female, a church singer, presented to her local physician with a six-month history of hoarseness, gastroesophageal reflux symptoms and mild left-side throat pain. By report, a posteriorly located left true vocal fold lesion was identified and removed endoscopically. The pathology examination revealed a benign granular cell tumour of the larynx. However, the recurrence of symptoms, now accompanied by mild odynophagia, developed post-operatively, prompting her referral to the University of Iowa for further evaluation and treatment.

Videoendoscopy revealed a smooth grey mass, involving the posterior third of the true left vocal fold (Figure 1). There was no cervical lymphadenopathy and the rest of the head and neck examination was negative.

Microscopic direct laryngoscopy was performed, with deep excision of the tumour. During surgery, it was observed that this mass was superficially infiltrating the underlying tissue. Post-operative histopathological examination, including S-100 immunohistochemistry staining revealed a benign GCT (Figures 2, 3). Although gross tumour removal was completely effected, microscopically extension was seen at the margin.

The patient presented normal post-operative videostroboscopy and recordings on computer analysed voice protocol (Kay labs, CSL, Computed Speech Laboratory system) were also normal. Although wider excision was offered, in view of the positive margins, the patient decided to defer any other procedure to the future.

Comment

GCT can be classified into two distinct subtypes based on clinical presentation: The rare congenital epulis (gingival GCT of infancy) (Morrison *et al.*, 1987; Fliss *et al.*, 1989), and the more common 'non infantile' GCT. Histologically, the types are indistinguishable. This tumour has an equal male-female presentation ratio (Noonan *et al.*, 1979) and some authors believe that it occurs more frequently in black people (63 per cent) (Frable and Fischer, 1976). It usually presents between the third and sixth decade of life (Noonan *et al.*, 1979). The most common region of GCT is in the head and neck, accounting for approximately 30 per cent to 50 per cent of all lesions (Thawley and Ogura, 1974), with the tongue as the single most common site of origin (Kenefick, 1978).

Multiple lesions in different sites of the body have been reported in approximately 10 per cent of patients overall, and the incidence is higher if the tumour is in the

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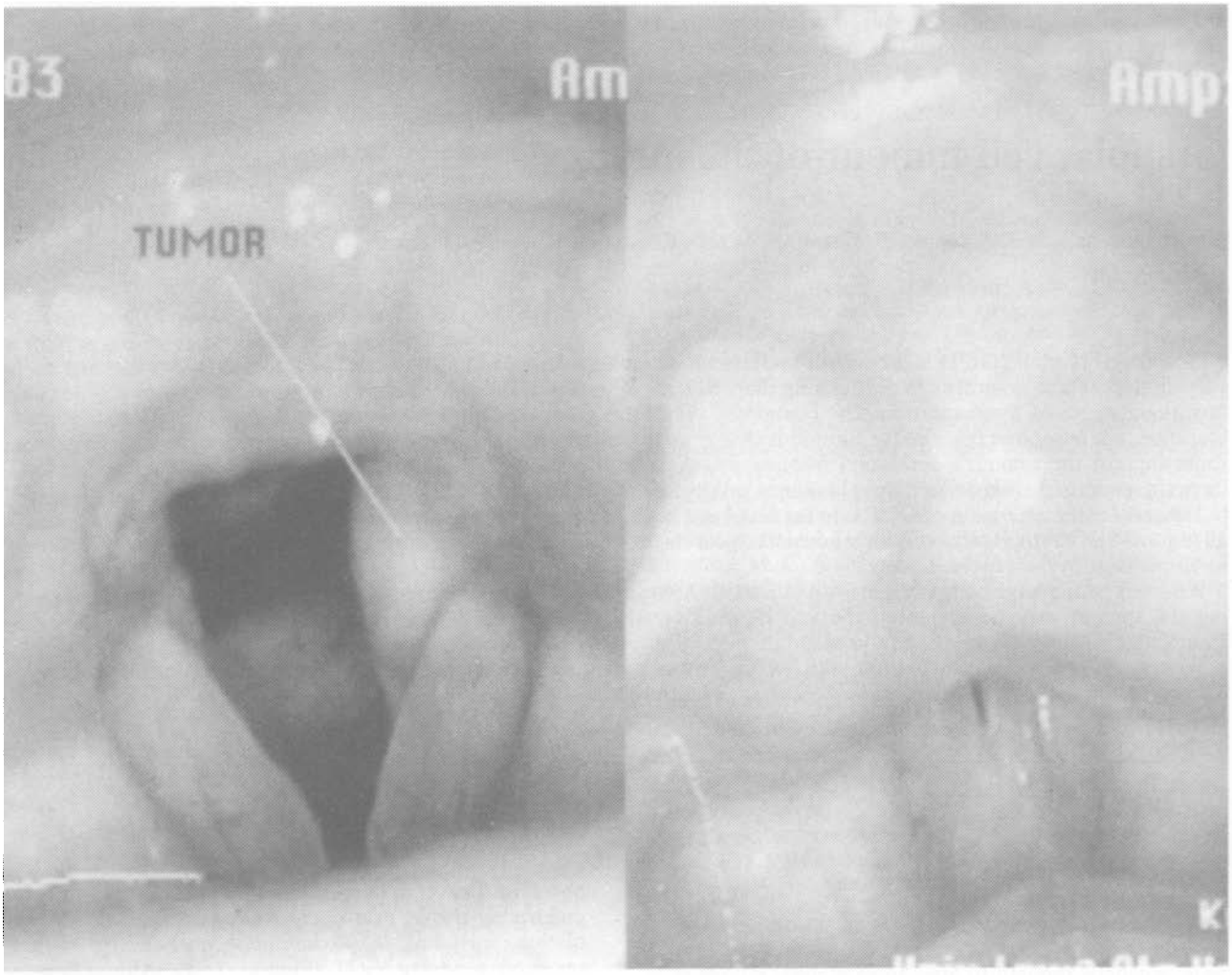

FIG. 1
Direct laryngoscopy exhibited an irregular greyish-white nodular mass, involving the posterior third of the true left vocal fold.

respiratory tract. The larynx is a relatively uncommon location for these tumours, accounting for 150 reported cases (Compagno *et al.*, 1975). The majority of tumours arise from the posterior aspect of the true vocal folds. Approximately half of these extend into the subglottis. Affected patients typically present with persistent hoarseness, stridor, haemoptysis, dysphagia, and otalgia, but the tumour may be nonsymptomatic and be discovered only incidentally during a routine examination. The diagnosis is usually made by histological examination from the tumour specimen by fine needle aspiration, frozen section, electron-microscopy, and immunohistochemistry. The gross appearance of the GCT is a greyish-yellow mass, usually smooth but firm, sessile or polypoidal, well circumscribed, and covered with mucosa. The tumour is firm to the touch, and the mucosa is usually intact, typically infiltrates into the surrounding structures, and there is no distinct capsule.

Benign granular cell tumours are neoplasms with a distinctive histological appearance. Classically, they are poorly circumscribed and consist of single and clustered rounded or polygonal cells with small, central, bland-appearing nuclei, typically hyperchromatic, although a mild degree of nuclear pleomorphism may be present. These tumours have an abundant eosinophilic cytoplasm filled with granules of varying sizes (Noonan *et al.*, 1979).

These granules are the defining characteristic of the GCT and are believed to represent lysosomes in varying stages of fragmentation. Often, degenerating cellular elements can be seen within the vesicles on ultrastructural examination, causing periodic acid-Schiff (PAS) possessiveness and reacting with Sudan black. Using electron-microscopy, Mittal concluded that the granules were formed by infoldings of degenerating cell membrane (Mittal, 1988). Angulate-body cells, resembling fibroblasts, are commonly found in association with granular cells, usually at the periphery of the tumour.

In differential diagnosis we must point out that a significant feature of the noninfantile GCTs is the association with pseudoepitheliomatous hyperplasia, which is present in about 50 to 65 per cent of cases. This characteristic is most apparent in the larynx and may be confused with a squamous cell carcinoma if the underlying GCT is not appreciated.

To date all reported cases of laryngeal granular cell tumours have been histologically benign. The overall incidence of malignancy is three per cent for those with extralaryngeal presentation (Compagno *et al.*, 1975). Thawley and Ogura stated that it should probably be axiomatic that squamous cell carcinoma should never be diagnosed when GCT is present (Thawley and Ogura, 1974).

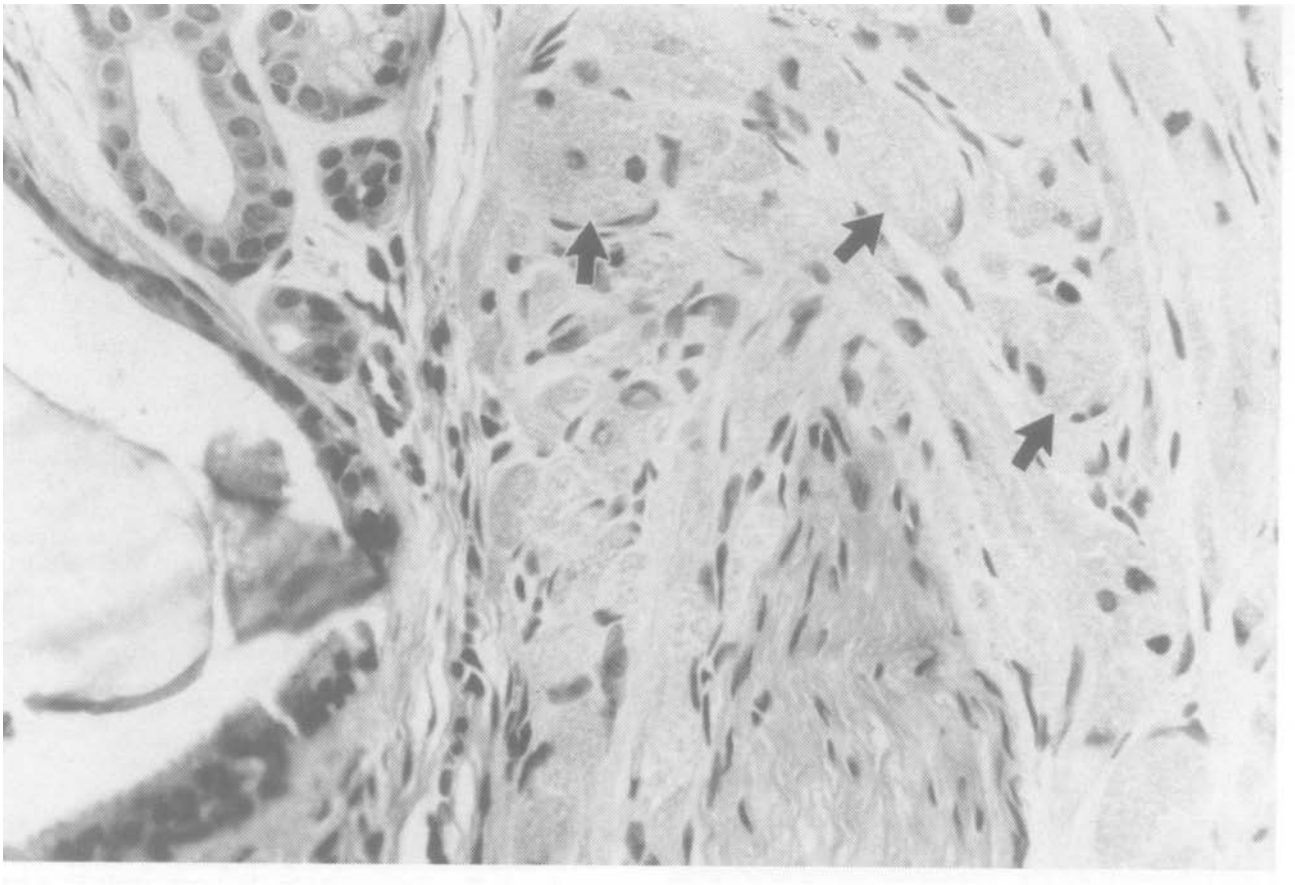

FIG. 2

Photomicrograph, exhibiting nonencapsulated proliferation of granular cells, (arrows), distributed in small clusters. Some of these cells surrounded and infiltrated small nerve twigs. The cells have a predominantly elongated or spindle shape, the nuclei are hyperchromatic, but only small nucleoli were seen (H & E; × 500).

Most investigators consider the lesions to be true neoplasms, but others have suggested that they represent degenerative changes from viral infection or an abnormal metabolic process (Troncoso *et al.*, 1988). Tumour cells may interdigitate with adjacent fibrous stroma, and there can be poor delineation at the periphery of the lesions, giving the impression of invasiveness.

The possible neurogenic origin is based on close association of these lesions with nervous tissue. It has been supported by the finding of neurofilaments and neurotubules in some GCT, as well as the sporadic occurrence of GCT in cranial, autonomic, and peripheral nerves. It should be mentioned that the occurrence of a flattened layer of cells with a continuous basal lamina resemble perineurium around tumour cells (Buley *et al.*, 1988). Schwann cells are capable of phagocytosis, which accounts for the finding of autophagocytic vacuoles. Immunohistochemical staining for the S-100 protein (Dhillon and Rode, 1983; Buley *et al.*, 1988) neuron-specific enolase and Leu-7 (NHK 1), also has provided further support for this theory (Abenoza and Sibley, 1987; Mazur *et al.*, 1990).

The histiocytic theory is supported by the finding of autophagocytic vacuoles and positive immunohistochemical staining in some tumours for α-1 antichymotrypsin and α-1 antitrypsin. Some believe that the granular cells are histiocytes storing altered myelin.

Recently, the myelomonocytic antigen CD68 has been demonstrated to be present in a small number of granular cell tumours. The neoplastic cells of the granular cell tumours and schwannomas strongly stained for CD68, whereas none of the neurofibromas, ganglioneuromas, ganglioneuroblastomas, or carcinoid tumours contained CD68 positive tumour cells (Smith *et al.*, 1991).

Complete excision with an attempt to maintain normal structures generally results in cure. Endoscopic removal, most often with the use of a laser, has been found to be an acceptable approach for small tumours of the airway. However, larger tumours may require laryngofissure or conservative resection. The recurrence rate in large series has been reported to be about eight per cent, estimating that all the recurrences followed resection with positive margins. However, the presence of a positive margin is not an absolute predictor of recurrence, and, in fact, the majority of tumours with positive margins do not recur (Kenefick, 1978). Radiation therapy has no proven role in the treatment of GCT.

In summary GCT of the larynx is an uncommon benign mass which requires a high index of suspicion and histological confirmation. The granules in the cytoplasm of the cells are infoldings of degenerating cell membranes. Pseudoepitheliomatous hyperplasia may be confused with squamous cell carcinoma. Therefore, immunohistochemistry and/or electron-microscopy should be performed to precise the peculiarities of the tumour. Complete excision with an attempt to maintain normal structures generally results in cure.

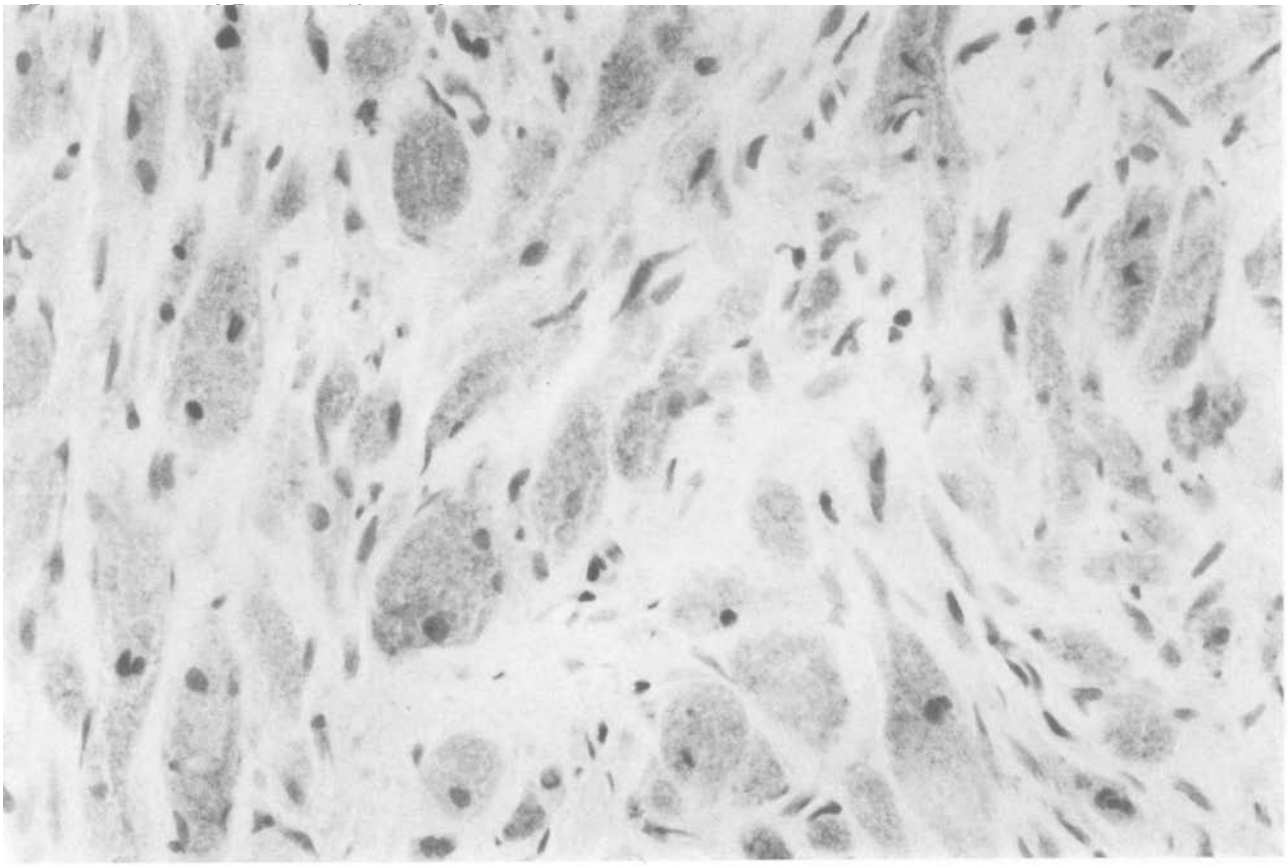

FIG. 3
S-100 immunostaining shows positive granular cells possessiveness, denoting its neuroectodermal origin (H & E; × 350).

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