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Pathology in Focus

Lipomas of the larynx and hypopharynx: a review of the literature with the addition of three new cases

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Abstract
Lipomas of the larynx and hypopharynx are uncommon mesenchymal neoplasms. This report discusses the clinical and pathological features of three cases of laryngeal and hypopharyngeal lipomas. Two of the cases occurred in females and one in a male. The ages of the patients were 28, 51 and 51 years respectively. Two of the cases involved the supraglottic larynx (left arytenoid and left vestibular fold); the third involved the pyriform sinus. Symptoms included airway obstruction, dysphagia, throat discomfort, a sensation of excessive secretions in the throat and an increase in snoring. The complaints occurred over periods ranging from several months to one year in duration. Clinically, a polypoid lesion described as yellow in appearance was seen. Histologically, the tumours were composed of mature adipocytes without evidence of pleomorphism, lipoblasts or infiltrative growth. Surgery was the treatment of choice and included simple but complete excision in two of the cases. In these two cases, surgery proved curative with follow-up periods of 11 and seven years, respectively. In one case, the initial tumour was removed in pieces. This lesion recurred 15 years after the initial resection and was totally excised at that time. This patient has been free of tumour for more than five years.

Key words: Lipoma; Liposarcoma; Larynx; Hypopharynx

Introduction

Primary mesenchymal tumours of the larynx and hypopharynx are uncommon tumours and among the primary laryngeal mesenchymal tumours, lipogenic neoplasms are rare (Barnes and Ferlito, 1993). Lipomas of the larynx and hypopharynx have been reported to represent approximately 0.6 per cent of benign tumours of the larynx (Jones *et al.*, 1984; Barnes and Ferlito, 1993). Zakrzewski (1965) reported one case of laryngeal lipoma and reviewed the world literature. In 1965, Zakrzewski cited the existence of 70 cases of lipomas in the region of the larynx. To date, including those cases reported following the study by Zakrzewski (1965) there are approximately 80 cases of laryngeal lipomas reported in the literature (Eagle, 1965; Lacomme and Laporte, 1968; Alekseev, 1969; Batasakis and Fox, 1970; Chizh, 1974; Pahor, 1976; Mansson *et al.*, 1978; O'Callaghan *et al.*, 1981; Remacle *et al.*, 1983; Jesberg, 1982; Chen and Weinberg, 1984; Jones *et al.*, 1984; Diop *et al.*, 1986; Som *et al.*, 1986; Reid *et al.*, 1987; Schrader, 1988; D'Auria *et al.*, 1990; Dinsdale *et al.*, 1990; Daniilidis and Megas, 1991; Ortiz and Weber, 1991; Rozas Aristy *et al.*, 1991; Gutsch *et al.*, 1993; Nonako *et al.*, 1993). This number of lipomas may be artificially high. It should be noted that a diagnosis of laryngeal liposarcoma may require multiple recurrences over the span of many years (Wenig *et al.*, 1990). The reason for this is that the morphological appearance for many of these malignant lesions is bland with only subtle changes suggesting their malignant potential. (Wenig *et al.*, 1990). The histological features diagnostic for malignancy (liposarcoma) may only become apparent in the recurrent neoplasm(s). As such, it is possible that many of the cases diagnosed and published as laryngeal lipomas, may represent low-grade liposarcomas. Thus, the incidence of benign lipogenic tumours (lipomas) of the larynx may be lower than actually reported. It is due to the rarity of these benign neoplasms that this study was undertaken. Emphasis is placed on the clinical and pathological features of these tumours with a discussion on the differentiation from their malignant counterparts.

Materials and methods

A search of the Otolaryngic Tumour Registry at the Armed Forces Institute of Pathology (OTR-AFIP) revealed three cases coded as laryngeal or hypopharyngeal lipoma. Haematoxylin and eosin stained slides were available in all cases. Clinical follow-up was obtained in all three cases. There were no cases of laryngeal or hypopharyngeal hibernomas identified.

Clinical features (Table I)

The three cases reported in this study included two females and one male. The ages of the patients were 28, 51, and 51 years respectively. Two of the cases involved the

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TABLE I
LIPOMAS OF THE LARYNX AND HYPOPHARYNX: CLINICAL FEATURES

Case	Age (years)	Sex	Symptoms	Clinical findings	Treatment and follow-up
1	51	M	Sensation of excessive secretions in throat and increased snoring of one year duration	Cystic mass (2.5 × 3.0 cm) in the pyriform sinus	Complete excision by DSM; free of disease over a 11-year period
2	28	F	Airway obstruction; symptoms began shortly after prior intubation for an unrelated problem	Yellow polypoid mass (0.6 0.8 cm) along the left vocal fold	Complete excision by DSM; free of disease over a year-year period
3	51;66*	F	Throat discomfort (bone in my throat); recurrent tumour associated with dysphagia	Cystic yellow lesion (2–3 cm) identified along the left arytenoid**	Primary tumour was removed in pieces by DSM; tumour recurred 15 years later with complete excision at that time by DSM; free-of-disease over a five-year period

*Ages at initial presentation and recurrence, respectively; **represents the appearance of the recurrent tumour; a description of the primary tumour was not available, this tumour was removed in 'pieces'; DSM–direct suspension microlaryngoscopy.

supraglottic larynx including the left arytenoid and left vestibular fold. The third case involved the pyriform sinus. The patient complaints included airway obstruction, dysphagia, throat discomfort described as a 'bone in my throat', a sensation of excessive secretions in the throat and an increase in snoring. These complaints occurred over periods ranging from several months to one year in duration. One patient stated that her symptoms began shortly after intubation for an unrelated medical problem. There was no link to any potential aetiological factors or agents such as excessive alcohol use, tobacco smoking, occupational or environmental exposure.

The endoscopic evaluation revealed a polypoid mass described as, soft to rubbery to cystic, and yellow in appearance. The tumours measured from 0.6 to 3.0 cm in greatest dimension. The endoscopic impression was that of a benign fatty tumour.

The treatment for all cases was by endoscopic removal. In two of the patients (*Cases 1 and 2*), complete surgical excision was accomplished resulting in the cure of the patients' tumour with follow-up periods of 11 and seven years, respectively. The initial tumour in the remaining patient (*Case 3*) was removed 'in pieces' via microlaryngoscopical techniques. Fifteen years following this excision, the patient's laryngeal tumour recurred. At that time, conservative but complete surgical excision was performed by transoral laryngoscopic suspension. This patient has been free of tumour over a five-year period since excision of the recurrent tumour.

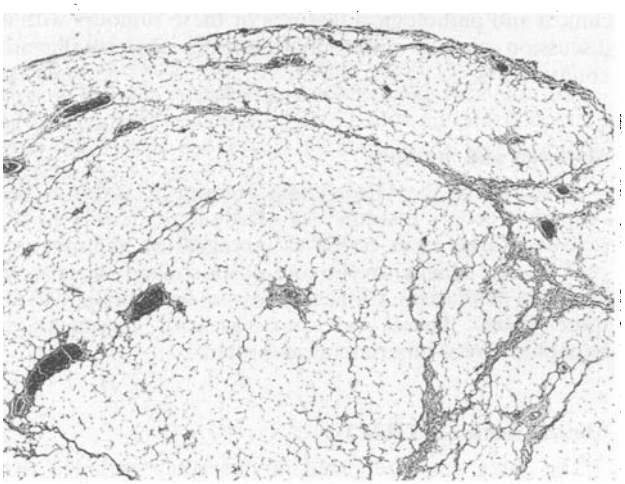

FIG. 1.
Laryngeal lipoma appearing as an encapsulated polypoid mass composed of mature fat. Scattered vascular spaces and thin fibrous strands coursing through the specimen can be seen.

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Histologically, the tumours were partly or completely encapsulated (Figure 1). The tumours were composed of uniform-appearing mature fat cells varying slightly in size and shape (Figure 2). A compressed but identifiable vascular framework could be seen between the distended adipocytes. Additional findings included the presence of spindle-shaped cells focally seen in one of the cases (Figure 3), and a myxoid stroma which was focally identified in the two other cases (Figure 3). The tumours did not demonstrate evidence of infiltration, or the presence of atypical adipocytes characterized by variability in size and shape with hyperchromatic nuceli. Lipoblasts were not present. The histology of the recurrent tumour in *Case 3* was identical to that of the primary tumour.

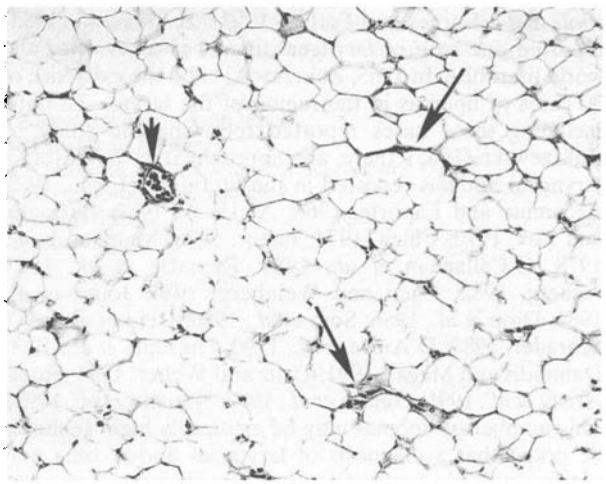

FIG. 2.
The cells of the lipoma are uniform, varying little in size and shape, and are without evidence of cellular atypia. The distended adipocytes compress the vascular framework (arrows) although an identifiable vascular space containing erythrocytes is seen (arrowhead).

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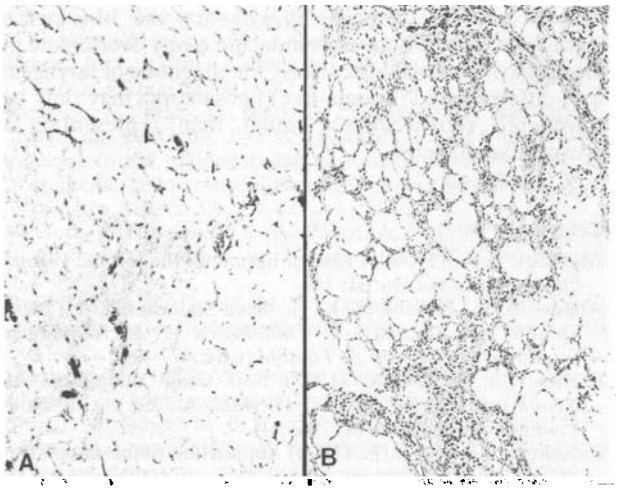

FIG. 3.

Histological variants of (laryngeal) lipoma include: (A) Lipoma with an associated myxoid stromal component which is seen along the left hand side; (B) lipoma with an associated spindle cell component. Both cases lack histological features which may be suggestive of a more aggressive lipogenic neoplasm.

Special studies such as histochemistry, immunohistochemistry or electron microscopy were unnecessary in the diagnosis or differential diagnosis of these tumours.

Discussion

Benign lipogenic neoplasms include lipomas which are benign tumours of mature adipocytes (white fat) and hibernomas which are benign tumours of brown fat ('lipoma' of brown fat). Of these two types of benign lipogenic neoplasms, lipomas are the most common type of benign lipomatous tumour identified throughout the body (Enzinger and Weiss, 1988) including those related to the larynx and hypopharynx (Barnes and Ferlito, 1993). Lipomas arise from the mature white fat cell (adipocyte, lipocyte) which is a mesodermally-derived cell. Adipose tissue is a normal component of the intrinsic larynx particularly in the area of the vestibular fold. In a pure anatomical sense, the pyriform sinus is part of the hypopharynx but has been referred to as the laryngeal portion of the pharynx (Soule, 1968). The clinical, pathological and biological parameters of hypopharyngeal (pyriform sinus) lipogenic tumours are virtually identical to those originating from the larynx. As such, the lipogenic tumours of the pyriform sinus are included within this study.

Lipomas of the larynx and hypopharynx primarily affect men and are tumours of adult life (Barnes and Ferlito, 1993). At the time of diagnosis, most patients are in their sixth decade of life or older. Two cases have been described in juveniles aged eight and 13 years, respectively (Zakrzewski, 1965; Dinsdale *et al.*, 1990). Laryngeal lipomas generally are solitary arising in the supraglottic larynx or project into the larynx from a hypopharyngeal mass. The more common supraglottic sites of involvement include the aryepiglottic fold, vestibular fold and epiglottis. At least one case report documents a subglottic lipoma (Zakrzewski, 1956). Symptoms include dysphagia, dyspnoea, acute airway obstruction, hoarseness, dysphonia, other voice changes, and a lump in the throat. The duration of symptoms may vary from a few months to several years. Rare cases have been reported in association with symmetrical lipomatosis (Madelung's disease or Launois-Bensaude syndrome) (Moretti and Miller, 1973).

The endoscopic appearance of laryngeal and hypopharyngeal lipomas varies from a submucosal mass to a polypoid intraluminal projection. Deeply situated tumours may require equally deep biopsy sampling in order to establish a diagnosis. The diagnosis of a lipogenic tumour of the larynx and hypopharynx is greatly facilitated by radiographical imaging (Remacle *et al.* 1983; Som *et al.*, 1986; Schrader, 1988; Dinsdale *et al.*, 1990; Ortiz and Weber, 1991). These studies demonstrate that adipose tissue typically has a low attenuation value on CT scan and is the only soft tissue with a density less than water (zero or negative Hounsfield units). In this way, the CT scan not only reveals the extent of the tumour but also establishes the lipomatous nature of these tumours.

The macroscopic appearance of laryngeal and hypopharyngeal lipomas includes a sessile to pedunculated, smooth to lobulated, well-delineated or encapsulated, light coloured solitary mass. The size of the lesion varies from deep seated (submucosal) lesions measuring a few millimetres to large polypoid lesions measuring up to 6.0 cm in greatest dimension. Histologically, lipomas are encapulated tumours composed of mature fat cells. The cells are uniform varying slightly in size and shape. Lipomas are richly vascularized but the vascular framework may be difficult to appreciate due to compression by the distended adipocytes. Secondary changes which can be seen include haemorrhage, calcification, cyst formation, fat necrosis, and infarction. Metaplastic components such as cartilage and bone may be seen in association with lipogenic tumours of all sites. Ultrastructurally, lipomas are composed of a single, central lipid vacuole with a peripherally situated nucleus and cytoplasm (Napolitano, 1963). The nuclei have prominent nucleoli and peripheral margination of the chromatin. The cytoplasm contains round to oval mitochondria, ribosomes, and smooth membrane-bound vesicles. Basal lamina may be seen enveloping the cells and numerous pinocytotic vesicles can be identified. In general, a diagnosis of lipoma does not require histochemical, immunohistochemical or electron microscopic evaluation. The myxoid lipomas will stain with alcian blue which is removed by prior treatment with hyaluronidase. Adipocytes will demonstate reactivity with S100 protein. However, the spindle cells of the spindle cell lipoma have been reported to be non-reactive with S100 protein (Fletcher and Martin-Bates, 1987).

Alteration of the usual type of lipomas by an admixture of various mesenchymal elements forming an intrinsic part of the tumour include myxolipoma and fibrolipoma. Both these types of lipoma have been reported in the larynx and hypopharynx (Jesberg, 1982; Dinsdale *et al.*, 1990; Rozas Aristy *et al.*, 1991). Myxolipomas display a prominent associated mucoid substance deposition. Fibrolipomas have a fibrous connective tissue component. Intramuscular lipomas, also referred to as infiltrating lipomas, have been reported in the larynx (Chen and Weinberg, 1984). These lipomas are characterized by the presence of mature adipocytes infiltrating into muscle. Morphological features possibly suggesting a malignant lipogenic tumour such as lipoblasts or atypical appearing adipocytes are not present.

Variants of lipoma include spindle cell lipoma, angiolipoma, pleomorphic lipoma, angiomyolipoma and benign lipoblastoma. Of these, only the spindle cell lipoma has been reported in the larynx (Nonako *et al.*, 1993). The spindle cell lipoma is characterized by mature adipocytes admixed with uniform, small spindle cells and eosinophilic-appearing collagen bundles set in a myxoid matrix with a vascular pattern varying from inconspicuous to prominent. Mast cells can be seen in association with the spindle cells. The spindle cells of the spindle cell lipoma demonstrate ultrastructural features similar to fibroblasts including

elongated nuclei, copious rough endoplasmic reticulum, microfilaments, ovoid mitochondria, and the presence collagen fibrils in the extracellular space (Enzinger and Harvey, 1975; Angervall *et al.*, 1976; Fletcher and Martin-Bates, 1987; Nonako *et al.*, 1993). One to several intracytoplasmic spherical osmiophilic lipid droplets can be seen. The basal lamina is ill-formed or absent.

The diagnosis of a lipoma as well as its variants does not usually present difficulties. However, in the larynx and hypopharynx, the principal entity to differentiate from a lipoma is a well-differentiated (lipoma-like) liposarcoma. Lipomas are encapsulated, are composed of uniform adipocytes lacking variation in size and shape, and do not have atypical lipocytes nor lipoblasts. In contrast, liposarcomas are infiltrative, have cytological evidence of pleomorphism and atypia, and contain lipoblasts. Further, lipomas will not recur following complete surgical extirpation whereas the well-differentiated liposarcomas of the larynx typically are associated with one or more recurrent tumours (Wenig *et al.*, 1990). Along these lines, *Case 3* reported in this study recurred 15 years following the initial surgical procedure. However, in spite of the recurrence, the histology of the recurrent tumour was identical to that of the primary neoplasm and did not demonstrate the criteria necessary for a diagnosis of liposarcoma (Wenig *et al*, 1990). The initial surgical procedure included removal of the laryngeal tumour 'in pieces'. Therefore, the recurrence of this tumour is directly related to inadequate surgical excision rather than representing a low-grade liposarcoma.

Myxoid lipomas of the larynx may be confused with a myxoid type of vocal fold polyp or the unusually occurring laryngeal myxoma. In contrast to these lesions, the myxoid lipoma demonstrates transition areas between fat and the myxoid foci. Myxoid liposarcomas can be identified in the larynx (Wenig *et al.*, 1990). However, myxoid liposarcomas have lipoblasts as well as a characteristic plexiform vascular pattern. The spindle cell lipoma may demonstrate prominent cellularity possibly resembling a variety of spindle cell neoplasms (benign or malignant) occurring in the larynx. However, the histological features of spindle cell lipomas should readily separate this tumour from other spindle cell neoplasms which demonstrate their own unique histomorphological patterns, cytomorphology and/or immunohistochemical antigenic profile.

Surgery is the treatment of choice for laryngeal and hypopharyngeal lipomas of all histological types and should prove to be curative. Small tumours can be removed endoscopically. Large tumours may require an external approach (lateral pharyngotomy, laryngofissure, subhyoid pharyngotomy). Regardless of the type of surgery employed, the surgical removal of the neoplasm should be complete in order to prevent a possible recurrence of the tumour. Given the tendency of lipomas to be circumscribed or encapsulated, complete surgical excision should be readily attainable. Recurrence of a purported laryngeal lipoma may be indicative of a well-differentiated liposarcoma. However, recurrence in and of itself is not an indication of malignant potential but may relate to inadequate surgical management. Histological evidence is required for a diagnosis of liposarcoma.

Conclusion

Laryngeal and hypopharyngeal lipomas are exceedingly rare tumours. Less than 90 cases are reported in the world literature. These tumours are benign and are cured by complete (conservative) surgical excision. Recurrence of the tumour may be the result of inadequate surgical excision. However, recurrent laryngeal lipomas may be indicative of a low-grade liposarcoma, the histological features of which often are subtle and easily overlooked in the surgical material. Therefore, the diagnosis of laryngeal well-differentiated (lipoma-like) liposarcoma may only be considered retrospectively rather than representing a prospective diagnosis.

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