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Rhabdomyoma of the larynx: a review of the literature with a summary of previously described cases of rhabdomyoma of the larynx and a report of a new case

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Abstract

A review of extracardial rhabdomyomas of the larynx reported in the literature is presented. A new case is added (the largest described yet). The diagnosis was based on routine histological and immunohistological staining, and electron microscopy. The extracardial rhabdomyomas were divided into three types according to histopathological findings: (i) adult; (ii) foetal cellular type; and (iii) foetal myxoid. There are 23 well-documented cases (including this case) of extracardial rhabdomyomas of the larynx; 15 of the adult type, four of the foetal myxoid type and four of the foetal cellular type. The differential diagnosis and the requisite diagnostic procedure is discussed. The tumour is benign. The treatment is surgical excision. Although rare, its existence should be kept in mind in the differential diagnosis of laryngeal tumours.

Key words: Rhabdomyoma; Larynx; Laryngeal neoplasms

Introduction

The term rhabdomyoma was introduced by Zenker (1864) to indicate a benign tumour showing skeletal muscle cells with varying degrees of differentiation and maturity (Boedts and Mestdagh; 1979; Modlin, 1982). In the literature prior to 1955 (Clime *et al.*, 1963) there has been some confusion about the diagnosis of a rhabdomyoma. It was considered a general diagnostic term for such tumours as granular cell myoblastoma, alveolar soft tissue sarcoma, and various neoplasms containing striated muscle elements, e.g. sarcoma botryoides, embryonal rhabdomyosarcoma, teratoma, gonadal tumours, nephroblastoma and mesenchymoma (Di Sant'Agnese and Knowles, 1980). The current definition of rhabdomyoma is a benign neoplasm of striated muscle tissue, consisting usually of polygonal, frequently vacuolated (glycogen containing) cells with a fine granular, deeply acidophilic cytoplasm resembling myofibrils cut in cross section. Cross striations are usually seen within the tumour cells (Enzinger and Weiss, 1983; Hyams *et al.*, 1988). Rhabdomyomas are considerably less common than rhabdomyosarcomas, and amount to no more than two per cent of all striated muscle tumours (Enzinger and Weiss, 1983). Rhabdomyomas are more frequent in the myocardium than in striated muscles. Fifty per cent of rhabdomyomas of the heart are associated with a hamartoma complex, including sebaceous adenomas, tuberous sclerosis, and hamartomas of the kidney and other organs. It is controversial whether these cardiac lesions are neoplastic tumours or the result of aberrant tissue development and therefore should be regarded as hamartomas (Enzinger and Weiss, 1983).

The rare extracardial rhabdomyomas are true neoplasms, and occur unrelated to other pathological manifestations (Boedts and Mestdagh, 1979; Enzinger and Weiss, 1983). Extracardial rhabdomyomas are most frequently found in muscles derived from the pharyngeal arches and 70 per cent of extracardial rhabdomyomas occur in the head and neck region. Most of those which occur outside this region are usually found in the female lower genital tract. There are only a few case reports describing extracardial rhabdomyomas from e.g. the mediastinum, the walls of the stomach and a few in the thigh (Eusebi *et al.*, 1988).

Among rhabdomyomas, three clinically and morphologically different types can be distinguished, which are all usually solitary, slowly growing lesions: (i) adult which is restricted to the head and neck area of adult persons. Characteristically it has a well-defined margin and is composed of sheets of closely packed, large, round, cells with granular eosinophilic cytoplasm, some containing cross striations; (ii) foetal cellular type which is an exceedingly rare lesion that may affect the head and neck region in elderly men, but prevails in children younger than four years of age. They are usually poorly defined and composed of immature, generally elongated spindle-shaped skeletal muscle elements in varying stages of differentiation with few mature cells; (iii) foetal myxoid type which is a rare tumour-like polypoidal mass with abundant loose, oedematous and myxoid stroma. The tumour may be found in the vagina and vulva of middle-aged women, and has in these cases been called a genital type of extracardial rhabdomyoma (Dehner *et al.*, 1972; Enzinger and Weiss, 1983; Helliwell *et al.*, 1988), or it is found in the head and neck region in children, especially in the post-auricular region (Di Sant'Agnese and Knowles, 1980; Konrad *et al.*, 1982).

By 1988 115 extracardial rhabdomyomas had been reported (Helliwell *et al.*, 1988), 87 of which occurred in the head and neck region. In the present review of 23 cases of extracardial rhabdomyomas in the larynx reported in the literature, 15 cases were of the adult type including this case, three of which were multifocal. Four cases were foetal cellular type and four foetal myxoid. Three of the cases reported have had a local recurrence.

Case report

A 51-year-old male presented with a history of slowly increasing hoarseness over one year. Apart from snoring for the last six months there were no other clinical symptoms. In the Depart-

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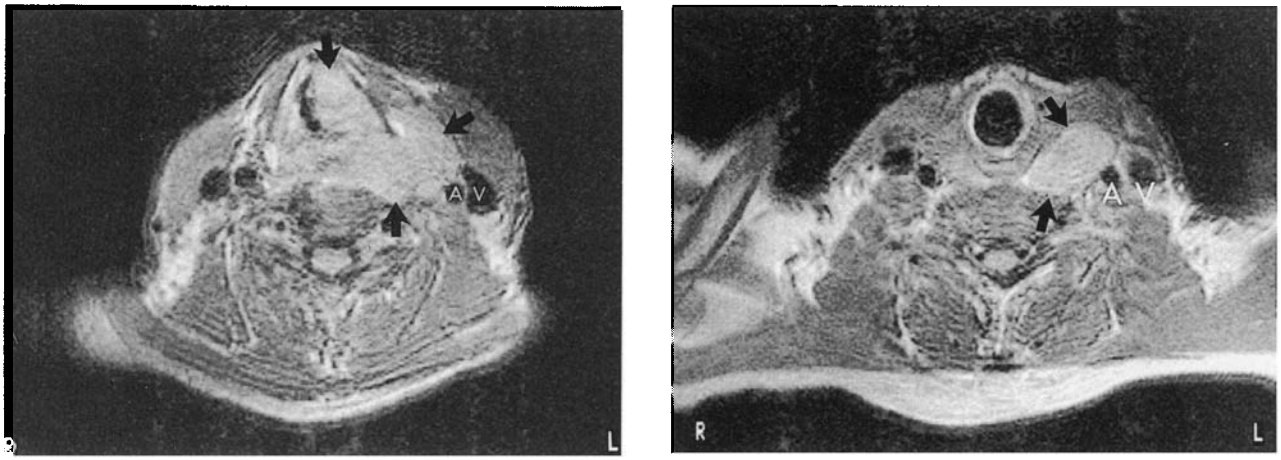

(a) (b)

FIG. 1

Axial MRI scans of the neck showing an adult rhabdomyoma of the larynx with a carniocaudal extension of 7.5 cm and a cross diameter of 4 cm: (a) at a level 1 cm over the vocal fold region; (b) at a level over the jugulum. The tumour is well delimited and noninvasive. It originates from the left ventricular fold with an extension through the cricothyroid membrane and behind the thyroid lamina into the parapharyngeal space (arrowed), displacing the left internal jugular vein (V) and the left carotid artery (A).

ment of Oto-Rhino-Laryngology at Vejle Hospital fibreoptic laryngoscopy showed the left ventricular fold protruding to the midline concealing the left vocal fold. At intonation the right vocal fold moved normally. Neck examination revealed no lymphadenopathy and an X-ray of the chest was normal. The results of routine laboratory tests were unremarkable.

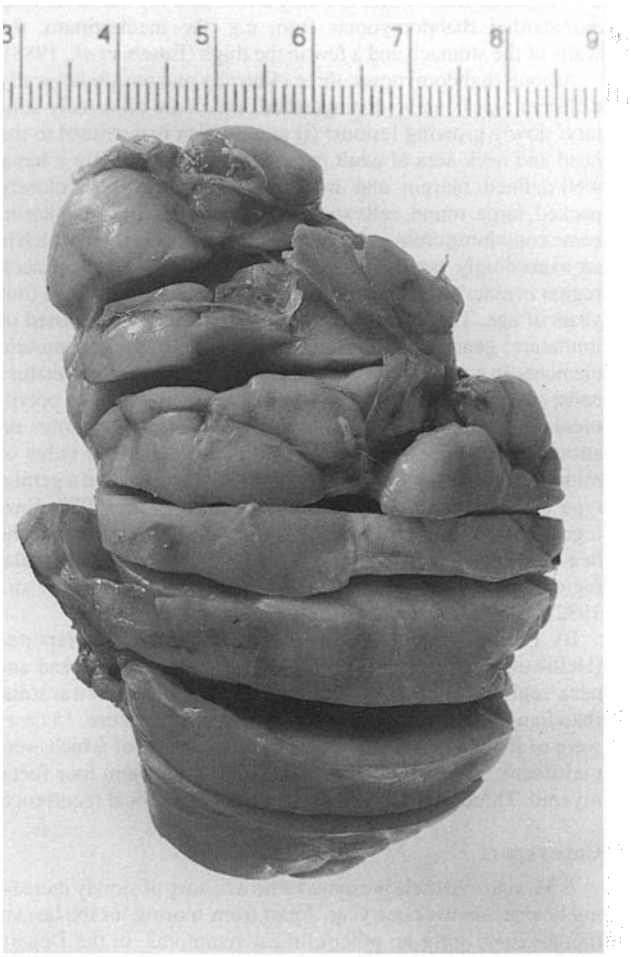

FIG. 2

Photograph of the laryngeal adult rhabdomyoma – a pink-brown well circumscribed rubbery tumour (7 × 4 × 2.5 cm).

Direct laryngoscopy under general anaesthesia was performed, demonstrating a large, smooth, submucous tumour in the left ventricular fold and the left laryngeal ventricle. The right side of the larynx was normal. A compact, smooth, mobile, submucosal tumour was found on the posterior wall of hypopharynx. It was removed *in toto* by excision, and the histopathological diagnosis from this tumour was chondroma. Two-thirds of the ventricular fold were extirpated for histological examination. The histopathological diagnosis was an adult type rhabdomyoma. The patient was subsequently transferred for further treatment to the ENT Department at Aarhus University Hospital. MRI scan of the neck demonstrated a tumour mass with a craniocaudal extension of 7.5 cm and a cross diameter of 4 cm (Figure 1). The tumour originated from the left ventricular fold with an extension through the cricothyroid membrane and behind the thyroid lamina into the parapharyngeal space, displacing the internal jugular vein and the left carotid artery. The tumour was well delimited and noninvasive, but in intimate contact with the vessels and the cervical plexus. No lymphadenopathy or destruction of the larynx skeleton was observed. A hemilaryngectomy was performed with radical removal of the tumour. A tracheostomy was performed, and an intralaryngeal stent applied for six weeks. There were no post-operative complications and no evidence of recurrence after one year. The patient has a tracheostomy, his voice is weak, but he is working full time.

Pathological features

The pink-brown, well circumscribed rubbery tumour (Figure 2) measured 7 × 4 × 2.5 cm, and was processed by routine histological methods. Sections were stained with haematoxylin-eosin (H & E), phosphotungstic acid-haematoxylin (PTAH) and immunohistochemical staining for myoglobin, desmin and vimentin. Finally, the tumour was examined by electron microscopy. All examinations showed an adult extracardial rhabdomyoma of the larynx.

Light-microscopical study

The tumour was composed of large polygonal, round or oval, occasionally elongated cells of varying size with abundant, pale, eosinophilic, finely granular cytoplasm. The cytoplasm often

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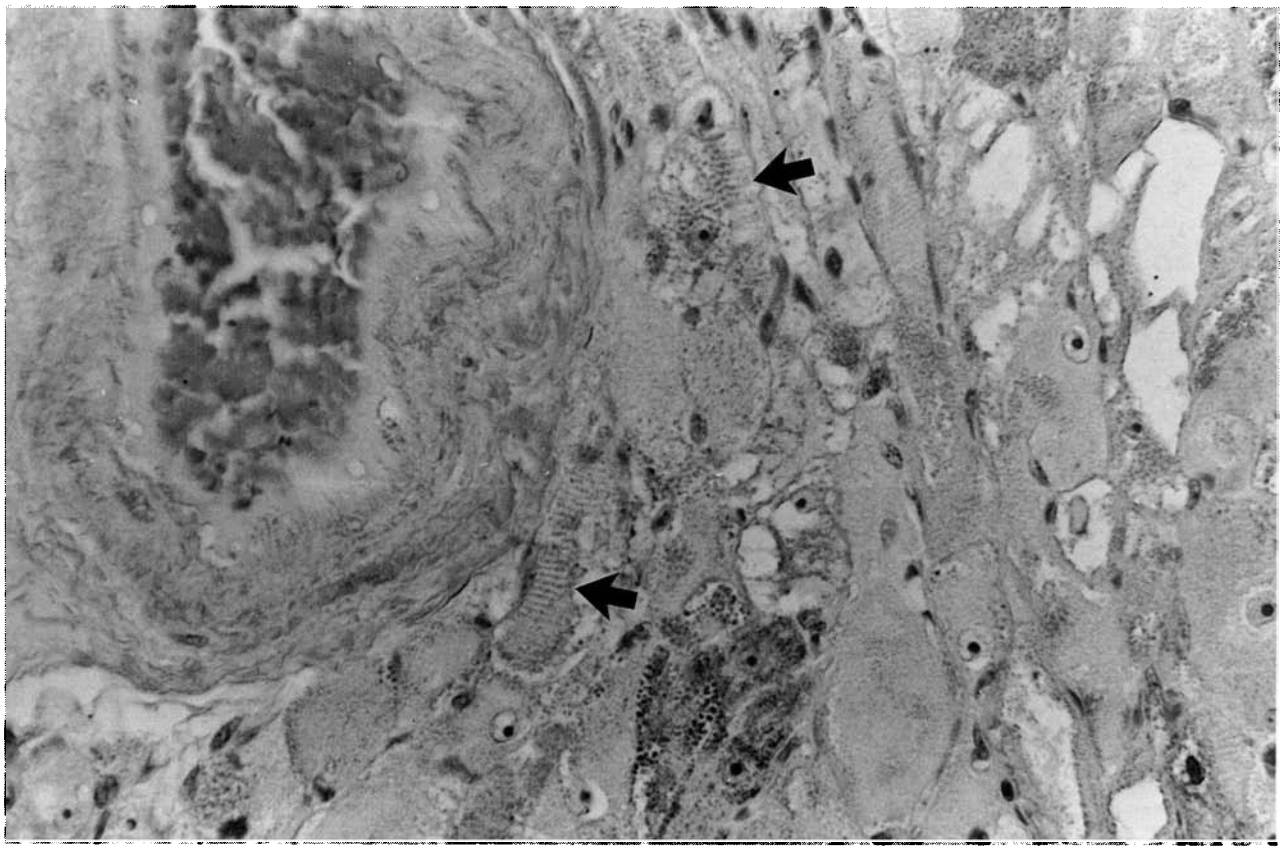

FIG. 3

Photomicrograph of an adult rhabdomyoma of the larynx. The tumour is composed of large, round or oval, sometimes elongated cells. Some cells show cross striations (arrowed). (PTAH × 450).

contained one or more large vacuoles. The nuclei were usually eccentric, round or oval, with a prominent acidophilic nucleolus. Multinucleation with two or three nuclei was frequent. Occasional cells showed distinct cross striations, visible in sections stained with PTAH (Figure 3). Many of the cells were vacuolated as a result of removal of glycogen during processing. Some cells had irregularly arranged basophilic crystal-like, rod-shaped, inclusions. The stroma was scarce, and contained some capillaries. Nuclear polymorphism, hyperchromatism or mitotic figures were absent.

Ultrastructural study

Ultrastructural studies (Figure 4) showed the resemblance to a striated muscle myofibrillar structure, but with a disturbance of the regular myofibril pattern. Hypertrophied Z-bands with thin myofilaments attached formed rod-shaped bodies corresponding to the crystal-like structures seen by light microscopy. Aggregates of myofibrils were scattered at random in the cytoplasm. In occasional cells they were more fully organized, forming parallel arrays producing the light-microscopical appearance of cross striation. Mitochondria were abundant. Glycogen granules were predominant in the more central cells and sometimes present in membrane-bound vacuoles.

Immunocytochemistry study

The tumour stained for myoglobin, desmin and vimentin showed myoglobin, desmin and some muscle lactin in the rhabdomyoblasts. There was no indication of vimentin or smooth muscle lactin in the cells.

Discussion

Rhabdomyomas of the larynx and neck occur in close relationship to the muscles developed from the unsegmented mesoderm, which belongs to the visceral (pharyngeal or branchial) arches, not from myotomes like the rest of the skeletal muscles. The musculature of each arch is supplied by special visceral efferent nerves. This characteristic embryology may explain why extracardial rhabdomyomas found mainly in the head and neck, especially in the larynx (Winther, 1976). The influence of the innervation of these tumours has not been evaluated. Normal myofibres depend on nervous innervation for terminal differentiation and some authors suggest that these tumours might have escaped such influence (Whitten and Benjamin, 1987). Extracardial rhabdomyomas of the larynx described before 1980 are listed by Di Sant'Agnese and Knowles (1980) and also by Granich *et al.*, (1983). Two of the cases listed by Granich and his coworkers are excluded, as their diagnosis is questionable, as pointed out by others authors (Bagby *et al.*, 1976; Kleinsasser and Glanz, 1979). The literature contains 23 well-documented cases of extracardial rhabdomyomas of the larynx (including this case) at present: 15 cases of adult extracardial rhabdomyomas, of which three are multifocal (Tables I and II); four cases of the foetal cellular type (Table III) and four cases of the foetal myxoid type (Table IV).

Epidemiology and symptoms

Extracardial rhabdomyoma, is three times more frequent in men than women. The age of the patients for all three types ranges from 16 to 82 years (mean 52 years), similar to that reported for adult extracardial rhabdomyomas in all regions of the body (Remacle *et al.*, 1983; Helliwell *et al.*, 1988). It seems that the adult and foetal types showed no clinical difference in the larynx, unlike the foetal types found elsewhere in the body, where half of the tumours occurred in children below the age of three years, affecting boys and girls equally (Helliwell *et al.*, 1988).

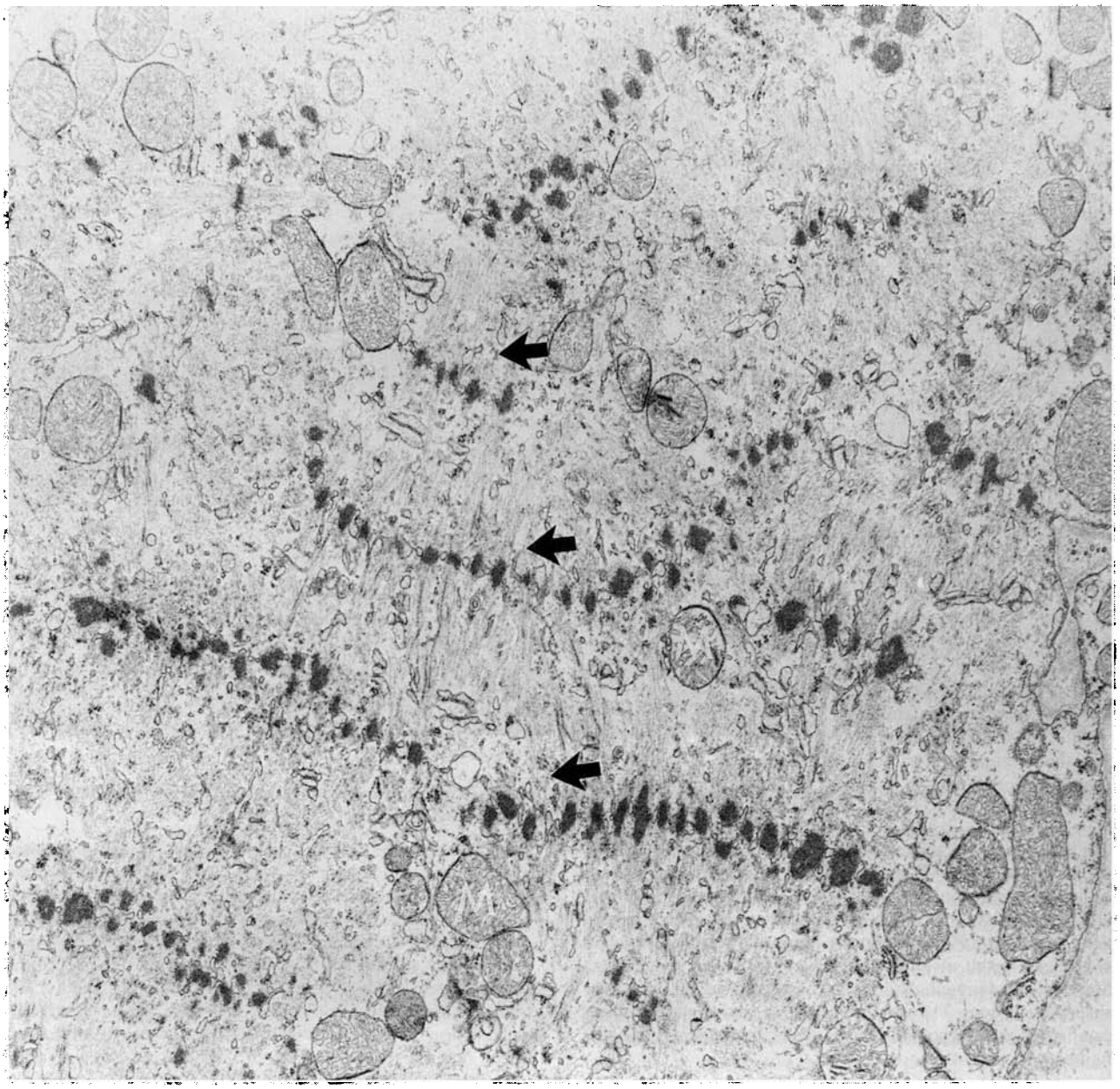

FIG. 4

Electron microscopic photograph of an adult rhabdomyoma of the larynx. Part of a single cell occupies the photographic field. The cell shows a resemblance to striated muscle myofibrillar structure, but here myofibrils are more fully organized, forming parallel arrays producing the appearance of cross striations (arrowed). Note numerous mitochondria (M). (× 41 6000).

The typical symptoms were hoarseness, foreign body sensation and dysphagia, not differing significantly from those caused by other benign neoplasms of the larynx. The duration of the symptoms is usually long, as might be expected of a benign neoplasm, but in one case the patient presented with an acute air passage obstruction (Kleinsasser and Glanz, 1979).

The tumour has been described as an intralaryngeal, often polypoid, mass in the vocal fold region. An extralaryngeal growth, as in our case has not been described previously. The size of the tumours reported ranged from 1 to 3 cm, and the present tumour (7 × 4 × 2.5 cm) is the largest extralaryngeal rhabdomyoma of the larynx described yet. The symptoms, in our case, were remarkably sparse as the tumour grew predominantly in the parapharyngeal space, causing only limited obstruction in the larynx.

Diagnosis

This case is a typical adult extracardial rhabdomyoma of the larynx. The histological diagnosis and the distinction between the three different types is usually easy (Clime *et al.*, 1963; Dehner *et al.*, 1972; Kleinsasser and Glanz, 1979; Di Sant'Agnese and Knowles, 1980; Konrad *et al.*, 1982; Enzinger and Weiss, 1983; Helliwell *et al.*, 1988). In dubious cases, electron microscopy examination may reveal thick and thin filaments with dense bodies, but these structures are present in only a few cells in all types of rhabdomyoma. However, H & E, PTAH and periodic acid Schiff (PAS) stains will enable a distinction to be made in most instances. The subgroup of extracardial rhabdomyomas can further be characterized by immunocytochemical studies staining for myoglobin, desmin and vimentin (Eusebi *et al.*, 1988; Helliwell *et al.*, 1988). Desmin is the most reliable marker for cells with skeletal or smooth muscle differentiation as it is present in both primitive and mature cells. Vimentin is present in primitive but not in mature skeletal muscle and myoglobin is present in much greater quantity in mature than foetal muscle. The foetal rhabdomyoma shows both desmin and vimentin in the primitive cells, and desmin and myo-

TABLE I
SUMMARY OF PUBLISHED CASES OF LARYNGEAL ADULT RHABDOMYOMA

Source	Age (years) Sex	Chief complaint	Duration	Examination results	Treatment	Morphological studies	Comment
Clime *et al.*, (1963)	48 M	Hoarseness	3 months	Cyst-like, (1.0 cm) mass in the right genniue vocal fold	Endoscopic excision	H & E	No recurrence after 1 year
Battifora *et al.*, (1969)	55 M	Hoarseness	3 years	Bulging submucosal (5.0 × 1.0 cm) mass in the left transglottic area	Laryngofissure, local excision	H & E, PAS, PTAH, trichome, EM	No follow-up reported
Bianchi and Muratti (1975)	52 F	Hoarseness	3 years	Submucosal 'pea-sized' nodule in the right false vocal fold	Endoscopic excision	H & E, PAS, PTAH	No recurrence after 7 months
Bagby *et al.*, (1976)	55 M	?	?	Submucosal (1.5 × 1.3 × 2.5 cm) mass in the right false vocal fold	Endoscopic excision	H & E, PTAH, tri-chome' EM	No recurrence after 2 years
Ebbesen *et al.* (1976)	64 F	Hoarseness, foreign-body sensation	6 months	Submucosal (1.5 × 1.0 × 1.0 cm) nodule in right ventricle	Endoscopic excision	H & E, PAS, PTAH, EM	No recurrence after 3 months
Winther (1976)	39 M	Hoarseness	3 years	Submucosal (0.5 × 0.5 × 0.5 cm) mass involving true vocal fold	Endoscopic excision	H & E	Recurrence 3 times in 1 year after repeated local excisions
Boedts and Mestdagh (1979)	76 F	Hoarseness	2 months	0.5 × 0.75 cm mass on left true vocal fold	Endoscopic excision	H & E, PAS, PTAH, trichome	No recurrence after 2 years
Kleinsasser and Glanz (1979)	16 M	Acute airway obstruction	Sudden onset	Tumour in the right transglottic area	Tracheotomy; total laryngectomy	H & E	Initial misdiagnosis of rhabdomyosarcoma
Helliwell *et al.*, (1988)	52 M	Hoarseness	6 months	Mild swelling of the left vocal fold	Lateral pharyngotomy removed 1.5 cm well-defined tumour	H & E, PAS, PTAH, trichome, EM, immunohisto-chemical staining	No recurrence after 1.5 years
Helliwell *et al.*, (1988)	66 M	Hoarseness	8 years	Smooth swelling (3 cm in diameter) arising just below the right vocal fold	Excision	H & E, PAS, PTAH, trichome, EM, immunohistochemical staining	No follow-up reported
Hamper *et al.*, (1989)	51 F	Dyspnoea, dysphagia	?	Tumourous protrusion in the area of both artenoid cartilages/ CT scan (3.5 cm mass) laterally on the left side of the larynx	4 cm tumour excised/ surgical removal of tumour	H & E, PTAH, Mason–Goldner, Astra blue, Giemsa, immunohistochemical staining	Recurrence after 12 years, first diagnosis as granular cell tumour, but revision of the initial diagnosis at recurrence
Present case (1992)	51 M	Hoarseness, snoring	1 year	MRI scan tumour parapharyngeal on the left side (7.5 × 4 cm) with origin from the left ventricular fold	Hemilaryngectomy	H & E, PTAH, EM, immunohistochemical staining	No recurrence after 1 year

H & E = haematoxylin-eosin; PTAH = phosphotungstic acid-haematoxylin; PAS = periodic acid Schiff; EM = electron microscopy.

globin in the more mature striated cells. The adult extracarchial rhabdomyoma is composed of comparatively mature cells staining for desmin and myoglobin, but not vimentin.

Immunocytochemical study of rhabdomyoma shows that adult rhabdomyoma contains foetal myosin, and that the tumour cells show the same level of myofibril differentiation as seen in neonatal skeletal muscle. Therefore the term 'adult' does not seem appropriate and the term neonatal rhabdomyoma is preferable for the adult type (Eusebi *et al.*, 1988; Helliwell *et al.*, 1988). This suggestion is supported by electron microscopy which revealed various degrees of myofibril differentiation similar to that seen in embryonic muscle cells (Battifora *et al.*, 1969; Bianchi and Muratti, 1975). Friedmann's investigations on experimentally produced rhabdomyo sarcoma in rats is according to the theory about the origin of these tumours from mesenchymatous tissue, which has retained the potential of differentiation to striped muscle (Friedmann, 1969). Foetal extracardial rhabdomyomas immunologically display all the characteristics of normal foetal skeletal fibres.

Differential diagnosis

Granular cell tumours may occur in the larynx. The similarity to adult extracardial rhabdomyomas is superficial and the different criteria have been precisely established (Coldman, 1963; Battifora *et al.*, 1969; Boedts and Mestdagh, 1979). Immunocytochemical study can help in the differential diagnosis, as granular cell tumours do not stain for desmin or myoglobin (Helliwell *et al.*, 1988).

The myxoid type of the foetal rhabdomyoma may be confused with simple polyps of the vocal folds, but careful routine microscopic examination with additional staining for desmin will show the striated muscle elements in the tumour. Myoglobin is a less useful marker as there are likely to be only a few posi-

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TABLE II
SUMMARY OF PUBLISHED CASES OF ADULT MULTIFOCAL RHABDOMYOMA

Source	Age (years) Sex	Chief complaint	Duration	Examination results	Treatment	Morphological studies	Comment
Coldman (1963)	82 M	Hoarseness	Long standing	Submucosal (1.0 cm) nodule in left true vocal fold	None. A finding at autopsy	H & E, PAS, PTAH, Sudan Black	Rhabdomyoma of sternomastoid muscle removed 20 years before
Gardner and Corio (1983)	60 M	?	?	Mass in the posterior wall of the left ventricle of the larynx	Excision	H & E	Adult rhabdomyoma superior to the left submandibular gland excised 6 months earlier
Nevill and McConnel (1981)	58 M	Dysphagia globulus	1 month	Submucosal (3.0 cm) mass in the left aryepiglottic fold extending into the left pyriform sinus	Transhyoid pharyngotomi. Local excision	H & E, PTAH	Adult rhabdomyoma in the floor of the mouth excised 4 years earlier. No recurrence after 2 years

H & E = hematoxylin–eosin; PTAH = phosphotungstic acid–haematoxylin; PAS = periodic acid Schiff.

tively staining cells, and vimentin is a nonspecific mesenchymal marker, also positive in simple polyps (Helliwell *et al.*, 1988).

The distinction between cellular variants of foetal rhabdomyoma and spindle cell sarcomas, especially embryonal rhabdomyosarcoma or leiomyosarcoma, may be very difficult. Careful light microscopy is essential, as sarcomas may also be characterized by increasing muscle cell differentiation toward the periphery of the tumour.

Recurrence and multifocality

Of the extracardial rhabdomyomas of the larynx, three have recurred, one of them three times (Winther, 1976). Two cases were of the adult type (Winther, 1976; Hamper *et al.*, 1989) one recurring after 12 years (Hamper *et al.*, 1989), one was of the foetal cellular type (Modlin, 1982). The interval of 12 years before relapse reflects the very slow growth rate of these tumours (Shemen *et al.*, 1992). Removal of the tumour may be technically difficult because of a close relationship to vital organs and recurrent tumours may be lobulated or multifocal at initial presentation (Winther, 1976; Modlin, 1982; Remacle *et al.*, 1983; Andersen and Elling, 1986).

Three of the adult extracardial rhabdomyomas of the larynx were multifocal, with an extracardial rhabdomyoma found in the sternomastoid muscle (Coldman, 1963), the floor of the mouth (Neville and McConnel, 1981) or superior to the submandibular gland (Gardner and Corio, 1983), all of them close to the larynx region.

Treatment

The treatment for these lesions is surgical, and endoscopic procedures may often be sufficient. Malignant transformation of the tumour has not been reported.

Acknowledgments

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TABLE III
SUMMARY OF PUBLISHED CASES OF LARYNGEAL FOETAL CELLULAR RHABDOMYOMA

Source	Age (years) Sex	Chief complaint	Duration	Examination results	Treatment	Morphological studies	Comment
Di Sant' Agnese and Knowles (1980)	53 M	Hoarseness	?	Polypoid mass in the vocal fold	Local excision	H & E, special unknown stains	No recurrence after 3 years
Modlin (1982)	34 F	Hoarseness	5 weeks	Polypoid mass in the right anterior vocal fold	Endoscopic excision	Not stated	Two recurrences treated first by right lateral pharyngotomy and finally by subglottic laryngectomy. No recurrence after 3 years
Granish *et al.* (1983)	31 M	Hoarseness	3 years	Submucosal, (3 cm) mass in the right false vocal fold	Lateral thyrotomy; local excision	H & E, PAS, trichome, EM	No recurrence after 1 year
Eusebi *et al.* (1988)	29 M	Hoarseness	Several months	Polyp (1.2 cm) in the right false vocal fold	Local excision	H & E, PAS, immunohistochemical staining	No recurrence after 2 years

H & E = haematoxylin–eosin; PTAH = phosphotungstic acid–haematoxylin; PAS = periodic acid Schiff; EM = electron microscopy.

TABLE IV
SUMMARY OF PUBLISHED CASES OF LARYNGEAL FOETAL MYXOID RHABDOMYOMA

Source	Age (years) Sex	Chief complaint	Duration	Examination results	Treatment	Morphological studies	Comment
Fertilo and Frugoni (1975)	50 M	Hoarseness	3 years	Polypoid (1.0 × 1.5 cm) mass in posterior commisure	Endoscopic excision	H & E, PAS, PTAH, van Gieson	No recurrence after 1 year
Di Sant' Agnese and Knowles (1980)	65 F	Hoarseness	?	Polypoid mass on vocal fold	Local excision	H & E	No recurrence after 1.5 years
Rosenman *et al.* (1986)	78 F	Hoarseness	2 months	Nodule (6 × 5 mm) in the posterior commissure	Local excision	H & E, PTAH	No recurrence after 2 years
Helliwell *et al.* (1988)	44 M	Sore throat	6 months	Polyp (0.5 cm) at the posterior commissure of the vocal folds	Excision	H & E, immunohisto-chemical staining, EM	No follow-up reported

H & E = haematoxylin–eosin; PTAH = phosphotungstic acid–haematoxylin; PAS = periodic acid Schiff; EM = electron microscopy.

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