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Review Article

Laryngeal paraganglioma. A review and report of a single case

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Abstract

Laryngeal paraganglioma originates in the neural crest cells in the laryngeal paraganglia. Two distinct types may be cited on the basis of clinical features, but biopsy is essential for diagnosis. By light microscopy, the Zellballen pattern appears pathognomonic. The treatment consists of surgical excision.

In this article, due to the rareness of the tumour, one case of laryngeal paraganglioma is presented. The general knowledge and the available literature are reviewed. The difficulties in the differential diagnosis are stressed and treatment principles are discussed.

Key words: Larynx; Paraganglioma

Introduction

Laryngeal paragangliomas arise from the laryngeal paraganglia that form a part of the widely distributed system of paraganglia of the vagus nerve. Laryngeal paraganglia are two paired structures in the larynx. The superior laryngeal paraganglia are located adjacent to the superior border of the thyroid cartilage in close association with the superior laryngeal nerve and artery, whereas the inferior laryngeal paraganglia may be located anywhere from the inferior horn of the thyroid cartilage to the cricotracheal area cartilage, and are in close association with the recurrent laryngeal nerve and inferior laryngeal artery. In addition, Kleinsasser (1988) demonstrated an inconstant paraganglion located anterior to the cricothyroid ligament. Rarely, laryngeal paragangliomas may be located in the pyriform sinus, within branches of the superior and inferior laryngeal nerves and in the capsule of the thyroid gland.

Since laryngeal paragangliomas were first described in 1955 by Andrews, and Blanchard and Saunders, more than a hundred cases have been reported. Lawson and Zak (1974) reported 18 cases and summarized all the laryngeal paraganglioma cases covered in the literature. Marks and Brookes (1983) reported the 29th case of malignant paraganglioma. The 62nd case was reported by Konowitz *et al.* (1988) who also listed all the cases in the literature. Recently, El-Silimy and Harvy (1992) reported the 93rd case. We found out that only one case of laryngeal paraganglioma has been reported in Turkey by Tezel *et al.* in 1989. We believe that there must have been other non-reported cases.

Ali *et al.* (1983) reported a case that complained of only burning pain in the throat and suggested for the very first time that there are two types of laryngeal paragangliomas according to the clinical features. They formulated Type I and Type II on the basis of clinical features and treatment methods. Type I was observed in approximately 70 cases, whereas Type II was noticed in 23 cases (El-Silimy and Harvy, 1992).

In Type I laryngeal paraganglioma the age range is eight to 86 years. The average age is 46 years. Common clinical features are hoarseness, dyspnoea, dysphagia, stridor, cough and haemotysis. The local recurrence (10 per cent) and metastasis rates are low. When present, metastases are usually seen in the skin, subcutaneous tissue and lymph nodes. The preferred treatment is local excision. The prognosis is good (El-Silimy and Harvy, 1992).

In Type II laryngeal paraganglioma, the age range is 40–73 years. The average age is 53 years. There is a predominance of males (4:1). Common clinical features are hoarseness, dyspnoea, dysphagia (El-Silimy and Harvy, 1992) and a persistent burning pain in the throat. The last feature is usually misinterpreted as glossopharyngeal neuralgia requiring neurectomia, chronic tonsillitis necessitating tonsillectomy (Ali *et al.*, 1983; Stanley *et al.*, 1986), or undifferentiated squamous cell carcinoma demanding radiotherapy (Hooper, 1972). The local

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recurrence and metastasis rates are as high as 40 and 73 per cent respectively. The metastases may occur in skin, subcutaneous tissue, lymph node, brain, lung, liver, bones. Contrary to Type I, the preferred treatments are radical excision of the primary lesion and local excision of metastasis. The prognosis is bad (El-Silimy and Harvy, 1992). The tumour site, pathology and immunohistochemical studies are identical in Type I and Type II. According to the review of literature by Barnes (1991), there is a predominance of females 2.8:1, regardless of type. Additionally, supraglottic, subglottic and glottic rates are 82 per cent, 15 per cent and three per cent respectively.

There is no relationship between the size of tumour and the clinical behaviour. The tumours are usually slow-growing. Therefore, patients often have symptoms for years before diagnosis. Laryngeal paragangliomas tend to be locally more aggressive than other paragangliomas in the head and neck region. Malignancy is more common when there is regional lymph node involvement or a distant metastasis present (Sykes and Ossoff, 1986). Local recurrence may be the first sign of malignancy (Crowther and Colman, 1987).

The histopathological appearance of the laryngeal paragangliomas possesses identical characteristics to other paragangliomas in the head and neck region. The typical appearance of paragangliomas may be described as a nest of cells called Zellballen. The Zellballen pattern, also called an alveolar pattern, is composed of chief epithelioid and sustentacular cells. The chief cells consist of granules that contain catecholamines. The sustentacular cells are arranged on the periphery of the Zellballen pattern (Konowitz *et al.*, 1988). The reticular fibres surround the cell cluster (Sneige *et al.*, 1983; Sykes and Ossoff, 1986; Kleinsasser, 1988; Barnes, 1991). The tumour contains a capillary network. Sneige *et al.* (1983) and Kliewer *et al.* (1989) reported that sustentacular cells were not seen in the malignant paraganglioma.

We are reporting this case-study because laryngeal paraganglioma is rare and a frequently misdiagnosed tumour. We hope that our case report will contribute to the estimation of the worldwide incidence of this tumour.

Case report

A 55-year-old woman was referred to Gülhane Military Medical Academy Otolaryngology–Head and Neck Department in March 1994. She presented with a one-year history of hoarseness, gradually increased dyspnoea and fullness in the pharyngeal region. The patient appeared anaemic and obese. She had an inspiratory stridor. There was no pain, dysphagia or haemoptysis. Indirect laryngoscopy and flexible fibreoptic endoscopic examination revealed a yellowish smooth surface, lobulated elastic mass 3×2.5 cm on the right band ventricle that was

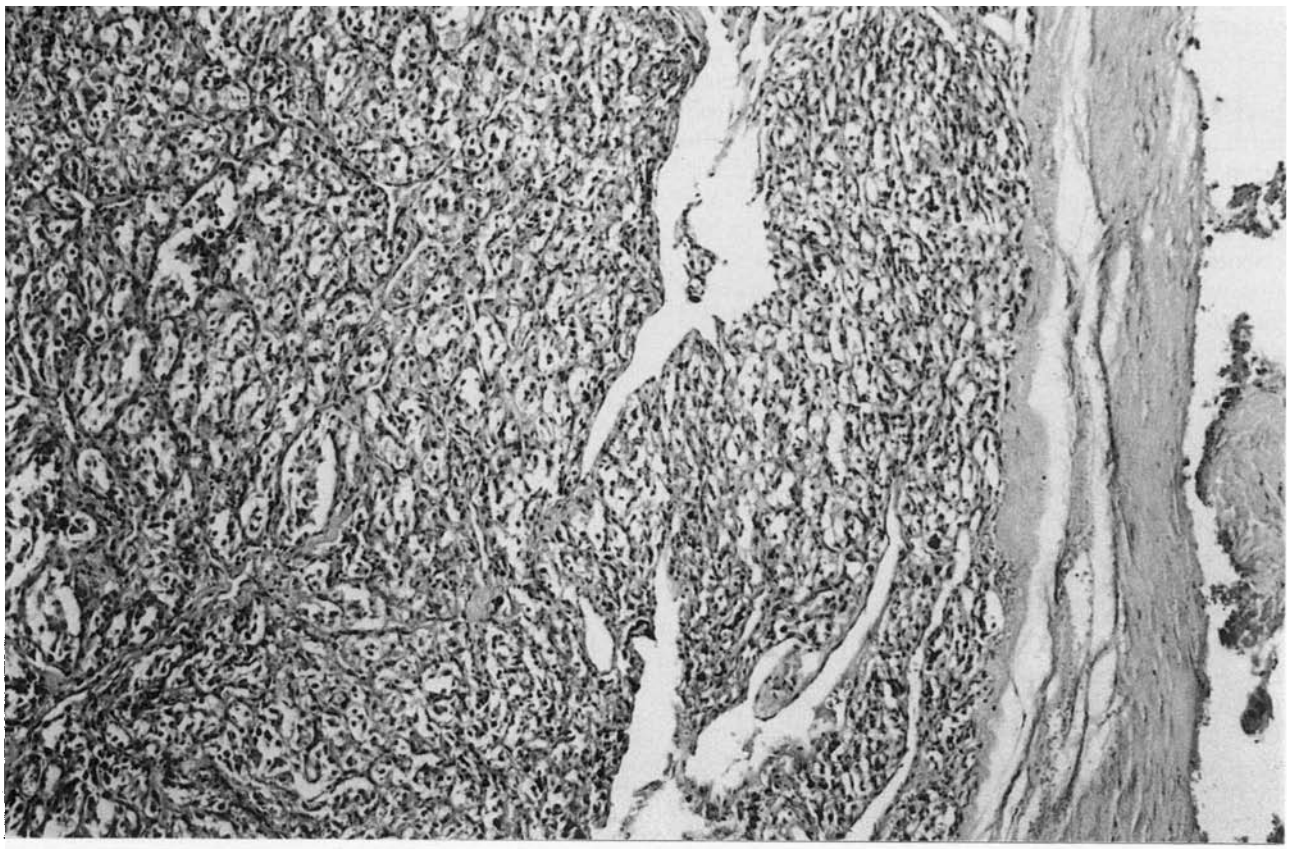

FIG. 1
The tumour was composed of groups of cells arranged in nest and cords.

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completely covered. Motion of the right vocal fold was restricted due to this mass on the right band ventricle. There was no palpable cervical lymph node. She was normotensive. Otoscopic and anterior rhinoscopic examination were normal. Cardiological and haematological examination revealed cardiac ischaemia and anaemia.

In the first instance, tracheotomy was performed because of respiratory distress which developed rapidly. Four days later, microlaryngoscopy was performed in order to decide whether to take a biopsy or excise the tumour by use of forceps. Microlaryngoscopy revealed a greyish-yellow lesion rich in capillaries on the right band ventricle with affected aryepiglottic fold and arytenoids. The lesion was about 3×2.5 cm. Right vocal fold mobilities were significantly diminished. A biopsy was taken, and there was profuse bleeding that could not be stopped with adrenaline application and cautery. The frozen section was negative for malignancy. Because of the persisting bleeding, laryngofissure was carried out. The lesion was completely removed. Deep haemolytic anaemia occurred during the post-operative course. On the ninth post-operative day, while aetiological research and supportive treatment for haemolytic anaemia were in progress, the patient's condition deteriorated gradually, and she died of myocardial infarction. Permission was not given for an autopsy.

For histopathological examination, the specimen was fixed in 10 per cent formalin, samples were embedded in paraffin and routinely processed. Sections from paraffin blocks were stained with haematoxylin-eosin, reticulum, mucin, PAS and Fontana. An immunohistochemical study was carried out on formaldehyde-fixed paraffin-embedded sections adopting the peroxidase-antiperoxidase (PAP) method. Mouse S-100 protein was obtained from Biogenex (USA) and used at a dilution of 1:200.

Pathological findings

Macroscopically, the mass, circumscribed by the thin and incomplete capsule of connective tissue, was red to brown, elastic and $3 \times 2.5 \times 1.5$ cm in size.

Histologically, the tumour was composed of groups of cells arranged in nests and cords (Figure 1). Nests of chief cells were separated by vascular channels creating an organoid pattern. The groups were formed by delicate bands of fibrovascular stroma, best demonstrated by the reticulum stain (Figure 2). The neoplastic cells consisted of polygonal or plump-shaped epitheloid cells. The cytoplasm was eosinophilic and rather granular in appearance. The degree of staining of the nuclei was variable. There were neither mitotic figures nor necrosis. No vascular invasion was identified, and PAS and mucin stains were negative. The Fontana stain was negative for argentaffine granules.

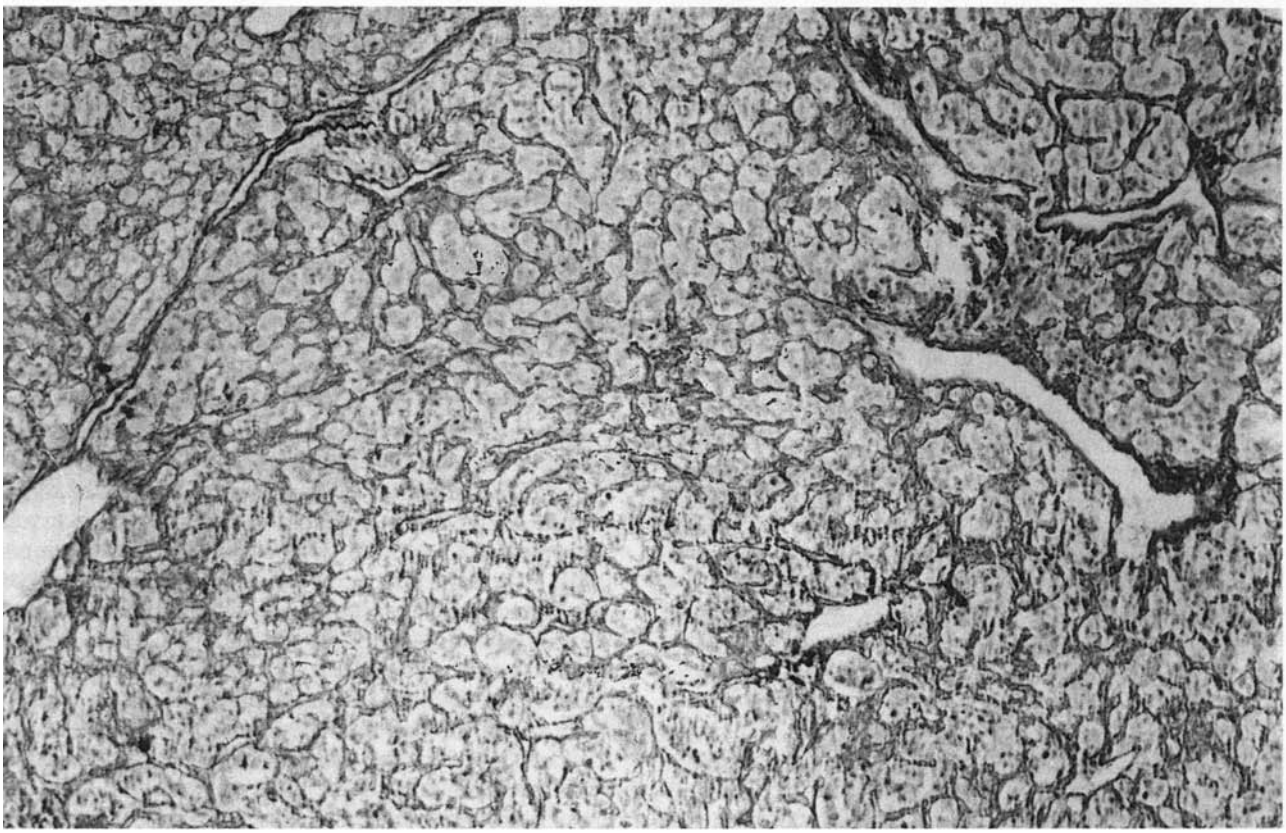

FIG. 2

The groups were produced by delicate bands of fibrovascular stroma (it was shown by using reticulum stain).

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Immunohistochemically, the delicate sustentacular network was demonstrated by anti S-100 protein.

Discussion

Laryngeal paragangliomas are rare. Therefore, the real incidence of the paraganglioma in all laryngeal tumours is not well-known. Laryngoscopic examination usually reveals the lesion. Type II laryngeal paraganglioma may not be disclosed by larygnoscopic examination due to its submucosal character (Ali *et al.*, 1983). Our case was consistent with Type I laryngeal paraganglioma on the basis of clinical features. The tumour was easily seen by laryngoscopic examination. However, it was interesting that the patient did not have symptoms for a long time.

In both Type I and Type II the lesion is usually located in the supraglottis, especially in the aryepiglottic fold, epiglottis, pyriform sinus, ventricle and arytenoid. El-Silimy and Harvy (1992) reported five cases of Type I versus only one case of Type II laryngeal paraganglioma involving the subglottis. Metastasis in skin, subcutaneous tissue and lymph node is usually painless in Type I, whereas in Type II, metastasis in skin and subcutaneous tissue is usually painful (Ali *et al.*, 1983; El-Silimy and Harvy, 1992). The causes of pain in the skin and subcutaneous tissue metastasis are not well-known. Tumour secretions were proposed as pain-producing substances (Ali *et al.*, 1983; Stanley *et al.*, 1986). However, these substances have not been found to date (Crowther and Colman, 1987). Milroy *et al.* (1991) reviewed the histology material of the patient reported by Ali *et al.* (1983), and reclassified the lesion as a large cell carcinoma. They supposed that the symptomatology of glossopharyngeal neuralgia occurs in large cell carcinoma rather than paraganglioma. Also, they pointed out that the presence or absence of pain is not important for subgrouping.

Macroscopically, the tumour is ovoid or round in shape, tan-brown in colour and possesses a diameter range from 1 to 7 cm. However, those features do not reflect the behaviour of the tumour (Marks and Brookes, 1983). Histologically, this tumour may be misinterpreted. Konowitz *et al.* (1988) reported that it was misinterpreted histologically in 16 of 62 laryngeal paragangliomas (26 per cent), which were in fact squamous cell carcinoma, adenocarcinoma, amelanotic melanoma, unspecified vascular tumours, haemangioma, malignant melanoma, haemangiopericytoma, lymphangioendothelioma and malignant glandular tumours. Neuroendocrine carcinoma, carcinoid tumour and adenocarcinoma may imitate the paraganglioma. Light and electron microscopy and immunohistochemical studies are useful to confirm the differences between these tumours (Konowitz *et al.*, 1988).

There is no distinct correlation between the tumours' histopathological appearance and clinical behaviour (Glenner and Grimley, 1974). Laryngeal paragangliomas are typically benign and rarely functional (Barnes, 1991). Lack *et al.* (1979) proposed that at least two of the following histopathological features were present in the malignant tumours; mitoses, necrosis of tumour cells, invasion of vascular spaces. This was not accepted by Barnes (1991). In necrotic lesions, invasion of vascular spaces is usually assessed with more difficulty. Therefore, confirming malignancy by an intraoperative frozen section is not possible in every case (Marks and Brookes, 1983). Levene (1981) put forward that the presence of pain might indicate malignant behaviour. It has been suggested that laryngeal paragangliomas should be considered as potentially malignant, regardless of their histological appearance. The motive of this suggestion is that paragangliomas comprising mitoses, cellular pleomorphism and polychromatism, indicating active, tumour histologically, may be benign in behaviour. In contrast, inactive tumours may metastasise. In benign laryngeal paragangliomas there is no recurrence after complete excision. In cases where local recurrence is observed, laryngeal paragangliomas tend to be malignant and to metastasise. It is difficult to confirm malignancy before the occurrence of metastasis. Thus, it is accepted that all paragangliomas should be considered as potentially malignant (Crowther and Colman, 1987). Ferlito *et al.* (1994) did not accept the 25 per cent malignancy rate previously reported, claiming that the diagnoses were not correct. Among 62 cases accepted by Ferlito *et al.* (1994), only one case of malignant laryngeal paraganglioma (reported by Rüfenacht *et al.*, 1985) was identified. Therefore, they proposed that the malignancy rate is less than two per cent. Rüfenacht's patient is the only case with neurological complications (Deleu and De Geeter, 1991).

There is no agreement concerning the malignant potential of laryngeal paraganglioma. As previously noted, it was reported that laryngeal paragangliomas exhibit a higher rate of malignancy than paragangliomas at other sites (Hooper, 1972; Lawson and Zak, 1974; Smith *et al.*, 1988). Moisa (1991) reported 68 cases with laryngeal paraganglioma, and stated that both early cervical metastasis and distant metastasis were seen in 22 per cent of those cases and mortality was 24 per cent. Therefore, he suggested that larygneal paraganglioma had considerable malignant potential and that biological behaviour must be considered indeterminate. This suggestion was not accepted by Wenig (1992). Some authors believed that the malignancy rate is 20–25 per cent (Hooper, 1972; Lawson and Zak, 1974; Smith *et al.*, 1988). Others stated that this rate was overestimated, laryngeal paraganglioma was benign, with little tendency to metastasise, and reported that malignant paraganglioma were often misdiagnosed carcinomas (Batsakis, 1979; Baugh *et al.*, 1987; Ferlito *et al.*, 1994). Brownlee and Shockley (1992) noted that this increased incidence, as high as 25 per cent, might indicate a different biological behaviour of the superior and inferior laryngeal paragangliomas because rate of malignancy was calculated on the basis of series that were weighted toward superior laryngeal lesions. They also stated that there were no malignant inferior laryngeal paragangliomas. However, a case reported by Olofsson *et*

al. (1984) should be accepted as malignant laryngeal paraganglioma (subglottic) due to metastasis of cervical nodes. According to the review of Ferlito *et al.* (1994), there were nine subglottic laryngeal paragangliomas. Therefore, the malignancy rate in the subglottic paraganglioma is one out of nine, contrary to the claim of Brownlee and Shockley (1992) concerning different biological behaviour of the superior and inferior laryngeal paragangliomas.

After Barnes (1991) described the laryngeal paragangliomas covered in the literature as acceptable and unacceptable, Ferlito *et al.* (1994) updated Barnes's analysis with new cases. Only 62 cases were accepted as true laryngeal paraganglioma by Ferlito *et al.* (1994). They proposed that most laryngeal paragangliomas, if not all, were benign and that allegedly malignant paragangliomas reported in the literature were actually atypical carcinoids.

Diagnostic procedures include indirect-direct laryngoscopy, endoscopic examination, biopsy, angiography and CT scan that are important in pre-operative evaluation. After laryngoscopic examination of our case, we did not perform a CT scan, due to difficulties encountered whilst taking a biopsy from the mass. Afterwards, the patient underwent laryngofissure due to profuse bleeding during biopsy. Definitive histological diagnosis may not always be possible by light microscopy, but electron microscopic, ultrastructural and immunohistochemical analysis may be necessary. As mentioned previously, the Zellballen pattern is characteristic of laryngeal paraganglioma. Ferlito *et al.* (1994) proposed that it was not pathognomonic, and could also be seen in other neoplasms especially in neuroendocrine carcinomas. Therefore, even if light microscopy suggests a diagnosis of laryngeal paraganglioma, diagnosis must be supported by electron microscopy, ultrastructural and immunohistochemical analysis (Marks and Brookes, 1983; Ferlito *et al.*, 1994). Histochemical analysis confirms the presence of argyrophilia. Argyrophilic granules are demonstrated on silver staining by the Grimelius technique. However, neuroendocrine carcinoma and mucosal malignant paraganglioma are also argyrophilic. Additionally, there may not be enough laryngeal paraganglioma cells to demonstrate argyrophilia. Therefore, the presence of argyrophilia may distinguish neuroectodermally derived neoplasms from adenocarcinoma of glandular origin (Konowitz *et al.*, 1988). The reticulum stain is not specific for laryngeal paraganglioma, but it shows the cell nests and fibrovascular stroma. Laryngeal paraganglioma cells also contain epithelial mucin, but mucicarmine and periodic acid-Schiff stains are also positive for neuroendocrine carcinoma.

On light microscopy, the small cell neuroendocrine carcinoma has an oat-like appearance, whereas the large cell carcinoma consists of plumper cells arranged in nests, cords, and acini. Carcinoid tumours have a trabecular pattern with ribbons and nest of cells, and also rich vascular stroma. On the contrary, a neuroendocrine carcinoma has a poor blood supply (Konowitz *et al.*, 1988).

Electron microscopy demonstrates neurosecretory granules that are seen in laryngeal paragangliomas as well as other neuroendocrine tumours. Of two cases reported by Sneige *et al.* (1983), one had a malignant paraganglioma. In that case, sustentacular cells were not seen by electron microscopy, and the irregular aggregates of cells were not bordered by a basal lamina. Ferlito *et al.* (1994) proposed that this case reported by Sneige *et al.* (1983) as a malignant paraganglioma was probably atypical carcinoid because of the calcitonin and carcinoembryonic antigen (CEA) revealed in tumour cells by immunostaining. Therefore, by electron microscopy, it may not be possible to differentiate between benign and malignant paragangliomas. Ultimately, the diagnosis of a paraganglioma may rest with an immunohistochemical evaluation (Konowitz *et al.*, 1988; Martinez-Madrigal *et al.*, 1991; Salim *et al.*, 1993; Ferlito *et al.*, 1994).

Immunohistochemical analysis includes demonstrating immunoreactivity of neuron-specific enolase (NSE), S-100 protein, chromogranin, cytokeratin, calcitonin and CEA. Neuron-specific enolase immunopositivity can be demonstrated in most paragangliomas (Konowitz *et al.*, 1988; Barnes, 1991; Martinez-Madrigal *et al.*, 1991; Milroy *et al.*, 1991; Molisa, 1991; Salim *et al.*, 1993; Ferlito *et al.*, 1994; Enzinger and Weiss, 1995). S-100 protein exists in glial cells of the central nervous system and Schwann cells of the peripheral nervous system, and is believed to be present in the sustentacular cells of the paraganglionic system (Konowitz *et al.*, 1988; Martinez-Madrigal *et al.*, 1991; Ferlito *et al.*, 1994). Korat *et al.* (1988) reported that glial fibrillary acidic protein (GFAP) was useful in the diagnosis of the paraganglioma because sustentacular cells stain for GFAP. Choi and Anderson (1985) demonstrated immunoreactivity of S-100 protein in all five cases with paraganglioma. Milroy *et al.* (1991) reported that all of the four cases with paraganglioma stained for S-100 protein and GFAP, thus they distinguished these tumours from large and small cell neuroendocrine carcinomas. Martinez-Madrigal *et al.* (1991) demonstrated that the immunostaining for S-100 protein was focally (+) or diffusely (++) positive for all cases (16 cases) with head and neck paraganglioma in the cytoplasm of sustentacular cells. Whereas, they reported that only two cases showed positivity for GFAP. Chromogranins are described markers (Lloyd *et al.*, 1983; Cohn *et al.*, 1984; Wilson and Lloyd, 1984). Among chromogranins, chromogranin A is the most useful marker in the neuroendocrine tumours (Lloyd, 1988). Milroy *et al.* (1991) reported that of four cases with paraganglioma, all were positive for chromogranin A. However, of 11 cases reported by Salim *et al.* (1993), only seven cases showed positivity for immunostaining of chromogranin. Martinez-Madrigal *et al.* (1991) stated that only one case in 16 patients was negative for chromogranin A. According to Ferlito *et al.*, 1994), the presence of chromogranin in the chief cells and S-100 protein in the sustentacular cells is characteristic of paraganglioma regardless of its site of origin.

In large and small cell neuroendocrine carcinomas different ratios have been reported, for positive immunostaining of chromogranin (Martinez-Madrigal *et al.*, 1991; Milroy *et al.,* 1991; Salim *et al.*, 1993). The absence of immunostaining for cytokeratin, calcitonin and CEA is a feature that supports diagnosis of paraganglioma (Ferlito *et al.*, 1994). Cytokeratin is a most useful immunological marker for differential diagnosis between paraganglioma and neuroendocrine carcinoma although the absence of cytokeratin does not preclude the diagnosis of neuroendocrine carcinoma, nor does it establish a diagnosis of paraganglioma (Martinez-Madrigal *et al.*, 1991; Salim *et al.*, 1993; Ferlito *et al.*, 1994). Some cases previously reported were cytokeratin positive (Mittal *et al.*, 1986; Johnson *et al.*, 1988). Milroy *et al.* (1991) reported that of 16 cases with large cell carcinoma, 12 were calcitonin positive. Also they stated that 13 cases with large cell carcinoma and two cases with small cell carcinoma were positive for low molecular weight cytokeratins. One case reported by Sneige *et al.* (1983) was accepted as malignant paraganglioma because sustentacular cells were not identified and there was calcitonin positivity. Cytokeratin staining results were not expressed. CEA was present in both primary and recurrent tumours. Therefore, these tumours were considered as atypical carcinoid (Wenig and Gnepp, 1989; Ferlito *et al.*, 1994). In their review of laryngeal paraganglioma, Salim *et al.* (1993) reported that neuropeptide Y and met-enchephaline immunoreactivity were positive. They also stated that tests for met-enchephaline and neuropeptide Y were negative in the most of large and small cell carcinomas. As a result, it could be stated that paraganglioma cells are negative for markers of epithelial differentiation (epithelial membrane antigen, CEA, cytokeratin), but positive for markers of neuroendocrine differentiation (chromogranin, neuron specific enolase, protein gene product-9.5, synaptophysin, Leu-7) (Ferlito and Friedman, 1991). In our case, an immunohistochemical study was performed and a sustentacular network was observed by anti-S-100 protein staining (Figure 2).

Angiography is useful to determine the size, and extent of the lesion and to detect the presence of other paragangliomas (Handel *et al.*, 1977). It is determined with arterial cross-flow whether or not the patient can tolerate the intra-operative ligation of the internal or common carotid arteries (Sykes and Ossoff, 1986). Contrarily, Konowitz *et al.* (1988) proposed that the superior thyroid and superior laryngeal artery could be ligated before the surgical procedure and angiography is not necessary in the assessment of laryngeal paraganglioma. Marks and Brookes (1983) suggested that angiography should be considered with lesions greater than 2 cm in diameter, and therapeutic embolization was necessary.

Paraganglia tissue and paraganglioma consist of epinephrine, norepinephrine, dopamine and seratonin. In the case of Vetters and Toner (1970) hypertension and cardiovascular lability were present. On fluorimetric essay, they found 0.145 mg of norepinephrine per gram of tumour. Justrabo *et al.* (1980) also found norepinephrine, epinephrine and calcitonin in a case that had malignant paraganglioma. According to Barnes (1991) and Ferlito *et al.* (1994) the cases reported by Vetters and Justrabo were probably atypical carcinoids due to microvilli seen on electron microscopy. On the other hand, Barnes (1991) stated that of the 34 acceptable cases only one case reported by Laudadio (1971), might be functional due to disappearance of tachycardia and hypertension after surgical excision. Sneige *et al.* (1983) reported that they found a positive reaction for calcitonin and vasoactive intestinal polypeptide (VIP) in their two cases. Additionally, in one case, they confirmed positive reaction to CEA both in primary and recurrent tumours, with a malignant clinical course. It was not accepted as paraganglioma because of positive immunostaining for calcitonin and CEA (Wenig and Gnepp, 1989; Barnes, 1991; Ferlito *et al.*, 1994). In our case, there were no signs leading to the suggestion of excessive cathecholamine secretion, and urinary vanylmandelic acid and 5-hydroxy-indol-acetic acid levels were normal.

Until the 1988 report of Konowitz *et al.*, four cases of multifocal paraganglioma involving the larynx with three carotid body tumours and one glomus jugulare tumour were seen. Additionally, one case of bilateral laryngeal paraganglioma was reported by Crowther and Colman (1987). Other paragangliomas of head and neck have a reported 10 per cent incidence of multicentricity (Lack *et al.*, 1977; Barak, 1982). On the other hand, of two reported paragangliomas of thyroid origin one had laryngeal involvement, whereas the other had tracheal involvement (Zak and Lawson, 1972; Kay *et al.*, 1975; Banner *et al.*, 1979; Massaioli *et al.*, 1979; Buss *et al.*, 1980; Mitsuda *et al.*, 1987; De Vries and Watson, 1989; Brownlee and Shockley, 1992). Smith *et al.* (1988) reported that there was no bilateral laryngeal paraganglioma as thyroid paraganglioma. However, the highest incidence of bilateral paragangliomas is 26 per cent in familial carotid body tumours (Barak, 1982).

Interestingly, one case with episodic growth of laryngeal paraganglioma during her two pregnancies was reported by Werner *et al.* (1992). Although they suspected that oestrogen or gestagen induced episodic growth, hormone receptors were not seen in the tumour tissue.

Surgical therapy is the mainstay of treatment in the larygneal paraganglioma. Surgery techniques that have been performed to date include endoscopic excision, partial or total laryngectomy with, or without modified or radical neck dissection, lateral pharyngotomy with excision, cryosurgery and laser surgery (Marks, 1983; Konowitz, 1988). Endoscopic excision, cryosurgery and laser surgery may be useful for treatment of small lesions (El-Silimy and Harvy, 1992). After endoscopic surgery, complications are recurrence and haemorrhage requiring laryngofissure as in the presented case. Partial laryngectomy is the mainstay of treatment (Konowitz *et al.*, 1988).

Crowther and Colman (1987) reported that laryngofissure is the treatment of choice with a good margin of clearance permitting the preservation of the function of the larynx. They suggested total laryngectomy when local recurrence occurs. Moisa and Silver (1991) recommended resection by the lateral pharyngotomy approach for supraglottic lesions, with ligation of the superior laryngeal artery as an initial step. Neck dissection must be performed when regional cervical metastasis occurs. It is usually accepted that radiotherapy is ineffective. Lawson and Zak (1974) concluded that laryngeal glomera are radioresistant having experienced that they withstood high dosage radiation (5500 R) without structural change. Contrarily, Lack *et al.* (1979) reported that radiotherapy increased the chief cells. Despite this, radiotherapy may be useful in palliative treatment of the metastasizing paraganglioma. Chemotherapy regimens are ineffective (Wetmore *et al.*, 1981).

A true estimate of survival is difficult to obtain. However, El-Silimy and Harvy (1992) reported that the prognosis is good for Type I lesions, whereas poor for Type II lesions. In the cases of painful lesions, prognosis is bad, mortality is higher compared to other cases (Schaefer *et al.*, 1980). Moisa (1991) reported that the five-year survival rate was 60 per cent. However, the incidence of malignancy was reported as approximately two to three (Barnes, 1991; Ferlito *et al.*, 1994). DNA analysis as a prognostic study has not yet provided useful information (Barnes, 1991; Milroy *et al.*, 1991).

Conclusion

In this review of literature, we reflected that laryngeal paraganglioma is an uncommon neoplasm with increasing frequency. Clinical symptoms are varying in terms of types. Diagnosis can often be reached by light and electron microscopy. Despite this fact, histopathological misdiagnosis may persist. Therefore, immunohistochemical analysis may be useful to distinguish between laryngeal paraganglioma and other neuroendocrine tumours. CT scanning is very important in pre-operative evaluation. The role of angiography is limited to demonstrating the vascular nature of paraganglioma. Tumour size and location are important in determining resection margins. Partial laryngectomy is an adequate method for control of tumour and preservation of voice function and nasal respiration. Total laryngectomy should be considered regardless of voice function in case of local recurrence after partial laryngectomy. Radiotherapy is not considered effective in the treatment of laryngeal paraganglioma. In addition, there is no proven role of chemotherapy.

As a result, the tumour defined as laryngeal paraganglioma should be considered in the differential diagnosis of laryngeal masses.

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