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Laser surgical treatment of laryngeal paraganglioma

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Abstract
Paragangliomas are rare benign neoplasms arising from the neural crest-derived paraganglia of the autonomic nervous system. In the larynx three different localizations of paraganglia are known. Most laryngeal paragangliomas arise from the supraglottic paraganglia. A review of the literature shows that the treatment of choice for laryngeal paragangliomas is surgical excision. Since the implementation of CO_2 laser surgery into laryngology in 1972, no reports of endoscopic laser surgical excisions of laryngeal paragangliomas have been published so far. We present the case of a 66-year-old female patient who suffered from a large ($4 \times 4 \times 3$ cm) left supraglottic paraganglioma. The tumour was completely excised utilizing the CO_2 laser. Histopathology and immunohistochemistry of the tissue presented the typical findings of a laryngeal paraganglioma. The pre- and post-operative management as well as the treatment strategies are discussed. To our knowledge the present case demonstrates for the first time a complete transoral CO_2 laser surgical resection of an advanced laryngeal paraganglioma.

Key words: Paraganglioma; Larynx; Laser Surgery

Introduction

Paragangliomas are benign neoplasms arising from the neural crest-derived paraganglia of the autonomic nervous system.[1] Extra-adrenal paraganglia have been identified in various localities in the human body. In 1743 Haller *et al.*[2] were the first to describe paraganglionic cells in relation to the carotid body. In the larynx three different localizations of paraganglia are known. In 1963 Watzka[3] described the regular occurrence of laryngeal paraganglia, which are usually located submucosally in the anterior superior portion of the vestibular fold along the course of the superior laryngeal nerve. One year later Kleinsasser[2] reported the constant presence of laryngeal paraganglia that were bilaterally situated a little more distally, close to the lateral margin of the cricoid cartilage in the cricotracheal membrane near the recurrent laryngeal nerve. Kleinsasser then founded the term 'Glomera laryngea superiores et inferiores'.[2] He also discovered the third laryngeal glomus, which is unpaired and located in front of the cricothyroid membrane (anterior laryngeal glomus).

Most laryngeal paragangliomas (82 per cent) arise from the supraglottic larynx[4] and are preponderantly located on the right aryepiglottic fold-false vocal cord region.[5] Laryngeal paragangliomas are three times more common in women and are typically benign.[4]

Clinical symptoms such as hoarseness, dysphagia, dysphonia, dyspnoea, stridor, sore throat, haemoptysis, neck mass, coughing, shortness of breath, foreign body sensation in the throat and ear pain have been reported.[4,6,7]

The macroscopical aspect of laryngeal paragangliomas is often described as reddish or bluish-red, lobulated submucosal masses of varying diameters that are usually covered with intact laryngeal mucosa.[8] On macroscopic sections paragangliomas occur as firm and rubbery masses with a red or brown surface. Paragangliomas may also be covered by a fibrous capsule.[6,9]

Microscopically the tumour is composed of chief cells arranged in clusters and round cell nests, which are also known as 'Zellballen', surrounded by a delicate stroma containing numerous vascular channels. Large vesicular nuclei and abundant granular eosinophilic cytoplasm of the cells are typical. Glandular structures are absent as is mucin.[4,9] Mitotic figures are rare.[5] Immunocytochemical findings of paragangliomas are characteristic staining of peripherally located sustentacular cells by S-100 protein and glial fibrillary acidic protein (GFAP). Furthermore an argyrophillic positivity is described. The tumour stains positive with chromogranin, synaptophysin, neuron specific enolase (NSE), protein gene product (PGP) 9.5, metencephalin and serotonin.[10] The absence of immunostaining for cytokeratin, calcitonin, bombesin, carcinoembryonic antigen (CEA) and epithelial membrane antigen (EMA) is a feature that supports the diagnosis of paraganglioma, as these antigens are identified in atypical carcinoid tumours.[6,9,11]

The major differential diagnosis of a laryngeal paraganglioma includes a carcinoid tumour, haemangiopericytoma, malignant melanoma, metastatic renal cell carcinoma, anaplastic carcinoma and medullary carcinoma of the thyroid.[4]

In their reviews of 1991 and 1994 respectively, Barnes and Ferlito analysed all cases of laryngeal paragangliomas published so far.[4,11] They accepted fewer than 70 cases as true laryngeal paragangliomas, according to certain criteria that had to be fulfilled. These criteria of acceptance are

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TABLE I
TREATMENT OF LARYNGEAL PARAGANGLIOMAS SINCE THE IMPLEMENTATION OF LARYNGEAL CO_2 LASER SURGERY (1972)

Author	Year	Cases	Origin	Size	Therapy
Tobin and Harris[20]	1972	1	supraglottic	6 x 4 cm	supraglottic laryngectomy
Helpap and Koch[21]	1974	1	supraglottic	–	surgical resection
Greenway and Heeneman[22]	1975	1	supraglottic	4 cm	subtotal supraglottic laryngectomy
Piquet *et al.*[23]	1976	1	supraglottic	–	extralaryngeal excision
Markowska *et al.*[24]	1976	1	glottic	pea size	surgery
Lack *et al.*[25]	1977	1	supraglottic	3.3 cm	surgical excision
Ani *et al.*[26]	1979	1	subglottic	–	local excision
Gallivan *et al.*[27]	1979	1	supraglottic	2.5 cm	surgical resection
Wilhelm *et al.*[28]	1980	1	supraglottic	walnut size	surgery
Neto[29]	1980	1	supraglottic	3.5 cm	surgery
Schaefer *et al.*[30]	1980	1	supraglottic	2 cm	supraglottic laryngectomy
Hordijk *et al.*[31]	1981	2	supraglottic	3 x 2 x 1.5 cm	cryosurgery prior to laryngofissure
			supraglottic	–	radiotherapy prior to laryngectomy
Basset *et al.*[32]	1982	1	supraglottic	2.5 cm	embolization, lateral pharyngotomy
Bielawna *et al.*[33]	1982	1	supraglottic	2 cm	surgery
Olofsson *et al.*[34]	1984	1	subglottic	–	laryngectomy
Davidge-Pitts[35]	1985	1	supraglottic	2.5 cm	partial supraglottic laryngectomy
Stanley *et al.*[36]	1986	1	supraglottic	0.5 cm	endoscopic excision
Baugh *et al.*[37]	1987	1	supraglottic	2 cm	partial laryngectomy
Zikk *et al.*[38]	1987	1	supraglottic	1 cm	excision via laryngoscopy
Konowitz *et al.*[15]	1988	1	supraglottic	–	endoscopic excision
Googe *et al.*[39]	1988	2	subglottic	–	laryngectomy
			subglottic	–	local excision
Bootz *et al.*[40]	1988	1	supraglottic	–	laryngectomy
Kliewer *et al.*[41]	1989	1	–	2.5 cm	–
Urso *et al.*[42]	1989	2	supraglottic	–	surgical resection
			supraglottic	–	surgical resection
Barnes[4]	1991	2	supraglottic	3.5 cm	supraglottic laryngectomy
			supraglottic	3 cm	lateral pharyngotomy with local excision of the tumour
Brandwein *et al.*[43]	1992	1	subglottic	2.5 cm	surgical resection
Rubin and Silver[44]	1992	1	supraglottic	–	supero-lateral thyrotomy
Werner *et al.*[8]	1992	1	supraglottic	2.9 x 1.8 x 1.4 cm	microlaryngoscopical resection
Contreras-Mejuto *et al.*[45]	1993	1	subglottic	0.9 x 0.7 x 0.8 cm	anterior thyrotomy with sample excision
Ferlito *et al.*[11]	1994	8	supraglottic	–	local excision
			supraglottic	–	–
			supraglottic	–	local excision
			supraglottic	2 cm	total laryngectomy
			supraglottic	5 cm	laryngectomy
			supraglottic	6 cm	pharyngotomy with local excision
			supraglottic	4 cm	local excision
			supraglottic	2.8 cm	local excision
Özünlü *et al.*[46]	1996	1	supraglottic	3 x 2.5 x 1.5 cm	laryngofissure
Pyd *et al.*[47]	1996	1	supraglottic	–	partial laryngectomy
Peterson *et al.*[48]	1997	1	subglottic	1.3 x 1.5 cm	partial laryngectomy and closure by muscle flap
Thirlwall *et al.*[19]	1999	1	supraglottic	–	conventional surgery and CO_2-laser surgical debulking in a 2nd step
Sanders *et al.*[16]	2001	1	supraglottic	approx. 4 cm	supraglottic laryngectomy
Sesterhenn *et al.* (present article)	2002	1	supraglottic	4 x 4 x 3 cm	complete endoscopical CO_2-laser surgical resection

listed in the review published by Barnes.[4] Since that time further cases of laryngeal paragangliomas have been published (Table I).

A review of the literature shows that the treatment of choice for laryngeal paragangliomas is surgical excision. Since the implementation of CO_2 laser surgery into laryngology in 1972,[12] no reports of endoscopic laser surgical excision of laryngeal paragangliomas have been published.

In the present case the complete and successful transoral resection of a large paraganglioma of the larynx utilizing CO_2 laser surgery is demonstrated for the first time.

Case report

A 66-year-old woman had been complaining about hoarseness and dysphagia for many years. She first saw a doctor in November 1996 after several episodes of haemoptysis. Indirect laryngoscopy showed a smooth deliminated tumour of the left supraglottic region, covering the entire left vocal fold. There were no palpable cervical lymph nodes or masses. The histopathology of a biopsy specimen showed vascular tissue with dilated vessels, oedema and fibrosis. There was no indication of any kind of malignancy. Because the attending physician was concerned that the bleeding episodes could recur and the endolaryngeal tumour could increase in size, he referred the patient to the Department of Otolaryngology, Head and Neck Surgery, University-Hospital of Kiel in 1997 with the presumed diagnosis of a supraglottic vascular malformation. The computed tomography (CT)-scans and angiograms showed a well-delineated tumour-like lesion in the supraglottic region. The tumour extended in the pre-epiglottic region and also in the left lateral side of the neck (Figures 1 and 2). In the subsequent microlaryngoscopical procedure the tumour was removed by CO_2-laser surgery transorally under general anaesthesia. Intra-operatively

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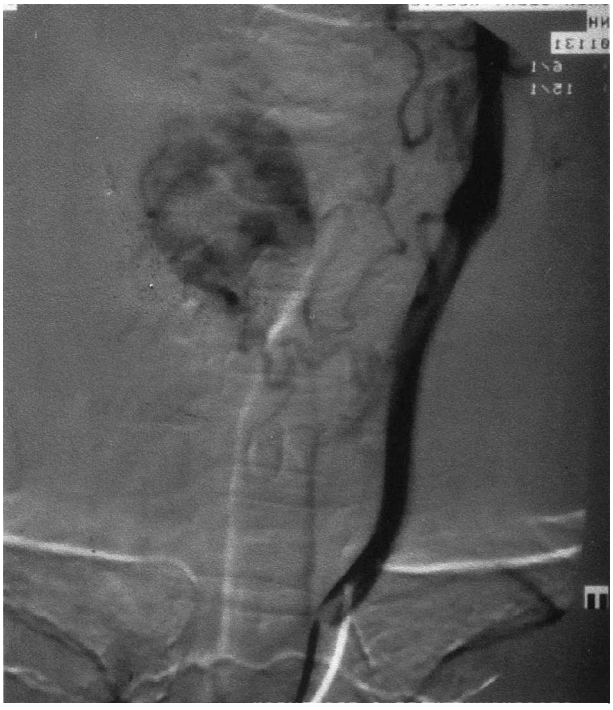

FIG. 1
Angiographic image demonstrating the extent and vascularity of a laryngeal paraganglioma.

the glottic space and the true and false vocal folds appeared completely free of tumour (Figure 3). Because of the extension of the strongly vascularized tumour, which was covered by intact mucosa (Figures 4 and 5), a partial left epiglottectomy had to be performed to achieve a better exposure of the tumour. Major vessels feeding the tumour were ligated with titanium clips. Thus, the tumour could be removed completely with safe margins (Figure 6). The resulting wound lesion was finally covered with fibrin glue and a naso-gastric feeding tube was placed. Peri-operatively the patient received i.v. antibiotics (cephalexin 1500 mg and metronidazole 400 mg) and prednisolone 250 mg. Post-operatively the patient was nursed in the intensive care unit and remained intubated and ventilated

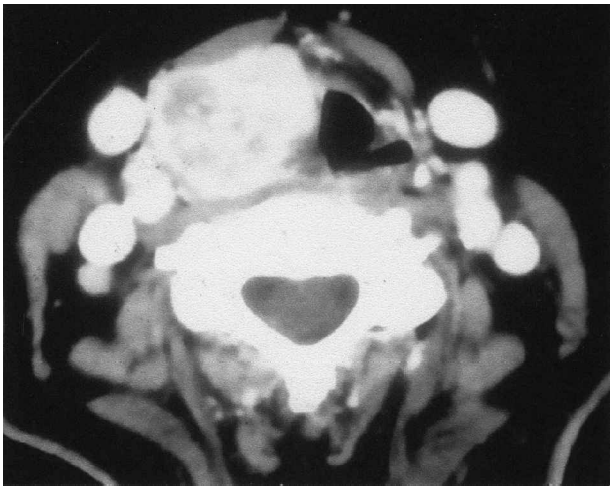

FIG. 2
Axial contrast enhanced CT-scan showing the laryngeal mass, which was found to be a laryngeal paraganglioma.

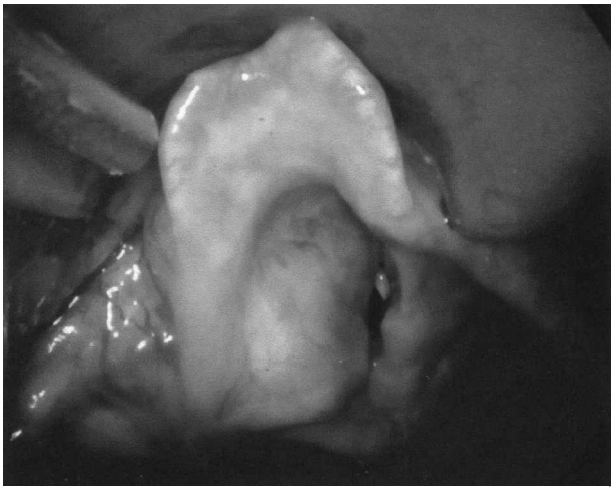

FIG. 3
Endoscopic exposure of the supraglottic laryngeal tumour.

for another 48 hours to avoid a tracheostomy. She was then extubated without any problems. The patient recovered nicely. Her breathing and swallowing were unimpaired. The initial hoarseness related to post-operative oedema and a reduced mobility of the left vocal fold, which improved under logopedic therapy. The further clinical course was uneventful, episodes of dyspnoea or bleeding did not occur. The patient was discharged from hospital without any complaints on the 14th post-operative day. A five-year follow-up has showed no recurrence. The patient is free of discomfort, speech and deglutition is normal.

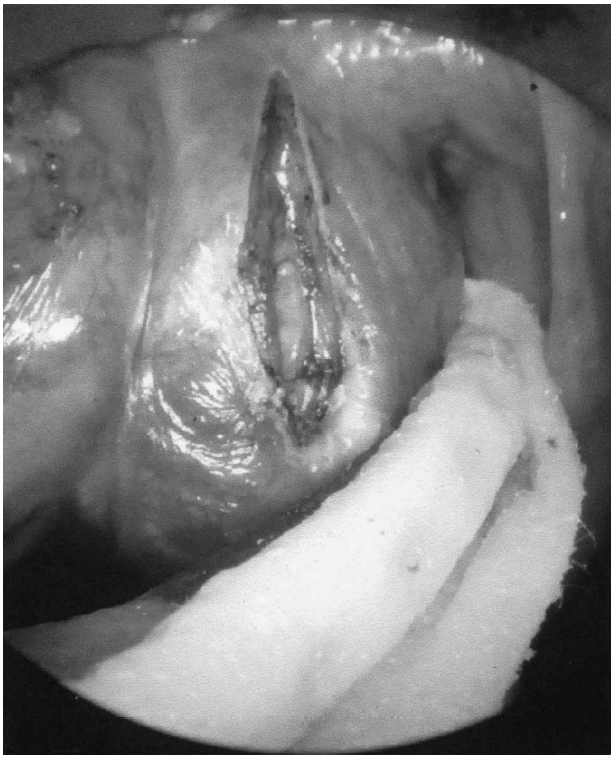

FIG. 4
CO_2 laser surgical incision of the overlying mucosa. Wet gauze is placed into the larynx to protect the endotracheal tube against accidental hits of laser beam.

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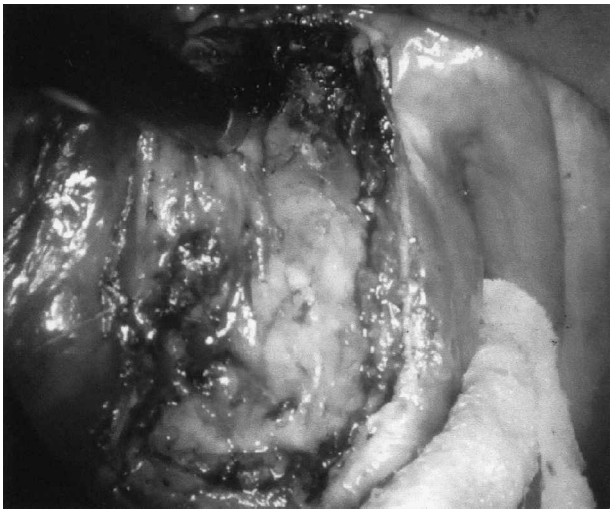

FIG. 5
Stepwise CO_2 laser surgical preparation along the capsule.

Histopathological findings

Macroscopically the surgical tumour specimen was $40 \times 40 \times 30$ mm in size and of soft consistency with a brownish-white surface (Figure 7). Microscopically the partially encapsulated tumour was composed of epithelial-trabecular tissue with some solid areas and thin fibrous tissue strands. The well-defined nests of epithelioid cells were arranged in distinct clusters ('Zellballen') (Figure 8). Focally distinct pleomorphic and giant nuclei were seen. Also pyknotic, hyperchromatic nuclei but less mitotic figures were observed. The tumour cells were separated by vascular channels containing erythrocytes creating an organoid pattern. The tumour margins were composed of angiomatous patterns with tumour cells with little cytoplasm. Immunohistochemical investigations of the tumour showed positive reactions for the neuroendocrine markers chromogranin, NSE and synaptophysin. The sustentacular cells stained positively with the S-100-protein. In contrast the reaction with NB84, which is a marker for neuroblastomas, was negative. The histopathological findings mentioned above led to the diagnosis of a 'paraganglioma laryngeale' partially of the angiomatous type.

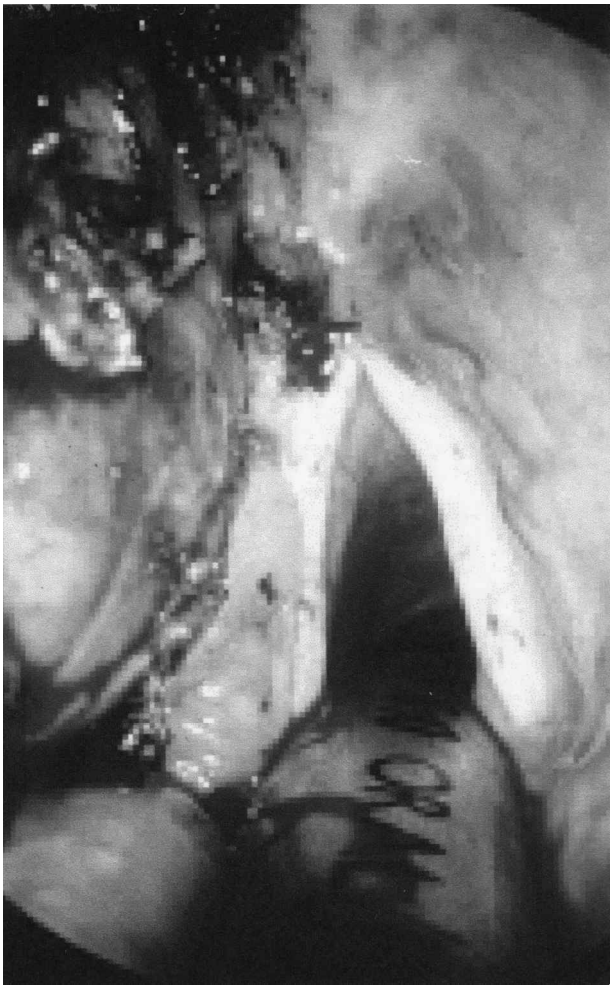

FIG. 6
Endolaryngeal aspect after complete CO_2 laser surgical removal of the tumour.

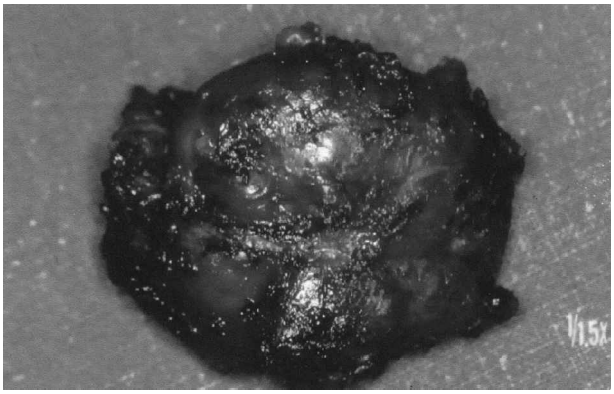

FIG. 7
Tumour specimen after complete CO_2 laser surgical excision.

Discussion

Paragangliomas of the larynx are rare neoplasms which have been reported increasingly since the early 1960s. Paragangliomas in the larynx may arise from three different localities, but they occur mostly in the supraglot-

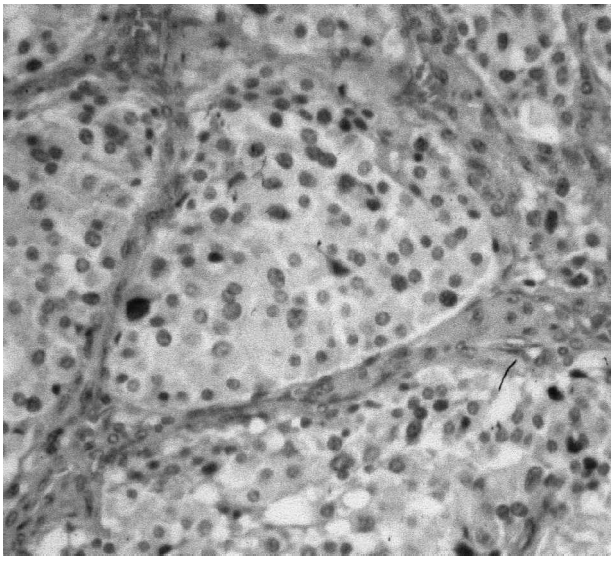

FIG. 8
Typical nesting of cells (Zellballen) in an haematoxylin-eosin staining.

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tic space. Since these tumours are highly vascularized and their size is not always easy to estimate from the laryngoscopical aspect, there may be misleading diagnoses such as vascular malformations.

Imaging procedures such as contrast-enhanced CT and, if necessary, magnetic resonance imaging (MRI) should belong to the standard examinations in questions concerning endolaryngeal tumours. Furthermore pre-operative angiography to evaluate the size, extent and especially the vascular structure and blood supply of the lesion, eventually in combination with selective embolization, may be extremely helpful.[13–17] Sanders also recommends a pre-operative arteriogram to determine the status of the circle of Willis which should help the surgeon in decision making, if the unlikely event of a carotid resection should occur.[16] From our point of view such procedures should be reserved to extended paragangliomas.

An accurate histological diagnosis of the tumour should in general be obtained by biopsy prior to definite treatment. Since paragangliomas are highly vascularized tumours one must be aware of the possibility of several haemorrhages through biopsies. Even needle biopsies may be hazardous. Furthermore, it has to be taken into consideration that laryngeal paragangliomas are usually covered by intact mucosa, so that a deep biopsy, if needed, is always necessary to avoid false diagnosis.

Since the blood supply of most supraglottic laryngeal paragangliomas is predominantly realized by the superior thyroid artery, some authors[4,14–16] recommend the ligation of the feeding vessel, which can easily be performed prior to resection of the lesion to minimize intra-operative blood loss. In the present case titanium clips were transorally placed to ligate the major feeding vessels.

The treatment of choice in all of the 46 analysed cases of laryngeal paragangliomas, which have been published since 1972, was surgical excision. A review of these 46 cases showed that classical surgical methods such as total laryngectomy (n = 7), supraglottic laryngectomy (n = 7) and surgical resection (n = 22) which was not further specified, were the major treatment strategies. The surgical approach varied between laryngofissure, lateral pharyngotomy and endoscopical access. In three cases of cryosurgery, radiation respectively and embolization were performed prior to surgery. Also in recurrent cases conventional surgery and excision was the treatment of choice.

Radiation, either pre-operatively or post-operatively and chemotherapy as an alternative to surgical treatment has been reported to be ineffective in the management of paragangliomas of the larynx.[4,13–15]

In recent years the endoscopical, laser-microsurgical resection of large laryngeal tumours has increased.[18] However, up to now not a single report about a complete endoscopical, CO_2 laser surgical resection of a laryngeal paraganglioma has been described. In 1999 Thirlwall *et al.*[19] reported a case where a child received emergency microlaryngoscopy and conventional tumour debulking because of a laryngeal paraganglioma. Initially this mass had been diagnosed as a capillary haemangioma. In a second session this child underwent further debulking with a carbon dioxide laser. After the lesion had recurred several times during a period of one year, and a laryngeal paraganglioma was diagnosed, this child underwent a partial supraglottic laryngectomy via an anterior pharyngotomy approach and removal of a large right supraglottic lesion.

Endoscopic excision alone was already refuted by many authors because of the reduced exposure in the endoscopic operation site. It has been criticized that severe life-threatening haemorrhage may prove difficult to control in endoscopic procedures and that the control of surgical margins may not be safe.[4,14,15] This could be true in those cases where the localization of the tumour is unfavourable, for example in the subglottic space. Also the use of different laser systems was found to be unsuccessful in many publications about the treatment of laryngeal paragangliomas.[4,11,13,15] In the present case it was successfully demonstrated, that extended ($4 \times 3 \times 4$ cm), supraglottic vascular lesions could safely be excised endoscopically (Figure 4). To get a better access to the advanced supraglottic tumour, depending on the localization, a partial epiglottectomy should be performed first. After mucosal incision and exposure of the capsule, the tumour may then be excised stepwise keeping the fibrous capsule intact. Larger vessels may be ligated easily by titanium-clips. After the complete removal of the tumour a large endolaryngeal wound results. To avoid post-operative bleeding fibrin glue may be used in certain cases to seal the wound.

- **This is a case report describing excision of a laryngeal paraganglioma using a CO_2 laser**
- **The paper is presented as it is the first such case excised with a laser**
- **The article also contains a discussion of the pre- and post-operative management of such cases**

The present case underlines that the use of the endoscopical CO_2 laser surgical resection of even extended laryngeal paragangliomas may be an alternative to conventional surgical excision, in selected cases, and deserves its place as an alternative treatment modality. Especially in cases of small lesions, endoscopical access to the tumour and the possibility of CO_2 laser-surgical excision should be considered.

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