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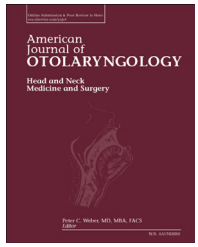

Treatment of cervical paragangliomas: Is surgery the only way?☆,☆☆

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ABSTRACT

Purpose: To analyze the results after surgery or stereotactic radiotherapy (SRT) in the treatment of cervical paragangliomas. Against this background, the decision-making algorithm used in the treatment of carotid body tumors (CBTs) and vagal paragangliomas (VPs) was reevaluated relative to the existing literature on the topic.

Materials and methods: Retrospective study between 2000 and 2012. A total of 27 CBTs and nine VPs in 32 patients were treated. Shamblin class I: 59.3% (n = 16); class II: 29.6% (n = 8); class III: 11.1% (n = 3). Treatment modalities were surgery, radiotherapy, or observation. The end points for analysis were long-term tumor control and integrity of the cranial nerves.

Results: 21 CBTs and seven VPs underwent surgery; SRT was performed in three CBTs and two VPs. Three CBTs were clinically observed. Permanent nerve paresis followed after surgery for CBTs in five patients (20%) and in all patients with VPs. No impaired cranial nerve function resulted after SRT. The median follow-up period was 4.7 years. The tumor control rate after therapy for CBTs and VPs was 100%. One CBT that received clinical observation showed slow tumor progression.

Conclusions: A surgical procedure should be regarded as the treatment of choice in patients with small CBTs. In larger CBTs, particularly in elderly patients with unimpaired cranial nerves, radical surgery should be regarded critically. As surgery for VPs caused regularly impairment of cranial nerves with functional disturbances of various degrees a comprehensive consultation with the patient is mandatory and nonsurgical strategies should be discussed.

1. Introduction

Head and neck paragangliomas (HNPs) are highly vascularized tumors, in which histopathological signs of malignancy are only seen in approximately 3% of cases [1]. HNPs show a mean growth rate of only approximately 0.2 cm per year [2]. They originate in paraganglionic tissue in the area of the carotid bifurcation (carotid body tumors, CBTs), the jugular foramen

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and tympanic plexus (jugulotympanic paragangliomas, JTPs), the vagal nerve (vagal paragangliomas, VPs), and the facial nerve [3,4]. HNPs may occur either sporadically or in the context of a hereditary familial tumor syndrome. Multilocular presentations of glomus tumors are observed in 10–20% of sporadic cases and up to 80% of hereditary cases. Hereditary HNPs are mostly caused by mutations in the succinate dehydrogenase complex (*SDHx*) genes, in particular *SDHD* [5]. The internationally accepted clinical classification of CBTs is the Shamblin system, with classes I–III corresponding to permanent postoperative side effects (Table 1) [6,7]. There is no internationally accepted classification system for VPs.

The paradigm used in the treatment of patients with cervical paragangliomas is apparently changing at present, with an increasing trend toward individualized therapeutic strategies. The literature provides good evidence for the effectiveness of a tailored and function-preserving surgical approach in the treatment of CBTs and VPs, as well as for primary or staged stereotactic radiotherapy (SRT) [8–12]. In selected patients, clinical observation appears to be an adequate strategy as well [2].

The purpose of the present study was to analyze the results in relation to long-term tumor control and integrity of the cranial nerves in patients receiving surgery or SRT in the treatment of cervical paragangliomas. Against this background, the decision-making algorithm used in our institution was reevaluated in relation to the existing literature on the topic.

2. Materials and methods

A total of 27 CBTs and nine VPs in 32 patients were treated between 2000 and 2012. The patients consisted of 10 men (31.3%) and 24 women (75%), with a mean age of 54.8 years (range 30–86 years).

2.1. *Algorithm for diagnostic work-up*

All patients with a cervical mass undergo ultrasonography of the neck as the initial diagnostic procedure at our institution, regardless of any imaging findings from external sources that may be available. Ultrasound is also carried out when patients have been admitted with an asymptomatic incidental imaging finding. To distinguish CBTs from VPs, particularly on ultrasonography, it is helpful to recall that CBTs typically displace the external carotid artery anteromedially and the internal carotid artery posterolaterally, while VPs displace both arteries anteriorly. Magnetic resonance imaging (MRI) was used for further diagnosis, particularly in cases of suspected VP, in order to delineate the cranial extension to the skull base. MRI angiography or computed-tomographic angiography was additionally carried out preoperatively. Digital subtraction angiography (DSA), with embolization of the afferent vessels, was performed only in a few patients, particularly in cases of suspected VP [13]. Germline mutations (*SDHx*) have been investigated routinely in our department since 2009 in patients with multiple presentations of HNPs, young patients, and patients with a positive family history, and fluorodihydroxyphenylalanine F 18 (^{18}F-FDOPA) positron-emission tomography (PET) or metaiodobenzylguanidine (MIBG) scintigraphy was carried out [5,14].

Table 1 – The Shamblin classification for carotid body tumors (CBTs).

Class	Characteristics
I	Tumors with splaying of the carotid bifurcation but little attachment to the carotid vessels
II	Tumors that partially surround the carotid vessels
III	Tumors that intimately surround the carotids

2.2. *Algorithm for treatment and decision-making*

Surgery is generally indicated as the treatment of choice, with the aim of achieving complete macroscopic resection of the tumor. When the caudal cranial nerves were found to be free of tumor or only partly infiltrated intraoperatively, every effort was made to preserve the neural structures — e.g., with microscopic dissection or subtotal resection. However, if cranial nerve deficits (CNDs) were evident preoperatively or the vagal nerve in particular showed complete tumor infiltration, the surgical procedure was more radical and the nerve was sacrificed. An indication for primary radiotherapy was only established rarely, but this was carried out particularly if a surgical procedure was likely to involve a high risk of damage to several intact cranial nerves. In addition, the indication for surgery or SRT depended on the patient's preferences and concomitant diseases. In patients with multiple HNPs, an individualized treatment strategy combining both surgical and nonsurgical methods was planned.

Ultrasound examinations and MRI were carried out at the annual check-ups. In addition to freedom from recurrences, criteria for successful tumor control following surgical procedures included a postoperatively stable residual tumor or a progression-free primary lesion following SRT.

2.3. *Planning and implementation of radiotherapy*

SRT was performed using a Novalis shaped-beam surgery center (Brainlab Ltd., Feldkirchen, Germany). The dosage was standardized to the reference point; individual doses of 1.8–2.0 Gy, conventionally fractionated, were administered up to 50–56 Gy [3].

The study was approved by the institutional review board at the University of Erlangen–Nuremberg.

3. Results

3.1. *Carotid body tumors*

The 27 CBTs in 24 patients (mean age 54.5 years) were categorized in accordance with the Shamblin classification as: class I: 59.3% (n = 16); class II: 29.6% (n = 8); and class III: 11.1% (n = 3). The most frequent symptom was a neck mass in 75% of cases (n = 18). Paresis of the vagal nerve and irritation of the cervical plexus were present in one case each (4.7%). In five cases (20.8%), the CBT was an incidental finding.