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Multiple paragangliomas of the head and neck - a case report

Mnogi przyzwojak głowy i szyi – opis przypadku

Tomasz Wojciechowski[1,2], Adrian Drożdż[3], Kazimierz Niemczyk[1]

[1]Department of Otolaryngology, Medical University of Warsaw, Poland
[2]Department of Clinical and Descriptive, Center for Biostructure Research, Medical University of Warsaw, Poland
[3]Students Scientific Group in the Department of Otolaryngology, Medical University of Warsaw, Poland

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ABSTRACT: Paragangliomas are rare, most commonly non-malignant tumors of the autonomic nervous system. Their location within the head is rather an exception than a rule, similarly as their multifocal prevalence. The authors of this paper present a case of a patient with bi-focal paraganglioma. The first symptom of illness was facial nerve palsy, diagnosed for the period of about 3 years. After making the initial diagnosis of tympanic paraganglioma, the tumor was operated. During the next 7 years, there was a reccurence within the temporal bone. What is more, periodic imaging examination showed a second foci within the neck, moreover asymptomatic. The authors discuss the natural development of paragangliomas in the region of head and neck and present the current knowledge about management of patients with a suspicion, diagnosis and treatment of this disease.

KEYWORDS: multiple paragangliomas, facial nerve, neck tumor, tinnitus

STRESZCZENIE: Przyzwojaki to rzadkie, najczęściej niezłośliwe nowotwory autonomicznego układu nerwowego. Ich lokalizacja w obrębie głowy jest raczej wyjątkiem niż regułą, tak samo jak ich wieloogniskowe występowanie. W niniejszej pracy autorzy prezentują przypadek chorej z dwuogniskowym przyzwojakiem. Pierwszym objawem choroby był niedowład nerwu twarzowego, który diagnozowano około 3 lat. Po postawieniu wstępnego rozpoznania przyzwojaka bębenkowego guz zoperowano. W ciągu następnych 7 lat nastąpiła wznowa w obrębie kości skroniowej. Ponadto w kontrolnych badaniach obrazowych uwidoczniono drugie ognisko w obrębie szyi, skądinąd bezobjawowe. Autorzy zastanawiają się w dyskusji nad naturalnym rozwojem przyzwojaków głowy i szyi, a także przedstawiają obecny stan wiedzy na temat postępowania z chorym przy podejrzeniu, a następnie rozpoznaniu i leczeniu tej choroby.

SŁOWA KLUCZOWE: mnogi przyzwojak, nerw twarzowy, guz na szyi, szumy uszne

INTRODUCTION

Paragangliomas are a rare, most commonly non-malignant tumors that originate from paraganglia of the sympathetic or parasympathetic nervous system [1]. Their prevalence is mainly sporadic, although in around 1 of 10 cases, there happen to be a part of genetic disorders such as hereditary paraganglioma, Carney complex or multiple endocrine neoplasia syndrome {Baysal, 2000 #3; Boedeker, 2011 #9}]. The natural course of these tumors' development is slow, and the symptoms are non-characteristic, making the path from the first symptom to accurate diagnosis and treatment possibly last for many years.

CASE REPORT

The case history of a currently 39-year-old patient begins in 2008 when the patient suddenly experienced right-sided facial nerve palsy. Initially diagnosed with borreliosis, after 3 years and a series of imaging studies she was taken into the Department of Otolaryngology at the Hospital in Siedlce for

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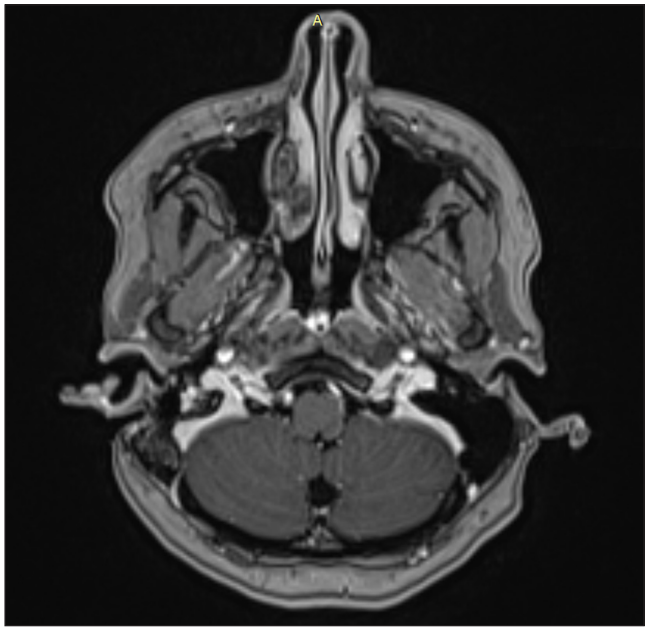

Fig. 1. ??????????????????????????????

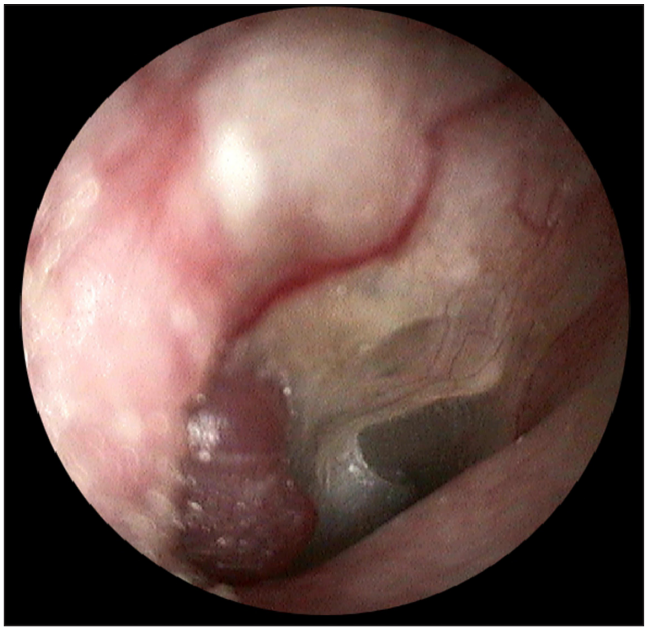

Fig. 2. ??????????????????????????????

Tab. I. Clinical classification of carotid body paraganglioma by Shamblin et al.

CLASS	TUMOR CHARACTERISTICS
Class I	Tumor delineates the common carotid artery bifurcation, but with a small adhesion to cervical vessels
Class II	Tumor partially surrounds carotid arteries
Class III	Tumor completely surrounds and encease carotid arteries

surgical treatment due to a tumor located in the middle ear air spaces on the right side, extending on the base of the skull medially towards the jugular foramen. The tumor was removed via antromastoidectomy. The tumor grew on the facial nerve. Due to total destruction of the facial nerve in the mastoid segment, simultaneous anastomosis of the facial nerve and hypoglossal nerve was performed. Histopathological examination confirmed the suspicion of tympanic paraganglioma. Since then, the patient remained under constant otolaryngologic care. In 2014, NMR of the head was performed with a description of decreased aeration within the mastoid process and the base of the petrous part of the temporal bone, however no pathology within the cerebrum and the cerebellopontine angle was observed. No signs of tumor recurrence at the operated area were observed. The area around the neurovascular bundle available for examination was free of any pathology. In June 2017, periodical NMR of the head was done, in which contrast enhancement with a diameter of 8mm is described at the operated area (image no. 1). Two months later, CT of the temporal bones was performed. It described a soft-tissue lesion of 1 cm3 just below the right posterior semicircular canal and the structure modeling the lower posterior wall of the external auditory meatus, which was later revealed in otoscopic examination (image no. 2). None of the above showed lesions along large vessels of the neck.

The patient reported to the Department of Otolaryngology, Medical University of Warsaw for second surgery and removal of suspected recurrence of tympanic paraganglioma. At the moment of admission to hospital, the patient suffered from facial nerve paralysis (House-Brackmann Grade 3). Moreover, she reported earache, hearing loss that lasted for half a year and constant, right-sided high-pitched tinnitus in the form of squeaking. Pure-tone audiometry was performed (image no. 3). The ailments that she experienced after the first surgery, i.e., headaches in the occipital region, vertigo (rocking, swaying dizziness), pulsating sensation and ear fullness had not changed their intensity over the previous few years. During hospitalization, NMR periodical examination from 2 months ago was assessed and existence of another tumor was concluded - this time, near the external opening of carotid canal (images no. 4 and 5). The lesion was not palpable and did not show any symptoms. The patient underwent lateral petrosectomy removing the residual tumor from the temporal bone, which occupied the vicinity of the internal carotid artery and internal jugular vein but did not cause symptomatic pressure on any of the above. During that same surgery, the second tumor was removed which did not join with the recurrence of the previously described paraganglioma. It was located at the base of the skull near the jugular foramen and shifted forward in the internal carotid artery with its mass covering a group of lower cranial nerves - it was dissected and entire-

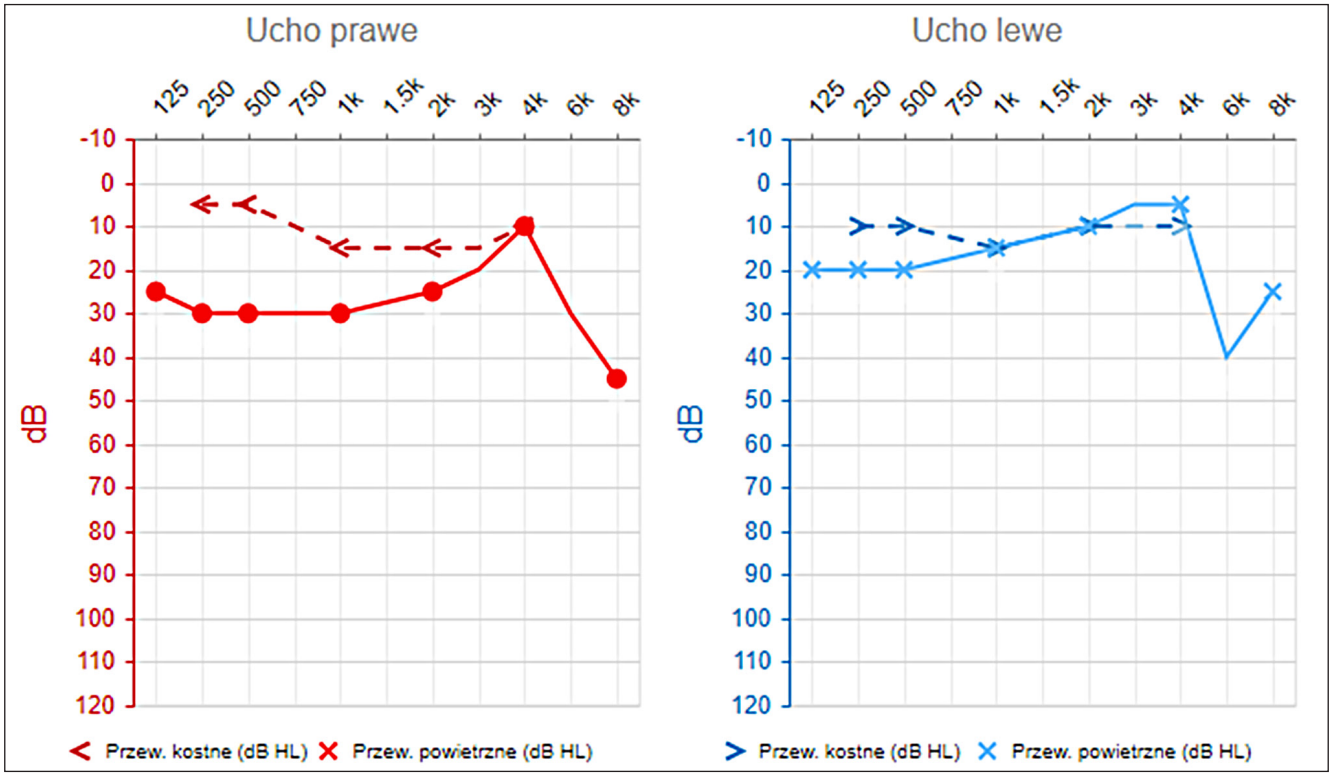

Fig. 3. ??????????????????????

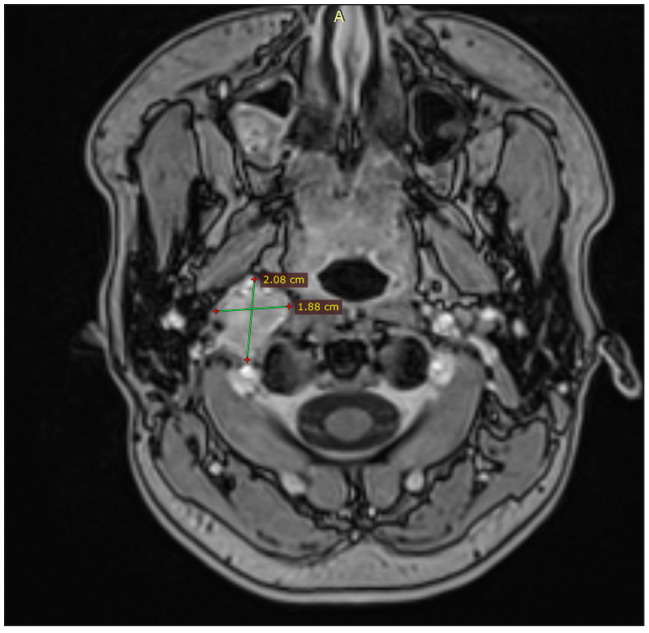

Fig. 4. ????????????????????????????

ly removed. Tumor point of origin could not be determined perioperatively. The lesion was connotated with nerves in this area. In histopathological examination, microscopically the image corresponded to paraganglioma (immunohistochemically positive for chromogranin A and synaptophysin). After surgery, nerve palsies (nerves IX, X and XII), corresponding to tumor location were found. Dysphagia and tongue mobility disorders decreased during hospitalization. The patient was discharged home on the ninth day following the surgery in good general condition. Next, she was referred to voice as well as dysphagia rehabilitation, and is currently experiencing subjective improvement. The patient remains under constant control of the hospital's otolaryngologic clinic.

DISCUSSION

Paraganglioma is a neuroendocrine tumor that originates from nonchromaffin paraganglic cells derived from the neural crest [1]. It is located near the fibers of the autonomic nervous system [2]. In both Polish as well as English literature, there are a few improper names of this tumor. This results from incorrect identification of paraganglioma with glomangioma or glomus tumors, which are of myoepithelial origin. Chemodectoma is an inaccurate term, as only glomus caroticum of the discussed ganglion cells appears as a chemoreceptor. Taking into account these inaccuracies, the name glomus tumor and chemodectoma should not be used [3, 4].

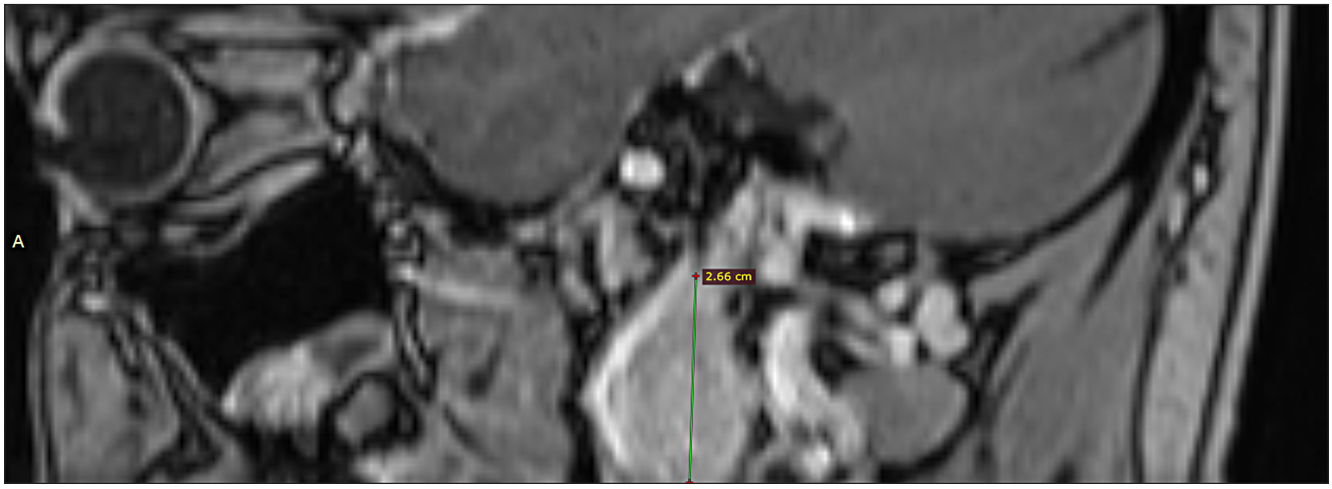

Fig. 5. ??????????????????

Tab. II. Classification of jugulotympanic paragangliomas according to Fisch et al.

CLASS	TUMOR CHARACTERISTICS
A	*Tumor limited to promontorium and mesotympanum*
B	Tumor occupies hypotympanum, bone over jugular foramen intact
C	
C_1	Erosion of the carotid foramen
C_2	Destruction of vertical segment of the carotid artery
C_3	Involvement of horizontal segment of the carotid artery, invasion of foramen lacerum
C_4	Invasion of foramen lacerum and cavernous sinus
De	Intracranial and epidural extension
De_1	Displacement of the dura less than 2cm
De_2	Displacement of the dura more than 2cm
Di	Intracranial and intradural extension
Di_1	Invasion of posterior cranial fossa <2cm
Di_2	Invasion of posterior cranial fossa 2-4cm
Di_3	Invasion of posterior cranial fossa >4cm

The most common location of paraganglioma in the head and neck region is glomus caroticum at the bifurcation of the common carotid artery [CCA] [5]. More uncommon locations are: jugular bulb, tympanic plexus, ganglia of the vagus nerve, ciliary ganglion, nasal cavity [6]. In the context of atypical location of the discussed case, it should be noted that due to origin, the above tumors in the head and neck region may theoretically be located around cranial nerve ganglia with autonomic parasympathetic fibers, i.e., oculomotor nerve (III), facial nerve (VII), glossopharyngeal nerve (IX) and vagus nerve (X). In practice, however, it seems pointless to search for cases referring to an origin other than the glossopharyngeal nerve (around the tympanic plexus, fossula petrosa or Hering's nerve) or the vagus nerve (ganglia in the jugular foramen area) [5, 6]. In the case described, the tumor's point of origin was probably the inferior ganglion of glossopharyngeal nerve. It is also noteworthy that paraganglioma can be located in the vicinity of sympathetic autonomic fibers, specifically along the sympathetic trunk and its ganglias. However, this is an extremely rare situation, although it has been described, for example, by Moyer and Bradford as the cause of Horner's syndrome [7].

Paragangliomas are rare tumors that constitute 0.6% of head and neck neoplasms and 0.03% of all neoplasms [8]. They are characterized by high vascularization, slow growth and usually a benign course. Tumor volume doubling time is estimated at approximately 10 years [9]. Depending on location, malignant tumors constitute from 2% to 19% of cases. Malignant progression of paraganglioma is usually found in lesions that originate from carotid body [6]. Due to lack of histopathological and immunohistochemical criteria of paraganglioma malignancy, such a situation is confirmed by the presence of metastases to the lymph nodes or distant metastases. [3, 4, 6]. Patients suffering from paraganglioma require long-term observation due to possibility of distant metastases even up to 30 years after surgery. They are most commonly found in the lungs, bones and liver [3, 8].

Paragangliomas are observed 3 to 4 times more often in women than in men [4]. They can occur at any age, however, the peak incidence occurs between 40 and 50 years of age [10].

The etiology of paragangliomas has not been fully elucidated. More frequent prevalence in people who live at high altitudes and suffer from chronic obstructive pulmonary disease gives rise to the suspicion of chronic hypoxia as a factor playing a

role in the formation of these tumors [3, 11, 12]. In addition to sporadic prevalence, the family prevalence of paraganglioma is well documented in literature. It may be occur in the form of paraganglioma syndromes [PGL1, PGL2, PGL3, PGL4] or belong to genetic syndromes such as: MEN, NF1 or VHL [3, 11, 13]. In 2000, Baysal et al. first described a succinate dehydrogenase complex subunit D gene mutation [SDHD] - one of the proteins of the mitochondrial respiratory chain [11, 13]. This mutation comprises the basis for development of PGL1 syndrome. PGL3 and PGL4 syndromes are associated with mutations in SDHC and SDHB genes, respectively [3, 6, 11]. Patients with these mutations comprise a group with greater risk of earlier illness and prevalence of multiple paragangliomas. Multiple paragangliomas are found in 80% of familial cases compared to 10-20% in sporadic cases [14].

The symptoms of paraganglioma depend on the primary location of tumor. Carotid body paraganglioma remains "clinically silent" for a long time. Then it manifests as a painless tumor slowly growing on the lateral surface of the neck [8, 15]. It is mobile, easier to move vertically rather than horizontally, which is referred to as a positive Fontaine sign [16, 17]. When spreading, it expands into the direction of the smallest tissue resistance resulting in dysphagia and lower cranial nerve deficits (IX, X, XI and XII) [18]. Paraganglioma located in the tympanic cavity or around the jugular bulb is usually manifested as pulsating tinnitus, accompanied by conductive hearing loss and ear fullness [19]. A typical otoscopic image is a livid-red mass behind the intact tympanic membrane. In case of jugular paraganglioma it may be accompanied by symptoms of damage to the lower cranial nerve group [19].

In addition to anamnesis and physical examination, it is necessary to conduct imaging studies to determine tumor location, size and vascularization. Ultrasonography is a cheap, non-invasive tool that is often the first stage in diagnosis of neck paragangliomas [20]. Carotid body tumor usually manifests as a homogeneous, well-defined, hypoechogenic mass. The use of Color Doppler can depict high vascularization of the paraganglioma [20]. Currently, the most important study in imaging paragangliomas of the head and neck is nuclear magnetic resonance [NMR] [5]. These tumors are visible as hyperintensive foci in the T2-weighted sequence and are subject contrast enhancement in the T1-weighted sequence [3, 5]. MRI allows to assess the possibility of tumor resection using the clinical classification of Shamblin et al. [21] [table 1]. It was developed in 1971 on the basis of the extent of carotid artery involvement and correlates with the probability of perioperative complications such as damage to the vessels and nerves of the neck [22]. During jugulotympanic paraganglioma diagnosis, computer tomography examination should be performed to assess the degree of bone destruction caused by tumor growth. Tumors of the jugular bulb are associated with invasion of bones around the jugular foramen, while in tympanic cavity paragangliomas, the bone remains intact. This evaluation is the base for classification according to Fisch et al. [Table 2], which comprises a tool helpful to the surgeon during the choice of operational approach [23].

Management of head and neck paragangliomas is controversial [19, 24]. Possible surgical treatment methods are: surgical resection, radiotherapy and embolization. At present, total surgical resection is the only method that gives a chance to completely cure the patient [22]. In selected cases, it is possible to combine the mentioned methods of therapy. Surgical procedure is commonly regarded as the method of choice for treatment of paragangliomas [17, 19, 25]. Since development of vascular reconstruction techniques, there has been a significant increase in the effectiveness of surgery. Percentage of healings after complete surgical resection of carotid body paragangliomas is 89-100% [25]. One of the main factors increasing mortality post-surgery is perioperative loss of lower cranial nerve function [17]. Radiotherapy is usually considered in case of non-surgical tumors. Its aim is long-term control of tumor size, the efficacy of which is influenced by, among all, the radiation dose [26]. Radiotherapy is associated with a lower risk of neurological deficits on the part of cranial nerves [26]. However, radiation is a factor that increases the risk of cancer and should be taken into account when choosing the method mentioned above, especially in younger patients [19]. In the absence of clear qualification criteria for treatment as well as guidelines for the management of head and neck paragangliomas, each patient should be treated individually and the choice of therapy method should also take into account factors such as: age, general condition or possibility of general anesthesia [9].

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Corresponding author: Corresponding author: Tomasz Wojciechowski, Department of Otolaryngology, Medical University of Warsaw, Poland; e-mail: wojciechowski.tk@gmail.com

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