Recurrence of a Resected Carotid Body Tumor Presenting as a Vagal paraganglioma

Spyros Papadoulas[1], Konstantinos Moulakakis[1], Nikolas Mastronikolis[2], Petros Zampakis[3], Maria Gkermpesi[4], Andreas Tsimpoukis[1], Stavros K. Kakkos[1]

[1]Vascular Surgery Department, Patras University Hospital, Patras-Greece
[2]ENT Department, Patras University Hospital, Patras-Greece
[3]Interventional Neuroradiology Department, Patras University Hospital
[4]Department of Pathology, Patras University Hospital, Patras-Greece

Abstract:

Purpose: To present a rare case of carotid body tumor recurrence presenting as a vagal paraganglioma. Vagal paragangliomas represent <5% of all head-and-neck paragangliomas with approximately 200 cases been reported in the literature.

Case report: An asymptomatic 25-year-old female was diagnosed with a vagal paraganglioma 3 years after an ipsilateral carotid body tumor resection. which had been fully excised as was shown by the pathology specimen examination and a recent Computed Tomography Angiography (CTA). Preoperative presumed diagnosis was based only on duplex scan and CTA. No biopsy was performed because it is contraindicated due to high vascularity of these tumors. Vagal Paraganglioma resection was easily performed because the patient was thin with a clean surgical field locating just distal to the previews operated area. Pathology specimen was conclusive for paraganglioma and his conjunction with the vagus nerve found on operation was indicative for a vagal paraganglioma., The patient remains without recurrence during the last 4 years.

Conclusion: This case emphasizes the necessity of a strict postoperative follow-up protocol after resection of paragangliomas, as recurrence is always possible.

INTRODUCTION

Head-and-neck paragangliomas (HNPGLs) are rare predominantly benign neuroendocrine tumors, comprising the 0.03% of all tumors and less than 0.5% of head-and-neck tumors, with an annual incidence of 0.001%.[1] The World Health Organization has classified HNPGLs as carotid body paragagliomas (PGLs), jugulotympanic PGLs, vagal PGLs, laryngeal PGLs, or miscellaneous PGLs.[2] Main treatment for cervical PGLs is surgery which leads to high curative rates. Unfortunately, a small rate of recurrence is apparent during years or even decades after treatment.[3] This was the case in our patient who was diagnosed with a vagal paraganglioma (VPGL) 3 years after surgery for a carotid body paraganglioma. We reviewed the literature about the presentation, clinical behavior, diagnosis, treatment, and appropriate follow-up of cervical paragangliomas focusing more on vagal ones.

CASE PRESENTATION

Author for correspondence:

Spyros Papadoulas

Vascular Surgery Department, Patras University Hospital, Patras-Greece

E-mail: Spyros.papadoulas@gmail.com

ISSN 2732-7175 / 2021 Hellenic Society of Vascular and Endovascular Surgery Published by Rotonda Publications

A 25-year-old female presented with an asymptomatic, non-palpable cervical mass revealed by ultrasonography (U/S), during the follow-up for a right carotid body tumor resection 3 years ago, 2.5cm in diameter. She was advised to have annual neck U/S, and neck, chest and abdominal Magnetic Resonance Imaging (MRI) on a 2-year basis. There was no family history.

Neck U/S revealed an oval, firm, well-defined, solid, hypoechoic mass at the lower neck. Computed tomography angiography (CTA) (fig 1) defined that the mass measured 2 x 1.5 cm in diameter, was located behind the common carotid artery (CCA) and was expanding laterally, displacing the internal jugular vein at the level of the sternoclavicular articulation. Chest and abdominal computed tomography scan were normal.

During the operating procedure, a longitudinal skin incision was performed along the medial border of the sternocleidomastoid muscle, initiating from the sternum, and extending cranially. The incision was a new distal extension of the previous incision, with only 1-2 cm overlap. The operation was not difficult because the operative field was different from the previous one. No adhesions were apparent. The CCA and the vagus nerve were dissected and looped. The mass was dissected free from the surrounding structures, but it was bonded with a short pedicle with the vagus nerve (fig 2). The pedicle was carefully transected and the vagus nerve was preserved. Regarding nerve recognition, we did not use neuro-

monitoring devices. After dissecting the tumor carefully, we realised its connection with the vagus and we therefore dissected the nerve free in the interspace between the common carotid artery and internal jugular vein. Hopefully, the nerve remained intact after excision as the tumor was not incorporated within the nerve.

The postoperative course was uneventful, and the patient was discharged on the 3rd postoperative day. Pathology specimen was conclusive for paraganglioma and his conjunction with the vagus nerve found on operation was indicative for a VPGL (fig 3). The patient was advised to have an annual neck U/S and a neck-chest and abdominal MRI every 2 years, remaining without recurrence during the last 4 years.

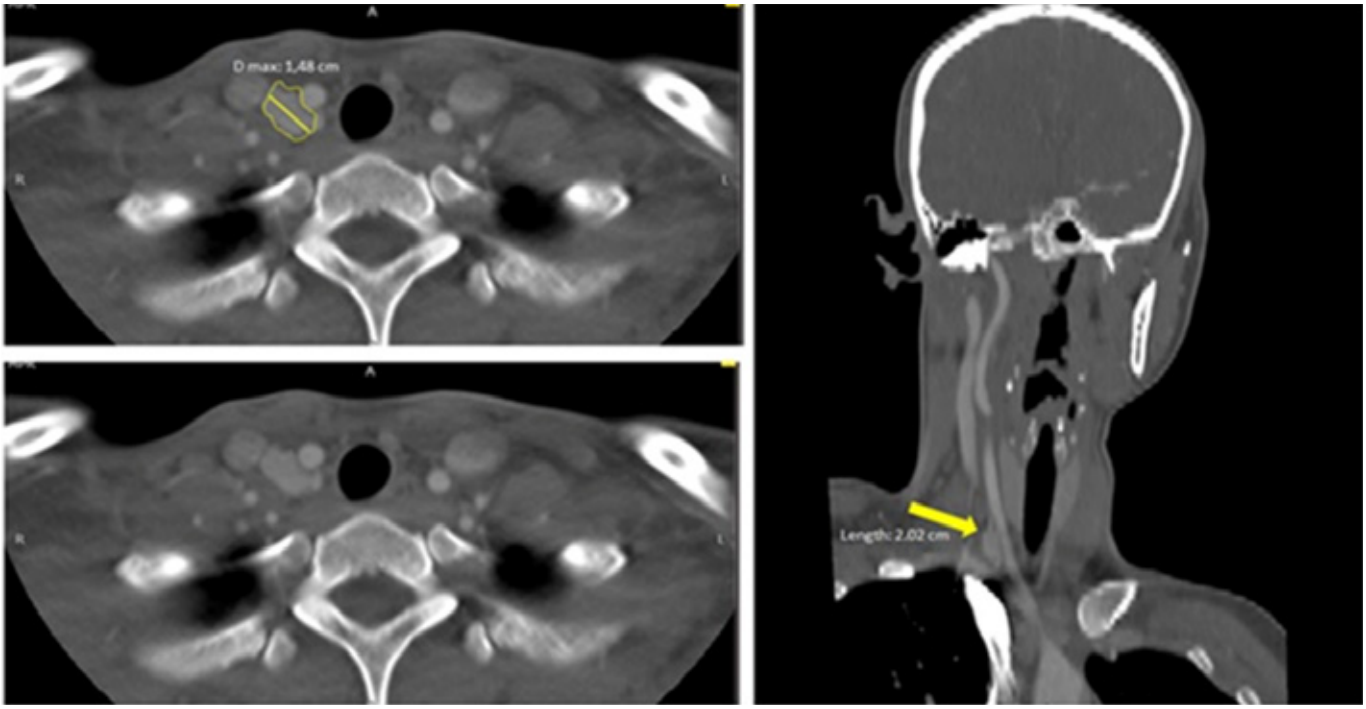

Figure 1. Computed Tomography Angiography showing the mass measuring 2X1 cm in diameter, located behind the common carotid artery and expanding laterally, displacing the internal jugular vein at the level of the sternoclavicular articulation.

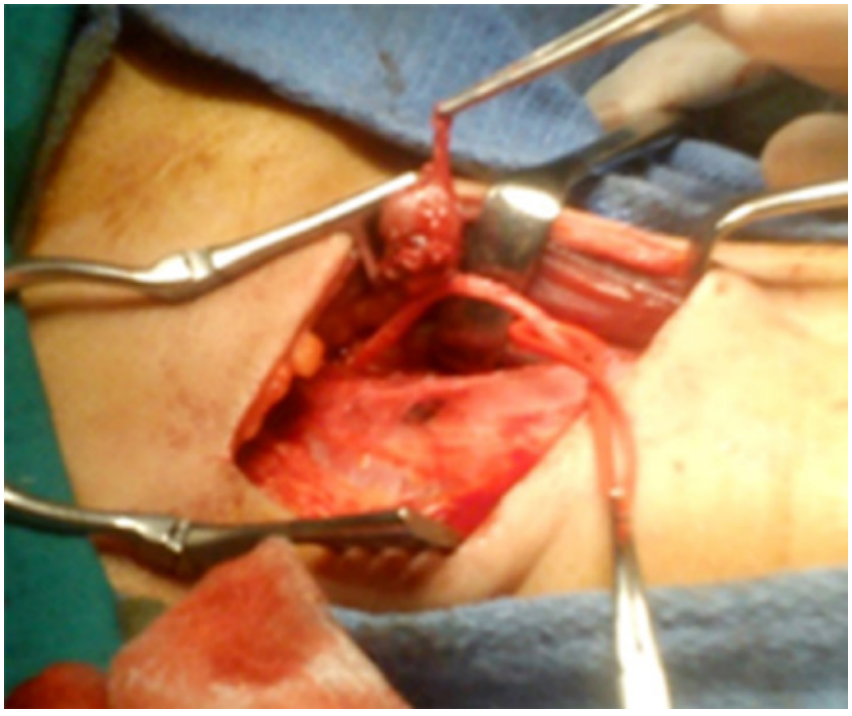

Figure 2. Paraganglioma was bonded with a short pedicle with the vagus nerve.

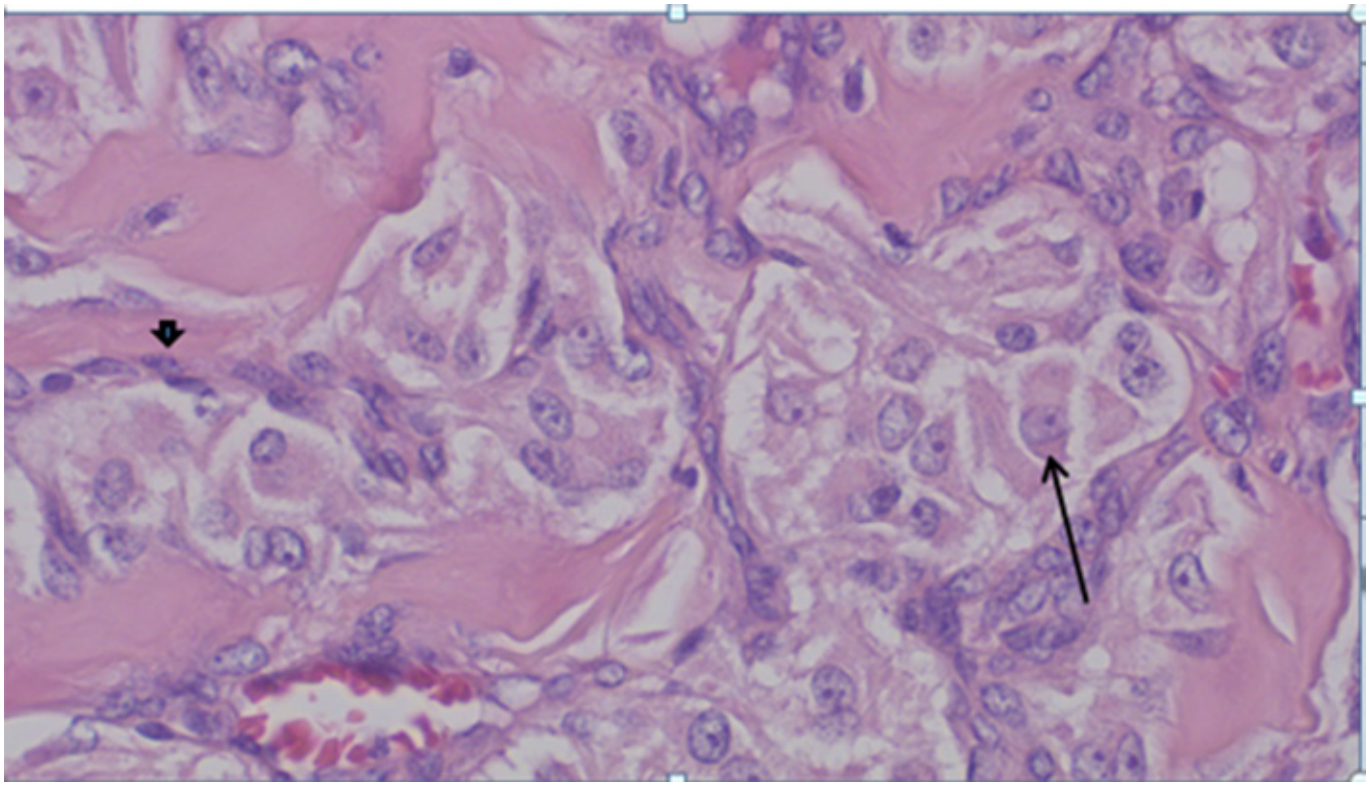

Figure 3. Pathology specimen of the vagal paraganglioma showing the organoid Zellballen pattern with chief cells (arrow) and sustentacular cells (arrowhead) (HE X400).

DISCUSSION

Paragangliomas are uncommon neuroendocrine tumors that develop along the autonomic ganglion chain from the head to pelvis and thus located in the pre-aortic and paravertebral area or skull base.[4] They may be parasympathetic or sympathetic and are usually benign and highly vascular. The parasympathetic tumors are usually asymptomatic and non-secretory, located mainly in the skull base in the distribution of IX and X cranial nerves. Adversely, sympathetic lesions are symptomatic and secretory (dopamine, norepinephrine, and/or epinephrine) and commonly located in the abdomen and pelvis.[5]

Head-and-neck paragangliomas are slowly growing tumors (average growth rate of 0.83 mm per year) and can be present for months to years before the onset of symptoms.

Small vagal PGLs (VPGLs) are usually asymptomatic, as in our case. Clinically, they are well-marginated and mobile laterally but fixed longitudinally.[4] They may be bilateral and/or multiple, mainly in familial forms or in metastases. Larger tumors may cause vagal nerve dysfunction (dysphagia, hoarseness, and vocal cord paralysis) and compression of the carotid sinus (syncope) or the sympathetic chain (Horner syndrome). Although VPGLs may arise anywhere along the vagus nerve, they are usually found at the inferior nodal ganglion (C1 level).

PGL genes are inherited in an autosomal dominant manner, relating to one of the succinate dehydrogenase (SDHx) genes. SDHD mutations are the most common in HNPGL and SDHB mutations in malignancy. Risk of malignancy is 10 to 19% for VPGLs. Malignancy is not a histologic finding but is suspected when they have rapid growth or when they metastasize in the cervical lymph nodes or at remote organs like lungs, bones, breasts, liver or in atypical sites. Distant metastasis is the only indicator of malignancy. Genetic testing is essential.

Diagnosis is based on imaging modalities. U/S demonstrates tumor hypervascularity. CT and/or MRI define the location, the hypervascularity and potential metastases. VPGLs appear with an intense homogenous contrast enhancement. They are located behind the internal carotid artery (ICA) and displace both the internal and external carotid arteries anteriorly, while the internal jugular vein is compressed and displaced posteriorly or laterally. Although usually confined to the carotid space, these tumors can grow superiorly into the posterior fossa, entering via the jugular foramen, or inferiorly to the carotid bifurcation. Biopsy is contraindicated as it may be complicated with massive bleeding. Positron emission tomography-CT should be performed to evaluate multiple tumors.[3]

It is recommended to perform initial MRI or CT-scan of the head, neck, chest, abdomen, and pelvis to define the primary lesion and to detect any synchronous, metachronous or metastatic tumors.[6] On admission the patient had already undergone chest and abdominal CT-scan under instructions of an oncologist at her hometown. The necessity for this imaging is the fact that Paragangliomas are found in the abdomen, pelvis, thorax, head and neck. Additionally, there is evidence that after resection of a PPGL a new tumor may arise (in a previously unaffected paraganglion) or recurrence (local or distant

as most recurrences are metastatic). Therefore, the imaging studies must be lifelong especially in patients with hereditary tumors (in around 40% of PPGLs) than in patients with sporadic tumors. Additionally, patients with PPGLs in syndromes such as multiple endocrine neoplasia type 2, von Hippel–Lindau disease, neurofibromatosis 1 or hereditary paragangliomas may develop non-PPGL tumors, more likely renal cancer, medullary thyroid carcinoma, or gastrointestinal stromal tumors.

Histologically, on gross examination paragangliomas are well-circumscribed firm and rubbery, ranging from 2-6cm in size. Microscopically they are similar to phaeochromocytoma. Typically, the organoid (Zellballen) of the normal paraganglion is seen.

There are insufficient data in the literature regarding the optimal treatment.[6] A multidisciplinary team approach is essential as is inquiry for a family history of PGLs, pheochromocytomas, renal cancer, and gastrointestinal stromal tumors.

Only around half of HNPGLs are growing. Due to the low risk of malignancy, and the potential invasiveness of large tumors, surgery is a prudent approach. Stereotactic radiosurgery, external radiation therapy, and a wait-and scan strategy are alternative treatments.[7,8] Consequently, rapidly growing and/or large VPGLs and those with an SDHB mutation should be managed with surgical resection and postoperative radiation in case of malignacy.[6] Embolization, in tumors measuring above 3 cm (especially for VPGLs and glomus jugulotympanicum) facilitates surgical resection with protection of surrounding cranial nerves and decreases intraoperative bleeding.[9] This is performed 24 to 48 hours preoperatively.[6] The 5-year survival rate is around 80% in lymph node metastases and 12% in distant metastases.[3] Radiotherapy is more appropriate in multiple growing tumors and peptide therapy with octreotide in metastatic disease.[6]

Regarding intraoperative complications, vascular injury is rare during resection of vagal paragangliomas but may occur in case of advance disease at the scull base and concern the petrous portion of the ICA. Lower cranial nerve injury is possible depending on the site and the size of the tumor. Deficits in cranial nerves (IX, X, XI, XII) may occur preoperatively in large tumors (>2cm) with skull base involvement or appear postoperatively (in 10-30% of cases). Each deficit is additive and multiple deficits may not be well tolerated leading to speech, swallow, and sensory disturbances. Finally, aspiration pneumonia, cardiac arrhythmias, sinus tachycardia, and orthostatic hypotension may arise. In some patients, tracheostomy or gastrostomy are unavoidable, especially in high vagus nerve injuries. These may be permanent in bilateral vagal palsy. Nerve deficits are less with radiotherapy.

It is possible a patient with a PPGL to develop another of the 5 type PPGLs. HNPGLs have a 10% risk of recurrence if they reimaged every 3.4 years.[5] Recurrences may occur decades after treatment and so surveillance is recommended.[5] In (SDHD) variant carriers, they face a risk from 7% after 2 years to 73% after 22 years (Bertine et al, Eur J Human Genetics 2018). There are no specific data in the literature about the risk of developing a vagal PGL after resection of a CBT.

Current guidelines do recommend genetic testing for all patients, in addition to hormonal measurements every year and imaging every 1-2 years, considering the first imaging 3 months postoperatively.[10] A lifelong follow-up should be individualized and offered in all patients.

CONCLUSION

This report highlights the importance of the strict follow-up that is necessary after resection of a paraganglioma, as was the carotid body tumor in our case. Early diagnosis before symptoms appear will aid in patient's quality of life and survival.

REFERENCES

1 Singh S, Madan R, Singh MK, Thakar A, Sharma SC. Head-and-neck paragangliomas: An overview of 54 cases operated at a tertiary care center. South Asian J Cancer. 2019;8:237-240.

2 Williams MD, Tischler AS. Update from the 4th edition of the World Health Organization classification of head and neck tumors: paragangliomas. Head Neck Pathol. 2017;11:88-95.

3 Kotsis T, Christoforou P. Vagal Paraganglioma: Surgical Removal with Superior Laryngeal Nerve Preservation. Vasc Specialist Int. 2019;35:105-110.

4 Guilmette J, Sadow PM. A Guide to Pheochromocytomas and Paragangliomas. Surg Pathol Clin. 2019;12:951-965.

5 Contrera KJ, Yong V, Reddy CA, Liu SW, Lorenz RR. Recurrence and Progression of Head and Neck Paragangliomas after Treatment. Otolaryngol Head Neck Surg. 2020;162:504-511.

6 Lloyd S, Obholzer R, Tysome J; BSBS Consensus Group. British Skull Base Society Clinical Consensus Document on Management of Head and Neck Paragangliomas. Otolaryngol Head Neck Surg. 2020;163(3):400-409.

7 Neumann HPH, Young WF Jr, Eng C. Pheochromocytoma and Paraganglioma. N Engl J Med. 2019;38:552-565.

8 Fatima N, Pollom E, Soltys S, Chang SD, Meola A. Stereotactic radiosurgery for head and neck paragangliomas: a systematic review and meta-analysis. Neurosurg Rev. 2020: 1-12

9 Prasad SC, Paties CT, Pantalone MR, Mariani-Costantini R, Sanna M. In: Mariani-Costantini R, editor. Carotid Body and Vagal Paraganglioma: Epidemiology, Genetics, Clinicopathological Features, Imaging, and Surgical Management. Paraganglioma: A Multidisciplinary Approach [Internet]. Brisbane (AU): Codon Publications; 2019 Jul 2. Chapter 5.

10 Plouin PF, Amar L, Dekkers OM, Fassnacht M, Gimenez-Roqueplo AP, Lenders JW, Lussey-Lepoutre C, Steichen O; Guideline Working Group. European Society of Endocrinology Clinical Practice Guideline for long-term follow-up of patients operated on for a phaeochromocytoma or a paraganglioma. Eur J Endocrinol. 2016;174(5): 1-10.