World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Non-resectable head and neck paraganglioma: A case series and literature review

Abdelkarim Uakkas *, Samia Khalfi, Kaoutar Soussy, Wissal Hassani, Fatima Zahraa Farhane, Zenab Alami and Touria Bouhafa

Department of Radiation Oncology, Hassan II University Hospital, Fez, Morocco.

World Journal of Advanced Research and Reviews, 2025, 26(01), 001-005

Publication history: Received on 21 February 2025; revised on 29 March 2025; accepted on 31 March 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.26.1.1019

Abstract

Paragangliomas or chemodectomas are rare neuroendocrine tumours arising from neural crest germ cells located in the sympathetic or parasympathetic system. They are generally benign but locally aggressive tumours. Surgery remains the standard treatment, but for certain tumours that are inoperable or deemed non-resectable due to the patient's general condition, the size of the tumour or local extension with intimate relationships with vascular-nerve structures, radiotherapy may constitute an alternative and exclusive therapeutic option that proves effective.

The aim of our study was to evaluate the epidemiological, clinical, para-clinical and evolutionary results, in particular local control and possible toxicities of exclusive irradiation of 6 cases of cervical paragangliomas judged to be unresectable. This case serie, accompanied by a review of the literature, highlights current diagnostic and therapeutic challenges in the management of cervical paraganglioma.

Keywords: Head and neck paraganglioma; Cervical paraganglioma; Radiotherapy of paraganglioma; Paraganglioma

1. Introduction

Paragangliomas represent a rare group of neuroendocrine tumors that are notably vascular and originate from neural crest cells. They can develop anywhere along the craniospinal axis, from the skull base to the sacrum (1). Approximately one-third of these tumors are inherited, with some cases occurring in association with familial syndromes such as multiple endocrine neoplasia type 2 (MEN 2), von Hippel-Lindau disease, or neurofibromatosis type 1 (2). While nearly two-thirds of paragangliomas arise within the adrenal gland, the extra-adrenal forms are most commonly reported in the abdomen and thorax, and less frequently in the head and neck region (3). Within the head and neck, carotid body tumors constitute the most frequent presentation (4). A significant proportion around 70–80% of head and neck paragangliomas remain asymptomatic; however, based on their anatomical location, they may produce various clinical manifestations, including a painless cervical mass, cranial nerve deficits leading to dysphagia or hoarseness, pulsatile tinnitus, hearing impairment, or other issues affecting speech, swallowing, and airway function (5). Diagnostic evaluation primarily relies on imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). Although these tumors are generally benign, their propensity to compress adjacent vascular and neural structures often necessitates surgical intervention. When complete surgical resection is not feasible due to patient-related factors or tumor localization, radiotherapy is considered, although the aim is typically to achieve tumor stabilization or partial regression rather than complete resolution (6). Notably, metastasis—defined as the spread of tumor cells to locations devoid of normal chromaffin tissue (including lymph nodes, liver, bone, and lungs)—has been observed in fewer than 5% of carotid body paragangliomas (7). We report a case series of 6 patients with non-resectable cervical paraganlioma treated exclusively with radiotherapy.

* Corresponding author: Abdelkarim Uakkas

2. Methods

A retrospective and analytical study was carried out on 6 patients with cervical paragangliomas collected in the radiotherapy - brachytherapy department of the oncology hospital, Hassan II University Hospital, Fez, over a period of 5 years, from January 2015 to December 2020.

3. Results

The mean age of the patients in our series was 55.5 years, with extremes ranging from 40 to 69 years. All six patients were female, with no notable pathological or family history of paraganglioma.

There were 4 cases of unilateral carotid paragangliomas - One case of jugulo-tympanic paraganglioma (of the petrous apex) - One case of tympanic paraganglioma. The average time to diagnosis was 21.6 months, with extremes ranging from 3 months to 5 years.

All our patients presented with a painless cervical mass, no other symptoms were found.

All patients underwent a CT scan, which was supplemented by an MRI scan in 3 patients. The diagnosis was made on the basis of the clinical and radiological work-up in 4 patients and on histological examination in the other 2.

All 6 cases had unresectable tumours, which led to exclusive radiotherapy with a total dose of 50 Gy in 25 fractions of 2 Gy each for 5 weeks. The average spread was 38 days. 3 patients received intensity modulated radiotherapy (IMRT), while the other 3 received three-dimensional conformal radiotherapy.

Regarding the follow-up of the patient, a history and physical examination was planned every 3 months for 2 years, and after that 2 times per year for 3 years and then, every 12 months. A head and neck scan was done after 6 months of the end of radiotherapy then annually.

With a follow-up time of 5 years, the short- and medium-term evolution was without the appearance of radiotherapy-related complications in four of our patients, two of whom suffered from grade I radiodermatitis associated with otorrhoea and an intermittent right-sided otalgia appeared in the case of the patient with a tympanic paraganglioma with a good evolution after appropriate symptomatic treatment.

Long-term evolution was marked by local control of tumour size in five of our patients (83%), with tumour progression in only one patient where malignancy was suspected given the appearance of bronchial carcinoid.

4. Discussion

4.1. Epidemiology

Paragangliomas constitute an uncommon category of neuroendocrine tumors that are exceptionally vascular and originate from neural crest cells. They may develop anywhere along the craniospinal axis—from the skull base to the sacrum. Although nearly two-thirds of these tumors occur in the adrenal gland, extra-adrenal paragangliomas are most frequently observed in the abdominal and thoracic regions, with a less common presentation in the head and neck area. Head and neck paragangliomas (HNPGLs) are typically slow-growing, vascular neoplasms arising from paraganglial cells associated with autonomic ganglia, with approximately 95% being non-secretory (Fig. 1). Current evidence suggests that over 50% of paragangliomas are linked to hereditary syndromes (8), most commonly involving germline pathogenic mutations in the genes encoding the succinate dehydrogenase (SDH) complex subunits. In sporadic cases, tumors tend to be solitary, unilateral, and manifest in patients between 40 and 70 years old, whereas hereditary cases are more frequently multifocal, prone to metastasis, and occur at a younger age (9).

4.2. Clinical prestation

Paragangliomas can be classified by their anatomical location into cervical lesions and those involving the temporal bone. Cervical paragangliomas mainly include carotid body tumors (CBTs), glomus vagale tumors (GVs), and, less commonly, paragangliomas of the cervical sympathetic chain. CBTs are the most prevalent subtype; they are generally benign, originate from the carotid body (10), and are often incidentally discovered on imaging or present as a painless, palpable, and occasionally pulsatile neck mass near the angle of the jaw. Symptoms may include hoarseness, dysphagia,

or autonomic disturbances resulting from compression of cranial nerves IX (glossopharyngeal) and X (vagus). Glomus vagale tumors, which usually arise along the vagus nerve—most commonly from its inferior ganglion—often present as asymptomatic high-neck masses but may also be accompanied by pulsatile tinnitus and deficits involving cranial nerves IX, X, XI (spinal accessory), and XII (hypoglossal) (10). Temporal bone paragangliomas are subdivided into glomus jugulare tumors (GJs), which originate from the jugular bulb near the skull base, and glomus tympanicum tumors (GTs), which develop in the middle ear cavity. These lesions most commonly cause pulsatile tinnitus and conductive hearing loss (11); additional symptoms such as dysphonia, shoulder pain or weakness, dysarthria, and facial paralysis are more suggestive of GJs rather than GTs (12). Classically, GTs are visualized as a reddish mass behind the tympanic membrane that blanches upon pneumatic otoscopy (13).

4.3. Diagnosis and imaging

The diagnostic workup for paragangliomas depends on whether the tumor is secretory or non-secretory. Secretory tumors require biochemical evaluation, whereas non-secretory HNPGLs are primarily diagnosed via imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). Given their hypervascular nature, paragangliomas typically exhibit pronounced contrast enhancement on CT and gadolinium enhancement on MRI. A characteristic imaging finding is the presence of flow voids on spin echo sequences, which creates a “salt and pepper” appearance (14). The imaging modality of choice is positron emission tomography (PET)/CT, which is valuable not only for tumor characterization but also for detecting metastatic disease (15, 16). Ultimately, diagnosis is based on the integration of clinical presentation, imaging results, and biochemical testing, with biopsy reserved for rare instances where further confirmation is necessary. Histologically, paragangliomas demonstrate a Zellballen (nested) architecture; the tumor cells are semi-epithelial with round, hyperchromatic nuclei, and mitotic figures are uncommon. There is typically no mucin production or glandular formation, and while immunohistochemical staining confirms neuroendocrine differentiation—with S100 protein staining observed in supporting cells—it is not mandatory for diagnosis (17).

4.4. Management

The treatment strategy for head and neck paragangliomas must balance the risks associated with surgical intervention—including potential cranial nerve deficits and other perioperative complications—against the tumor’s impact on the patient’s quality of life. Surgical treatment is generally indicated when there is tumor progression or the onset of new symptoms. In functional tumors, preoperative management may require α-adrenergic blockade (with the addition of β-blockers if necessary). For resectable carotid body tumors (CBTs) in otherwise healthy patients, gross total resection (GTR) remains the gold standard, as incomplete treatment can lead to local invasion and potential metastasis (18). In cases of glomus vagale tumors (GVs), patients usually become symptomatic before presentation, at which point observation is typically no longer an option. The extent of surgical resection in these patients is influenced by factors such as age and overall health; for elderly yet fit individuals, a more conservative resection that preserves cranial nerve function (or GTR with vocal cord medialization) may be preferred (19), while younger patients are generally managed with GTR (20). Traditionally, glomus jugulare tumors (GJs) have been managed with GTR, achieving high rates of tumor control despite considerable morbidity due to their lateral skull base location, proximity to lower cranial nerves, local invasiveness, and high vascularity.

Radiotherapy (RT) has historically been used as an adjunct to surgery; however, in patients who are poor surgical candidates, have recurrent disease, or present with unresectable tumors, RT can serve as a primary treatment to inhibit tumor growth and delay the need for surgery (21). Given its potential for serious adverse effects—such as osteoradionecrosis, secondary malignancies, and vascular ischemic events—RT is generally reserved for cases showing tumor progression on serial imaging (22). Recent advancements in RT techniques have reduced associated morbidity, thereby expanding its role as a viable alternative to surgery in select cases

5. Conclusion

In summary, head and neck paragangliomas represent a rare and heterogeneous group of neuroendocrine tumors that pose significant diagnostic and therapeutic challenges. Advances in imaging modalities, particularly PET/CT, have markedly improved diagnostic accuracy, while the integration of biochemical and histopathological assessments continues to refine our understanding of these lesions. Although surgical resection remains the cornerstone of treatment for resectable tumors, especially in cases of carotid body tumors, radiotherapy has emerged as a crucial therapeutic option. In our patient cohort, radiotherapy was the primary treatment modality, demonstrating effective tumor control while preserving quality of life, particularly in cases where surgery was contraindicated or carried high risk. Moreover, the recognition of a substantial hereditary component, primarily linked to SDH gene mutations, underscores the importance of genetic counseling and family screening. Future research should focus on optimizing

multimodal treatment strategies, further elucidating the molecular underpinnings of paragangliomas, and refining radiotherapeutic techniques to enhance outcomes. Collectively, these efforts will contribute to improved patient care and a more nuanced understanding of paragangliomas in clinical practice.

Compliance with ethical standards

Disclosure of conflict of interest

All authors have no conflict of interest to declare.

Statement of ethical approval

This case report was conducted in accordance with ethical guidelines.

Statement of informed consent

The patient provided informed consent for the publication of this case report.

References

[1] W.M. Mendenhall, R.J. Amdur, M. Vaysberg, C.M. Mendenhall, J.W. Werning. Head and neck paragangliomas. Head Neck, 33 (2011), pp. 1530-1534

[2] A.P. Gimenez-Roqueplo, P.L. Dahia, M. Robledo. An update on the genetics of paraganglioma, pheochromocytoma, and associated hereditary syndromes. Horm Metab Res, 44 (2012), pp. 328-333

[3] N. Burnichon, A. Cascón, F. Schiavi, N.P. Morales, I. Comino-Méndez, N. Abermil, et al. MAX mutations cause hereditary and sporadic pheochromocytoma and paraganglioma. Clin Cancer Res, 18 (2012), pp. 2828-2837

[4] D.C. Jianu, D.F. Muresanu, M. Petrica. Diagnosis of carotid body paragangliomas by various imaging techniques. Rom J Neurol, 7 (2014), pp. 161-166

[5] E.P. Corssmit, J.A. Romijn. Clinical management of paragangliomas. Eur J Endocrinol, 171 (2014), pp. 231-243

[6] P. Gilbo, C.G. Morris, R.J. Amdur, J.W. Werning, P.T. Dziegielewski, J. Kirwan, et al. Radiotherapy for benign head and neck paragangliomas: a 45-year experience. Cancer, 120 (2014), pp. 3738-3743

[7] C. Suárez, J.P. Rodrigo, W.M. Mendenhall, M. Hamoir, C.E. Silver, V. Grégoire, et al. Carotid body paragangliomas: a systematic study on management with surgery and radiotherapy. Eur Arch Otorhinolaryngol, 271 (2014), pp. 23-34

[8] Horton C, LaDuca H, Deckman A, Durda K, Jackson M, Richardson ME, Tian Y, Yussuf A, Jasperson K & Else T 2022 Universal germline panel testing for individuals with pheochromocytoma and paraganglioma produces high diagnostic yield. Journal of Clinical Endocrinology and Metabolism 107 e1917–e1923

[9] Ikram A & Rehman A 2022 Paraganglioma. In StatPearls. Treasure Island, FL, USA: StatPearls Publishing

[10] Offergeld C, Brase C, Yaremchuk S, Mader I, Rischke HC, Gläsker S, Schmid KW, Wiech T, Preuss SF & Suárez C et al.2012 Head and neck paragangliomas: clinical and molecular genetic classification. Clinics 67(Supplement 1) 19–28

[11] Carlson ML, Sweeney AD, Wanna GB, Netterville JL & Haynes DS 2015 Natural history of glomus jugulare: a review of 16 tumors managed with primary observation. Otolaryngology–Head and Neck Surgery 152 98–105.

[12] Moore MG, Netterville JL, Mendenhall WM, Isaacson B & Nussenbaum B 2016 Head and neck paragangliomas: an update on evaluation and management. Otolaryngology–Head and Neck Surgery 154 597–605.

[13] Sweeney AD, Carlson ML, Wanna GB & Bennett ML 2015 Glomus tympanicum tumors. Otolaryngologic Clinics of North America 48 293–304

[14] Taïeb D., Kaliski A., Boedeker C.C., et al. Current approaches and recent developments in the management of head and neck paragangliomas. Endocr. Rev. 2014;35:795–819

[15] Lenders J.W., Duh Q.Y., Eisenhofer G., et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J. Clin. Endocrinol. Metab. 2014;99(6):1915–1942

[16] Bozkurt M.F., Virgolini I., Balogova S., et al. Guideline for PET/CT imaging of neuroendocrine neoplasms with 68Ga-DOTA-conjugated somatostatin receptor targeting peptides and 18F-DOPA. Eur. J. Nucl. Med. Mol. Imaging. 2017;44(9):1588–1601

[17] Gimm O., DeMicco C., Perren A., Giammarile F., Walz M.K., Brunaud L. Malignant pheochromocytomas and paragangliomas: a diagnostic challenge. Langenbecks Arch. Surg. 2012;397(2):155–177

[18] 18. Burgess A, Calderon M, Jafif-Cojab M, Jorge D & Balanza R 2017 Bilateral carotid body tumor resection in a female patient. International Journal of Surgery Case Reports 41 387–391

[19] Shin SH, Piazza P, De Donato G, Sivalingam S, Lauda L, Vitullo F & Sanna M 2012 Management of vagal paragangliomas including application of internal carotid artery stenting. Audiology and Neuro-Otology 17 39–53

[20] Prasad SC, Paties CT, Pantalone MR, Mariani-Costantini R & Sanna M 2019 Carotid body and vagal paragangliomas: epidemiology, genetics, clinicopathological features, imaging, and surgical management. In Mariani-Costantini Red. Paraganglioma: a multidisciplinary approach. Brisbane, AU: Codon Publications

[21] Jackson CG, McGrew BM, Forest JA, Netterville JL, Hampf CF & Glasscock ME 2001 Lateral skull base surgery for glomus tumors: long-term control, 3rd ed. Otology and Neurotology 22 377–382

[22] Lassen-Ramshad Y, Ozyar E, Alanyali S, Poortmans P, van Houtte P, Sohawon S, Esassolak M, Krengli M, Villa S & Miller R et al.2019 Paraganglioma of the head and neck region, treated with radiation therapy, a Rare Cancer Network study. Head and Neck 41 1770–1776