Rare Cervical Paragangliomas: Diagnostic and Therapeutic Challenges in Three Cases

Introduction

Paragangliomas are rare neuroendocrine tumors arising from extra adrenal paraganglionic issue derived from neural crest cells. while they may develop anywhere from the skull base to the sacrum base to the sacrum cervical paragangliomas also known as head and neck paragangliomas account approximately 3% of all paragangliomas and primarily involve the carotid body vagal or jugulotympanicregions (1) .These tumors are typically benignbut may exhibit locally aggressive behavior. They are more frequently observed in females in 67 % of cases and most commonly diagnosed between the third and seventh decade of life .(4) Complete surgical resection remains the treatment of choice, however the rich vascular supply and proximity to critical neurovascular supply and proximity to critical neurovascular structure often render surgery high risk.Radiotherapy is a viable alternative, though its efficacy varies. Accurate imaging is essential for diagnosis, and genetic analysis plays a key role in patient monitoring.We present three cases involving female patients with painless cervical masses. Imaging confirmed the diagnosis, and biological assessments were performed. Due to tumor size and invasion, surgical intervention was deemed unsuitable, leading to radiotherapy as the preferred treatment.Our study aims to provide an overview of the clinical presentation diagnostic process and therapeutic strategies for cervical paragangliomas through a series of three illustrative cases .

Case report

Case 1

A 42-year-old female with no comorbidities or significant family history presented with a slowly growing right lateral cervical mass evolving over 8 years. A CT angiography of the supraaortic trunks revealed a highly vascularized lesion at the carotid bifurcation (36 × 34 × 66 mm) encasing both the internal and external carotid arteries over more than 180° while maintaning patency and compressing the internal jugular vein .MRI angiography revealed a hyperintense lesion on T1 and T2 with homogeneous enhancement, (41x29x64mm) (Figure 1) consistent with a Shamblin III right carotid paraganglioma (Figure 1).Normetanephrines were elevated (6.08 times normal) .Pathogenic mutation in exon 1 of the VHL gene was detectedsuggesting von Hippel-Lindau disease. MIBG scintigraphy showed a soft tissue mass at the carotid bifurcation (39 x29 x 43 mm) without tracer uptake suggesting a non-functional paraganglioma despite biochemical secretion potentially reflecting a false negative MIBG scan . Surgery was contraindicated due to tumor size and vascular involvement as confirmed by multidisciplinary team consensus.The patient receives external beam radiotherapy (IMRT) at 54 Gy in 27 fractions. Follow up CTAP showed tumor regression (34 x 23 x 44 mm) .Plasma metanephrines and pituitary function were monitored .

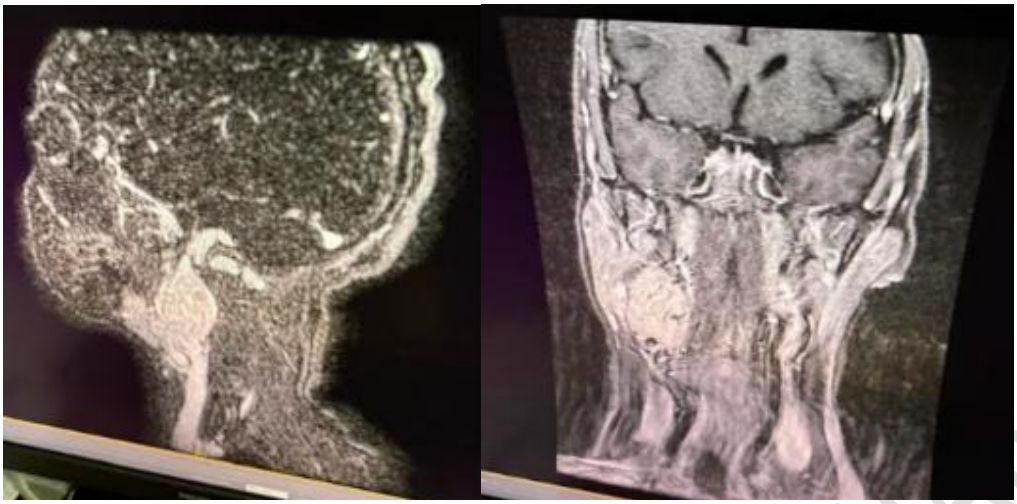

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Figure 1 : sagittal (a)and axial (b) cross section from a CT angiography of the supra aortic trunks showing the right carotid paraganglioma measuring 41x29x64 mm in diameter prior to radiotherapy

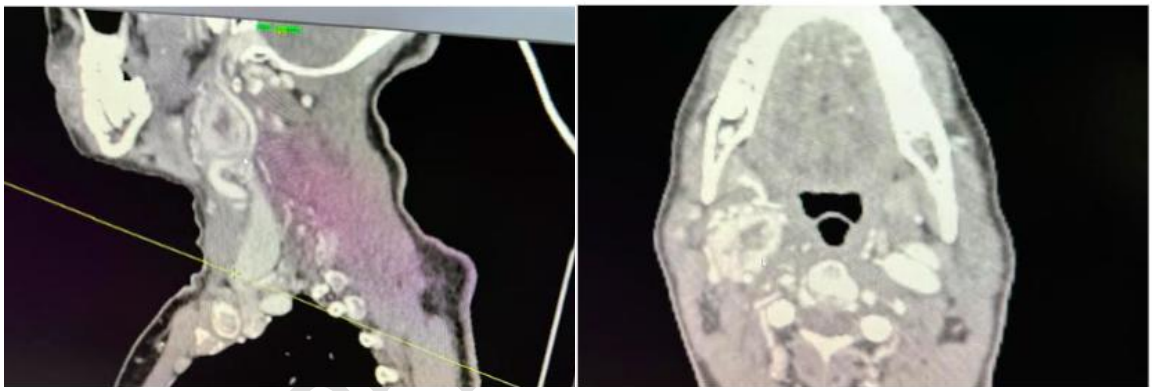

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Figure 2 : Sagittal (a) and axial (b) cross sections from a post radiotherapy CT angiography of the supra aortic trunks showing a reduction in the size of the right carotid paraganglioma decreasing from 41x29 to 64 to 34x23x44 mm in diameter

Case 2

A 38-year-old female with no comorbidities or relevant family history presented with a left lateral cervical mass progressing over 2 years. CT angiography revealed a heterogeneous lesion with central necrosis and intense arterial phase enhancement(35 × 37 × 55 mm) encasing encased the common carotid artery over more than 180° with maintained patency . Normetanpéhrine were considered normal.Testing for NEM, NF1, and VHL was negative.SDHx was not performed due to financial constraints.MIBG scintigraphy showed increased tracer uptake in the cervical region , suggesting a functioning paraganglioma . the discrepancy with normal biochemical markers may indicate a biochemical false negative

,possibly due to low or intermittent catecholamine secretion although rare a false positive MIBG scan cannt be entirely ruled out . Surgery was ruled out due to tumor extension and vascular involvement. The patient underwent IMRT with a totale dose of 56 Gy in 28 fractions. Control imaging revealed stable disease with a size of 37 x 30 x 57 mm.

Case 3

A 71-year-old female with no comorbidities or significant family history presented with a right lateral cervical mass evolving over 3 years. cervical ultrasound identified a hypervascular, multilobulated jugulocarotid formation (44,4 × 25,8 mm) initially suspected to be a cystic lymphangioma . However subsequent MRI angiography confirmed hypervascularlesion consistent with right carotid paraganglioma(35 × 38.5 × 45 mm)) encasing the internal and external carotid arteries and compressing the internal jugular vein . CTAP reveleadmass under the mandible (44 × 37 × 60 mm)(Figure 3)with heterogeneous enhancement and involvement of the thyoid larynx and internal jugular vein with loss of fat planes . Plasma metanephrines were negative while chromogranin A was elevated supporting the neuroendocrine nature of the tumor but the discordance suggests a biochemical false negative for catecholamine possibly due to intermittent or low level secretion.Genetic testing (NEM, VHL, RET) was requested and results were pending at the time of reporting.MIBG scintigraphy showed increased uptake in the right lateral cervical region,confirming a functional right cervical paraganglioma despite negative plasma markers suggesting a biochemical false negative or false positive imaging .Due to tumor's size and anatomical extension surgery was contraindicated by multidisciplinary consensus .External beam radiotherapy using IMRT was indicated and the patient is currently awating initiation with a follow up visit scheduled for treatment planning .

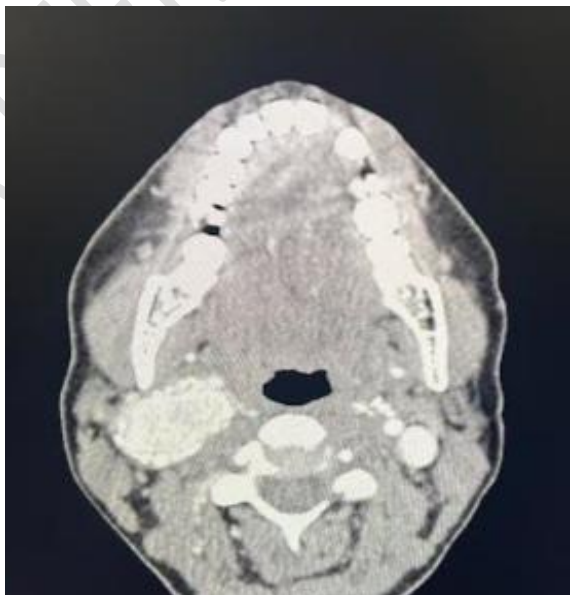

Figure 3 :Axial cross section of a contrast enhanced CT angiography showing a right carotid paraganglioma measuring 44x37x60 mm in diameter prior to radiotherapy

Discussion

Head and neck paragangliomas HNPGLs are the most frequent form of extra-adrenal paragangliomas, representing approximately 70% of all cases. These tumors arise from parasympathetic paraganglia and are typically non-secreting and benign.A strong female predominance is reported in the literature, with a mean age around 47 years (3). Our series matches this this finding, as all three patients were women, although one patient was notably older (77 years), likely reflecting a delayed diagnosis. HNPGLs have also been associated with high-altitude residence due to chronic hypoxia, a hypothesis relevant to our geographic context. While the most of HNPGLs are non-functional and benign, their genetic underpinnings are crucial to understand due to a high rate of hereditary transmission. Up to 40% of cases involve germline mutations, primarily affecting the SDHx gene complex. Mutations in SDHB are particularly associated with aggressive or metastatic disease, whereas SDHD mutations are more commonly linked to benign presentations.In our study, genetic testing was performed in all three patients, revealing a pathogenic VHL mutation in one case. This aligns with Group 1 mutations in the current classification, involving pseudohypoxic pathway activation. The identification of this mutation led to genetic counseling for the patient and her family. However, SDHB immunohistochemistry and extended gene panel screening were not performed, limiting our genetic characterization. Clinically, cervical PGs often present as painless neck masses. All our patients presentedthis typical symptoms, with additional pulsatility in two cases, suggestive of carotid body origin. Biochemically, although only 4–5% of HNPGLs are reported to be catecholamine-secreting(3), one of our patients had positive methoxy derivatives, indicating secretory activity, this discrepancy may be explained by the small sample of size of our case series.Radiologically, MRI angiography remains the gold standard, with characteristic “salt-and-pepper” appearance and detailed vascular mapping. This was essential for diagnosis and preoperative planning in our patients. Of note, one case was initially misdiagnosed as a cystic lymphangioma on ultrasound, corrected by MRI. Functional imaging with ^{123}I-MIBG was positive in two patients (2)(6). While MIBG has low sensitivity for non-metastatic HNPGLs according to recent data, our findings suggest variable performance, possibly influenced by tumor functionality or size.Surgical resection is the only curative treatment but carries a significant risk of cranial nerve and vascular complications. The Shamblin classification helps guide surgical risk. All three tumors in our series were Shamblin III, indicating advanced disease and contributing to the challenging resections. This likely reflects delayed diagnosis, with an average of five years from symptom onset to treatment.Due to the high surgical risk and tumor extension, all three patients were managed with intensity-modulated radiotherapy (IMRT). This technique allowed good local control with minimal complications. Tumor regression was observed in one case, stability in the second, and is under evaluation in the third (5). Our experience is consistent with published data showing excellent local control with IMRT or stereotactic radiotherapy, especially for inoperable or high-risk patients.Post-treatment surveillance requires both clinical and imaging assessments. MRI is recommended every 6–12 months initially, then annually. Biochemical monitoring is also important, particularly in functional tumors. In our series, all patients are under regular follow-up, with no evidence of recurrence or progression to date.The prognosis of HNPGLs is generally favorable in non-metastatic cases, with 5-year survival exceeding 90%. However, quality of life can be significantly affected by treatment-related sequelae such as dysphonia, swallowing disorders, and psychological distress (1)(3).Our series illustrates several key points: the female predominance of HNPGLs,

the potential for secretory behavior even in classically non-functional tumors, and the diagnostic challenges that can delay treatment. The identification of a VHL mutation underscores the importance of genetic screening. However, the small number of cases, absence of extended genetic analysis (e.g., SDHB staining), and relatively short follow-up limit the generalizability of our conclusions.(4)(6)

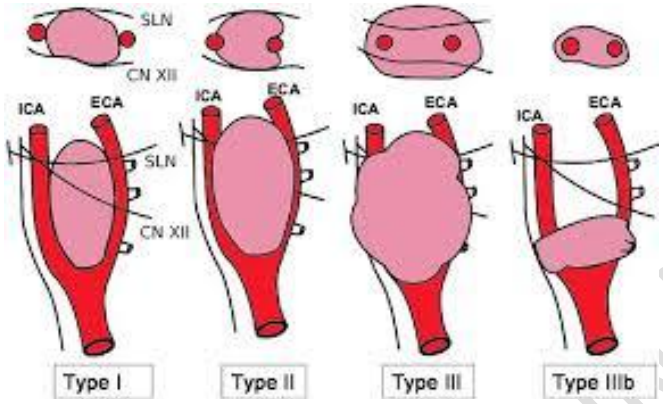

Figure 4 : Shamblin classification of cervical paraganglioma

Conclusion

Cervical paragangliomas are rare but potentially challenging tumors due to their vascularity, anatomical location, and possible hereditary background. Our case series highlights the importance of early diagnosis, thorough imaging, and genetic evaluation. In high-risk or inoperable cases, modern radiotherapy techniques such as IMRT offer an effective, well-tolerated alternative to surgery, with promising local control. Long-term multidisciplinary follow-up remains essential to monitor for recurrence, manage functional syndromes, and provide appropriate genetic counseling when indicated.

Références

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