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The use of scintigraphy for diagnosing and evaluating paraganglioma: an integrative review

Uso da cintilografia para diagnóstico e avaliação do paraganglioma: uma revisão integrativa

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Abstract

Paraganglioma is a tumor of the endocrine system with a significant hereditary characteristic that affects younger people, causing headaches, palpitations, and diaphoresis. This tumor may be present in the head and neck region as a carotid body tumor and has a low incidence of metastasis. Although several tests can be used, such as computed tomography and magnetic resonance imaging, scintigraphy is useful for diagnosing and assessing paraganglioma. Online databases, such as Scielo, Oxford Academic, PubMed, and The Journal of Nuclear Medicine, were used to compare the relationship between scintigraphy and paraganglioma. Data were analyzed based on the germline classifications of the paraganglioma and the Shamblin classification for prognosis and surgical risk. The imaging exam and the new drugs used in the exams increased the life expectancy and quality of life of affected patients. Also, these approaches have been a major advance in nuclear medicine.

Keywords: Paraganglioma; Scintigraphy; Carotid body; Tumor

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Resumo

O paraganglioma é um tumor do sistema endócrino com característica hereditária significativa que afeta pessoas mais jovens, causando dores de cabeça, palpitações e diaforese. Esse tumor pode estar presente na região da cabeça e pescoço como um tumor do corpo carotídeo e tem baixa incidência de metástase. Embora vários exames possam ser utilizados, como tomografia computadorizada e ressonância magnética, a cintilografia é útil para o diagnóstico e avaliação do paraganglioma. Bancos de dados online, como Scielo, Oxford Academic, PubMed e The Journal of Nuclear Medicine, foram utilizados para comparar a relação entre cintilografia e paraganglioma. Os dados foram analisados com base nas classificações da linha germinativa do paraganglioma e na classificação de Shamblin para prognóstico e risco cirúrgico. O exame de imagem e os novos medicamentos utilizados nos exames aumentaram a expectativa de vida e a qualidade de vida dos pacientes afetados. Além disso, essas abordagens têm sido um grande avanço na medicina nuclear.

Palavras-chave: Cintilografia; Corpo carotídeo; Paraganglioma; Tumor

INTRODUCTION

Paraganglioma is an endocrine tumor closely linked to genetic anomalies, with some genes recorded as endothelial PAS domain protein 1, dihydrolipoamide S-succinyltransferase, and succinate dehydrogenase complex flavoprotein subunit A. Similar to pheochromocytoma, this tumor secretes catecholamines, and it is more likely to be inherited than other tumors[1]. The clinical presentation usually appears between 11 and 13 years and includes episodic symptoms of palpitations, headaches, and diaphoresis[2,3]. Metastasis is usually absent, and malignancy is not associated with poor prognosis[4]. Around 70% to 80% of head and neck paragangliomas are symptomless[5] and can be presented as carotid body tumors, which are irrigated by their vasa vasorum and the arterial branches of the external carotid artery. The carotid body is anatomically described as a structure measuring about 3.5 cm that can be found at the bifurcation of the common carotid artery at the level of its adventitial layer[6,7].

Biochemical tests, one of the evaluation tests, are used to detect the excess of catecholamines or metanephrines. Then, imaging exams (e.g., computed tomography or magnetic resonance imaging) are conducted. However, imaging tests to assess the functional aspect are recommended to exclude the hypothesis of metastasis and assess regional extension or a suspected paraganglioma; the scintigraphy with I-123 metaiodobenzylguanidine can be conducted in this context[2,8]. Some drugs help to detect this tumor because they interact with specific paraganglioma receptors, such as 6-18F-fluoro-l-3,4-dihydroxyphenylalanine, 18F-FDG, and 68 analogs of Ga-DOTA-somatostatin. Thus, scintigraphy is important for managing and treating paraganglioma[9,10].

METHODOLOGY

This literature review was performed in the Scielo, Oxford Academic, and PubMed databases, using the descriptors Radionuclide Imaging and Paraganglioma for the MeSH search and Scintigraphy and Paraganglioma for the DeCS search; descriptors were combined using the boolean operator “AND”. The inclusion criteria were congruence with the theme, relevance to the research, publication date between 2018 and 2023, and studies published in English, French, or Portuguese. Exclusion criteria were non-conformity with the topic, irrelevance to the research, articles published in other languages not included in the inclusion criteria, and more than five years since publication. A total of 1,015 articles were found in the search, and 10 were included in the review.

RESULTS AND DISCUSSION

A detailed analysis showed that a specialized evaluation of pheochromocytoma or paraganglioma is needed to clarify the clinical management and the expected prognosis. A biochemical interpretation was also conducted to provide individualized follow-up. Three clusters were formed based on the underlying germline or somatic mutations of the pheochromocytomas and paragangliomas: clusters 1A and 1B related to pseudohypoxia (cluster 1); cluster 2 associated with kinase signaling; and cluster 3 linked to Wnt 3 signaling. These clusters are also clinical, biochemical, and imaging signatures that can guide clinical therapy, specifying the individual intervention for each one. However, the inoperable or metastatic disease cluster does not yet have a proper intervention in clinical practice, suggesting the need for personalized genetic treatment as a routine procedure in these cases[1].

The analysis also evidenced the importance of imaging for evaluating and managing pheochromocytomas and paragangliomas, which often even guides treatment. In the study, the discovery of susceptibility genes associated with these tumors improved the understanding of clinical phenotypes and imaging. Thus, imaging is essential as it can detect the subtypes of pheochromocytoma and paraganglioma. Several radiopharmaceuticals were created to target specific receptors and metabolic processes of pheochromocytomas and paragangliomas, including 131 I/ 123 I-metaiodobenzylguanidine, 6-18 F-fluoro-l-3,4-dihydroxyphenylalanine, 18 F-FDG, and 68 Ga-DOTA-somatostatin analogs[10].

One investigation of demographic, clinical-pathological, and radiological data included 104 patients (33 men and 71 women, mean age 54.6 ± 13 years) with cervical paraganglioma in the carotid bifurcation between 2003 and 2017. The radiological analysis showed that ten patients had bilateral tumors; thus, 114 patients received treatment during this period, and all underwent surgery. After the procedure, seven patients had hoarseness, two had facial paralysis, one had dysphagia, and one had Horner’s syndrome[5].

The 114 patients underwent the Shamblin classification to stratify surgical risk and potential vascular complications. The highest percentage found was Shamblin II (n = 66; 57.9%). The Shamblin classification is shown in Table 1[5].

Table 1. The Shamblin classification according to Basel & Bozan[5].

Type	Description	Prevalence of paraganglioma according to Basel & Bozan[5] n = 114 (100%)
I	Localized tumors that do not extend beyond the carotid body (< 6 cm)	15 (13.2%)
II	Tumors that partially extend beyond the carotid vessels (Up to 6 cm)	66 (57.9%)
III	Large tumors that completely bypass the carotid vessels (> 6 cm)	33 (28.9%)

Source: Basel & Bozan, 2021[5].

Each patient can undergo a different type of surgery, depending on what is most appropriate for each case. Those with tumors larger than five centimeters can be treated with spring embolization and surgical resection. Patients with Shamblin III can undergo surgical resection with a polytetrafluoroethylene graft. Although these surgeries can present complications, recent studies showed that patients did not have a lasting sequelae[5].

Paraganglioma is considered a neuroendocrine tumor that can be named pheochromocytomas or extra-adrenal paragangliomas when they appear in the adrenal glands or outside the adrenal glands, respectively. Most pheochromocytomas and paragangliomas are benign, with a few spreading to other sites. When the biochemical results are positive, imaging tests can be performed to confirm the diagnosis, in which the location, course, and best surgical treatment are defined. PET-CT with Ga-DOTA-SSA is the best diagnostic option. Scintigraphy can be very effective as it is a safe, non-invasive, and efficient method for locating pheochromocytomas and paragangliomas outside the adrenal glands, providing functional and anatomical data. Metaiodobenzylguanidine scintigraphy is indicated to evaluate the whole body since it shows the correct topography of the tumor. Tomography or magnetic resonance imaging is used to show anatomically where they meet and with whom they converge[10].

CONCLUSION

The use of metaiodobenzylguanidine is a great ally for diagnosing paraganglioma. Oth-

er substances can also be used, such as 131 I/ 123 I-metaiodobenzylguanidine, 6-18 F-fluoro-l-3,4-dihydroxyphenylalanine, 18 F-FDG, and Ga-DOTA-somatostatin analogs, which have proved to be more effective. These drugs are an achievement in nuclear medicine that directly impacts the life expectancy and quality of life of affected patients. Paraganglioma is a rare disease, and most studies are scarce and generally retrospective. In addition, the pharmaceutical industry lacks investment in research into new drugs. Thus, surgery is considered the definitive choice of treatment and should be encouraged since the percentage of patients with sequelae and complications is relatively low. However, considering the topography of the tumor, very close to large vessels and neural structures, the surgery can still be considered a challenge for inexperienced surgeons. When evaluating a patient with paraganglioma, physicians must decide whether the surgery will be conducted, considering the risks or benefits and life expectancy. Moreover, preoperative embolization can also be chosen for large tumors, which increases the success rate of the surgery.

CONFLICT OF INTEREST

Nothing to declare

AUTHOR CONTRIBUTIONS

LLAL - Research, Writing - original writing, Writing - proofreading and editing; **MRS -** Research, Writing - original writing, Writing - proofreading and editing; **LBMN** - Research, Writing - original writing, Writing - proofreading and editing; **NSFRS -** Research, Writing - original writing, Writing - proofreading and editing; **BXL** - Research, Writing - original writing, Writing - proofreading and editing; **HGS** - Conceptualization, Research, Methodology, Supervision, Writing - original writing, Writing - revision and editing. All authors approved the final version.

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