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Case Report

Paraganglioma of the Carotideal Glomus Bibliographic Review of a Rare Tumor about a Case

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Abstract

Paragangliomas (PGL) are neuroendocrine tumors that occur in the ganglia of the autonomic nervous system. They share their embryonic origin with pheochromocytomas. They are differentiated from the latter by their low catecholamine secretory power, their extra-adrenal location, low malignant potential and lower incidence and prevalence. The heterogeneity with which they present makes their clinical presentation very varied and diagnosis a challenge. The indicated treatment will depend on the extent of the disease and relationship with adjacent structures, prioritizing surgical resection for its localized form as standard.

The clinical case of a patient with a diagnosis of carotid glomus paraganglioma is presented below, as a kickstart for the development of this topic of interest due to its low frequency of appearance.

Keywords: Paraganglioma; Pheochromocytoma; Pheochromocytoma/Paraganglioma Síndrome; Carotid Glomus

Introdución

Feochromocytomas and PGL form part of a group of neoplasms that arise from the chromatins cells of the neural tissue that is found in the adrenal cord and sympathetic and parasympathetic nodes, respectively [1,2].

PGLs, of interest in this review, represent 25% of this neuroendocrine tumor subtype, are mostly of benign strain and are usually highly vascularized. They may occur in sympathetic nodes of the chest cavity (10%), abdominal (75%) and/or pelvic (5%), which can secret norepinephrine or dopamine [3]. Those located in the parasympathetic nodes are most often located at the neck and base of the skull (10% of the total) and in a 95% are hormonally inactive [4]. They account for 0.6% of all head and neck cancers [5].

The estimated overall incidence of head and neck PGLs (PGLCyC) is 0.3 - 1 cases per 100,000 inhabitants, with a subtle female predisposition. They are usually located in the jugular bulb, the glosopharyngeal or vague nerve or in the carotid body [6]. While most are benign, those that are accompanied by histological characteristics such as central necrosis, hypervascularity or increased mitotic activity tend to be considered malignant. (It should be noted that these factors are not entirely reliable). Between 6% and 19% of all PGLCyCs develop metastases, which are mainly limited to the regional lymph nodes, but can also occur remotely, in the lungs or bone skeleton (6% to 13% of cases) [7]. Carotid body PGLs (PGLCCs) constitute up to 60% of all PGLCyCs. They occur especially between the fourth and sixth decades of life, although the range of appearance is wider [8]. They are slow-

growing and develop specifically in the anterolateral face of the upper neck, in the sector better known as the carotid "glomus", whose function is to regulate breathing through the detection of oxygen levels thanks to their chemoreceptor activity. Although most PGLs are generally sporadic, an increasing percentage of cases may be part of a family genetic syndrome [9]. The incidence of PGLCCs is generally higher in populations living in geographical areas above 2,000 metres above sea level [10], in this respect, it has been proposed that environmental hypoxia could eventually modulate a genetic predisposition for its development [11]. It represents a surgical challenge due to its proximity to the internal and external carotid arteries. Clinical and therapeutic management is even more challenging because PGLCCs can occur bilaterally and/or in multiple forms, especially in family forms. 12 Early identification leads to R0-targeted surgery that is usually curative and key to a favourable prognosis. Similarly, the prognosis ranges from very long life expectancy to a 5-year survival rate of 11.8% in patients with remote metastases [12].

Caso clínico

She is presented to the oncology department of the Hospital General de Agudos Dr. T. Álvarez, a female patient of 62 years of age, derived from the vascular surgery department.

The following data were collected for the first time: personal history of deep vein thrombosis (TVP) in the lower right member in 2010 and family history of paraganglioma in a sister, diagnosed in the year 2022 with surgical resection of the same and controls so far without recurrence of disease. As a history of current disease refers to the detection, by self-examination, of a hardened mass in the left lateral-cervical region.

An Angio tomography is performed (04/07/2023) which reports: zone of hypervascularization at the level of the source of internal and external carotid, which fistulizes the jugular vein. It looks like a carotid glomus.

In August 2023, he underwent surgical resection of the injury. (Figure 1).

Patological anatomy: carotid glomus according to histological and immunohistochemical findings (IHQ) CK AE1/AE3 negative; synaptophysine positive; S100 positive in sustentacular cells. Immunophenotype compatible with carotid glomus paraganglioma. Resection margins in contact with the injury. Mitosis 1:30 per field.

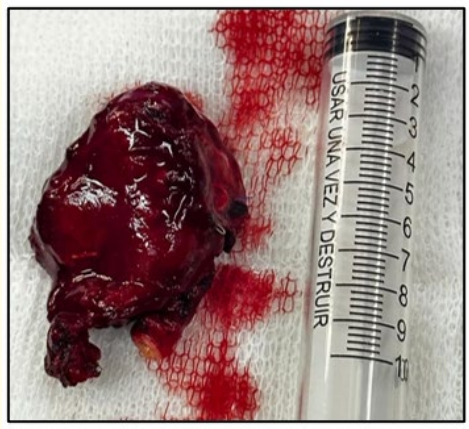

Figure 1: Carotid glomus tumor resection macroscopy piece.

Postoperative studies

- Laboratory (04/12/2023): urinary catecolamines: urinal norepinephrine 330 ug/24 hs; urinal adrenaline 241 ug/24 hs. V Vainillin Mandelic Acid 13.8 mg/24 hs.
- Ecodoppler of neck vessels (02/01/2024): in left lateral cervical region hypoecogenic formation of net edges, ovoid of 18 x 10 mm, with low central and peripheral resistance arterial flow. It could be compatible with adenomegaly.
- Axial computed tomography of the brain, chest, abdomen and pelvis with intravenous contrast (11/01/2024): in close relation to the external carotid a rounded injury of 16 x 11 mm is observed, with intense enhancement after contrast administration. No evidence of remote secondary education.
- Nuclear Neck Magnetic Resonance with Gadolinium (08/02/2024): Presence of solid contrast enhancing nodular image, located behind the submaxillary gland, measuring 21 x 15 x 21 mm.

With these findings, the case is presented to a multidisciplinary tumor committee and is interpreted as a local recurrence of illness, irresectable, so it is decided to apply for radiosurgery, which is carried out in February 2024.

Currently, the patient is in good general condition. It is presented as an adverse effect of radiant treatment dysphonia G1, so it is in phonoaudiological rehabilitation. April 2024 control studies show no evidence of disease recurrence.

Discussión

PGLs have their importance and interest in relation to the low incidence rate. Their clinical presentation is equally unpredictable. Completely asymptomatic cases with incidental presentations in imaging studies have been described, such as, in another extreme, cases with florid symptomatology (functioning tumors) with signs and symptoms of the sympathetic system of fight or flight such as dry mouth, redness of the face, palpitations, midriasis, restlessness, constipation, fatigue, excessive sweating, headache, tremors, panic-like symptoms and generalized weakness by exhaustion. It can also occur with blurred vision, dizziness, weight loss, excessive thirst or hunger, mood disturbances, high glucose levels, and weight loss. However, the most classic presentation is the triad of headache, palpitations, and abundant sweating [13]. Tumors below the neck tend to give more overlapping pictures such as headaches, palpitations, sweating, abdominal or chest pain, hypertension, and palsy.

The diagnosis of PGL is carried out with biochemical analyses to exclude a secretor component, although its finding is rare. Dosage of catecolamines and metanefrins in plasma and urine should be performed. In non-secretory PGLCCs, imaging such as tomography and resonance imaging are mandatory as a method for tumor localization, surgical planning and follow-up [13].

For functional imaging, 18F-fluorodeoxyglucose positron emission tomography (PET TC with FDG) is the study of choice [14]. The PET TC of fluorodeoxyglucose, given the avidity of the metastases by fluorodesoxiglucosa, or metayodencylguanidine (MIBG), may also be used to assess the presence of metastasis, although the latter is lower [15]. It should be noted that ultrasound remains a good initial diagnostic method for patients with suspicion of carotid body paraganglioma.

Diagnosis is usually based on functional imagery, and confirmative biopsies are rarely performed.

Histologically, PGLs are characterized by presenting a thin capsule, with an alveolar growth pattern nested or "Zellballen" around few or numerous cells. These cells are from amphophilia to rosacea; they are usually epithelial but can also be fuse-shaped. PGL cells have a round hyperchromatic nucleus with mitosis (Figure 2).

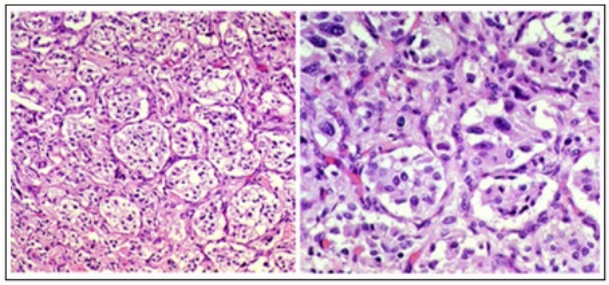

Figure 2: PGL epithelium in microscopic field. Cells in trabecular pattern. (Adaptado de Silloo B Kapadia, MD.)

Immunohistochemistry shows the expression of neuroendocrine markers (chromogranin, synaptophysine and neuronal-specific enolase) in the main cells and the disappearance of S100-positive sustentacular cells; they are not necessary for diagnosis [16,17].

PGLCCs are classified according to Shamblin criteria (basados en los resultados de los hallazgos en la RMN). Class I tumors are localized with extension of carotid bifurcation but with little connection to the adjacent blood vessels (A), Class II tumors partially surround the carotida (B) and Class III tumors intimately surround the Carotides (C) [18]. (Figure 3).

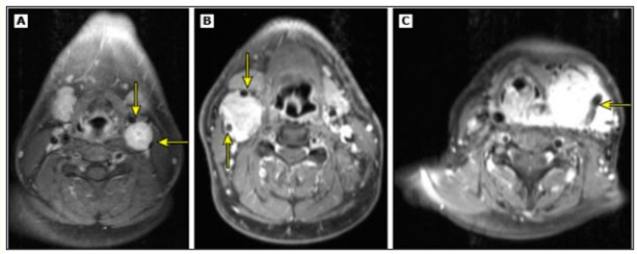

Figure 3: Clasificación según los criterios de Shamblin por RNM (Adaptado de: Boedeker CC).

Ranking by Shamblin criteria by RNM (Adapted from: Boedeker Most PGLs are sporadic, however, approximately 10% are associated with family syndromes. Among them, the most known and common germinal line mutation is in the Succinate dehydrogenase (SDH) gene, closely related to the family paraganglioma. This gene is responsible for the transfer of electrons to the respiratory chain through ubiquinone (coenzima Q). The SDH complex consists of 4 subunits (described as tumor suppressing genes) SDHA and SDHB (catalytic subunities), SDHC and SDHD (subunidades de anclaje). All mutations in SDHB, C and D cause hereditary paraganglioma syndromes (PGL4, PGL3 y PGL1, respectivamente) [19-21].

On the other hand, three more well-known genetic syndromes have been described, such as Von Hippel-Lindau (VHL), Multiple Endocrine Neoplasia Type 2 (MEN-2) and Neurofibromatosis Type 1 (NF1), which reflects mutations in the VHL, RET and NF1.18 gene respectively. These are mainly associated with feochromocytomas, but occasionally can also occur with paragangliomas. All are characterized by an autosomal dominant pattern of inheritance with variable penetration. The risk of developing tumors and the degree of malignancy varies depending on the type of pathogenic variant [22].

The therapeutic decision will be closely related to the location and relationship with adjacent structures, the size and functionality of the tumor.

If the disease is localized, as in most cases, surgery is the standard treatment, especially when it comes to a functioning tumor. Radiation therapy could be reserved for when attempting to avoid the complications of surgery or when it is a recurrence of a disease not passible to surgical resection. In some cases, when the tumor is small, slow-growing and non-functioning, observation may be considered [23,24].

In those patients with advanced disease, therapeutic options are more limited and complex. Among them is the iobenguano I-131. Another option to consider is chemotherapy, especially in combination schemes with cyclophosphamide, vincristine and dacarbazine or doxorrubicin. Tyrosine kinase (ITK) inhibitors such as sunitinib, with low level of evidence, have also been evaluated [15-27].

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