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Paragangliomas, Etiology, Review of 1070 Series of Cases Hospital De Especialidades Centro Médico La Raza

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Abstract

Objective: Present the frequency of atypical histological lineage paragangliomas on a third level hospital.

Introduction: Paragangliomas, also known as neuroendocrine tumors, are rare and can appear in distinct places throughout the human body where chromaffin cells are present. Such examples include blood vessels and nerves. Thirty percent are in head and neck compartments; after carotid paragangliomas, the yugulotimpanic follow in frequency and then the vagal ones by 5%. Onlyone percent of paragangliomas located in the head and neck are functional compared with those located in other parts of the body that tend to be functional, most commonly causing hypertension.

Methods: An ambispective, observational, descriptive review was conducted, including patients operated on by paraganglioma from 1987 to January 2023; 99.4% were initially diagnosed as carotid origin.

Results: A total of 1070 patients were captured. 998 patients were female (93.2%). 1,063 of paragangliomas were carotid (99.3%), 2 were vagal (0.18%), 1 was yugulotympanic (0.09%) and 3 were in other locations (0.28%). One was reported as a Schwannoma. None of the tumors were reported as being hyperfunctional.

Conclusion: The angiographic visualization of these lesions can confuse their diagnosis and cause an erroneous follow-up with a poor prognosis, since it is described that vagal paragangliomas recur in 17%.

Keywords: Paragangliomas; extirpation; extra adrenal

Abbreviations: PG: Paragangliomas; CPG: Carotid paragangliomas; VPG: Vagal paragangliomas; YTPG: Yugulotimpanic paragangliomas

Introduction

Paragangliomas (PG), also known as neuroendocrine tumors when located in regions other than the adrenal glands, are rare and can develop where chromaffin cells are present. Such places include blood vessels and nerves [1]. 30% are in head and neck compartments where carotid paragangliomas are the most frequent;90% are benign; they are more common on the female sex; these lesions occur in patients living in localities with more than 2000 meters above sea level, which conditions chronic hypoxia; Genetic predisposition has also been found. As in the case of Mexico, in which, most of the patients, come from the City of Pachuca Hidalgo, a town at 2432 m above sea level and with a predominant gene was the SDHD in 16% of patients. Probably the same factor influenced a family with bilateral, multicentricandmalign stripe lesion even though they lived in Morelia, Michoacan, a locality 1920 meter above the sea level.

About PG located in head and neck, Carotid Paragangliomas (CPG) are the most frequent. Followed by the Yugulotimpanics (YTPG) and Vagal Paragangliomas (VPG) which represent less than 5% [2-4].

Even Though they are considered tumors capable of producing and storing catecholamines, only 1% of head and neck paragangliomas are functional. Those located in the thorax, abdomen or pelvis can secrete vasoactive hormones that cause hypertension [2,4]. Approximately 10% of these tumors are related to genetic predisposition, where multi-locate presentations are more likely to occur [5].

VPG is a non-chromaffin tumor which arises predominantly in the accumulations of paraganglionic cells within the perineurium of the vagus nerve, associated with one of its own three nodes [3,6], mainly the lower ganglion or nodose ganglion (sensory) that innervates the chemoreceptors of the aortic bodies and the baroreceptors of the aortic arch (extracranial portion of the nerve), which determines the clinical presentation and growth pattern dependent of the type of lesion, remaining in this case, in the cervical region; Not so, with those that originate from the middle or upper ganglia, which extend intracranially [7]. They also develop in hypoxic scenarios.

It has been mentioned that a percentage of PG that are not originated on head or neck are vasoactive and include bladder PG, which may result with hypertensive paroxysms accompanied during urination [8].

YTPG is a tumor that can affect the ear, upper neck, and skull base, as well as nerves and surrounding blood vessels. It grows in the temporal bone, at the level of the jugular foramen, where the jugular veins and some nerves leave the skull. It involves the middle and inner ear. The aforementioned area contains nerve fibers (glomus bodies) that respond to temperature or blood pressure changes; it usually occurs between the seventh and eighth decade of life and its cause is unknown; they have been linked to genetic mutations of the enzyme Succinate Dehydrogenase (SDH) gene [9,10].

This tumor is rarely malignant; its treatment is multidisciplinary which include previous embolization and surgical management, it is complemented with radiotherapy when its complete removal is not possible; more than 90% of patients are cured [3,9].

Our objective was to determine the frequency of the different strains of head and neck paragangliomas in our entitled population.

Material and Methods

From 1987 to January 2023, the records of patients who underwent surgery in our medical unit were analyzed, with the diagnosis of PG in any location; the presumptive diagnosis in 99.4% was CPGof the neck masses. Our sample consisted of Older adults of both sexes; age went from 21 to 82 years old (mostly older patients who specifically asked for surgical procedure). Diagnostic tools included clinical findings, Doppler ultrasound, CT scan and angiography; all discerned by the Shamblin classification.

Results

From 1987 to January 2023, 1070 PGs were collected, 998 were in female patients (93.2%); of these, 96 correspond to the post-pandemic period, with stage III predominance on the Shamblin classification (60.7%), followed by stage II (35.7%) and stage I (3.5%).

Due to the pandemic, a patient requested to be operated outside of our institution; it turned out to be a Schwannoma, whose symptomatology was Tinnitus and right hemiface pain; the lesion had a high location, which captured the contrast medium.

In this series, two women were not included, one with a YTPG on the right side that was going to be operated together with neurosurgery and otolaryngology, with otorrhagia and an intracerebral injury which unfortunately died before the procedure due to bleeding; another patient with a right 10 cm diameter PGC and an ipsilateral 7 cm thyroid mass with a family history of carotid and abdominal aorta PGs was sent to radiotherapy.

We had a patient with an hypogastric artery and bladder PG [11] another patient from the seventh decade of life with a PG and an adenocarcinoma, where the histopathological report found out to be a metastasis of an pulmonary adenocarcinoma confirmed by immunohistochemistry (Figure 1); the patient was discharged in good conditions and was lost to follow up, failing to establish if he had neoplasms in other places [12]. Another patient who underwent surgery with the diagnosis of cervical PG turned out to be Castleman disease (Figure 2) confirmed by histopathological study [13], who did not enter this PG series. A patient of the third decade of life, with genetic load for DM2 by maternal line, presented with a Zuckerkandl organ PG (Figure 3) clinically symptomatic since childhood with pulsatile headache, diaphoresis, palpitations and anxiety. The lesion was located between the abdominal aorta and the inferior vena cava. It was managed jointly with the endocrinology and internal medicine services in the preoperative period 7 days prior to surgery with phenoxybenzamine 1 mg / kg PO or prazosin 2-5 mg PO every

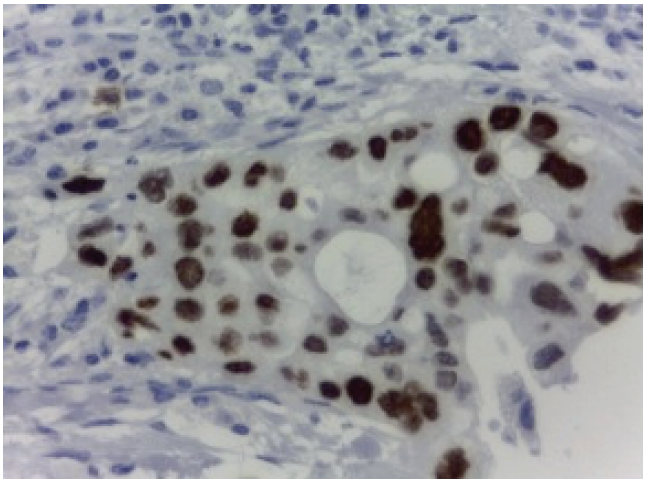

Figure 1: Image with Thyroid Transcription Factor (TTF-1) stain, the staining reaction is nuclear, demonstrating its pulmonary origin.

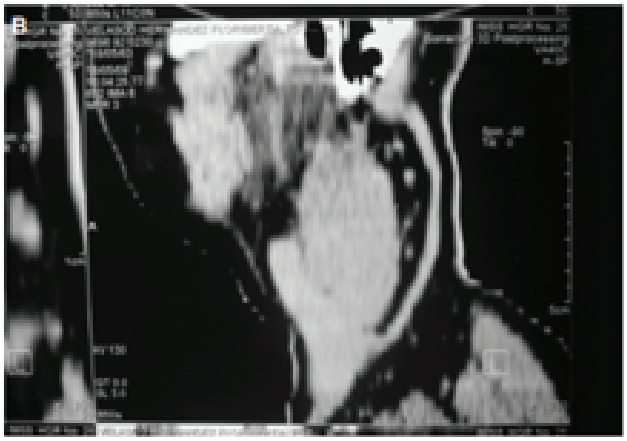

Figure 2: CT Angiography demonstrates a single well-defined left lateral-cervical tumor of approximately 7 cm, which captures contrast material.

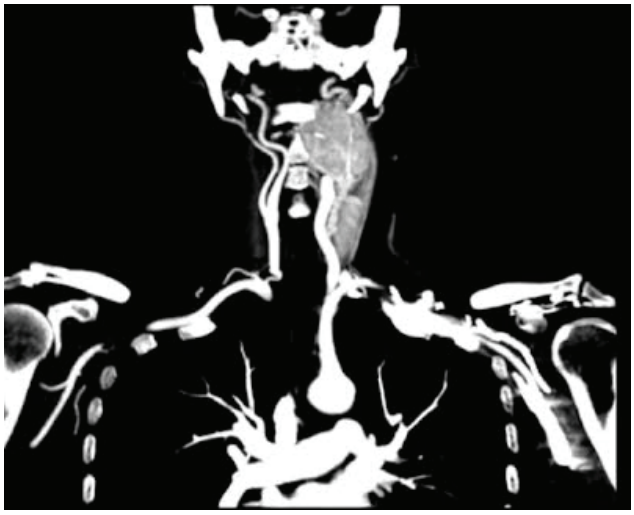

Figure 4: CT angiography of a VPG.

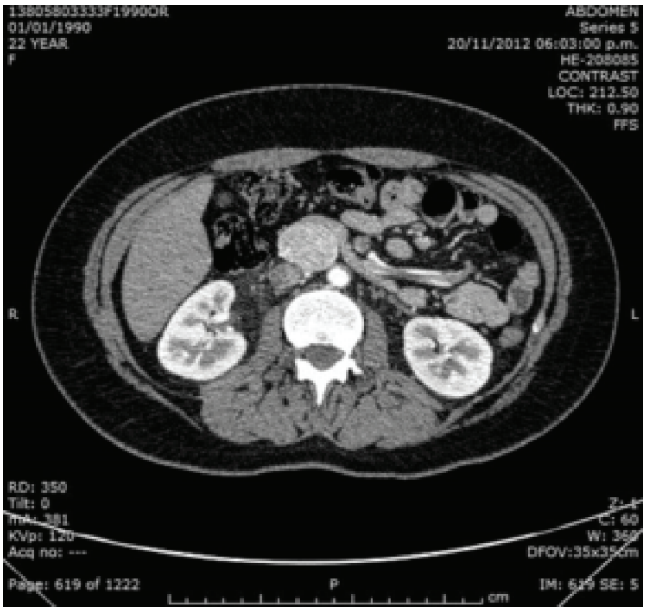

Figure 3: Abdominal computed tomography with IV contrast which evidences a well-defined mass on left paraaortic localization of 43x32x32 mm heterogeneous with hypodense center; reinforced with the contrast medium.

12 h, increasing the dose until BP was 130/80 mmHg seated and 100 mmHg systolic in a sitting position; and a HR between 60 to 70 bpm. Subsequently was managed with metoprolol 95 mg PO every 12 h maintaining HR between 60 to 70 bpm sitting and 70 to 80 bpm standing [14].

We have an image of a sixth decade patient who was asymptomatic, without neurological signs, with a VPG (Figure 4).

We didn't have any hyper-functioning type; in a subgroup study, metanephrines were determined in 26 patients, finding high plasma metanephrines levels in 80.7% of patients (above 60pg/ml of values established as normal); after surgery it remained elevated in 50% and decreased in 19 patients with a maximum decrease of 129 pg/ml, with an average of 30 to 90 pg/ml in 10 patients and from 91 to 120 pg/ml in 3 patients [15].

Discussion

The presence of a pulsatile mass in the carotid triangle suggests the presumptive diagnosis of PG. Asymptomatic patients with a PG and family history should be screened with a radioactive isotope (octreotide) to rule out the presence of multiple lesions not clinically diagnosed [16].

CPG can be sporadic or familial. Cases Of disease occur in 10%; they are transmitted in an autosomal dominant manner through the 11q23 locus5 gene and have a high incidence of presenting bilaterally (33%, according to reports). In 79% of head and neck PGs, a mutation in the D subunit of the SDH gene has been found, which has suggested the presence of multiple paragangliomas. We must bear in mind that even when mortality is low (1-2%) and morbidity high (40%), it is a pathology whose management, sometimes, must be multidisciplinary, not only in surgery, but in its diagnosis, taking into consideration previous neurological deficits that will influence its postoperative results and in bilateral ones, we must consider the baroreflective deficit whose symptoms are minimized or not diagnosed [17].

Erroneously in our environment, we catalog all the lesions as cervical PG of arterial origin if it captures contrast medium and for an inadequate anamnesis, when described, that the VPG, capture the contrast medium by Discussion.

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not only in surgery, but in its diagnosis, taking into consideration previous neurological deficits that will influence its postoperative results and in bilateral ones, we must consider the baroreflective deficit whose symptoms are minimized or not diagnosed [17].

Erroneously in our environment, we catalog all the lesions as cervical PG of arterial origin if it captures contrast medium and for an inadequate anamnesis, when described, that the VPG, capture the contrast medium by the vasa nervorum, and after resection, the surgical pieces are sent to the Department of Pathology, with the diagnosis of CPG, so they are misdiagnosed by this reference.

In VPG, the surgery apparently may be simpler due to minimal blood loss; however, it is technically difficult in many cases, and should have a multidisciplinary management both due because of the approach, the location, and nerves involved which can result in sequelae from the damage during surgery, requiring intense rehabilitation, so radiotherapy is a good option in selected patients. In addition, we must not forget that there are reports of malignancy (Druck et al.), so if possible, we must perform complete resection [18].

As Dr. Quiñones mentions, "With respect to CPG, whether they are malignant or not, the morphology is not conclusive; the neoplasm may appear pleomorphic and not malignant or viceversa; however, if there is invasion of the capsule or vascularity, it should be considered potentially malignant, especially when there is well-documented metastasis, an unequivocal sign of malignancy. Most PGs are benign despite their histological appearance; it is necessary to resect them completely (if possible) and send them for full macroscopic and histopathological study" [19].

During the COVID-19 pandemic (2019-20), no patient with this pathology was intervened; it is noteworthy that during the post pandemic period, stage III of the Shamblin classification predominated with 60.7% (96 patients), against 46% in the period prior to the pandemic [20], when described, increasing in size from 1.5 to 2 mm per year; it would be necessary to investigate, if it was due to inactivity or hypoxia secondary to multiple factors. A good question would be, how many of these patients probably suffered from COVID?

It should be noted that our analysis showed high concentrations of metanephrines in 80.7% of patients (above 60pg/ml values established as normal) and even after surgery, remained above 50% of the cases, which could guide us, that in our population most of the Carotid Body Tumor (CBT) are hyperfunctioning [15].

Our study, even with the comorbidities that mainly affect our entitled population, confirmed what is already described about head and neck PGs and their different strains, the family factor in malignant behavior.

It is also important to consider in our research, the number of cases for the conclusions issued, since there are no reports in the universal literature, with greater casuistry, although on the other hand, histopathological reports in most cases, lack appropriate analysis and are vitiated by the reference diagnosis when cataloguing the surgical pieces, as CPG. Another inconvenient was we couldn't do to all the patients genetic studies because of our institution economic situation.

Conclusion

The angiographic visualization of these lesions can confuse their diagnosis and lead to erroneous follow-up, with disastrous consequences, since it is described that the VPG, recur in 17% [21].

The genetic factor is important (16%) and not only the height that conditions chronic hypoxia.

In conclusion, not all lesions that are stained are PG and the fact that they are stained, does not mean that they are not vagal.

Conflict of Interest

Authors declare no conflict interest.

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