Case Report

Recurrent Primary Intrasellar Paraganglioma

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We describe a case of an 81-year-old male presenting with bitemporal visual field defects and blurry vision in the right eye. The patient was found to have a recurrent primary paraganglioma in the sellar and suprasellar region requiring a repeat transsphenoidal endoscopic resection. Immunohistochemical examination confirmed paraganglioma with the classic zellballen appearance which stained positive for chromogranin, synaptophysin, and S-100 in the periphery. Paragangliomas (PGLs) in the sella turcica are a rare entity; only 19 cases have ever been reported in the literature. PGLs in the sellar region are often misdiagnosed or diagnosed in a delayed fashion. Earlier diagnosis of this locally aggressive tumor and meticulous debulking can prevent morbidity secondary to the tumor’s compressive effects. This report highlights the effectiveness of surgical interventions in treatment of paragangliomas. More research is still needed to determine the need for adjuvant therapies such as radiation.

1. Introduction

Paragangliomas (PGLs) are rare, nonepithelial neuroendocrine neoplasms (NEENs) [1] that arise from neural crest cells and generally occur in locations where paranglia normally are found [2]. There are two main types: parasympathetic and sympathetic [3]. Parasympathetic are usually in the head and neck and nonfunctional, while sympathetic are typically in the thorax, abdomen, retroperitoneum, and pelvis and are functional [3–5]. The most well-known type of paraganglioma is a pheochromocytoma which originates in the adrenal medulla [5]. While all PGLs have neurosecretory granules, those classified as functional secrete catecholamines leading to symptoms such as secondary hypertension, flushing, increased perspiration, headaches, and tremors [6]. Only 1–3% of PGLs in the head and neck are functional [7].

In the head and neck, PGLs account for only 0.6% of all tumors [8]. Of all PGLs, only 3% occur in the head and neck region [7]. PGLs are found along parasympathetic parganglia of the glossopharyngeal and vagus nerves with the most common site being the carotid body (75%) and the second being the temporal bone (16%) [3, 8, 9]. Other sites such as vagal, laryngeal, subclavian, aorticopulmonary, and cardio pulmonary are also documented [3].

60–70% of carotid body PGLs present as a nontender, enlarging mass in the lateral neck often with a bruit and can lead to cranial nerve IX, XI, and XII deficits [7]. Vagal PGLs are also nontender, slow growing neck masses in the lateral neck with the majority at the angle of the mandible. Symptoms consist of pulsatile tinnitus and in one to two thirds lower cranial nerve palsies in X, IX, XI, and XII [7].

When PGLs are intracranial, over 90% are from the temporal bone, in the jugular foramen or middle ear (termed
typanic) [10]. Jugular PGLs present as an enlarging mass around the jugular bulb leading to decreased venous blood return on that side and resultant rerouting to the contralateral sigmoid sinus [7]. These often lead to pulsatile tinnitus, an audible bruit over the ear, dizziness, or hearing loss [7]. Tympanic PGLs typically present as a small mass in the tympanic membrane or external auditory canal associated with tinnitus and hearing loss [7]. PGLs generally present as an enlarging mass with symptoms based on the topographic location.

Sellar PGL generally presents as an enlarging sellar mass most often associated with vision loss/impairment and headaches [11]. To our knowledge, there are only 19 cases reported of primary sellar paragangliomas. We present a case of a recurrent paraganglioma of the sellar and suprasellar region and compare our findings to the current literature.

2. Case Presentation

An 81-year-old male with a history of atrial fibrillation on warfarin, hypertension, and glaucoma initially presented with progressively worsening blurry vision. On physical examination, he was found to have visual field defects, with no other cranial nerve sensory or motor defects. Additionally, there was no evidence of endocrinopathy or autonomic changes noted.

On radiologic evaluation, the patient was found to have a sellar mass pressing on the optic chiasm, most consistent with a pituitary microadenoma. Two years earlier, he underwent a transseptal transphenoidal resection of the pituitary tumor at another institution to decompress the optic chiasm. Histopathological evaluation of the resection had features of a paraganglioma. Postoperatively, there was no progression of his visual deficits.

Several months later, the patient presented to our clinic with worsening visual problems especially blurry vision on the right side and decreased short-term memory. He also reported two episodes of epistaxis within the prior ten days. He denied having any problems with balance or episodes of headaches. On physical examination, he had decreased bitemporal fields and an increased right inferior field but can still see hand movements in both superior quadrants on the right side. Visual acuity in the left eye was good. The pupils were equal, round, and reactive to light. The extraocular movements were intact. The remainder of the physical exam was unremarkable.

On imaging, MRI demonstrated a lobulated 1.9 cm × 2.1 cm × 2.3 cm T2 hyperintense homogeneous enhancing mass causing expansion of the sella turcica and extending into the suprasellar cistern compressing the optic chiasm and the right optic nerve (Figure 1). There was also extension into the medial aspect of the cavernous sinus.

Transphenoidal endoscopic resection with intraoperative MRI and CT Stealth stereotactic navigation was used to extensively decompress the optic nerve and chiasm and resect the paraganglioma. Intraoperative MRI demonstrated a gross-total resection of the tumor (Figures 2(a) and 2(b)).

On histopathological evaluation, the tumor displayed features of a paraganglioma. The tumor cells were arranged in relatively well-defined nests (“zellballen”) (Figures 3(a) and 3(c)) surrounded by a delicate network of reticulin fibers. These were highlighted in the sections stained with the silver impregnation method (Figures 3(b) and 3(d)). Relatively large elongated cells, with clear cytoplasm (principal cells), were the most prominent component of nests. The sustentacular cells were difficult to detect in the routine stained sections. Only a rare mitotic figure was identified, and areas of necrosis were not observed. By immunohistochemistry, the tumor cells were positive for synaptophysin (Figure 4(a)), chromogranin (Figure 4(c)), NCAM (neural cell adhesion molecule, CD56) (Figure 4(d)), and neuron-specific enolase (Figure 4(e)). The sustentacular cells were strongly immunoreactive for S100 protein (Figure 4(b)). Focally, the tumor cells were also positive of cytokeratin (AE1/AE3) (Figure 4(f)). They were not immunoreactive for calretinin or neurofilament protein.

The patient is currently symptom-free with no recurrent tumor on repeat imaging 2.5 years after surgery.

3. Discussion

Paragangliomas arise from neural crest cells, but the exact pathogenesis of sellar PGLs is not completely understood. A widely accepted hypothesis indicates paraganglionic cells from cranial nerve IX (tympanic or ciliary branches) migrate into the cavernous sinus that is just adjacent to the sella turcica [12].

The differential diagnosis for sellar tumors is large and includes pituitary adenomas (85%), craniohypophyngiomas (3%), Rathke cleft cysts (2%), meningiomas (1%), and metastases (0.5%) [13]. Other rare masses such as oncocytomas, neurohypophysis granular cell tumors, hypophysitis, and pituicytomas are also seen [14]. Paragangliomas in this
Intraoperative T2-weighted MRI: (a) sagittal and (b) coronal views following resection of paraganglioma with the cross-sectional slice indicated by the vertical lines.

Paraganglioma with a distinct nested pattern of the tumor cells ("zellballen") in sections stained with hematoxylin-eosin (H&E) (a, c); the nested pattern was highlighted by a silver impregnation for reticulin fibers (b, d). Figures a and b 100x; figures b and c 400x.
region are an extremely rare diagnosis and often initially misdiagnosed.

According to a recent literature review, sellar paragangliomas are most commonly initially diagnosed as a pituitary adenoma (77.8%) followed by meningioma, craniopharyngioma, and macroadenoma [11]. Of the 19 other sellar PGL case reports, 9 were initially misdiagnosed (4 as adenomas, 2 as meningiomas, 2 as macroadenomas, and 1 as a craniopharyngioma while 10 other cases did not report on misdiagnosis) [11]. Our patient was initially misdiagnosed with a pituitary adenoma.

The most common presenting symptom for sellar PGLs, as seen with our patient, is visual disturbances. Of the 19 sellar PGLs, patients’ symptoms on presentation were visual disturbances/vision loss (63.2%, 12/19), headaches (47.4%, 9/19), hyperhidrosis (10.5%, 2/19), and one patient (5.3%, 1/19).

Figure 4: Strong immunoreactivity in principal cells for synaptophysin (a), chromogranin (c), CD56 (d), and neuron-specific enolase (e). Sustentacular cells with strong immunoreactivity for S-100 protein (b). Focally, the tumor cells were also positive for AE1/AE3 (cytokeratin) (f); figures a–f, 200x.
including this report, the average age with standard deviation of 48.3 ± 21.1 years with a wide range from 14 to 84 years. The female to male ratio is 2:1 (8:1 in high altitude) for carotid, 2:1–8:1 for vagal, 3:1–9:1 for tympanic, and 3:1 for laryngeal PGLs [17]. On the contrary, 20 sellar PGLs had a male predilection with 14 males (70%) and 6 females (30%; M:F ratio of 2.3:1). Bilateral and/or multifocal PGLs occur in 10–25% of carotid, 20–40% of vagal, often with carotid and/or vagal PGLs for tympanic, and rarely for laryngeal PGLs [17]. None of the 20 sellar PGLs, including the present study, were reported to be bilateral or multifocal [11]. The metastatic risk also varies by type: 4–6% in carotid, 16% in vagal (metastatic vs. multifocal was not clear), 2% in tympanic, and 2% in laryngeal [17]. Only 1 of the 20 sellar PGLs (5%) was noted to have metastasis [14]. Additionally, none of the 20 sellar PGLs had elevated catecholamine levels [11, 12]. CT and MRI are the most common imaging studies used in diagnosis with sensitivity of 95–100% and specificity of 67–70% [18]. PGLs enhance on contrast CT and gadolinium MRI [19]. PGLs have low signal on T1-weighted and high signal on T2-weighted MRI, as seen in our patient’s hyperintense homogeneous sellar PGL (Figure 1) [19]. One classic sign, seen more in head and neck PGLs than those in the trunk, is a “salt and pepper” appearance composed of flow voids creating low-signal intensity and hemorrhage.
20), persistent hyposthenia in 5% (1/20), basal ganglion infarction in 5% (1/20), headaches in 5% (1/20), and hypopituitarism in 5% (1/20) [11]. Patients with single-site PGLs after surgical resection have an equivalent life expectancy to age-matched disease-free individuals [6]. However, around 30% of patients have recurrence of their paraganglioma [18]. Patients with familial forms are 3.4 times more likely to have recurrence than those with sporadic disease [25]. Of these patients with recurrence, 50% have had distant metastasis [25]. Follow-up is highly recommended since many patients have persistence or recurrence of disease. Patients should be encouraged to undergo genetic testing to identify if there is a syndromic link. Postoperatively, patients should undergo annual surveillance with an MRI or CT to ensure the tumor has not recurred. Postoperatively, patients should undergo annual surveillance with a MRI or CT to ensure the tumor has not recurred [6]. Patients with functional PGLs should also undergo annual biochemical screening [6].

4. Conclusions

While, rare, paragangliomas should be kept on the differential for a sellar lesion. If there is a high index of suspicion based on symptoms, family history, elevated catecholamines, etc., an additional workup should be considered. Surgery is the mainstay of treatment, with no clear consensus for adjuvant therapy in the literature.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References


