CASE REPORT

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Vagus nerve schwannoma in the parapharyngeal space: surgical, histological and immunohistochemical aspects. A case report

VLAD ANDREI BUDU[1)], IOAN ALEXANDRU BULESCU[2)], CRISTIANA GABRIELA POPP[3)], BOGDAN CONSTANTIN MOCANU[1)], CARMEN AURELIA MOGOANTĂ[4)]

[1)]*Department of ENT, "Prof. Dr. Dorin Hociotă" Institute for Phono-Audiology and Functional ENT Surgery, Bucharest, Romania*
[2)]*Department of Anatomy, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania*
[3)]*Department of Pathology, Colentina Clinical Hospital, Bucharest, Romania*
[4)]*Department of ENT, Faculty of Medicine, University of Medicine and Pharmacy of Craiova, Romania*

Abstract

Tumors of the parapharyngeal space are rare accounting approximately for 0.5% of all head and neck tumors. In the retrostyloid space, schwannomas are a more common finding, in contrast to other tumors. Usually, they present with a variety of slight symptoms until they grow in size and compress surrounding organs. Surgical treatment of parapharyngeal space tumors is difficult; due to the anatomical complex area, they develop in, and include several approaches, according to its size and relations. In this paper, we present a case of a 63-year-old female with a vagus nerve schwannoma in the parapharyngeal space. Beside the surgical difficulties, the resected tumor had a peculiar histopathological aspect (large areas of degeneration and atypia and little typical palisading) that compelled a thorough histological and immunohistochemical evaluation for positive and differential diagnosis.

Keywords: schwannoma, parapharyngeal tumors, vagus nerve, cervical surgery.

Introduction

The parapharyngeal space (PPS) is the space surrounding the pharynx in its posterior and lateral aspects. Nowadays, the term PPS is recognized as the classic lateropharyngeal space. In this paper, we will consider the PPS as the space extending on each side of the pharynx, from the skull base, to the esophagus. PPS is an inverted pyramidal-shaped potential space [1–3], divided into two compartments, the prestyloid and retrostyloid. In the prestyloid compartment, we can find branches of the mandibular nerve, the internal maxillary artery, ascending pharyngeal artery, pharyngeal venous plexus, minor or ectopic salivary glands, surrounded by fat and connective tissue. The retrostyloid compartment contains vital vascular and nervous structures like the internal carotid artery, internal jugular vein, cranial nerves from IX to XII, the cervical sympathetic chain, the glomus bodies and lymph nodes [1–3].

Pathological masses found in PPS are varied in structure and contain congenital or developmental lesions and neoplasms. Common congenital masses include branchial cysts, originating in the second branchial apparatus, most likely from the second branchial pouch, located deep to the tonsillar fossa, in the medial part of PPS [1, 4]. Also, teratomas may rarely occur in PPS, mostly in newborns and infants [1, 5].

The majority of authors consider that PPS tumors account for less than 0.5% of head and neck neoplasms [1, 6–8]. According to their origin, they can be divided into primary tumors, metastatic, and tumoral extensions from related regions. Tumors extending from other regions into PPS are most common [4]. Primary neoplasms arising in PPS are either salivary gland tumors or neurogenic tumors [1, 9]. Primary salivary tumors in PPS originate from minor salivary glands, most commonly presenting as pleomorphic adenomas. Neurogenic tumors are second most common in prestyloid PPS, and most common in retrostyloid PPS [9]. Common tumor types are schwannomas, neurofibromas and paragangliomas. Other masses that could appear in PPS are vascular malformations and lesions like lymphangiomas, cavernous hemangiomas, and aneurysms [1, 4, 10, 11].

Surgical treatment of PPS tumors is a true surgical challenge due to the complex anatomical relations of the region, as well as the difficult approach to the area. Different surgical approaches can be used, like transcervical, transcervical-transmandibular, transparotid-transcervical, infratemporal and transoral [12].

We are presenting a case of a 63-year-old patient with a right parapharyngeal mass, which was excised through a trans-cervical approach. The location and anatomical relations of the tumor suggest that it was a tumor involving the vagus nerve. Histological and immunohistochemistry analysis revealed that the tumor was in fact a schwannoma.

Case report

A 63-year-old female presented complaining of difficult swallowing, sensation of pharyngeal foreign body and slight tumefaction in the right side of the neck, symptoms appearing approximately two years before presentation. Clinical examination revealed a bulging mass in the wall of the right oropharynx, protruding behind the right tonsil

and posterior pillar, which were medially displaced. Indirect laryngoscopy and laryngeal endoscopy showed normal mobility of both vocal folds, slight displacement of the lateral pharyngeal wall. Palpation of the cervical regions revealed in the right retromandibular and submandibular region the inferior part of a hard, well-differentiated mass, in continuity with the bulging in the oropharynx. The clinical diagnosis was of a right parapharyngeal tumor. The patient underwent contrast-enhanced computed-tomography of the skull base and cervical regions, which showed the 8×6 cm, right parapharyngeal mass, in the retrostyloid compartment, in direct contact with the lateral wall of the pharynx, displacing anteriorly the internal carotid artery and posteriorly the internal jugular vein. The lesion was well defined, inhomogenous, with a central hypodense area, appearance suggesting a hypovascular tumor. Also, the patient underwent a pre-operative selective angiography of the carotid arteries, which showed the anterior displacement of the internal carotid, and no direct major vessels to the tumoral mass.

The tumor was excised *in toto* through a transcervical approach, with cross-section of the posterior belly of the digastric and stylo-hyoid muscles, and dissected from the carotid artery and internal jugular vein using blunt dissection (Figure 1).

No important blood vessels for the tumor were observed during surgery. After excision, the tumor was sectioned and its interior was observed macroscopically. The examination showed an 8×6 cm, solid ovoid mass tumor, well encapsulated with a yellow-reddish appearance. The inside of the tumor was observed and it had a yellow, fatty consistency (Figure 2). The tumor was well circumscribed, encapsulated and the cut surface had a soft tan, "fish-flesh" homogenous appearance, without signs of hemorrhage or necrosis.

The specimen was largely sampled, immediately immersed in 10% buffered formalin and then routinely processed and then were paraffin embedded and sectioned in 3 μm slices. The slides were stained with Hematoxylin–Eosin (HE). An immunohistochemical indirect three-stage method was also performed using peroxidase and as substrate 3,3'-diaminobenzidine hydrochloride (DAB) (brown). We used antibodies from LabVision: S100, vimentin, GFAP, CD99, CD117, CD34, α-SMA, AE1/AE3 and Ki67 with external negative and positive adequate controls.

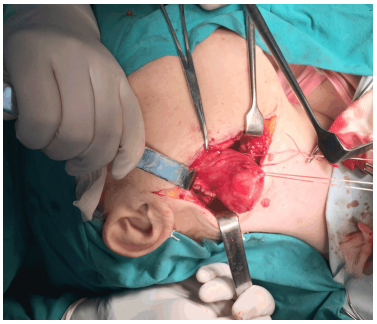

Figure 1 – ***Intraoperative aspect. Transcervical approach, revealing the tumor.***

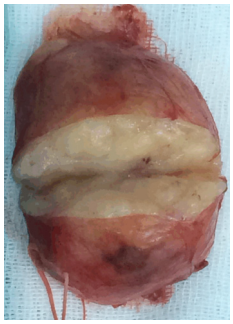

Figure 2 – ***Operative specimen. Well-encapsulated tumor, with greasy content.***

Histological assessment of surgical specimen revealed a solid tumoral proliferation, mostly hypercellular composed of fusiform cells with spindled nuclei and abundant eosinophilic cytoplasm. Focally there were identified tumor cells with significant nuclear pleomorphism, hyperchromatic, bizarre nuclei, but without significant atypia and with very scarce mitotic figures (1/50 HPF – high power field). Central, the tumor had more hypocellular, but atypical areas, with myxoid stroma hyalinized small-size vessels. In tumor periphery, some areas with palisading nuclei around fibrillary processes (Verocay bodies) were identified. A diagnosis of schwannoma was formulated and immunohistochemical tests were used for confirmation (Figures 3 and 4). They revealed that the tumor cells were diffusely positive for S100 protein, vimentin and glial fibrillary acid protein (GFAP) and negative for cytokeratins, CD99, CD117, CD34 and alpha-smooth muscle actin (α-SMA). Ki67 index was <1% (Figures 5 and 6).

Final diagnosis was schwannoma with areas of ancient schwannoma.

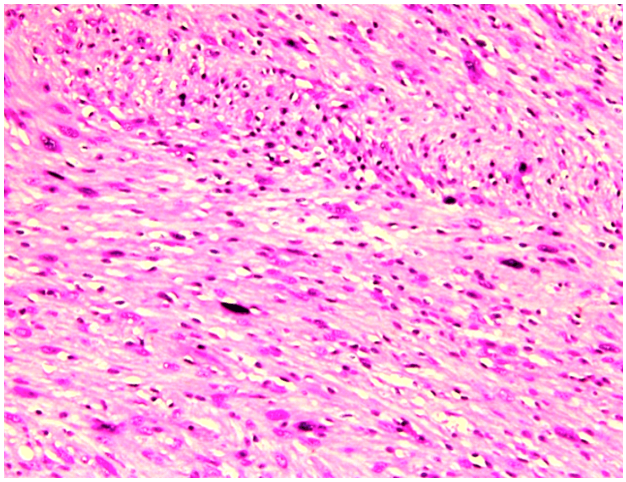

Figure 3 – ***Ancient schwannoma aspect with large, hyperchromic nuclei. Hematoxylin–Eosin (HE) staining, ×200.***

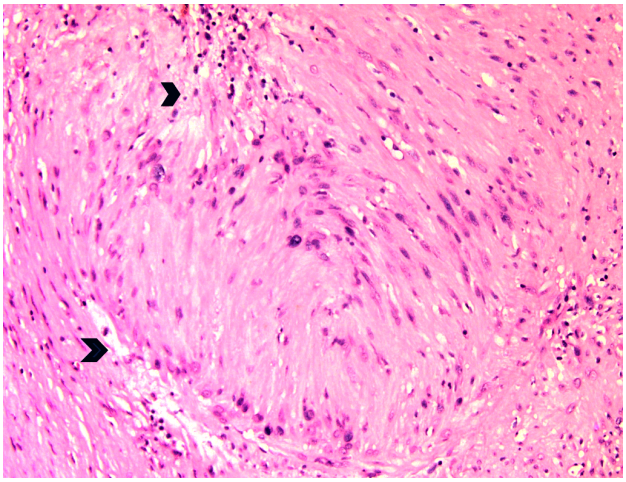

Figure 4 – ***Higher magnification view of a very characteristic Verocay body. Palisading typical, elongated nuclei disposed in concentric rows around eosinophilic material. Note also some basophilic, myxoid material in stromal compartment (arrowheads). HE staining, ×400.***

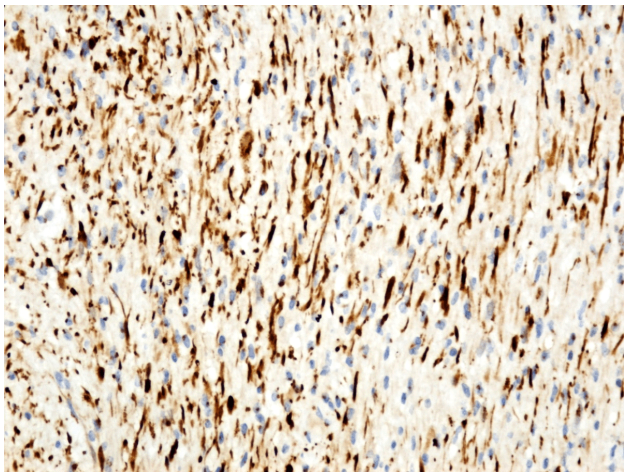

Figure 5 – ***Diffuse positive staining for S100 indicating neural origin of the tumor. S100 immunostaining, ×200.***

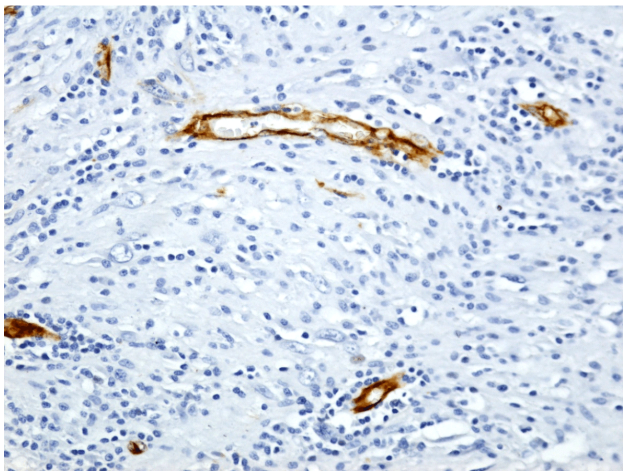

Figure 6 – ***CD34 negative in tumor cells, positive in endothelial cells (highlights some small vessels, some of them with hyalinized walls – arrowhead). It excludes a vascular tumor and also a GIST. CD34 immunostaining, ×200.***

Discussion

Due to the deep position of PPS, its anatomical relations, and vital vascular and nervous structures it contains, tumors appearing in this space are very difficult to diagnose and treat. Tumors arising in the PPS are rare, most of them presenting with few symptoms like dysphagia, dyspnea, cranial nerve deficits, pain, trismus [12]. Clinical examination is difficult; therefore, imaging studies are crucial in diagnosis of PPS masses. Imaging studies have been important in pre-operative management of the case presented in this paper, when we used both contrast-enhanced CT and angiography, in order to discover more information about the mass in PPS. Relations to the internal carotid artery and internal jugular vein offer important information about the origin of the tumor. Salivary gland tumors are always found anterior to the internal carotid artery and when they grow large enough they displace the artery posteriorly [1, 13]. Also, in the case of neurogenic tumors, the nature of displacement of the internal carotid and internal jugular can help determine the nerve of origin for the tumor, as well as differentiating it from other types of tumors [13, 14]. Due to the anatomical position of the vagus nerve, a schwannoma arising from it would normally displace the internal carotid artery anteriorly and medially and the internal jugular vein towards posteriorly and laterally, while a schwannoma of the cervical sympathetic chain displaces anteriorly both the internal carotid artery and internal jugular vein. In the case presented by us, contrast-enhanced CT and angiography both showed anterior displacement of the internal carotid and posterior displacement of the internal jugular vein. This arrangement suggested a vagus nerve tumor.

Surgical management of PPS tumors is considered the best treatment, and several surgical resection techniques are described in literature [12, 15–18]. They are classified as transoral, transcervical, transparotid-transcervical, transcervical-transmandibular or infratemporal. We used a transcervical approach that provided good access and also minimal damage to other structures.

Neurogenic tumors of the parapharyngeal space arise from neural crest cells that differentiate into nerve sheath cells and sympathoblast [6]. The main types of neurogenic tumors are schwannomas and neurofibromas. They both have the Schwann cell as their parent cell, but neurofibromas also originate from the perineurium, being linked to the nerve of origin [6, 19]. Therefore, differential diagnosis between the two can be challenging. Schwannomas usually grow longitudinally and extend along the length of the nerve; they can be separated surgically from their nerve of origin. Microscopy can usually distinguish between schwannomas and neurofibromas [20].

Histological aspect of schwannomas is that of an encapsulated neoplasm with two components known as Antoni A and B areas. Antoni A are cellular zones, consisting of monomorphic spindle-shaped Schwann cells, with poorly defined eosinophilic cytoplasm and pointed basophilic nuclei. Verocay bodies are cellular palisading around fibrillar, eosinophilic material and they were identified only in the periphery of this tumor, in dense cellular, non-atypical areas [21]. Usually, Antoni A areas predominate, as in our case, in which it was identified only a central Antoni B area (loose, myxoid, hypocellular with large, stellate atypical cells).

Histological problem of this case was the significant cellular atypia identified not only in Antoni B areas, but also in more cellular parts of the tumor. These findings require a thorough differential diagnosis with more aggressive tumors, as fibrosarcoma, malignant peripheral nerve sheet tumor, extra-digestive gastrointestinal tumor or low-grade leiomyosarcoma.

Immunohistochemical stains were performed and their results were sustaining the initial schwannoma diagnosis. S100 protein and GFAP were positive indicating a neural tumor, while smooth muscle actin was negative excluding therefore a muscular tumor. Also were negative: AE1/AE3 were (excluding a carcinoma), CD117 (excluding a GIST) and CD34 (excluding a vascular tumor and a solitary fibrous tumor). S100 demonstrates neuroectodermal origin of tumors and is considered an exclusion immunohistochemical marker. Usually, schwannomas show diffuse, intense and homogenous nuclear and cyto-

plasmic S100 immunostaining, as opposed to neurofibromas that show focal and variable immunostaining patterns, consisting of various cell populations [22]. In our case, diffuse positivity for S100 excluded a fibrosarcoma or a non-neural tumor.

Low Ki67 index was also an important feature, apparently opposing the presence of atypia. Although not surprisingly (we already identified a very low mitotic rate on routine staining), Ki67 confirmed the fact we are facing a benign tumor despite its polymorphous and atypical appearance.

Conclusions

In this case, symptoms appeared approximately two years before presentation. Preoperative cross-sectional contrast-enhanced computed-tomography was very important in the case management, showing the anatomical relations and suggesting its origin and structure thus allowing a surgical excision through a transcervical approach. Histological differential diagnosis included a malignant soft tissue tumor (fibrosarcoma or leiomyosarcoma), an extradigestive gastrointestinal stromal tumor and a fibrous histiocytoma. Difficulty of this case was represented by the presence of extensive hypercellularity with large, hyperchromatic nuclei and small, peripheral areas with specific aspect (palisading and Verocay bodies). Histological examination and immunostaining were crucial in establishing the diagnosis.

Conflict of interests

The authors declare that they have no conflict of interests.

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Corresponding author

Ioan Alexandru Bulescu, MD, PhD candidate, Department of Anatomy, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, 8 Eroilor Sanitari Avenue, Sector 5, 050474 Bucharest, Romania; Phone +40722–763 807, e-mail: ibulescu@gmail.com

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