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Case Report

Nasopharyngeal Angiofibroma in 48-Year-Old Female. Case report with Uncommon Presentation and Brief Review of the Literature

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Abstract

Nasopharyngeal angiofibroma is a benign yet locally aggressive tumor. It most commonly occurs in males before the age of 20 years old. It is uniquely comprised of fibrous stroma and a mixture of blood vessels with abundant endothelial and fibroblast cells making it very intricate and delicate. This tumor usually arises in the nasopharynx region near the choanae. Being a space-occupying lesion, it can locally compress nearby structures leading to various clinical presentations such as difficulty in nasal breathing, recurrent severe epistaxis, and unilateral facial swelling. The pathogenesis is unclear, but it may be associated with puberty and circulating hormones. Diagnosis of this tumor is made with complete patient history, physical examination, radiography, nasal endoscopy along with using specialized imaging like arteriography, computer tomography and MRI. Here we present a case of nasopharyngeal angiofibroma in a 48-year-old woman, and we review the literature.

KEYWORDS: Nasopharyngeal; Angiofibroma; Benign; Vascular

ABBREVIATION

NA: Nasopharyngeal angiofibroma, **JNA**: nasopharyngeal angiofibroma, **IHC**: Immunohistochemistry.

INTRODUCTION

Nasopharyngeal angiofibroma (NA), also known as juvenile nasopharyngeal angiofibroma (JNA), or fibromatous or angiofibromatous hamartoma of the nasal cavity is a benign tumor of the nasopharynx [1]. It is a rare (<1% of head and neck tumors) benign mesenchymal neoplasm composed of a vascular proliferation within a cellular, densely collagenized stroma, typically originating in the nasopharynx, most commonly affecting adolescent males [2]. The most common site of initiation is posterolateral wall of the nasopharynx, precisely at the trifurcation of the sphenoidal process of the palatine bone, the roof of the pterygoid process and the horizontal process of the vomer [3]. Patients usually present at late stage of the disease with typical complaints of nasal obstruction. Extensive local growth of tumor may cause facial swelling, proptosis, diplopia with disturbance in speech and conductive hearing loss [4]. The severity of the clinical features depends on the extent of the tumor. Progressive unilateral nasal obstruction with septum deviation to the contralateral side in 80-90% of cases and recurrent epistaxis, often torrential in 45-60% of the cases. Rhinorrhea can also present with nasal intonation of the voice. In very large tumors anosmia may be present.

On examination it most commonly appears lobular and has rubbery texture with red-pink color to it. (5). Nasopharyngeal angiofibroma characteristically demonstrates angiogenesis and vascular proliferation situated within the posterior nasal cavity, sphenopalatine foramen, and nasopharynx. There are suggestions that hormonal influences, chromosomal abnormalities, and overexpression of vascular growth factor receptors play a role, but much of this is still open to debate, and the exact mechanism remains unknown. Given the extensive vascularity of this tumor, recruitment of adjacent arterial supply and aggressive growth can cause osseous erosion and extension into the orbits, skull base, frontal and middle cranial fossae, and other high-value territories that can make treatment difficult [6]. The current standard treatment of choice and standard of care is surgical resection of the tumor. [7]. NA is known to recur after surgery. Most recurrences occur within four years after surgery and hence annual/bi-annual follow up is required for at least five years [8].

CASE PRESENTATION

A 48-year-old woman presented with progressive left sided nasal obstruction for 6 months. She also reported several episodes of epistaxis and rhinorrhea. No significant medical history was noted except for total hysterectomy for removal of multiple fibroids and cholecystectomy for multiple cholesterol stones. Physical examination revealed a firm and friable mass in the nasopharynx.

Diagnostic nasal endoscopy was performed, and it revealed a deviated nasal septum to the right, and a single smooth pink, tan lobulated mass in posterior part of left nasal cavity occupying the

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entire left choana. Angiography identified a highly vascularized mass with a central feeding vessel. CT studies showed a 3.5 cm homogenously enhancing lesion in the posterior part of the left nasal cavity extending into the nasopharynx with widening of left sphenopalatine foramen. Imaging studies suggested a vascular lesion and for this reason a small biopsy sampling or fine needle aspiration sampling were not recommended to avoid potential hemorrhage. The differential diagnosis included possible antrochoanal polyp, hemangioma, or an adenoid mass. Imaging studies did not exclude possible nasopharyngeal malignancies. Although nasal angiofibroma was also included in the differential, it was not high in the list due to presentation in a 48-year-woman.

The mass was surgically removed after preoperative embolization. The excised lesion was a 3.5 cm vascular rounded, circumscribed, unencapsulated mucosa covered mass with spectrum of different color ranging from pale white to a pink and wine-colored (**Figure 1A**). Microscopic examination showed benign fibrovascular lesion composed of collection of vascular spaces of various sizes, ranging from dilated branching vessel of various thickness to slit-like capillaries (**Figure 1B**). The background of the central cellular vascular areas showed a mixed fibrous edematous stroma with scattered thrombi in the dilated vessels (**Figure 1C**). No nuclear atypia or abnormal mitotic activity were noted. Immunohistochemistry (IHC) studies were utilized for definitive diagnosis and the cells were positive for vimentin, SMA, and h-caldesmon in the smooth muscle wall of the large vessels and CD31 and CD34 highlighted the endothelial cells lining of the vessels. The stroma was strongly positive for estrogen. The cells were negative for cytokeratin AE1/AE3 and CD117. The histomorphology and the IHC profile were diagnostic of nasopharyngeal angiofibroma.

Patient was followed up for three years with no evidence of recurrence then was lost to follow up. During the time of follow up, all symptoms disappeared.

DISCUSSION

Juvenile nasopharyngeal angiofibroma (JNA) is a relatively uncommon, benign neoplasm of the nasopharynx, with an incidence of 1 case per 150,000 individuals. Although it can occur at any age, young adults, and adolescents between the ages of 14 and 25 are primarily affected, and there is a significantly distinct male predominance [9]. There are also reports that individuals from India and the Middle East appear to have an increased incidence when compared to those of European descent [17]. It was first described by Hippocrates in 5th century AD, and he called it as 'hard polyp'. It affects almost exclusively male adolescents with median age of 15 years; raising suspicion about the role of sex hormones in its pathogenesis [10]. JNA classically presents as a painless, progressive unilateral nasal obstruction. Epistaxis, rhinorrhea, and pain may also be seen. Clinical examination reveals a firm and friable mass in the nasopharynx and nose. As this tumor is aggressive and expansile, it invades adjacent structures causing further symptoms. Impaired Eustachian tube function, facial deformity, proptosis, and changes in visual acuity may be seen. Invasion of the intracranial region may lead to cranial nerve palsy. Angiofibromas originating outside the nasopharynx may appear as an intraoral mass in the retromolar or buccal space area [11].

Based on the clinical and radiological features, JNA is classified into three types. Type I includes lesions fundamentally localized to the nasal cavity, paranasal sinus, nasopharynx, or pterygopalatine fossa. Type II is a JNA extending into the infratemporal fossa, buccal region, or orbital cavity with anterior and/or minimal middle cranial fossa extension but intact dura mater. Type III is a calabash-like massive tumor lobe in the middle cranial fossa [16]. The etiology of JNA itself remain elusive. Because of the tumor's vascularity, early studies of JNA hypothesized a vascular etiology due to incomplete regression of the first branchial artery which remnants at the superior margin of the sphenopalatine foramen [12]. Significantly higher immune staining with CD34, vascular endothelial growth factor, flt-1 and flk-1 in JNA, when compared to orbital cavernous hemangiomas, indicates its vaso-proliferative nature. This supports the hypothesis that the vascular endothelial cells may become postembryonic undifferentiated mesenchymal cells and

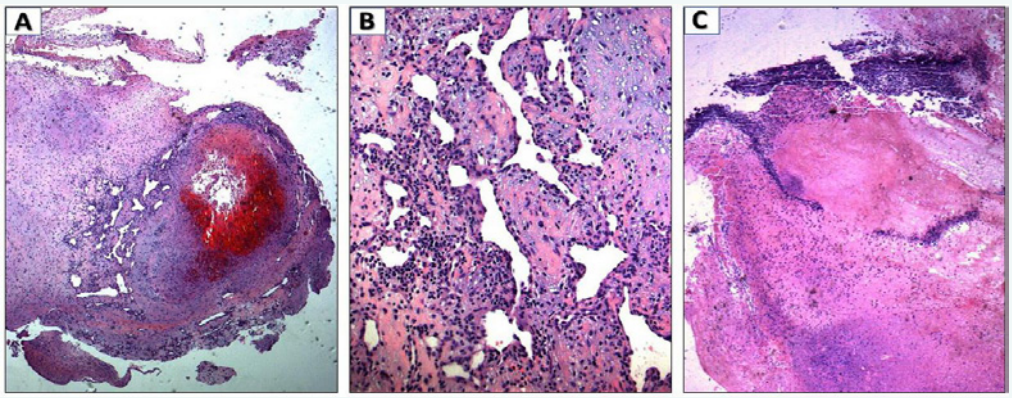

Figure 1 Pathological examination of the nasopharyngeal angiofibroma. 1A: Vascular rounded, circumscribed, unencapsulated mucosa covered mass, showing central vascular component with feeding artery and surrounding stromal fibrous components. Low power view (H&E stain x20). **1B:** Vascular component showing irregularly anastomosing vascular channels lined up by bland benign endothelial cells (H&E stain x40) **1C:** Stromal part of the mass showing fibro-collagenous tissue and large vessels filled with fibrin (H&E stain x40).

can be induced into other mesenchymal nonhemopoietic cell phenotypes [13].

Occurring predominantly in adolescent males, several investigations have been conducted to determine the relationship between JNA and sex chromosomes. Chromosomal studies of JNA using the comparative genomic hybridization showed a number of chromosomal abnormalities in the JNA. DNA gains are more common than DNA losses with the exception of the frequent loss of chromosome Y. Vascular endothelial growth factor (VEGF) as well as vascular endothelial growth factor receptor-2 (VEGFR-2) and platelet-derived growth factor (PDGF) have also been described and associated with vessel density in JNA [14]. Previous studies have reported the presence of androgen, estrogen, and progesterone receptors. Some hypothesize this is the reason for the predominant adolescent male incidence, as the increase in androgen production in puberty stimulates the growth and vascular expansion of the tumor. Others have shown that tumor growth can occur at any time, even after treatment, from testosterone administration. This concept has support from case reports of nasopharyngeal angiofibroma in older women that have since downregulated their estrogen and progesterone production, suggesting that estrogen has a protective effect but further confounded by case reports of nasopharyngeal angiofibroma being discovered in pregnant females, suggesting that androgen influence is not important. Thus, the importance of hormonal influence remains unclear [18]. The most significant interest in these deletions is their association with the TP53 suppressor gene, as well as the human epidermal growth factor receptor 2 (HER2), involving the HER2/NEU oncogene, both well known in the realm of tumor growth and malignancy.

Other nasopharyngeal angiofibroma associations reported include familial adenomatous polyposis (FAP) and Gardner syndrome, with an altered APC gene expression in this subset of nasopharyngeal angiofibroma [19]. Histopathologically angiofibroma is composed of fibrocollagenous stromal proliferation with an admixture of variably vascular space. Vascular component is comprised of thin-walled, small to large vessels varying on appearance from stellate to staghorn to barely conspicuous, owing to mark compression by stromal fibrous tissue. Stroma is composed of fibrous tissue with fine or coarse collagen fibers whereas its cells are spindle shaped and stellate with plump nuclei and tend to radiate around vessels [15]. Macroscopically this tumor appears as a rounded, circumscribed, unencapsulated mucosa-covered mass. The color depends on the vascular component and may vary from pale white in less vascular lesions to a pink and wine-colored mass in highly vascularized ones [13].

Differential diagnosis includes antrochonal polyp, rhinosporidiosis, Sino-nasal malignancy chordoma, nasopharyngeal cyst and pyogenic granuloma. In recent studies the most common is the antrochoanal polyp, originating from the maxillary sinus and extending through the maxillary ostium into the nasal cavity. Sino-nasal polyps can also originate from or extend into the nasopharynx. However, they will typically not extend into the sphenopalatine foramen or pterygopalatine fossa. Osseous remodeling is smooth, not destructive. Polyps will demonstrate peripheral enhancement without central enhancement, unlike nasopharyngeal angiofibroma. Also seen in teens/young adults with nasal obstruction, but rarely results in epistaxis [6].

Early diagnosis and treatment are required for a good prognosis in JNA. Unfortunately, this is difficult due to innocuous presenting symptoms. Advanced lesions with orbital and intracranial extension are difficult to treat and may recur often. When diagnosed early the patients are treated with a combination of preoperative embolization and surgical resection providing a good prognosis.

Angiofibroma can be diagnosed using CT, MRI, and magnetic resonance angiography. CT is the most important preoperative test because it is useful in showing the destruction of bony structures and widening of foramen and fissures at the skull base [3,16]. Trans-nasal Endoscopic nasal surgical excision of the mass is preferred for small tumors. Other surgical approaches are, Trans-palatal approach, lateral rhinotomy, midfacial degloving may be considered along with preoperative embolization, arterial ligation, or use of sclerosing agents in large tumors. Incomplete excision of the mass leads to residual mass and recurrence. Other methods of treatment that have been employed are irradiation, and cryotherapy [20,21].

Preoperative embolization, considered as standard treatment nowadays, has shown to minimize the blood loss. Retrospective study conducted by Pei et al [23]. Hormonal therapy in the way of androgen receptor blockers such as flutamide is an additional possible adjuvant therapy. These have been shown to help reduce tumor size prior to surgical resection or in the setting of recurrence, but do not have curative results on their own [22]. Surgical complications can include much of the same, with the addition of scarring and facial deformity. Hormonal therapy, if employed, can lead to feminization as a complication or at least undesirable side effect in adolescent boys.

The most significant complication of JNA is blood loss, primarily in the operative/procedural setting, and can be fatal in the absence of proper precautions. Exophthalmos, facial/orbital deformity, vision loss, and loss of extraocular movements can occur from orbital invasion by the tumor. Vision loss can also be a potential complication of nontarget embolization if there is internal carotid artery branch involvement. Other severe complications of preoperative embolization include arterial vasospasm, facial palsy, infarction, or cranial nerve injury. More self-limiting, less severe complications include facial swelling, pain or abnormal sensation, headache, or nausea/vomiting [6]. NA is known to recur after surgery. Most recurrences occur within four years after surgery and hence annual/bi-annual follow-up is required for at least five years [8]. Recurrent tumors must be managed individually, taking into account location, age, complications and the possibility of spontaneous resolution. This would better define the treatment strategy [23]. it is also known as juvenile angiofibroma (JAF), or fibromatous or angiofibromatous hamartoma of the nasal cavity.

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