

Nasopharyngeal angiofibroma in an elderly female patient: A rare case report

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Abstract. ‘Juvenile’ nasopharyngeal angiofibroma, which accounts for <1% of all head and neck neoplasms, occurs predominantly in males between 10 and 18 years of age. The small number of patients older than 30 years confirms that presentation after this age is exceptional. Only rare cases of nasopharyngeal angiofibroma in female patients have been documented to date, and some authors believe that sex chromosome studies are indicated in such cases. The pathogenesis of nasopharyngeal angiofibroma remains unknown, but it has been hypothesized that it is a testosterone-dependent tumor. We herein report a particularly rare case of a 68-year-old woman diagnosed with nasopharyngeal angiofibroma and describe the diagnostic and therapeutic workup. This case describes, to the best of our knowledge, the oldest patient reported in the literature.

Introduction

‘Juvenile’ nasopharyngeal angiofibroma (NA) occurs almost exclusively in males, but has also been documented in females, albeit infrequently (1-5). When a diagnosis of NA is made in a female patient, caution is necessary to exclude the possibility of a conventional nasal or antrochoanal polyp with fibrosis. The presentation age ranges from 10 to 25 years (2), whereas a few cases of NA patients aged >30 years have been reported in the literature (6).

NA is a vascular tumor that accounts for <1% of all head and neck neoplasms, with a higher reported incidence in India (2,7); it originates from the sphenopalatine foramen and involves both the pterygopalatine fossa and the posterior nasal cavity (8,9). Despite being histologically benign, NA is locally invasive and is associated with a high rate of persistence

and recurrence mainly due to incomplete resection during surgery (10).

The aim of the present study was to report a particularly rare case of a 68-year-old female patient who was diagnosed with NA and describe the diagnostic and therapeutic workup.

Case report

A 68-year-old woman was admitted to the ENT Clinic of Sapienza University Hospital (Rome, Italy) in May 2015 with an 18-month history of nasal obstruction, episodes of left-sided hearing loss, discharge of mucus in the nasopharynx, occasional headaches and snoring. The patient was otherwise healthy, with no reported comorbidities. She had gone into menopause 11 years earlier and, up to that point, she had had regular menstrual cycles and two pregnancies.

The patient underwent endoscopic examination of the upper airways that revealed a whitish, non-ulcerated, non-bleeding large mass in the posterior nasal cavity extending to the nasopharynx. Endoscopy was followed by magnetic resonance imaging (MRI) examination of the head and neck with gadolinium contrast, which confirmed the presence of a polypoid lesion sized 3.2x2.6 cm in the posterior nasal cavity, without invasion of the roof or posterior wall of the nasopharynx. There were no enlarged lymph nodes in the upper part of the neck (Fig. 1).

The patient underwent functional transnasal endoscopic removal of the mass under general anesthesia; consistent bleeding occurred during surgery. The mass was entirely removed and was found to be of firm, elastic consistency. The specimen was sent for histological examination; hematoxylin and eosin staining demonstrated that the mass was composed of proliferating blood vessels of variable shape and size, intermixed with a connective tissue stroma. The wall of the vessels was formed only by endothelial cells (CD34⁺). The connective tissue was fibrocellular, with an irregular pattern and plump fibroblasts (Fig. 2). Immunohistochemical analysis was performed with actin staining for smooth muscle; the perimeter of the mass appeared as a thin rim of smooth muscle cells topped by endothelium (vimentin⁺ and CD68⁺). Ki-67 immunostaining demonstrated only a few positive cells, confirming low cell proliferation rate and excluding the possibility of a conventional nasal or antrochoanal polyp with fibrosis (11).

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The postoperative course was uneventful, and no disease recurrence was observed during the last follow-up visit in March 2018, nearly 3 years after surgery.

Discussion

NA is a rare benign tumor affecting almost exclusively adolescents and young adults who have been symptomatic for 15 to 24 months prior to seeking medical treatment (2,11-13). Only a few studies have reported NA in women (3-5). Neel *et al* (10) and Conley *et al* (14) in two case series including 150 and 38 cases, respectively, reported no female patients. In a systematic review of the literature, Gruber *et al* (15) found only 28 female cases.

NAs are mainly diagnosed in patients aged between 14 and 25 years, with a mean age of 15 years (2,16,17). The small number of patients aged >30 years confirms that a presentation after this age is quite rare (6,18,19). Isolated cases of angiofibroma arising outside the nasopharynx have been reported, most commonly in the maxillary (32%) and ethmoid (10%) sinuses (20). These tumors are clinically distinct from NA, they develop at a slightly older age and occur more commonly in women. Based on these facts, the case of a 68-year-old woman with NA is considered as particularly rare due to both the sex and the age of patient; to the authors' best knowledge, this is the oldest patient with NA reported in the literature.

The etiology of NA is debated; it has been hypothesized that NA i) arises from the periosteum (21), ii) is a distinct type of hemangioma (22), iii) is a connective tissue response of the nasopharyngeal periosteum to an ectopic nidus of vascular tissue, possibly of the inferior turbinate type (23), and iv) is a specific type of fibromatosis (24).

The occurrence of NA in women has been seldom reported; to explain the male predominance in NA it has been hypothesized that NA may be a testosterone-dependent tumor that arises from a fibrovascular nidus in the nasopharynx that lies dormant until the onset of puberty (25). At this time, coincident with the increase in testosterone levels, the tumor grows and becomes symptomatic. Estrogens, acting in an antagonistic manner, inhibit the release of trophic hormones from the pituitary gland, causing a decline in testosterone production and, therefore, a decrease in the size of the tumor (26). The hormonal theory suggests that high estrogen levels act protectively in women; Johns *et al* observed a reduction of the mass with estrogenic therapy in 6 patients (27), while Johnsen *et al* reported that testosterone therapy was associated with tumor enlargement (28).

In the present case, the occurrence of NA after menopause may also support the idea of this hormonal impact. It may be hypothesized that the patient's NA had undergone natural regression during the years of increased estrogen production and then started proliferating after menopause due to the decreased hormonal levels. The fact that the patient had regular menstrual cycles suggests the absence of abnormal variations in her hormonal levels throughout her fertile life. The high levels of estrogen and progesterone during her two pregnancies may have also delayed the appearance of the tumor. However, the case of NA in a pregnant woman reported by Péloquin *et al* in 1997 favors the likelihood of other congenital or inflammatory factors contributing to the pathogenesis of NA (29).

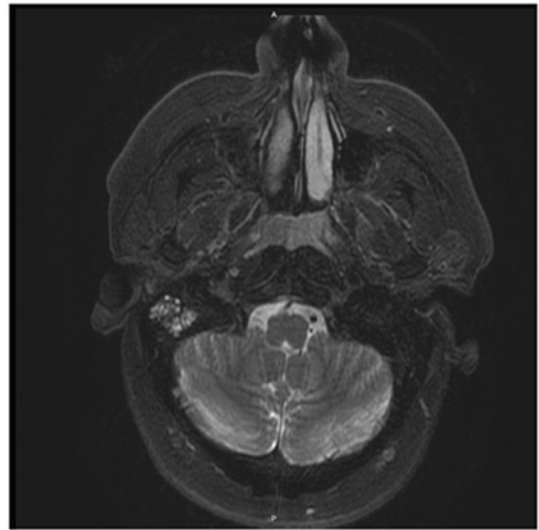


Figure 1. Magnetic resonance imaging (MRI) of the head with gadolinium contrast revealed a polypoid lesion sized 3.2x2.6 cm in the posterior nasal cavity extending to the nasopharynx, without invasion of the roof or the posterior wall of the nasopharynx.

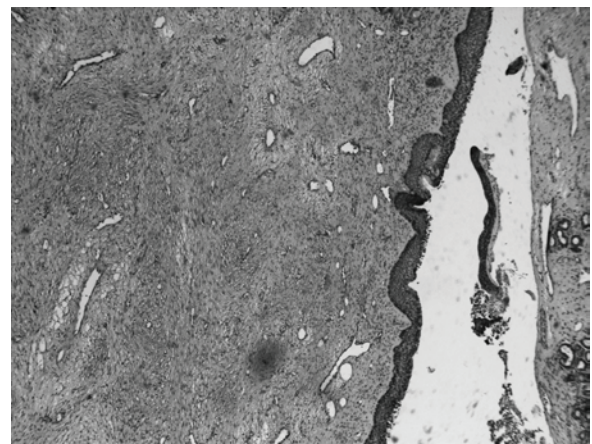


Figure 2. Histological examination of the specimen (hematoxylin and eosin staining at x100 magnification) revealed that the mass was composed of proliferation of blood vessels of variable shape and size intermixed with a connective tissue stroma. The wall of the vessels was formed only by endothelial cells (CD34⁺). The connective tissue was fibrocellular, with an irregular pattern and plump fibroblasts.

The preoperative diagnosis of NA is mainly based on a careful history and nasal endoscopic examination and is supplemented by imaging using computed tomography or MRI scans; however, final diagnosis must be based on histological and immunohistochemical examination. Biopsies to establish histological diagnosis are contraindicated due to the risk of substantial bleeding; however, with the advancements in angiography, diagnosis and embolization of the tumor-feeding vessels may be performed at the same time. In older patients, the tumor becomes fibrotic and bleeding is usually not a major concern although consistent bleeding may occur during surgery, as in the present case.

The surgical approach to NA resection depends on the stage of the tumor based on the Fisch classification (30).

In conclusion, NA is a rare, vascular, benign tumor that typically affects adolescent boys. The etiopathogenesis

remains unknown; the most important theories are genetic and hormonal, although the latter may not apply to all cases, since NA has been reported in a pregnant woman. In the present case, the sex and age of the patient are particularly rare for this condition and warrant suspicion of NA in any patient presenting with a nasopharyngeal mass and recommendation of an angiographic examination to prevent dangerous intra- and postoperative bleeding.

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Ethics approval and consent to participate

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Patient consent for publication

The patient provided written informed consent for the publication of any associated data and accompanying images.

Authors' contributions

MR and MF wrote the paper, IV and SM provided clinical assistance and contributed to paper writing, MV and AG performed the surgery and provided critical review of the paper. All the authors have read and approved the final version of this manuscript.

Competing interests

The authors declare that they have no competing interests to disclose.

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