A Comprehensive Approach to Juvenile Angiofibroma: Diagnosis, Staging, and Surgical Management

Shrestha BL, Shrestha P

Department of ENT-HNS,

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences,

Dhulikhel, Kavre, Nepal.

Corresponding Author

Bikash Lal Shrestha

Department of ENT-HNS,

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences,

Dhulikhel, Kavre, Nepal.

E-mail: bikashotology267602@gmail.com

Citation

Shrestha BL, Shrestha P. A Comprehensive Approach to Juvenile Angiofibroma: Diagnosis, Staging, and Surgical Management.*Kathmandu Univ Med J*. 2024;87(3):340-5.

ABSTRACT

Juvenile angiofibroma of nasopharynx is a benign but locally aggressive tumor predominantly affecting adolescent males, characterized by hypervascular growth in the nasopharynx. Early diagnosis and appropriate management are crucial to prevent complications. Symptoms typically include nasal obstruction, epistaxis, and hearing loss. Imaging techniques, such as contrast-enhanced CT and MRI, play a pivotal role in assessing tumor size, vascularity, and involvement of surrounding structures. Angiography, followed by embolization, is commonly used to reduce intraoperative bleeding risk. The treatment of choice is surgical resection, which can be performed via an endonasal, transpalatal, or combined approach, depending on tumor extent. In cases of inoperable tumors or recurrence, radiation therapy may be considered. Although nasopharyngeal juvenile angiofibroma has a favorable prognosis when treated early, close monitoring for recurrence is necessary, as it can reappear even years after surgery. Multidisciplinary management involving otolaryngologists, radiologists, and oncologists is essential for optimal outcomes.

KEY WORDS

Diagnosis, Embolization, Juvenile angiofibroma, Nasopharynx, Surgery

INTRODUCTION

The earliest known mention of juvenile nasopharyngeal angiofibroma (JNA) dates back to the fifth century B.C. in Hippocrates time who was the first to document the condition. This benign but highly vascular tumor is also referred to as juvenile angiofibroma (JAF), or fibromatous and angiofibromatous hamartoma of the nasal cavity.[1,2]

There is some debate regarding its exact origin, with some studies suggesting it arises from the sphenopalatine foramen and the posterior nasal cavity, while others propose a more nasopharyngeal or choanal origin. Regardless of the origin, JNA accounts for a small fraction (0.05-0.5%) of all head and neck tumors. Although histologically benign, it exhibits aggressive behavior, often invading the nasal concha, septum, and pterygoid bone. Larger tumors can extend into the nasal cavity, nasopharynx, pterygopalatine fossa, and even the different sinuses. In severe cases, it can involve the orbit and intracranial regions, with involvement seen in 10-37% of cases.[3-7]

JNA is highly vascular, with the internal maxillary artery, a branch of the external carotid artery, being the primary source of blood. Larger tumors may have multiple arterial supplies, including contributions from the ascending pharyngeal artery, middle meningeal artery, accessory meningeal artery, and facial artery. In certain cases as per different researches, branches of the internal carotid artery, particularly the vidian and ophthalmic arteries, may also be involved.[8,9]

A recent systematic analysis of 828 cases found supply with internal carotid artery in 35.6% cases and bilateral supply in 30.8% cases.[10]

Etiology

The exact cause of juvenile nasopharyngeal angiofibroma (JNA) remains unclear, and there are several theories currently being debated. One common hypothesis suggests that the tumor may arise from a vascular malformation, such as an arteriovenous malformation (AVM), or potentially from remnants of the first branchial arch. These remnants could explain why JNA typically forms near the sphenopalatine foramen, as incomplete regression of

the arch during development might leave behind these structures. Additionally, the expression of certain receptors that promote vascular growth, particularly vascular endothelial growth factor (VEGF), fibroblast growth factor receptor (FGFR), expression of laminin alpha (considered to be a marker for early angiogenesis) may help explain the tumor's highly vascular nature.[5,11,12]

Another theory links JNA to hormonal influences, particularly during puberty, when increased androgen production might stimulate the growth and expansion of vascular tissue in the tumor. Studies have found androgen, estrogen, and progesterone receptors on JNA cells, which could explain why the condition mainly affects adolescent males. Some researchers suggest that the growth of the tumor could even be triggered by testosterone therapy. However, this hypothesis is complicated by cases of JNA in older women or pregnant individuals, where hormonal changes don't seem to follow the same pattern, making the role of hormones in JNA growth still uncertain.[13]

There are also genetic factors that may play a role in the development of JNA. For example, deletions on chromosome 17 have been linked to the tumor, particularly involving genes like TP53, a well-known tumor suppressor gene, and HER2, which is associated with other cancers. Additionally, genetic conditions such as familial adenomatous polyposis (FAP) and Gardner syndrome, which involve mutations in the APC gene, have been reported in people with JNA.[14,15]

Recently, there has been growing interest in the potential connection between JNA and human papillomavirus (HPV). HPV has a well-established role in tumor formation, similar to the Epstein-Barr virus, raising the possibility that it could also contribute to the development of JNA.[16]

Epidemiology

Juvenile nasopharyngeal angiofibroma (JNA) is a rare tumor that primarily affects adolescent males, making up about 0.05% to 0.5% of all head and neck tumors. Studies suggest a higher prevalence in populations from India and the Middle East compared to those of European descent.[2] Its reported incidence varies, ranging from 1 in 150,000 to 1 in 1.5 million individuals.[3-5] In rare cases, females may also develop JNA, and in these instances, further investigation through immunohistochemical and genetic testing is recommended to identify underlying genetic factors such as mosaicism.[13,17]

Pathophysiology

Nasopharyngeal angiofibroma is characterized by significant vascular growth and angiogenesis, particularly within the posterior nasal cavity, sphenopalatine foramen, and nasopharynx. Although several potential contributing factors have been suggested, including hormonal influences, chromosomal abnormalities, and the overexpression of vascular growth factor receptors, the precise cause remains uncertain. Due to the tumor's extensive vascular network, it can draw blood supply from surrounding arteries, promoting rapid growth. This aggressive nature can lead to bone erosion and cause the tumor to invade the orbits, skull base, and both the frontal and middle cranial fossae, presenting significant challenges for treatment.[3,5,9]

Histopathology

Juvenile nasopharyngeal angiofibroma (JNA) is characterized by a combination of fibrous tissue and vascular proliferation. Histologically, JNA is made up of an abundant network of thin-walled blood vessels, which are often dilated and irregular in shape. The vessels are usually a mix of capillaries, venules, and occasionally arterioles. These vascular components are surrounded by a collagenous stroma populated by fibroblasts, smooth muscle cells, and occasionally lymphocytes. The fibrous areas contribute to the tumor's dense appearance, while the vascular regions give it its highly vascular nature.[2,4]

The tumor exhibits two key histopathological features: the vascular pattern, where blood vessels are prominent, and the fibrous pattern, which consists of collagenous tissue with scattered fibroblasts. In some cases, epithelial remnants may be seen, but these are generally inconspicuous. Smooth muscle actin (SMA) and CD34 are commonly used in immunohistochemical staining to highlight the vascular elements and endothelial cells within the tumor, respectively.[18,19]

Despite its benign nature, JNA can show aggressive features due to its rapid growth and local invasion. Mitotic activity is typically low or absent, indicating that the tumor remains benign despite its destructive behavior. Histologically, it is considered non-malignant, and the lack of atypia in the tumor cells is a characteristic feature.

The endothelial lining of the vascular channels is typically a single layer and expresses various vascular markers, including CD34, CD31, von Willebrand factor, and endoglin. Notably, the presence of endoglin has been associated with both the vascular density of the tumor and its potential for recurrence.[18,19]

Clinical Features

The clinical presentation varies depending on the size and location of the tumor but commonly includes:

Nasal Obstruction: Due to the tumor's growth within the nasopharynx, patients often experience significant nasal congestion and blockage.

Epistaxis: One of the hallmark symptoms of JNA, resulting from the tumor's vascular nature and frequent rupture of blood vessels.

Facial Swelling: In some cases, patients may present with swelling in the face, particularly around the cheek area, due to tumor extension into adjacent structures such as the maxillary sinus.

Hearing Loss: If the tumor extends into eustachian tube, it may lead to conductive hearing loss.

Headache: It is due to pressure effect on the skull base and cranial nerves.

Orbital Symptoms: In severe cases, the tumor can extend into the orbit, causing symptoms such as proptosis or diplopia.

Neurological Symptoms: Larger tumors may invade the skull base and cranial nerves, leading to neurological symptoms like visual disturbances, cranial nerve palsies, and even intracranial extension.

Investigations

A variety of diagnostic methods are used to confirm the presence of JNA and assess its extent. These include:

Endoscopy: Nasal endoscopy is often the first step in identifying the tumor. It shows smooth, hypervascularised lesion originating behind the middle turbinate, which is laterally displaced against lateral wall.

CT Scan: Computed tomography (CT) is helpful for evaluating the extent of the tumor and its involvement with adjacent bone structures (e.g., the nasal septum, maxillary sinuses, and pterygoid fossa). It is particularly effective in assessing the bony destruction caused by tumor growth. It shows the area of origin invariably located at the level of pterygopalatine fossa with erosion of the base of the medial pterygoid plate.[20]

Further evaluation with CT angiography can help determine the extent of vascularity and vascular supply for preoperative planning. Examination for unilateral enlargement of the external carotid and/or internal maxillary artery can help delineate the situs of the vascular source.[1,3]

MRI: Magnetic Resonance Imaging (MRI) is the most effective imaging modality for evaluating the soft tissue components of JNA, particularly its extent into the nasopharynx, orbits, and cranial base. It provides excellent soft tissue contrast and can help determine the tumor's relationship to critical structures, such as cranial nerves and the internal carotid artery. MR is also good for distinguishing extension into the cavernous sinus, sphenoid sinus, or perineural extension through the skull base or into the orbit. The presence on both T1 and T2 weighted sequences of several signal voids within the lesion indicating major Intralesional vessels(salt and pepper appearance) is hallmark of JNA.[21,22]

Angiography: Cerebral angiography may be performed to assess the vascularity of the tumor, identify its feeding vessels (e.g., internal maxillary artery, ascending pharyngeal artery), and guide preoperative embolization. This can help reduce intraoperative bleeding.[23]

Biopsy: Although not commonly performed due to the vascularity of the tumor, a needle biopsy may be indicated in unusual or difficult cases. However, imaging is typically sufficient for diagnosis.

Immunohistochemistry: Immunohistochemical markers, such as CD34, CD31, and von Willebrand factor, are used to confirm the vascular nature of the tumor. This is especially useful when the diagnosis is uncertain or when differentiating JNA from other types of head and neck mass.[18]

Differential diagnosis

The differential diagnosis for juvenile nasopharyngeal angiofibroma (JNA) includes several conditions with overlapping clinical features and imaging characteristics.[17]

Sinonasal polyps, often inflammatory in nature, can become hypervascular but typically have less vascularity than JNA. These polyps, such as the antrochoanal type, originate from the maxillary sinus and extend into the nasal cavity but do not invade deeper structures like the sphenopalatine fossa. They also lack central enhancement.

Rhinosporidiosis, a granulomatous disease affecting the mucous membrane of nasopharynx, the floor of the nose and inferior turbinate, may confuse with Juvenile angiofibroma.

Olfactory neuroblastoma (esthesioneuroblastoma), a tumor of the olfactory neuroepithelium, can present similarly with nasal cavity masses. These tumors often appear as dumbbell-shaped lesions on imaging, with intracranial extension centered at the cribriform plate. They may also show cystic areas, restricted diffusion, and necrosis, and are more common in females.

Rhabdomyosarcoma, a soft tissue sarcoma, can occur in the head and neck, especially in younger patients, with involvement of the nasopharynx, orbit, or paranasal sinuses. This tumor typically presents with mild to moderate enhancement and diffusion restriction, distinguishing it from JNA's more avid enhancement.

Encephaloceles are brain tissue protrusions through a skull base defect, typically anterior to JNA, and do not enhance on imaging.

Finally, nasopharyngeal carcinoma, a malignancy primarily in adults, arises in the nasopharynx and demonstrates mild enhancement and more extensive osseous destruction compared to JNA.

Staging

Various staging systems for juvenile nasopharyngeal angiofibroma (JNA) have been developed to guide surgical approaches and predict treatment outcomes. The Radkowski and Andrews-Fisch staging systems are among the most widely used, with the University of Pittsburgh Medical Center (UPMC) introducing a newer system focusing on endoscopic evaluation and vascularity.

In 2010, Snyderman et al introduced the UPMC system, a staging model that emphasizes endoscopic evaluation and residual vascularity, particularly after preoperative embolization. It stages the disease from I (localized to

the nasal and nasopharyngeal regions) to V (involving intracranial extension with residual vascular supply from the internal carotid artery). This system is especially relevant in modern surgical planning and treatment of JNA.[24]

The Andrews-Fisch system shares similarities with Radkowski's but includes an extra stage for intracranial spread. Stage I is confined to the nasal and nasopharyngeal areas, Stage II involves the pterygopalatine fossa or sinuses, and Stage IIIa is defined by orbital or infratemporal fossa extension. Stage IIIb accounts for extradural extension into the parasellar region, while Stage IV includes intradural extension, further split into subcategories based on the involvement of critical areas like the cavernous sinus or optic chiasm.[25]

The Radkowski system uses a three-tiered approach. Stage I is divided into two subcategories: Ia, where the tumor is confined to the nasal cavity and nasopharyngeal vault, and Ib, where it extends into the sinuses. Stage II involves extension into the pterygopalatine fossa, with further distinctions: IIa for minimal involvement, IIb for full fossa involvement, and IIc when the tumor reaches the infratemporal fossa. Advanced Stage III is characterized by skull base and intracranial extension. Subcategories include Stage IIIa, which involves minimal cranial fossa or pterygoid plate involvement, and Stage IIIb, where intracranial extension is present, often with cavernous sinus involvement.[26]

Another staging system has been proposed by Janakiram TM et al, mainly to show the potential of endoscopic resection in advanced stage JNA.[27]

Treatment

The primary treatment for juvenile nasopharyngeal angiofibroma (JNA) is surgical resection which dates back to Hippocrates.[28] Given the tumor's extensive vascular nature, preoperative embolization is often performed to reduce the risk of excessive bleeding during surgery. This procedure involves the use of digital subtraction angiography (DSA) to identify the arterial supply, particularly from the external and internal carotid arteries. Embolization materials include gelatin sponge, polyvinyl alcohol particles, and microcoils. In cases where precise embolization is required, microcoils are used. The decision to avoid certain arteries, particularly those close to cranial nerves, helps prevent iatrogenic nerve injury. Preoperative embolization is particularly beneficial for higher-stage tumors with more robust vascular supplies, while its utility is less pronounced in earlier-stage tumors.[29]

Not all experts agree on the routine use of preoperative embolization. In fact, the changes caused by this procedure at the tumor's periphery have been shown to increase the risk of leaving residual tissue. Another reason to avoid preoperative embolization is the easy accessibility of small juvenile angiofibromas from the maxillary artery, which can be clamped before dissecting the lesion.[30]

Historically, the lateral rhinotomy was the standard surgical approach, but today, multiple surgical options exist, and in some cases, a combination of approaches may be needed. These can include transpalatal, transfacial, transnasal, sublabial/Le Fort I, transmaxillary, and infratemporal corridors.[7] In many instances, an endoscopic approach is used, often supplemented by procedures such as an anterior maxillotomy or craniotomy when necessary.[31] During surgery, controlled hypotension is often employed under general anesthesia to reduce bleeding, and epinephrine may be used to shrink the nasal mucosa, providing a clearer view. Depending on tumor size, parts of the inferior and middle turbinates may need to be resected, and the ethmoid air cells and maxillary ostium may be opened to improve access to the tumor, particularly when the posterior wall of the maxillary sinus must be removed.

Instruments like monopolar and bipolar electrocautery help control bleeding, although they may damage surrounding tissues. Alternatives, such as ultrasonic or laser-assisted cautery, are also employed, with the latter using an Nd:YAG laser to provide more focused cautery.[28]

For larger tumors, especially when multiple feeding arteries are involved then the external carotid arteries are usually addressed first, followed by the more challenging segments supplied by the internal carotid artery or those with intracranial extension. This strategy helps minimize blood loss by segmenting the tumor's vascular territories. Depending on the tumor's extent, it may be necessary to drill or remove portions of the skull base, particularly to access arteries like the vidian or pterygoid canal. Special care is taken when there is a dural tear to avoid complications like intracranial vasospasm or meningitis.[31,32]

Although surgery is the treatment of choice, radiation therapy may be used as an adjunct for residual or recurrent tumors, particularly in advanced cases or those with intracranial extension that cannot be fully resected. The role of radiation therapy remains controversial due to concerns about long-term side effects, such as the potential development of secondary malignancies. However, studies have reported local control rates between 85-91% when radiation therapy is used as an adjuvant, with low rates of severe complications.[2] When radiation is used as the primary treatment, success rates range from 80-88%, but tumor burden often persists, and long-term radiation-related complications are a concern.[8,33] Various radiation modalities, such as stereotactic radiosurgery (gamma knife), intensity-modulated radiation therapy (IMRT), and conventional external beam radiation, all show similar success rates. Among these, IMRT may offer a better balance between disease control and minimizing long-term morbidity.[8] However, post-radiation, re-operative morbidity remains a concern, as irradiated tissue can be more friable,

complicating subsequent surgical procedures. For instance, patients may experience delayed cerebrospinal fluid (CSF) leaks following surgery and stereotactic radiosurgery, requiring additional endoscopic interventions.[34]

Hormonal therapy, specifically the use of androgen receptor blockers like flutamide, has been investigated as an adjuvant therapy. These agents may reduce tumor size prior to surgery or in cases of recurrence, though they do not provide a cure on their own.[35]

The use of chemotherapy for JNA remains largely unsupported by evidence. Some limited data suggest variable patient responses, from no recurrence to partial response, highlighting the need for further research into the role of cytotoxic drugs in the treatment of JNA.[35]

Post-operative follow up

It is based on periodic endoscopic and imaging examination, which should be performed for a minimum of 3 years. Because the most residual tumor tends to grow submucosally so CECT or MRI plays crucial role in their early detection.[31]

Prognosis and complications

Nasopharyngeal angiofibroma (JNA) is generally a benign tumor, which often results in a favorable prognosis. However, the prognosis can be affected by advanced disease, incomplete resection, or recurrence. Studies indicate that up to 33% of advanced JNA cases (Radkowski stage III) are unresectable. Among those who undergo surgery, recurrence rates can range from 30% to 38%, leading to additional complications from tumor regrowth and further invasion. In cases with residual or recurrent disease, adjuvant radiotherapy may be considered. While effective, radiation therapy carries a small risk of secondary malignancies, including basal cell carcinoma and squamous cell carcinoma, within the treated area. Rarely, JNA may undergo malignant transformation, particularly after radiotherapy, with some cases developing well-differentiated tumors or undifferentiated sarcomatous forms, which worsen the prognosis.[8,17]

The most significant complication of JNA is excessive blood loss during surgery or other procedures, which can be life-threatening if not managed appropriately. Orbital invasion by the tumor may lead to exophthalmos, vision loss, or the loss of extraocular movements. Non target embolization during preoperative embolization can also affect vision if internal carotid artery branches are involved. Other serious complications of embolization include arterial vasospasm, cranial nerve damage, facial palsy, or tissue infarction. Less severe complications include facial swelling, pain, headaches, or nausea. Surgical interventions may also result in facial scarring or deformity. Hormonal therapy, if used, can lead to undesirable side effects like feminization in adolescent males.[6]

Recent advances

There are studies about use of proton therapy (PRT) in advanced Juvenile angiofibroma with good control of tumor. They mentioned about the use of PRT with a dose of 45 Gy is a safe and effective therapeutic option for the treatment of advanced JNA. Notably, reducing potential long-term radiation-induced complications is of utmost importance, especially considering the young age of patients with JNA and their considerable life expectancy.[36]

REFERENCES

1. Makhasana JA, Kulkarni MA, Vaze S, Shroff AS. Juvenile nasopharyngeal angiofibroma. J Oral Maxillofac Pathol. 2016 May-Aug;20(2):330.
2. López F, Triantafyllou A, Snyderman CH, Hunt JL, Suárez C, Lund VJ, et al. Nasal juvenile angiofibroma: Current perspectives with emphasis on management. *Head Neck.* 2017 May;39(5):1033-1045. [PubMed]
3. Szymańska A, Szymański M, Czekajska-Chehab E, Szczerbo-Trojanowska M. Invasive growth patterns of juvenile nasopharyngeal angiofibroma: radiological imaging and clinical implications. *Acta Radiol*. 2014 Jul;55(6):725-31.
4. McKnight CD, Parmar HA, Watcharotone K, Mukherji SK. Reassessing the Anatomic Origin of the Juvenile Nasopharyngeal Angiofibroma. *J Comput Assist Tomogr*. 2017 Jul/Aug;41(4):559-564.
5. Alshaikh NA, Eleftheriadou A. Juvenile nasopharyngeal angiofibroma staging: An overview. *Ear Nose Throat J*. 2015 Jun;94(6):E12-22.
6. Allensworth JJ, Troob SH, Lanciault C, Andersen PE. High-grade malignant transformation of a radiation-naïve nasopharyngeal angiofibroma. *Head Neck.* 2016 Apr;38 Suppl 1:E2425-7.
7. Park CK, Kim DG, Paek SH, Chung HT, Jung HW. Recurrent juvenile nasopharyngeal angiofibroma treated with gamma knife surgery. *J Korean Med Sci*. 2006 Aug;21(4):773-7.
8. Mallick S, Benson R, Bhasker S, Mohanti BK. Long-term treatment outcomes of juvenile nasopharyngeal angiofibroma treated with radiotherapy. *Acta Otorhinolaryngol Ital*. 2015 Apr;35(2):75-9.
9. Overdevest JB, Amans MR, Zaki P, Pletcher SD, El-Sayed IH. Patterns of vascularization and surgical morbidity in juvenile nasopharyngeal angiofibroma: A case series, systematic review, and meta-analysis. *Head Neck.* 2018 Feb;40(2):428-443.
10. Mehan R, Rupa V, Lukka VK, Ahmed M, Moses V, Shyam Kumar NK. Association between vascular supply, stage and tumour size of juvenile nasopharyngeal angiofibroma. *Eur Arch Otorhinolaryngol*. 2016 Dec;273(12):4295-4303.
11. Marshall AH, Bradley PJ. Management dilemmas in the treatment and follow-up of advanced juvenile nasopharyngeal angiofibroma. *ORL J Otorhinolaryngol Relat Spec.* 2006;68(5):273-8.
12. Starlinger V, Wendler O, Gramann M, Schick B. Laminin expression in juvenile angiofibroma indicates vessel's early developmental stage. *Acta Otolaryngol.* 2007 Dec;127(12):1310-5.
13. Ralli M, Fusconi M, Visconti IC, Martellucci S, de Vincentiis M, Greco A. Nasopharyngeal angiofibroma in an elderly female patient: A rare case report. *Mol Clin Oncol.* 2018 Dec;9(6):702-704.
14. Schick B, Veldung B, Wemmert S, Jung V, Montenarh M, Meese E, et al. p53 and Her-2/neu in juvenile angiofibromas. *Oncol Rep*. 2005 Mar;13(3):453-7.
15. Guertl B, Beham A, Zechner R, Stammberger H, Hoefler G. Nasopharyngeal angiofibroma: an APC-gene-associated tumor? *Hum Pathol.* 2000 Nov;31(11):1411-3.

16. Mishra A, Sachadeva M, Jain A, Shukla NM, Pandey A. Human Papilloma virus in Juvenile Nasopharyngeal Angiofibroma: possible recent trend. *Am J Otolaryngol.* 2016 Jul-Aug;37(4):317-22.

17. McGarey PO, David AP, Payne SC. Nasopharyngeal angiofibroma in a 32-year-old man. *BMJ Case Rep.* 2018 Feb 08;2018.

18. Beham A, Regauer S, Beham-Schmid C, Kainz J, Stammberger H. Expression of CD34-antigen in nasopharyngeal angiofibromas. *Int J Pediatr Otorhinolaryngol.* 1998 Aug 01;44(3):245-50.

19. Wang JJ, Sun XC, Hu L, Liu ZF, Yu HP, Li H, et al. Endoglin (CD105) expression on microvessel endothelial cells in juvenile nasopharyngeal angiofibroma: tissue microarray analysis and association with prognostic significance. *Head Neck.* 2013 Dec;35(12):1719-25.

20. Castellana R, Fanelli G, Lunardi G, Rosset M, Piccolo S, Ariozzi I, et al. Imaging findings of juvenile nasopharyngeal angiofibroma invading orbital apex and middle cranial fossa: a case report. *Egypt J Radiol Nucl Med*. 2023; 54 (160).

21. Das A, Bhalla AS, Sharma R, Kumar A, Thakar A, Vishnubhatla SM, et al. Can Diffusion Weighted Imaging Aid in Differentiating Benign from Malignant Sinonasal Masses?: A Useful Adjunct. *Pol J Radiol*. 2017;82:345-355.

22. Ikubor JE, Okolugbo NE, Okhakhu AL. Radiological features of juvenile nasopharyngeal angiofibroma. *J West Afr Coll Surg*. 2013 Oct-Dec;3(4):84-91.

23. Haubenreisser H, Bigdeli A, Meyer M, Kremer T, Riester T, Kneser U, et al. From 3D to 4D: Integration of temporal information into CT angiography studies. *Eur J Radiol*. 2015 Dec;84(12):2421-4.

24. Snyderman CH, Pant H, Carrau RL, Gardner P. A new endoscopic staging system for angiofibromas. *Arch Otolaryngol Head Neck Surg*. 2010 Jun;136(6):588-94.

25. Andrews JC, Fisch U, Aeppli U, Valavanis A, Makek MS. The surgical management of extensive nasopharyngeal angiofibromas with the infratemporal fossa approach. *The Laryngoscope*. 1989 Apr;99(4):429-37.

26. Radkowski D, McGill T, Healy GB, Ohlms L, Jones DT. Angiofibroma. Changes in staging and treatment. *Arch Otolaryngol Head Neck Surg*. 1996 Feb;122(2):122-9.

27. Janakiram TN, Sharma SB, Kasper E, Deshmukh O, Cherian I. Comprehensive preoperative staging system for endoscopic single and multicorridor approaches to juvenile nasal angiofibromas. *Surg Neurol Int*. 2017 Apr 26;8:55.

28. Mair EA, Battiata A, Casler JD. Endoscopic laser-assisted excision of juvenile nasopharyngeal angiofibromas. *Arch Otolaryngol Head Neck Surg*. 2003 Apr;129(4):454-9.

29. Butler CR, Scholfield DW, Madani G, Sandison A, Clarke PM. Current Management and Controversies of Juvenile Angiofibromas. *Int J Head Neck Surg.* 2018; 9(1):32-37.

30. Vlăescu AN, Ioniţă E, Ciolofan MS, Mogoantă CA, Voiosu C, Rusescu A, et al. Current approach of juvenile nasopharyngeal angiofibroma: a case series. *Rom J Morphol Embryol*. 2022 Jan-Mar;63(1):105-111.

31. Snyderman CH, Pant H. Endoscopic Management of Vascular Sinonasal Tumors, Including Angiofibroma. *Otolaryngol Clin North Am*. 2016 Jun;49(3):791-807.

32. Ye D, Shen Z, Wang G, Deng H, Qiu S, Zhang Y. Analysis of factors in successful nasal endoscopic resection of nasopharyngeal angiofibroma. *Acta Otolaryngol.* 2016;136(2):205-13.

33. Wiatrak BJ, Koopmann CF, Turrisi AT. Radiation therapy as an alternative to surgery in the management of intracranial juvenile nasopharyngeal angiofibroma. *Int J Pediatr Otorhinolaryngol*. 1993 Dec;28(1):51-61.

34. Min HJ, Chung HJ, Kim CH. Delayed cerebrospinal fluid rhinorrhea four years after gamma knife surgery for juvenile angiofibroma. *J Craniofac Surg*. 2014 Nov;25(6):e565-7.

35. Scholfield DW, Brundler MA, McDermott AL, Mussai F, Kearns P. Adjunctive Treatment in Juvenile Nasopharyngeal Angiofibroma: How Should We Approach Recurrence? *J Pediatr Hematol Oncol*. 2016 Apr;38(3):235-9.

36. Hoeltgen L, Tessonnier T, Meixner E, Hoegen P, Kim JY, Deng M, et al. Proton Therapy for Advanced Juvenile Nasopharyngeal Angiofibroma. *Cancers*. 2023; 15(20):5022.