# ORIGINAL ARTICLE

# AZHAR MAROOF RASHID-AMR Staging of Juvenile Angiofibroma: A New Staging System based on Anatomical Spread of the Disease – 25 Years Experience at Mayo Hospital, Lahore, Pakistan

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## ABSTRACT

**Objective:** The purpose of this study is to frame a simple method of staging the juvenile angiofibroma. A new staging system is introduced as Azhar Maroof Rashid -AMR staging based on the anatomical spread of the disease process in our past 25 years clinical experience.

**Study design**: Retrospective study

**Place and duration of study**: This study was conducted in department of ENT Unit 1, Mayo Hospital, Lahore associated with King Edward Medical college/University Lahore. It spanned over a period of 25 years from June 1988 to July 2012.

**Material and method**: A total of 30 consecutive recorded patients with suspected juvenile angiofibroma were evaluated preoperatively by history, examination, plane radiology, contrast enhanced CT scan and four vessels subtraction angiography depending on the availability and indication. Patients with recurrent disease were also included in the study.

**Results:** All patients were male. The average age of the patients was 16 years (SD 18.5±6.5). They ranged in age from 12 to 25 years. 6 (20 %) patients presented with recurrent disease.

**Conclusion**: Intradural extension could not be demonstrated radiologically as well as peroperatively in our past 25 year's experience. Therefore, in the new classification dural involvement was not taken into account.

**Key words:** Angiofibroma, Juvenile, Staging

## INTRODUCTION

Juvenile angiofibroma (JA) is the commonest benign tumor of nasopharynx exclusively found in males and has aggressive submucosal local spread. This non encapsulated and extremely vascular tumor arises in the tissues within the sphenopalatine foramen. It accounts for less than .5 % of all head and neck tumors. Nasopharyngeal part is covered with pink to reddish mucus membrane while extra pharyngeal part is grey to white in color. Histologically overlying mucosa often demonstrates squamous metaplasia. Their blood vessels typically lack the smooth muscle and elastin fibers which contribute for the sustained bleeding. It develops almost exclusively in pre pubertal and adolescent males though there are reports of this tumor being found in children, the elderly, young and even pregnant women.[1]

Abbreviations: Azhar Maroof Rashid (AMR), Juvenile angiofibroma (JA)

It presents with severe intermittent epistaxis and progressive nasal obstruction. There may be associated features like chronic anemia, hearing loss, anosmia, cheek swelling, broadening of nasal dorsum and pulmonary quality of voice. More extensive tumors can invade the orbit and cavernous sinus leading to headache, facial pain, proptosis and visual loss due to tenting of optic nerve. Tumor can be seen through anterior rhinoscopy and it may be prolapsed from the anterior nares. Posterior rhinoscopy in a cooperative patient may display a pink or red mass filling the nasopharynx. The soft palate is often displaced inferiorly by the bulk of the tumor and in advanced cases JA can be visible in the oropharynx.[2]

From the sphenopalatine foramen, tumor migrates medially beneath the mucus membrane of nasopharynx to fill the postnasal space. Anterior face of the sphenoid sinus may be encroached with sinus invasion. The tumor then follows the line of least resistance and grows forward into nasal cavity where it may acquire secondary attachment. Growth in lateral direction may take place from the

sphenopalatine foramen to pterygopalatine fossa causing forward bowing of posterior wall of the maxillary sinus. Eventually tumor comes to occupy the infratemporal fossa and when insufficient room remains for further expansion, it invades the orbital fissures leading to proptosis. It may erode greater wing of the sphenoid bone so as to make contact with dura of the middle cranial fossa, destroying the superior bony region triangulated by the foramen rotundum, foramen ovale, and foramen lacerum. Further extension from the middle cranial fossa tends to respect the dural barrier, such that the tumor remains lateral to the cavernous sinus. Tumor enters the cavernous sinus by eroding the inferior wall of sphenoid sinus through the nasopharynx and may displace the maxillary nerve. Tumor doesn't invade the skull base by cellular infiltration like malignant carcinomas but lead to bone absorption by local pressure.[3]

The highest incidence is found in Subcontinent and Egypt The occurrence of these tumors almost exclusively in adolescent males supports the hypothesis that an alteration of pituitary androgen estrogen axis contributes to the pathogenesis of JA, but many studies have failed to identify any endocrinologic abnormality. Several theories have been considered to explain their origin like vascular malformation, growth of embryonic residues, abnormal response to the nasopharyngeal periosteum, remains of fetal erectile tissue and genetic mutations of the beta-catenin gene. The most widely accepted theory is that the tumor is derived from the embryologic chondrocartilage during the development of the cranial bones. [4, 5]

Androgen receptors are present in at least 75 % of the tumors. Vascular endothelial and insulin like growth factors have been demonstrated and it correlates with Ki67 proliferative marker. Spontaneous cases of regression following puberty have been described.[6,7]

Diagnosis is based on history and examination and is supplemented by imaging studies. CT scan is useful in evaluating position of the mass and bony details of the craniofacial structures while MRI has advantage of showing extensions of JA into orbit, cheek and middle cranial fossa. When doubt exists about their accuracy, subtraction angiography is undertaken to evaluate the site and size of the tumor, source of blood supply and its embolization with polyvinyl alcohol particles. The main blood supply of JA comes from internal maxillary artery, but other arteries such as ascending pharyngeal, vidian, unnamed branches of internal carotid and rarely the vertebral artery may contribute to their vascularization. The vascular blush in post nasal space and the adjacent area is diagnostic of the condition and obviates the need for transnasal biopsy which can provoke brisk hemorrhage.[8]

Surgery is the main stay of treatment although radiotherapy, hormonal therapy, cryotherapy, elctrocoagulation and chemotherapy have all been described in the literature. The role of preoperative embolization to decrease intraoperative blood loss is controversial as it may obscure tumor extensions peroperatively and increases the likelihood of recurrence. Estrogen and Flutamide (non steroidal androgen receptor blocker) had been used to shrink the tumor size but their effects are variable and are associated with secondary feminizing effects. There have been 65 documented ways of removing JA with about 10 logical approaches including transpalatal, retropalatine, transnasal transmandibular, transzygomatic, lateral rhinotomy, weber fergusson, mid facial degloving, endoscopic transnasal, infratemporal fossa and craniofacial resection. [9, 10,11,12]

The transpalatal approach would be suitable if angiofibroma is confined to nasopharynx. Tumors that have gone into the nasal cavity and pterygopalatine fossa, a lateral rhinotomy combined with medial maxillectomy may suffice to deliver the tumor. For larger tumors which invade the infratemporal fossa, access can be achieved with Weber Fergusson by lazy S incision or by facial degloving approach. These approaches can afford access to both components of the swelling and its central stalk. The objective of either incision is to expose the maxillary antrum sufficiently so that anterior, posterior, medial and lateral walls of the antrum can be removed leaving orbital floor and upper alveolar arch as two distinct shelves. So the nasal cavity, nasopharynx maxillary antrum, pterygopalatine and infratemporal fossa all are converted into one large continuous space.[13,14]

Endoscopic excision can be considered for the lesions extended upto pterygopalatine fossa with limited medial invasion using one or two surgeon's technique. Extensive tumors with intracranial disease or with involvement of cavernous sinus are better resected by extended Weber Fergusson combined with temporal fossa approach. Advanced inoperable disease with intracranial extensions has also been treated by external beam radiotherapy. Radiotherapy is delivered in several fractions to achieve a total dose of 30-55 Grey. Regression is

very slow and it may take 2 to 3 years to achieve radiological stabilization. Treatment failure within 2-3 years in these patients with residual tumor may be managed by salvage surgery. Complications varies with the surgical technique used and may include nasal crusting, vestibular stenosis, palatal fistula, infra orbital nerve deficit, ectropion of lower eyelid, opthalmoplegia and visual loss.[14, 15]

## OBJECTIVE

Reporting, presentation and geographical distribution of JA varies in different parts of the world. The purpose of this study is to frame a simple method of staging the juvenile angiofibroma, which would allow us for an accurate preoperative tumor assessment and surgical planning. We have introduced a new staging system as Azhar Maroof Rashid-AMR Classification based on our clinical experience, radiological findings and anatomical spread of the disease process.

## MATERIAL AND METHOD

A total of 30 consecutive recorded patients with suspected JA were evaluated preoperatively by history, examination, contrast enhanced CT scan and four vessels subtraction angiogram if available and required. Patients with recurrence were also included in the study. Retrospective analysis was undertaken to propose a new staging system. Informed consent for the surgery was taken after being briefed about the nature of the procedures.

All patients were operated and surgical technique was tailored according to the extent of the disease.

Demographic profile and relevant data was recorded in a standard proforma. Data was entered in SPSS version 11, a computer based software programme. Mean and standard deviation were computed for qualitative variable like age. Descriptive statistics like percentages were computed for categorical variables like surgical approaches used according to stage of the tumor and anatomical spread of the disease process.

## RESULTS

All patients were male. The average age of the patients was 16 years (SD 18.5±6.5). They ranged in age from 12 to 25 years. 6 (20 %) patients presented with recurrent disease. 9 (30 %) patients with AMR stage II were operated by transpalatal approach while 3 (10 %) patients with transpalatal combined with lateral rhinotomy approach having stage I, II and III disease respectively. 4 (13.3 %) patients with stage II & III disease were operated by lateral rhinotomy alone and 1 (3.33 %) with stage II disease by retropalatine approach. However 10 (33.3 %) with stage IV and 2 (6.66 %) patients with stage II and V disease were operated by Weber Fergusson and modified Weber Fergusson approaches respectively. 1 (3.33 %) patient was operated by extended Weber Ferguson temporal fossa approach having stage IV disease.
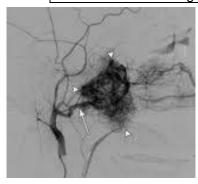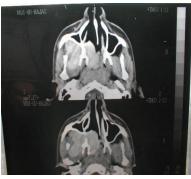
**Table 1:** Descriptive statistics of age (n=30)

**Table 2:** Anatomical spread of the disease

| Site | Patients | % | | |
|---|---|---|---|---|
| Mean | 16 | Nose/shenopalatine foramen | 29 | 96.6 |
| Standard deviation | 18.5±6.5 | | | |
| Range | 13 | Nasopharynx | 30 | 100 |
| Minimum | 12 | Maxillary sinus | 6 | 20 |
| Maximum | 25 | Ethmoid sinus | 1 | 3.33 |
| | | Sphenoid sinus | 1 | 3.33 |
| | | Pterygopalatine fossa | 18 | 60 |
| | | Infratemporal fossa | 13 | 43.3 |
| | | Cheek | 1 | 3.33 |
| | | Orbit | 10 | 33.3 |
| | | Intracranial extradural | 1 | 3.33 |
| | | Oropharynx | 1 | 3.33 |

**Table 3:** Surgical approaches used according to stage of the tumor

| Surgical approach | Patients | % | AMR grade |
|---|---|---|---|
| Transpalatal | 9 | 30 | II |
| Transpalatal lateral rhinotomy | 3 | 10 | I-II-III |
| Lateral rhinotomy | 4 | 13.3 | II-III |
| Retro palatine | 1 | 3.33 | II |
| Weber Fergusson | 10 | 33.3 | IV |
| Modified Weber Fergusson | 2 | 6.66 | II-V |
| Extended Weber Fergusson temporal fossa | 1 | 3.33 | IV |



**Picture 1:** Tumor blush of maxillary artery on angiogram
**Picture 2-3:** Contrast enhanced CT scan axial and coronal views showing tumor extensions to nasopharynx, sphenoid sinus, pterygopalatine and infratemporal fossa (AMR Stage IV).

## DISCUSSION

Hippocrates in 410-470 Bc have been said to remove a hard nasal polyp through a midline nose splitting incision and it is suggested that it was a juvenile angiofibroma. Later on Liston at University College London performed the first successful resection of angiofibroma on a 21 year old man on 6th September 1841. They removed the tumor by performing total maxillectomy through a Weber Ferguson incision without anesthesia. In the recent past surgical resection has been the preferred treatment for the extracranial JA since 1955.[16]

Many staging systems of JA have been proposed in the past but with some controversies. In 1981, session's et al suggested a staging system according to benign behavior of the tumor. But we cannot have a clear cut demarcation about the treatment modality to be followed for each stage in this system. In 1984, Chandler suggested another classification based on the system proposed for the nasopharyngeal cancer by the American joint committee. However this staging system does not reflect the benign behavior of the tumor and does not differentiate extra nasopharyngeal sites except the sphenoid sinus and intracranial cavity. In 1989, Fisch and Andrews proposed new staging systems with special emphasis on dural involvement. These systems do not cover all the aspects of tumor extension and recurrence. In 1996, Radkowski modified the Session Classification stressing the importance of tumor extension posterior to pterygoid plates and cavernous sinus. This system has been involved mainly with management of the smaller tumors as there are more subdivisions and less utility.[17,18,19,20,20,21]

**Azhar Maroof Rashid-AMR Staging of Juvenile Angiofibroma**

I- Tumor confined to the site of origin, sphenopalatine foramen, basioccipit and basisphenoid.
II- Tumor with extension to nasopharynx, oropharynx, nasal cavity and/or pterygopalatine fossa.
III- Tumor with extension to orbit or paranasal sinuses except sphenoid sinus.
IV- Tumor with extension to cheek, sphenoid sinus, temporal or infratemporal fossa.
V- Tumor with intracranial extradural extension or with involvement of the cavernous sinus

In the last decade advances in embolization techniques, use of angled endoscopes and changes in the sites of recurrences brought the need for a new classification system. Similarly the need for a uniform classification has also been

expressed by other authors. In the light of these advances, data from our series and the literature we have suggested a new classification according to the anatomical spread of the disease and named it as Azhar Maroof Rashid-AMR staging of JA. This new staging system would help in interinstitutional comparison of the treatment outcomes. Fisch classification reflects its main contribution in cavernous sinus, pituitary fossa and optic chiasma. We consider that JA is basically an innocent tumor, which just extend wherever it finds area of least resistance. Intradural involvement is though anatomically possible but almost never exists because till the time tumor extends to deeper structures of the brain, patient either bleeds profusely or might succumb to bleeding. Moreover it is not possible radiologically to distinguish whether tumor extends intradurally or not. We believe that tumor keep on expanding in extradural space and in most of the cases actual dural penetration never exist. Though possibility of intradural extension cannot be denied, there is only one documented case in the literature that fulfilled this criteria. Intradural extension could not be demonstrated radiologically as well as peroperatively in our past 25 year's clinical experience. We did not even observe any case which has involved optic chiasma, pituitary fossa or cranial nerves. Therefore, in the new classification dural involvement was not taken into account. We have not demonstrated bone destruction of shenopalatine foramen as well, as suggested in Fisch stage I. [22]

We have simplified our classification in 5 stages and involvement of oropharynx was also included as demonstrated in our series. We recommended the surgical approaches suited for each AMR Grade (Table 3) based on the anatomical spread of the tumor (Table 2). We did not operate any case with endoscopic approach because of its limited access and high rate of recurrence (Table 3). Average age of the patients in our series was 16 years which was in accordance with Onersi M et al. It was 14 years by Gupta AK et al, 15 years by Bales C et al and 17 years by Tang IP et al. Maximum age limit was 25 years in our patients and it was close to Gupta AK and Tang IP, where it was 28 years.[8,12,22,23]

Recurrence rate was 20 % in our patients and it was same as observed by Bales C et al in their series. Recurrence rates as high as 30%–50% have been reported by McCombe A et al. In 1992, Gullane et al and in 2004 Castello FM reported a 36% recurrence after surgery. Prolonged clinical and radiological monitoring is necessary and disease free status of 5 years after primary surgery probably represents the cure [10,23,24,25]

## CONCLUSION
Intradural involvement is though anatomically possible but never comes across because actual dural penetration is unlikely. Moreover it is not possible radiologically to distinguish whether tumor extends intradurally or not. Intradural extension could not be demonstrated radiologically as well as peroperatively in our past 25 year's clinical experience. We did not even observe any case which has involved optic chiasma, pituitary fossa or cranial nerves. Therefore, in the new classification system dural involvement was not taken into account.

## REFFERENCES
1. Windfuhr JP, Remmert S. Extra nasopharyngeal angiofibromas: etiology, incidence and management. Acta Oto-Laryngologica 2004; 124: 880-9.
2. Hwang HC, Mills SE, Patterson K, Gown AM. Expression of androgen receptors in nasopharyngeal angiofibroma: an immunohistochemical study of 24 cases. Modern Pathology 1998; 11: 1122-6.
3. Tayagi I, Syal R, Goyal A. Recuurent and residual juvenile angiofibromas. J Laryngology Otology 2007; 121:460-7.
4. Schiff A. Juvenile nasopharyngeal angiofibromas: a history of pathogenesis. Laryngoscope 1969.69; 981:1016.
5. Abraham SC, Montgomery EA, Giardello FM, Wu TT Frecuent beta-catenin in juvenile nasopharyngeal angiofibromas. Am J Pathol 2001; 158:1073-78.
6. Dohar J, Duvall A. Spontaneous regressions of juvenile nasopharyngeal angiofibroma. Ann Otol Rhinol Laryngol 1992; 101:469-471.
7. Coutinho-Camillo CM, Brentani MM, Butogan O, Torloni H, Nagai MA. Relaxation of imprinting of IGF ii in juvenile nasopharyngeal angiofibroma. Diagnostic Molecular Pathology 2003; 12; 57-62.
8. Tang I P, Shashinder S, Gopala Krishnan G, Narayanan P. Juvenile nasopharyngeal angiofibroma in a tertiary centre: ten-year experience. Singapore Med J 2009; 50 (3): 261.
9. Petruson K, Rodriguez- Catarino M, Petruson B, Finizia C. Juvenile nasopharyngeal angiofibromas:in pre-operative embolized and

non-embolized patients. Acta Oto-larygologica 2002; 122: 96-100.

10. McCombe A, Lund VJ, Howard DJ. Recurrence in juvenile angiofibromas. Rhinology 1990; 28: 97-102.

11. Gates GA, Rice DH, Koopmann CF, Schuller DE. Flutimide-induced regression of angiofibromas. Laryngoscope 1992; 102; 641-4.

12. Gupta AK, Bansal S. Nasopharyngeal angiofibroma-staging and selecting a surgical approach; changing trends. Clinical Rhinology 2009; 2(3):5-10.

13. Nicolai P, Berlucchi M, Tomenzoli D, Cappiello J, Trimarchi M, Maroldi R et al. Endoscopic surgery for juvenile angiofibroma-when and how. Laryngoscope 2003; 113: 775-82.

14. Pryor SG, Moore EJ, Kasperbauer JL. Endoscopic versus traditional approaches for excision of juvenile nasopharyngeal angiofibroma Laryngoscope 2005; 115:1201-7.

15. Reddy KA, Mendenhall WM, Amdur RJ, Stringer SP, Cassisi MJ. Long-term results of radiation therapy for juvenile nasopharyngeal angiofibromas. American Journal of Otolaryngology 2001.22; 172-5.

16. University College Hospital. Tumor of the upper jaw-bone- excion and recovery. Lancet 1841; 1: 67-8.

17. Sessions RB, Bryan RN, Naclerio RM, Alford BR. Radiographic staging of juvenile nasopharyngeal angiofibroma. Head Neck Surg 1981; 3:279-283.

18. Chandler JR, Goulding R, Moskowitz L, Quencer RM. Nasopharyngeal angiofibromas: staging and management. Ann Otol Rhinol Laryngol 1984; 93:322-29.

19. Andrews JC, Fisch U, Valavanis A et al. The surgical management of extensive nasopharyngeal angiofibromas with the infratemporal fossa approach. Laryngoscope 1989; 99:429-37.

20. Fisch U, Matox D. Microsurgery of skull base. Stuttgaurt: Thieme 1988; 348-53.

21. Radkovski D, Macgill T, Healy GB, Ohlms L, Jones DTY. Angiofibromas. Arch Otolaryngol Head Neck Surg 1996; 122:122-29.

22. Onersi M, Ogretmenoglu O, Yucel T. Juvenile nasopharyngeal angiofibroma: a revised staging system. Rhinology 2006; 44:39:45.

23. Bales C, Kotapka M, Laurie A, Al Ravi M, Weinstein G, Hurts R et al. Craniofacial resection of advanced juvenile nasopharyngeal angiofibroma. Arch Otolaryngol Head Neck Surg 2000. 128 ;( 9):1071-8.

24. Gullane PJ, Davidson J, O'Dwyer T, Forte V. Juvenile angiofibroma: a review of the literature and a case series report. Laryngoscope 1992; 102:928-33.

25. Castillo FM, Ramos AJ, Bravo F, Acosta FD, Villarejo PL. Endoscopic surgery of nasopharyngeal angiofibroma. Acta Otorhinolaringol Esp 2004; 55: 369-375.