

Juvenile Nasopharyngeal Angiofibroma: Correlating Histology, Surgical Approach and Blood Loss

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ABSTRACT

Juvenile nasopharyngeal angiofibroma (JNA) is locally destructive benign vascular tumor for which surgical excision has always been the treatment of choice, in spite of the availability of various other treatment modalities. Complete removal at the maiden attempt has always been the key to a successful outcome. Recurrences (or rather residuals) discourage both the surgeon and patient.

This prospective study was carried out in the Department of Otorhinolaryngology, Sir Sayajirao General Hospital, Vadodara, Gujarat, between August 2002 and 2015. We have studied 28 patients with JNA for growth patterns, histological characteristics and to compare various surgical modalities. Besides other investigations a detailed histological examination of the tumor was performed which suggested that as the tumor ages, the stroma predominates and the vessels are compressed into slits. In actively growing tumor the vascular component predominates. The percentage of open vascular channels is directly proportional to the bleeding while the intervascular fibrosis is inversely related. Surgical excision of JNA is the preferred modality of treatment. Surgical approach is sometimes the most tricky decision. Choosing the right approach is akin to walking on the thin rope with adequate exposure on one side and postoperative scar on the other.

Keywords: Adolescence, Angiogenic tumor, Epistaxis, Fibroangioma, Histopathology, Juvenile nasopharyngeal angiofibroma, Nasopharyngeal neoplasms, Surgical approval.

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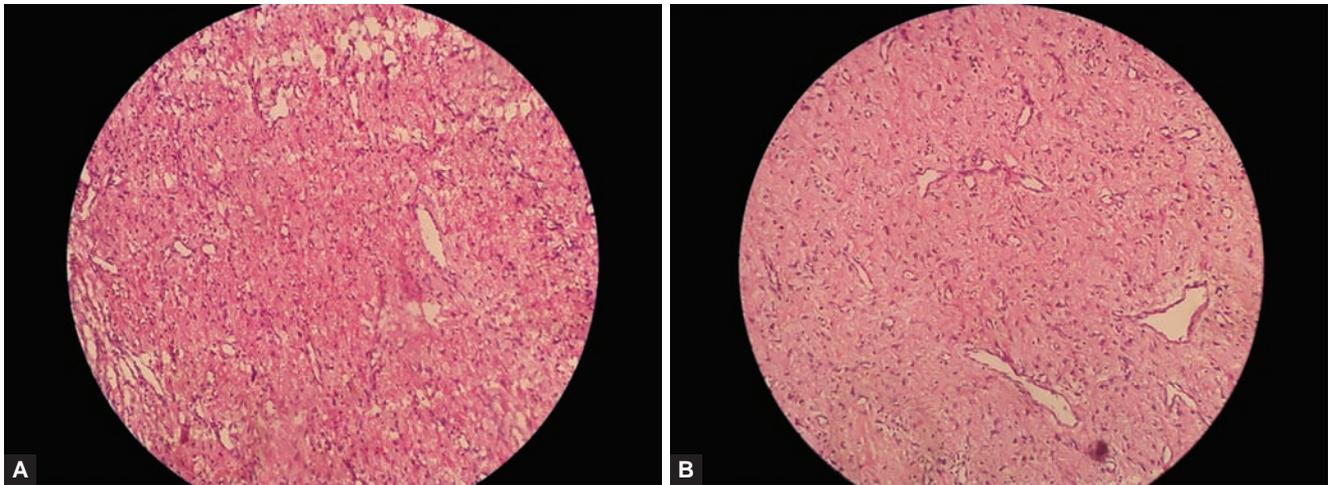
INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is quite an uncommon benign vascular tumor occurring almost exclusively in adolescent males. It usually presents with a triad of unilateral nasal obstruction, episodes of spontaneous nasal bleeding and nasal/nasopharyngeal mass. It accounts for less than 0.5% of head-neck tumors. Its incidence has been slated to be as low as one in 50,000 otorhinolaryngological new patients. Intracranial extension has been found in 10 to 20% of patients with JNA at presentation.

It is a benign tumor but locally aggressive eroding adjacent bone and growing into the cranium and infratemporal region. The extent is determined accurately by imaging techniques including computed tomography (CT) scan¹ and magnetic resonance imaging (MRI). Angiography and embolization are considered obligatory specially if planning for endoscopic approach.

On gross examination, the tumor usually is sessile, firm, rubbery, lobulated and red-pink to tan-grey in appearance. The tumor may be polypoidal or pedunculated. There is no true capsule, but the tumor is well demarcated from surrounding tissues. Microscopic appearance shows the appearance of fibroblasts-ovoid to spindle shaped, with a generous amount of connective tissue. In the compact stroma are blood vessels of different sizes and shapes lined by plump endothelial cells but with little or no smooth muscles or elastic fibers (Figs 1A and B). As the tumor ages there may be predominance of stroma so that the vessels are compressed into slits.

The surgical management of JNA has undergone considerable technical advancement during the last 50 years. Earlier (till about 8–10 years back) even in our hospital all cases were excised through an open approach in the absence of adequate imaging studies and state-of-the-art high definition nasal endoscopy system. The inability to identify the extensions of the tumor preoperatively made the surgeon to look for alternative and safer methods of treatment and subsequently much attention was given to hormonal therapy and external beam radiation. Feminizing features developing due to hormonal therapy and potential complications of radiotherapy² made the surgeons consider surgical removal as the gold standard for management of JNA.



Figs 1A and B: Juvenile nasopharyngeal angiofibroma slides showing more fibrous and less vascular component

With the advent of improved diagnosis using CT scans, MRIs, angiography with embolization and more through the selective surgical approaches designed to remove the tumor with all its extensions the surgical treatment is considered the definitive management. Advent of high definition nasal endoscopy system has helped in managing favorable tumors through the endonasal route.

Management of JNA aims to provide the patient with a tumor free healthy life with as little a cosmetic disfigurement as possible. The most reliable way to achieve this objective is by excising the tumor completely³ with all its extensions with minimal possible blood loss and postoperative morbidity. Many surgical approaches have been tailored to ensure a wide exposure with each having their own merits and demerits. Various approaches to nasopharynx⁴ and nasopharyngeal structures like transpalatal, lateral rhinotomy, maxillary swing⁵ and endoscopic endonasal have been evolved to provide good exposure and a complete excision of tumor. Combined neurorhinologic approaches have also been described for large tumors. Preoperative embolisation⁶ has been found to significantly decrease intraoperative bleeding.

Presuming the hormonal dependency, numerous attempts have been made to alter the tumor with hormonal therapy. Gates⁷ in a pilot study demonstrated hormonal pharmacoreduction of angiofibroma using flutamide which interferes with binding of testosterone.

Postoperative histopathology confirmed the clinical diagnosis in all cases included in the study. An attempt was made to grade the histological changes on basis of perivascular fibrosis, intervascular fibrosis and percentage of open channels (taking an average of 20 high power fields). This grading (0–5) done by a senior pathologist was then compared with blood loss and age of the patient.

All the patients were followed up regularly after discharge initially every week for 1 month, followed by every month for 3 months and subsequently every 3 months.

MATERIALS AND METHODS

This is a study of 28 cases of JNA that underwent primary or revision surgery carried out at department of otorhinolaryngology and head-neck surgery, SSG Hospital and Medical College, Vadodara, during the period from August 2002 to 2015.

After a thorough clinical history and examination patients were subjected to nasal endoscopy and CT scan of paranasal sinuses with and without injection of intravenous contrast with axial, coronal and sagittal cuts.

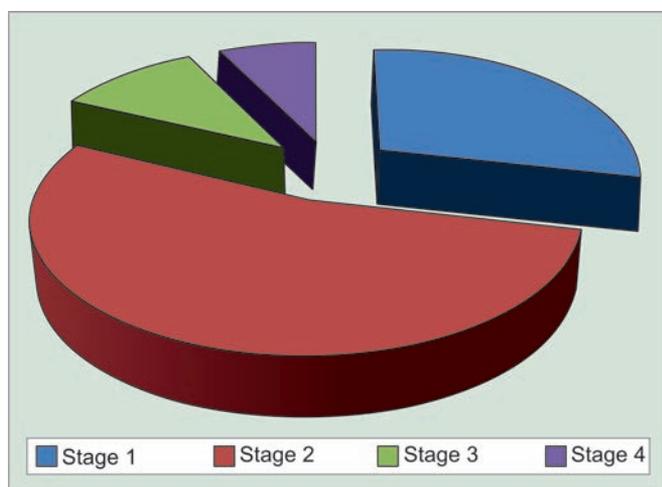
Complete hemogram, S.LFT, S.RFT, RBS, bleeding profile, etc. were routinely performed in all cases. Staging of all patients was carried out as per Fisch's staging system⁸ based on CT scan findings.

Preoperative angiography and embolization was done in one case with involvement of cavernous sinus. High cost resisted us from asking for these procedures routinely. Both intraoperative and postoperative findings were systemically recorded. Various surgical approaches were used like endonasal, transpalatal, lateral rhinotomy and maxillary swing. Approach was chosen considering merits and demerits of each vis a vis extent of tumor. The recovery of the patient in postoperative period was carefully observed with regard to the morbidity associated with each surgical approach used.

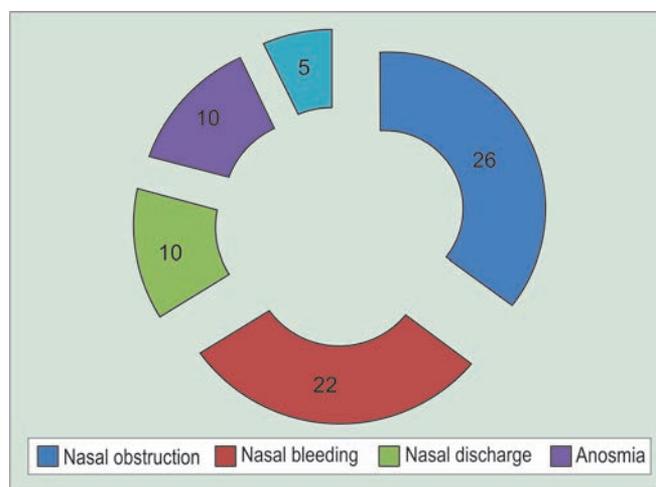
RESULTS AND ANALYSIS

The commonest age group seen in our study was between 17 and 20 years. The youngest patient in our study was 11-year-old and the oldest was 24 years old. All the patients in this study were males.

Depending upon the presentation to us, the patients were divided into two groups: primary group A (not previously operated) and recurrent group B (operated previously) (Graph 1). Majority of patients belonged to group A which included 24 patients while group B had four patients.



Graph 1: Number of patients in different stages



Graph 2: Presenting complaints

Of the patients in group B, two were operated previously in our institute itself; one for stage I tumor by transpalatal approach and second for stage II tumor by lateral rhinotomy approach. Another patient who was in stage III before first surgery and was operated by lateral rhinotomy approach at some other had to be shifted to our hospital within 2 weeks with anterior nasal packing *in situ*. All these patients were then operated again by a lateral rhinotomy approach.

The most common presenting symptom in our study was nasal obstruction and epistaxis. Rhinorrhea was present in six patients, while headache was present in four patients (Graph 2). Most of the primary cases in our study (18 of 24) had preoperative duration of symptoms less than 1 year, while in all recurrent cases duration of symptoms was more than 1 year.

Of the 28 patients who underwent surgery right side was involved in 16 cases and left was involved in 12 cases. In our study the tumor involved the posterior part of the nasal cavity and the nasopharynx in all the cases. The pterygopalatine fossa was involved in 15 of 28 cases. The sphenoid sinus (13 of 28) was next most common site to be involved. The ethmoid sinus was involved in nine cases, while the infratemporal fossa was involved in seven cases. Three patients had involvement of orbit and cavernous sinus.

Most of the tumors in our study were in stage II (15 of 28). There were eight patients in stage I, three patients in stage III and two patients were in stage IV.

Transpalatal approach was used only in stage I tumors while the endonasal approach was used in stage I and limited stage II tumors. Lateral rhinotomy was used in stages I, II and III tumors. The transfacial maxillary swing approach was used in stages II, III and IV tumors.

The average blood loss in our study for stage I tumors was approximate 950 ml, while for stage II was 1100 ml. The approximate average blood loss for stage 3

was 1050 ml while for stage 4 was also about 2200 ml. It was observed that the average blood loss in our study in transpalatal approach for stage I tumors was 900 ml, while for lateral rhinotomy approach (stages I, II, III) was 1100 ml. The approximate average blood loss for endonasal approach for stages I and II was about 1200 ml while for maxillary swing approach for stages 2, 3 and 4 was 1200 ml.

The data suggest that with increasing age of the patients the fibrosis (both intervacular and perivascular) tends to increase and the percentage of open channels decrease. This fibrosis has an impact on bleeding in an individual case which is clearly reflected in Graph 3.

In our study, one patient (stage 4) had residual postoperative persistent tumor because of the proximity of the tumor to optic nerve in the region of orbital apex, which was managed postoperatively with oral estrogens and the patients is symptom free. Two patients had recurrent tumors for which a second surgery was performed. All other patients are on regular follow-up and disease free.

DISCUSSION

The mean age of the patients in our study was 17 years. As this is an age group of productive life, a tumor (angiofibroma) in this age is a big handicap in work/ education. In the series of Chandler⁹ (1984), the mean age was 16 years (74%). In our study, all the secondary cases having recurrence were in the age group of 16 to 20 years (4 of 4 cases). In our study, all the patients were male, similar to the series of Antonelli et al¹⁰ (1987) and Witt et al¹¹ (1983). This totality of male incidence of this disease suggests that chromosomal studies be carried out with biopsy diagnosis.

Most of the patients in our study presented with complaints of nasal obstruction (26 out of 28) and recurrent episodes of nasal bleeding (22 out of 28), ten patients had an additional complaint of associated nasal

discharge. Ten patients had additional complaints of headache, five had loss of olfaction. In the series of Witt et al¹¹ (1983) 73% of patients presented with nasal bleeding, nasal obstruction was present in 60% of patients and 23% had rhinorrhea. In the series of Antonelli et al¹⁰ (1987) nasal obstruction was present in 84% of patients, epistaxis in 68% of patients.

Of 28 patients who underwent surgery, right side was involved in 16 cases and left was involved in 12. In the series of Witt et al¹¹ (1983), right side was involved in 12 of 31 patients (39%).

In our study, the tumor involved the posterior part of nasal cavity and the nasopharynx in all cases. The pterygopalatine fossa was involved in 15 of 28 cases. The sphenoid sinus was next most common site to be involved in 13 cases. The ethmoid sinus was involved in nine cases while the infratemporal fossa was involved in seven cases. Three patients had involvement of orbit and cavernous sinus. In the series of Nicoli et al¹² (2003) nasal cavity and the nasopharynx was involved in 14 of 15 cases (93%). 13 of 15 patients (86%) had involvement of pterygoid process and pterygopalatine fossa. Twelve of 15 cases (80%) had involvement of sphenoid sinus. Three of 15 cases (20%) had involvement of infratemporal fossa. While in the series of Witt et al¹¹ (1983) the sphenoid sinus and orbit was involved in 38% of cases and pterygopalatine fossa was involved in 27% of cases. The infratemporal fossa was involved in series of Witt et al¹¹ (1983) in 11% of cases only.

Most of the tumors in our study were in stage II (15 of 28). There were eight patients in stage I, three patients in stage 3 and two patients in stage 4. In the series of Nicolai et al¹² (2003) 9 of 15 cases were in stage 2 (60%), 4 of 15 cases (26%) were in stage 3 and 14% in stage 1. In the series of Antonelli et al¹⁰ (1987) stage 3 tumors were most frequent (63%).

In our study, we used lateral rhinotomy in 18 patients, transfacial maxillary swing in four patients, endonasal in four patients and transpalatal in two patients.

Transpalatal approach was used only in stage 1 tumors. This approach is relatively easy and operative time is not more but provides an adequate access¹³ for the removal of angiofibroma but gives poor access of lateral nasopharynx. Also the paranasopharyngeal region is exposed inadequately hence the extensions of the angiofibromas into this region are also not dealt with. Palatal fistula as a complication may result if adequate precautions are not taken.

The endonasal endoscopic approach was used in stage 1 tumors and in limited stage 2 tumors. It has a distinct advantage of being cosmetically superior and the least operative time. Its main disadvantages are a limited access,

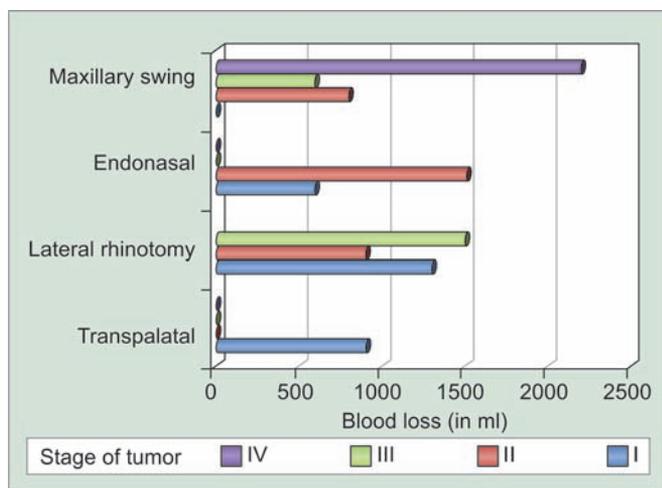
restricted visibility, difficulty in controlling the bleeding and tumors must be delivered through the mouth. If used in conjunction with preoperative embolization¹⁴ to reduce the vascularity of the tumor, this approach can prove to be far superior to others.

Lateral rhinotomy was used in stages 2 and 3 tumors. This approach is not difficult to perform and provides a good exposure of nasopharynx, the sphenoid and ethmoid sinuses. This approach however does not provide a good exposure of infratemporal fossa. A good tumor clearance can be achieved for stage 2 and limited stage 3 tumors. This approach carries the disadvantage of facial scarring if meticulous facial repair is not performed. Also one needs to drill the interior and posterior walls of maxillary sinus to reach the lateral most extent of the tumor which may hamper the future growth of maxilla in younger patients. The patients may also complaint of epiphora due to injury to the lacrimal apparatus and frequent problematic crusting due to the excessive raw area created. Of late we have started using ligaclips for controlling internal maxillary artery. We have also started stenting the lacrimal system to prevent blockage later on.

Maxillary swing approach was used in stages 2, 3 and 4 tumors. This approach although slightly difficult to perform for beginners, carries the distinct advantage of adequate exposure of nasopharynx and the paranasopharyngeal structures which include the pterygopalatine and infratemporal fossa. Although the operative time for this approach is more the tumor clearance using this approach is complete and blood loss corresponds to the stage of the tumor. It has an advantage of immediate control of bleeding by ligation of internal maxillary artery which lies there completely exposed. Contrary to what happens the soft tissue and bony reassembly is relatively easy to perform.¹⁵ This approach can be associated with complications like maxillary necrosis, palatal fistula, malocclusion and poor cosmesis - if proper precautions are not taken. The infraorbital nerve needs to be cut while swinging the maxilla laterally and subsequently an infraorbital nerve neurography needs to be performed to prevent anesthesia of cheek.

In our study, only one patient had massive hemorrhage from tumor due to involvement of cavernous sinus and intracranial extension (stage 4) which was controlled by ligation of internal maxillary artery and by packing with surgical.

From Graph 3, it is seen that average blood loss in our study in transpalatal approach for stage 1 tumors was 900 ml, while for lateral rhinotomy approach (stages 1, 2, 3) was 1100 ml. The approximate average blood loss for endonasal endoscopic approach for stages 1 and 2 was about 1200 ml; while for maxillary swing approach for



Graph 3: Blood loss in various stages and surgical approaches

stages 2, 3, 4 was also about 1200 ml. The data in our study suggest that the blood loss in JNA depends to a large extent upon the stage of tumor which cannot be controlled in anyway. However to prevent excessive loss of blood during surgery an adequate exposure must be achieved.

The overall approximate average blood loss for excision of JNA was 1120 ml in our study. In the study of Chandler et al⁹ (1984) the average approximate blood loss was 1500 ml in the series of Witt et al¹¹ (1983) using the weber fergusson transantral approach the average approximate operative blood loss averaged about 2600 ml in the series of Nicoli et al¹² (2003) using endonasal endoscopic approach the mean blood loss was approximate 372 ml.

Grading of histological change in JNA on the basis of perivascular fibrosis, intervascular fibrosis and percentage of open channel (taking an average of 20 HPF) was done. This was then compared with the blood loss and age of the patient. This is a pioneer work performed in our study for which not literature was available. Being a rare disease, the study group comprised of only 28 cases, hence no definite conclusions could be reached but it was found that percentage of open channels was directly proportional to the blood loss while the intervascular fibrosis and age was inversely related to the blood loss.

In our study initially nasal crusting was present in almost all operative cases JNA. After 3 months of follow-up this continued to be problematic in 7 of 28 (25%) cases. Two patient two developed scar retraction of Moure's lateral rhinotomy incision and developed an unsightly facial scar. One of these patients had presented to us with recurrence with an anterior nasal pack *in situ*.

One patient developed minor malocclusion of the jaws due to the orotracheal intubation used in a patient where maxillary swing was done. This was because the occlusion status in that patient could not be assessed prior to extubation. This was later rectified by the use of intermaxillary wiring for 3 weeks. Occlusion was good in other cases of maxillary swing where preoperative

tracheostomy was performed and the occlusions could be assessed intraoperatively.

In one case with the orbital involvement the tumor was left untouched (residual tumor) in the region of orbital apex. This patient was the given estradiol in the postoperative period and the patient is on a regular follow-up with no complaints. In two other patients' recurrent tumor was detected in the nasopharynx on routine follow-up endoscopic examination within 8 weeks of surgery. The recurrent tumor was excised in both cases with an endoscopic approach. Hence the problem of recurrent tumor was encountered in 2 of 28 cases. All other patients are on regular follow-up and disease free. In the study of Nicoli et al¹² (2003), the recurrence rate was 7% and in study of Witt et al¹¹ (1983) it was 13%.

CONCLUSION

Juvenile nasopharyngeal angiofibroma is a benign but locally invasive tumor. Microscopically, the tumor consists of a vascular component in a fibrous stroma. In actively growing tumors the vascular component predominates and the vessel wall generally consists of a single endothelial lining. It is suggested that percentage of open channels is directly proportional to the blood loss while the intervascular fibrosis and age are inversely related to the blood loss. This observation in our study of histological picture is a pioneer work which opens the doors for further research in this direction.

The surgical management of JNA is preferred modality of treatment. The choice of the best surgical approach is the most critical decision. Complete excision of the tumor can be done and reoccurrence prevented by a good exposure of the tumor with various approaches which must be tailored to the individual patients depending on the stage (CT findings), keeping in mind the merits and demerits of all the approaches.

The reoccurrence is a result of aggressive rapidly growing tumors. However the choice of a wrong approach with regard to the stage of the tumor can lead to an inadequate clearance and a residual tumor. Therefore an ideal approach should be able to deal with all the possible extensions of this tumor without jeopardizing the basic anatomy of the region and taking care of postoperative morbidity and cosmesis.

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