Original Article

Comprehensive preoperative staging system for endoscopic single and multicorridor approaches to juvenile nasal angiofibromas

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Abstract

Background: Juvenile nasal angiofibromas (JNA) is a benign lesion with high vascularity and propensity of bone erosion leading to skull base invasion and intracranial extension. It is known to involve multiple compartments, which are often surgically difficult to access. With evolution in surgical expertise and technical innovations, endoscopic and endoscopic-assisted management has become the preferred choice of surgical management. Over the last four decades, various staging systems have been proposed, which are largely based on the extent of nasal angiofibroma. However, no clear guidelines exist for the stage-appropriate surgical management. In this study, we aim to formulate a novel staging system based on the analysis of high quality preoperative imaging and propose detailed surgical guidelines related to disease stages as observed in 242 primary cases of JNA.

Methods: A retrospective analysis of the case records of 242 primary JNA cases was performed at our center. Patients were staged according to various existing staging systems as well as our own new staging system, and outcome variables were compared with respect to intraoperative blood loss, multiple staged operations, and tumor recurrences. Operative records were studied and precise endoscopic surgical guidelines were formulated for each stage.

Results: Comparing the intraoperative blood loss seen in stages of various classifications, it was found that intraoperative blood loss correlated best and statistically significantly with stages in the newly proposed Janakiram staging system when compared to the existing staging systems. Staged operations were performed in a total of 7/242 patients, and there was a significant association between the requirement of a staged operation and tumor extent (Fischer's exact test, $P < 0.001$). Tumor recurrence was seen in 22 cases and the pterygoid wedge

was found to be the most frequent site of recurrence initially. As the extent of resection improved with better surgical technique over time, recurrences were only found in superior orbital fissure, around the internal carotid artery, and in the middle cranial fossa.

Conclusion: This new Janakiram staging system is based on preoperative imaging data from one of the largest JNA case series reported thus far. Respective guidelines reliably stratify patients into treatment groups with definite surgical approaches and predicts outcome. Improved surgical approaches in the modern endoscopic era have redefined JNA management with improved outcome. This study shows the importance of precise presurgical imaging and the choice of the most suitable surgical approach in reducing morbidity and mortality in JNA surgery.

Key Words: Endoscopic excision, JNA, staging system

INTRODUCTION

Juvenile nasal angiofibromas (JNA) is a benign neoplastic lesion encountered in the anterior skull base, and is characterized by significant vascularity and a propensity of bone erosion with intracranial extension.[18] Most authorities agree that surgery is the preferred modality of treatment, at least for primary tumors.[5] JNA frequently involves multiple anatomical compartments which are difficult to access.[5] With growing expertise in endoscopic techniques and advancements in imaging, the endoscopic route has evolved as the preferred approach for surgical management of JNA even at advanced tumor stages.

Optimal imaging is an indispensable tool in the assessment and is the key element in planning surgery for JNA. Adequately classifying the stage and precise extent of such a distinct pathology is essential, and will determine the most suitable operative approach as well as the extent of resection that can be achieved. This in turn has profound implications on the prognosis.[6]

Any staging system must continuously be updated to reflect changes in our knowledge of tumor characteristics or our understanding of recurrence patterns and how these features relate to available treatment options.[19,9] This new staging system, therefore, stratifies tumor extension into distinct subgroups and correlates the extent of disease to stage-appropriate definitive treatment strategies.

In the present study, we analyze preoperative records of 242 consecutive JNA patients treated at our center over a period of 9 years. Based on our experience, we propose and evaluate a new classification system that is derived from preoperative imaging data. Each stage in this classification system assigns patients to a specific treatment group with a defined surgical approach appropriate to address specific issues encountered in the respective anatomical compartment. Preoperative computed tomography (CT) data was analyzed in detail

to especially understand the degree of tumor invasion into the skull base and beyond. With this classification-based surgical approach, we explore the suitability of exclusive single transnasal corridor surgery as well as endoscopic multicorridor approaches for these tumors. Based on our experience, we demonstrate that, with endoscopic multicorridor approaches, we can stretch the limits of endoscopic JNA resection to a new level. Only a small number of tumors that are very extensive will remain beyond management via such endoscopic-controlled multicorridor approaches, and should, in our opinion, be resected by endoscopic-assisted open approaches.

Furthermore, in this study, new insights were gained regarding the possible site of JNA origin and the common pathways of tumor spread, which can be inferred from observations made during surgery.

We discuss the implications of this assessment for the overall management strategies of JNA, and it will be shown that this classification clearly correlates to the prognosis of the patient.

MATERIALS AND METHODS

The entire medical and radiographic records of patients who underwent endoscopic resection of JNA at our center between January 2005 and January 2014 were retrospectively analyzed.

Two hundred and forty-two primary cases of JNA were identified for inclusion in this cohort analysis; all the included patients were young males between 10 and 25 years of age. Cases were categorized and assigned to groups according to the proposed Janakiram staging system (JSS). The JSS takes into account the sites of skull base involvement and the pattern of JNA extension based on preoperative imaging (see below). The most suitable approach and operative technique is then chosen according to this assigned stage.

Imaging

Preoperative evaluation included contrast-enhanced CT scan (0.625 mm) of the skull base and paranasal sinuses obtained in three-dimensional projections in both bone and soft tissue windowing. In advanced tumor cases with orbital, parapharyngeal, or intracranial extension, additional magnetic resonance (MR) imaging with contrast was obtained.

Patients with lesions in close proximity to or with involvement of the internal carotid artery (ICA) underwent additional conventional transfemoral angiography for identification of the tumor supplying vessels. Cases that involved the ICA to a significant degree underwent balloon occlusion testing to assess cross circulation. Preoperative embolization was not deemed necessary and hence not performed in any of our cases. Intraoperative navigation was used for all cases infiltrating the greater wing of sphenoid, tumors encasing the ICA, infiltrating the cavernous sinus, or extending intracranially. To avoid ICA injuries, microvascular Doppler sonography was used to localize the vessel intraoperatively.

Postoperative evaluation included a contrast-enhanced CT within 36 hours of surgery to identify any residual tumor burden. In cases in which any significant residual tumor mass was displayed, patients were taken back to the operation room electively for a second surgery session. In all cases of ICA transposition, a second conventional angiography was performed postoperatively.

Postoperative follow-up data included CT scanning immediately after resection, as described above, and at 6 months postoperatively, along with nasal endoscopic examinations every 3 months for the first year after surgery and every 6 months for the following 3 years as well as a comprehensive clinical exam at each visit. Additional scan was obtained if the endoscopy revealed any suspision for recurrence. Recurrent disease was defined as new tumor seen on subsequent imaging studies during the follow-up observation period after an initially negative postoperative scan.

Staging system

The JSS is based on tumor extent as seen on preoperative contrast-enhanced CT. It consists of 5 stages and substages as they relate to endoscopic surgery, as well as one separate advanced stage for rare JNA extensions, which are beyond the access of endoscopic approaches. Our staging system advocates a tailored surgical strategy for each anatomical tumor configuration depending upon the various compartments involved. The staging system employed at our center for JNA is presented in Table 1 and illustrated in Figures 1–4. Cases with similar anatomical configuration and comparable extent of disease are assigned to a distinct JSS Figure 5, which is approached in a consistent manner by our surgical protocol; then, we analyzed the impact of this categorical

Table 1: The staging system employed at our center for JNA

Stage 1a	Pterygoid wedge and/or paranasal sinus
Stage 1b	With extension to nasopharynx
Stage 2a	With extension in nasal cavity and/minimal involvement of pterygopalatine fossa
Stage 2b	Involvement of infratemporal fossa
Stage 2c	Involvement of infratemporal fossa with extension to cheek/pterygoid fossa/inferior orbital fissure/laterally along the greater wing of sphenoid
Stage 3a	Involvement of quadrangular space/Meckel's cave
Stage 3b	Involvement of cavernous sinus/engulfing carotid artery
Stage 4a	Prestyloid parapharyngeal tumor extension above the lower border of the mandible
Stage 4b	Intracranial intradural extension
Stage 5	Massive parapharyngeal, maximal intracranial extensions, and bilateral JNA
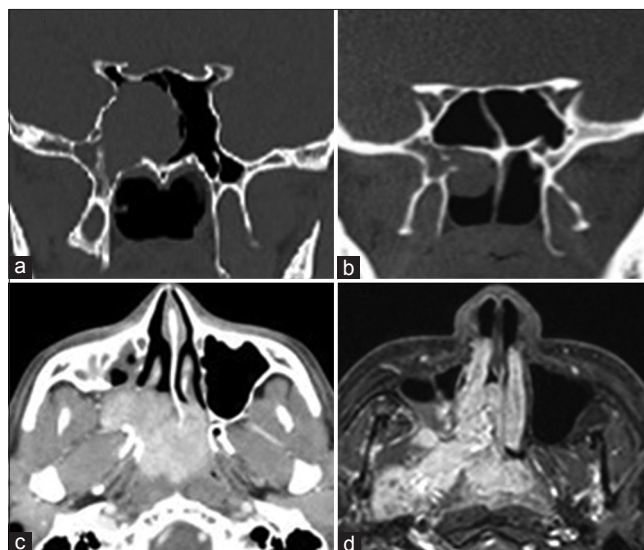
Figure 1: Preoperative imaging in Janakiram staging system. (a) Tumor seen involving pterygoid wedge and paranasal sinus on a coronal section CT scan (Stage 1a). (b) On a coronal section CT scan, tumor seen extending to the nasopharynx (Stage 1b). (c) Axial section CT scan showing tumor extension to the nasal cavity and pterygopalatine fossa (Stage 2a). (d) Tumor seen extending to the infratemporal fossa in an axial section (Stage 2b)

approach on prognosis. The surgical approaches in this geared system are gradually expanded in a stepwise manner from a rather simple middle meatal antrostomy to a complex modified Denker at our center[9] for maximum exposure and increased surgical maneuverability. When transnasal endoscopic surgery via a single trajectory reaches its limits and gross tumor resection is not feasible, endoscopic multicorridor approaches were employed for further and eventually complete excision of the tumor. Based on this staging system, we suggest that even very advanced tumors – that display extension into complex and difficult to reach anatomical areas – can be approached via multiple corridors or may be dealt with

in more than one surgical session. Finally, the system includes a stage that comprises rare tumors with extreme extensions that are beyond the access of endoscopic multicorridor approaches. The most suitable access to such massive tumors is best via external approaches, and therefore, these cases (two cases) are not included in the statistical analysis of this endoscopic staging system. The management or external approach for such tumor depends upon the surgeons' choice and expertise.

Surgical planning

General transoral endotracheal anesthesia was administered. Hypotensive anesthesia (htA) was maintained using a nitroglycerine infusion. Goal in hypotensive anesthesia is to achieve mean arterial pressures of 60–70 mmHg and systolic blood pressure values at about 80–90 mm Hg. Hemodynamics were closely monitored with invasive access throughout the case. The four-handed binostril technique was used in all cases except in stage 1 cases.

In the following paragraph [Table 2], we describe the surgical approach for each stage.

Statistical analyses

A number of variables (tumor extension based on presurgical imaging, surgical approaches chosen, direct vascular control by ligation of the feeder vessels, intraoperative blood loss, occurrence of residual or recurrent disease, and need for staged surgery) was analyzed for tumor staging and subsequently correlated to clinical outcome.

The database of our cohort was also used to classify our patient series according to other already established staging systems.[1,5,22,24,28,29] The respective outcomes were then correlated with the distinct stages of the proposed JSS and compared to those of the existing classification systems. Blood loss was recorded during surgery and amounts were correlated to the respective surgical approaches using the Spearman rank correlation. The number of cases that required a staged procedure as well as the observation of tumor recurrence during the postsurgical observation period was also correlated to the respective "classification stage" using Fischer's exact test. Statistical significance was defined when the calculated level was at or below 0.05 (Software SPSS version 21 IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.).

RESULTS

Demographics

Between January 2005 and January 2014, a total of 242 JNA patients were identified as requiring surgery and were subsequently operated in our department. All patients were males. The mean age at surgery was 17.3 years (range = 10–25 years). All patients were fully worked up and their tumor was categorized according to

Table 2: Proposed stagewise surgical approach

Stage 1a – Tumor limited to pterygoid wedge with or without sphenoid sinus [Figure 5]

The exposure requires anterior and posterior ethmoidectomy with wide sphenoidotomy. The blood loss is controlled by cauterization of the posterior nasal branch of the sphenopalatine artery followed by tumor excision. The pterygoid wedge is drilled and the residual tumor can be accessed and delivered.

Stage 1b – Extension into pterygoid wedge and sphenoid sinus with or without involvement of the nasopharynx [Figure 5]

The exposure is achieved by wide middle meatus antrostomy. The sphenopalatine artery, descending palatine artery, and vidian artery can be cauterized or clipped to devascularize the tumor. The tumor is finally dissected off the nasopharynx and delivered. The pterygoid wedge is drilled away and residual tumor is removed.

Stage 2a – Tumor with minimal extension into the pterygopalatine fossa with or without involvement of the nasal cavity [Figure 5]

Exposure is obtained by medial maxillectomy with removal of the medial part of the posterior wall of maxillary sinus. A posterior septectomy/septal window is added to facilitate access with a four-handed binostril technique. Ligation of internal maxillary artery is done for devascularization. This vessel has to be carefully dissected and identified lateral to the tumor margin.

Stage 2b – Extension to pterygopalatine fossa/infratemporal fossa [Figure 5]

Endoscopic medial maxillectomy is performed for tumor exposure. Tumor dissection is carried out after ligation of the internal maxillary artery, which is dissected lateral to the tumor margin.

Stage 2c – Involvement of infratemporal fossa with or without further extension into pterygoid space/inferior orbital fissure/laterally along the greater wing of sphenoid/cheek area [Figure 5]

Transient clamping of the external carotid artery on the same side is recommended and carried out prior to starting the endoscopic procedure to control the blood loss for stage 2C and beyond.

In this setting, a modified endoscopic Denker's approach[9] is used to expose the angiofibroma at its most lateral extent before commencing the tumor dissection. Trigeminal branch V2 is identified and should be preserved as it also serves as a landmark for inferior orbital fissure. In JNA cases with tumor extension into the inferior orbital fissure, the bony margins are drilled away with a 3 mm diamond drill burr to facilitate exposure and allow extirpation of this part of the tumor.

Any tumor anterior to the pterygoid wedge is debulked first to enable drilling of the involved cancellous bone.

Stage 3a – Involvement of quadrangular space/Meckel's cave [Figure 5]

In cases with extension in to the quadrangular space or Meckel's cave, a modified Denker's approach with clamping of the external carotid artery is again performed. The tumor is debulked first so that the pterygoid wedge can be accessed, as described above. The drilling of the greater sphenoid wing superiorly is important for better proximal exposure, which aids in removing tumor from crevices in the cancellous bone. It rarely extends laterally or superiorly to the anatomical path of V2. Further posterolateral extension beyond the pterygoid wedge is limited by middle cranial fossa dura. As the tumor respects the dura, it can be meticulously dissected away from it with gentle traction.

The vidian nerve is then identified and can be freed by drilling out bone from the 6 to 9 o clock position. The anterolateral wall of the sphenoid is removed next. The paraclival ICA is identified. The bone over the medial wall of the paraclival ICA is drilled away. The lingular process is identified and removed, which allows mobilization of the ICA. The paraclival

Contd...

Table 2: Contd...

ICA can now be gently transposed medially, which creates additional space to resect any tumor extending into Meckel's cave.

Stage 3b – Involvement of cavernous sinus and/or engulfment of the carotid artery [Figure 5]

In this stage, the tumor resection till the level of the pterygoid wedge is performed, as described in the earlier stages. It can be delivered via the oropharynx, as described above. The tumor is carefully debulked in close proximity to the ICA. The microvascular Doppler probe can be used to identify the exact position of the ICA. Feeder vessels arising from the ICA supplying the tumor can be cauterized. The tumor around the ICA is carefully debulked in a piecemeal manner. The position of the ICA needs to be confirmed as well as its distance to the workspace that has been developed before opening the cavernous sinus. Tumor can now be gently dissected off the sinus wall while taking care not to injure cranial nerves. Intraoperative monitoring and direct nerve stimulation is used for identification and monitoring of the integrity of cranial nerves. Electrodes are introduced in superior rectus (CN III), superior oblique (CN IV), temporalis (CN V), and lateral rectus muscle (CN VI) for electromyogram (EMG). Triggered, spontaneous, and neurotonic EMG responses are monitored and used for the identification of cranial nerves as well as to avoid injury. Tumor is dissected away carefully when in vicinity of these nerves without injuring them. Any bleeding can be controlled with warm saline irrigation and homeostatic agents (e.g., Floseal™ or Surgiflo™). In primary cases, the tumor is usually only attached to the endosteal layer surrounding the ICA.

Stage 4 – Involvement of prestyloid parapharyngeal space above the lower border of the mandible and/or with minimal intracranial extension lateral to the superior orbital fissure

In cases of such widespread tumor extension we employed multiple corridors or changed our strategy to an endoscopic-assisted external approach.

To this end, the surgical procedure can be divided into two steps, each tailored to the tumor extension. Clamping of external carotid artery on the same side is done to minimize the blood loss and should be done before starting the endoscopic procedure.

For the transnasal corridor, again a modified Denker's approach is used to expose the angiofibroma to its most lateral extent before tumor dissection is carried out. V2 is again identified and preserved. The tumor is cleared from the sinonasal corridor step by step, as described above.

Stage 4a – Prestyloid parapharyngeal tumor extension above the lower border of the mandible [Figure 5]

4a – In cases with parapharyngeal extension, a transoral corridor should be adopted. In this approach, the tumor bulge is identified in the soft palate and an intraoral incision is made anterior to the anterior pillar. The mucosa, submucosa, and fibers of palatoglossus and superior constrictor pharyngis are dissected to visualize and expose the tumor. With constant traction on the inferior part of the tumor, the mass is bluntly dissected along the tumor bed in the prestyloid space. It is then pushed superiorly to be delivered via the infratemporal fossa. The attachment of the tumor to any residual mass is now sharply cut near the foramen ovale. The intraoral part of the JNA – depending on its size – is delivered intraorally or through the nasal cavity. Hemostasis is performed and the incision is closed in a water-tight manner to prevent infection.

Stage 4b – Minimal intracranial extension [Figure 5]

In cases with tumor extension through the superior orbital fissure into the intracranial compartment (middle cranial fossa and towards the temporal lobe), the tumor can best be accessed via a transorbital endoscopic approach. An incision at the level of the brow or inferiorly to it is made to enter the supraorbital area. The periorbita is moved and elevated to allow drilling of the greater wing of the sphenoid bone. This

Contd...

Table 2: Contd...

corridor is bounded laterally by the temporalis muscle, posteromedially by the superior orbital fissure, and superiorly by the dura of the anterior cranial fossa. Using this corridor, the tumor is exposed lateral to the superior orbital fissure, and microsurgical dissection is performed with regular cauterization of the blood vessels using bipolar cautery prior to delivery of the tumor mass.

Stage 5 – Massive parapharyngeal, maximal intracranial extensions, and bilateral JNA

These include rare extensions of JNA that are beyond the access of multicorridor endoscopic approach. They can be dealt with external endoscopic-assisted approaches.

In two cases with poststyloid parapharyngeal extension or bilateral JNAs, the author prefers an external approach to access the tumor. The external approach implemented by the author is a bilateral facial translocation approach proposed by Ivo Janecka. However, the author does not advocate any specific external approach. The choice of external approach is at the discretion of the provider.
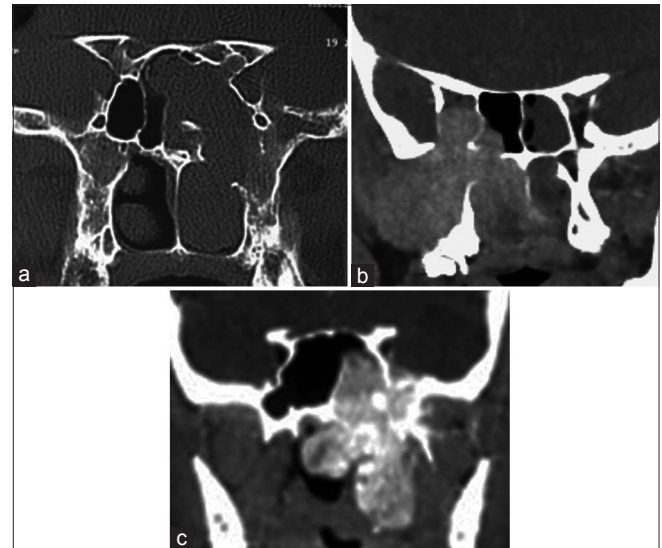
Figure 2: Preoperative imaging in Janakiram staging system (Stage 2c) tumor spread beyond the infratemporal fossa. (a) Tumor spread along the greater wing of sphenoid. (b) Tumor spread in the inferior orbital fissure. (c) Tumor in the pterygoid fossa

the JSS. A comparison of the JSS to other existing staging systems is presented in Table 3. The subgrouping of the patients in stages is presented in Table 4.

Imaging

On analysis of preoperative CT imaging studies of the entire cohort of 242 native JNA cases, the pterygoid wedge and floor of sphenoid sinus were the most commonly involved skull base structures. On further detailed analysis of the imaging studies, it was noted that the epicenter of the tumor could be localized to the pterygoid wedge in all our cases. The vidian canal was identifiable as a separate structure in 19% of our JNA cases.

The nasopharynx and the pterygopalatine fossa were involved in 98.4% and 95.8% of the cases, respectively. The tumor was observed to frequently extend via an

Table 3: Staging systems

Classifications	Stages	Based on	Approach	No. of patients in retrospective analysis
Sessions *et al.*[27]	I-III	CT	Open	12
Chandler *et al.*[5]	I-IV	CT	Open	13
Andrews *et al.*[1]	I-IV	CT	Open	14
Radkowski *et al.*[24]	I-III	CT	Open	23
Onerci *et al.*[22]	I-IV	CT	Endoscopic	36
Snyderman *et al.*[28]	I-V	CT and pre/post-embolization angiogram	Endoscopic	35
Janakiram *et al.*	I-IV	CT	With proposed endoscopic stage-wise surgical planning	242
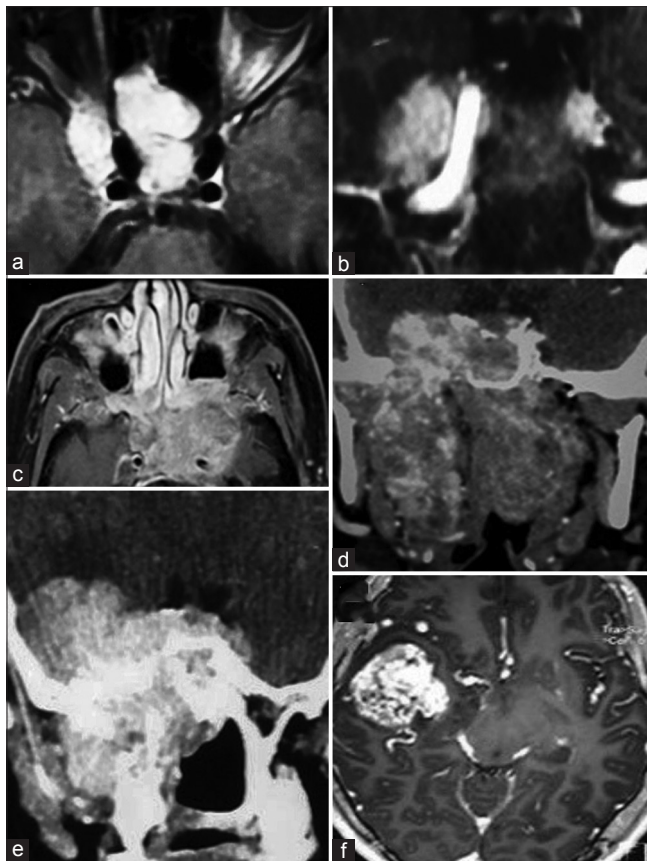
Figure 3: Preoperative imaging in Janakiram staging system. (a, b) Axial and coronal views of tumor in the Meckel's cave (Stage 3a). (c) Axial cut showing tumor engulfing the internal carotid artery (Stage 3b). (d) Tumor seen extending in to the parapharyngeal space in a coronal section (Stage 4a). (e, f) Coronal and axial sections showing intracranial tumor extension in to the middle cranial fossa (Stage 4b)

Figure 4: Postoperative CT scans. (a) postoperative CT scan of a Stage 1a. (b) similar postoperative scans of stage 2b. (c) Stage 2c with extension in the IOF. (d) Postoperative CT scan stage 2c with extension to the pterygoid fossa. (e) Postoperative CT scan of stage 2c with extension to cheek. (f) Postoperative CT scan of a stage 3b JNA. (g) Postoperative CT scan of a stage 4a JNA

anterolateral pathway reaching into the infratemporal fossa in 89.66% of the cases. Once tumor was present in the infratemporal fossa, it showed multidirectional spread along pathways of low resistance.

Orbital extension through the inferior orbital fissure was seen in 25.6% of the cases. This pathway was typically also associated with involvement of the infratemporal fossa. The pterygoid fossa was involved in 21.9% of the cases in our patient cohort. The greater wing of sphenoid was involved in 45.8% of the patients. Finally, we observed that the tumor extended from the pterygoid wedge along the greater wing of sphenoid into the middle cranial fossa in 2.1% of the patients.

A second typical pattern observed was that of the tumor extending posteriorly towards the quadrangular space with erosion of the base of pterygoid and the greater wing of the sphenoid. The quadrangular space was found to be involved in 30.1% of the cases. Tumors extending
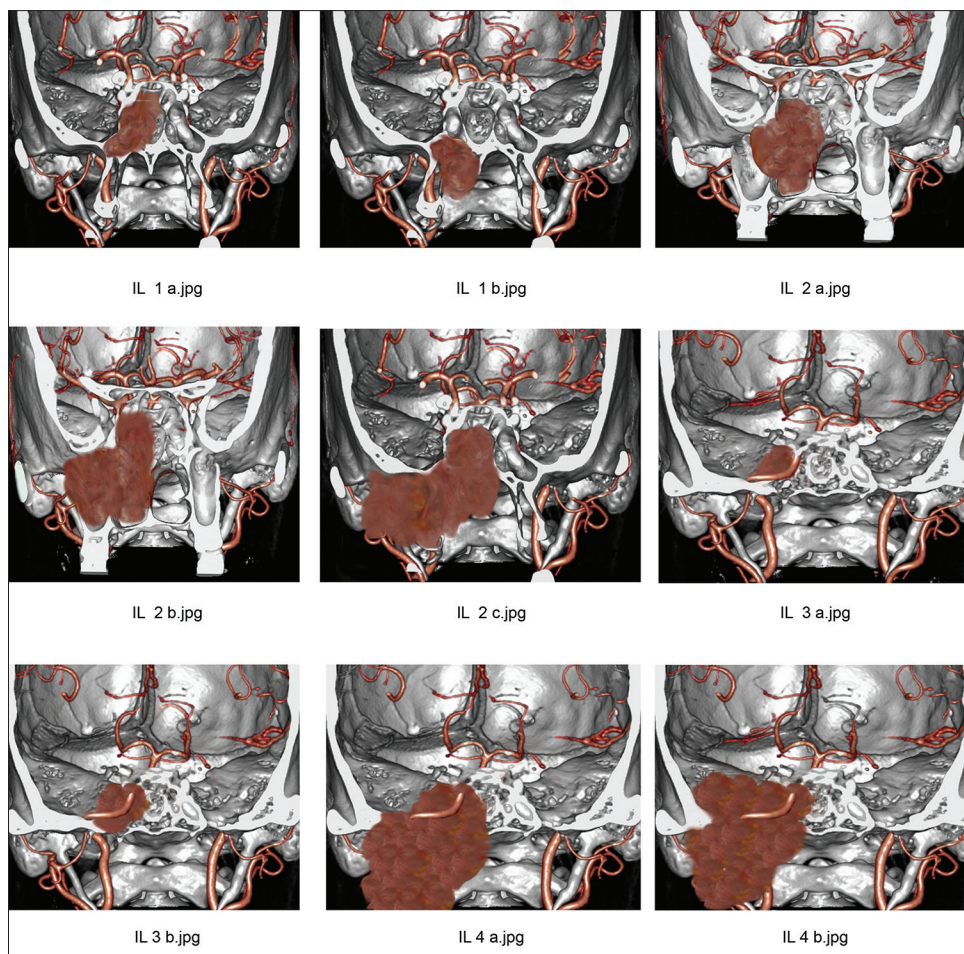
Figure 5: Stage 1a – Coronal cut section showing JNA in the pterygoid wedge area and occupying the sphenoid sinus. Stage 1b – JNA in the pterygoid wedge area and extending to the nasopharynx. Stage 2a – JNA extending in the nasal cavity and minimal involvement of pterygopaltine fossa. Stage 2b – JNA extending to the pterygopalatine fossa. Stage 2c – JNA involving the infratemporal fossa. Stage 3a – JNA extending to the quadrangular space. Stage 3b – JNA engulfing the internal carotid artery. Stage 4a – JNA extending to the Prestyloid parapharyngeal space. Stage 4b – JNA extending intracranially

Table 4: Patient distribution in various stages in our system

Stage	Extension	No.
Stage 1a	Pterygoid wedge and/or paranasal sinus	3
Stage 1b	With extension to nasopharynx	7
Stage 2a	With extension in nasal cavity and/minimal involvement of pterygopaltine fossa	15
Stage 2b	Involvement infratemporal fossa	21
Stage 2c	Involvement infratemporal fossa with extension to check/pterygoid space/ inferior orbital fissure/laterally along the greater wing of sphenoid	123
Stage 3a	Involvement of quadrangular space/Meckel's cave	46
Stage 3b	Involvement of cavernous sinus/Engulfing carotid artery	17
Stage 4a	Prestyloid parapharyngeal tumor extension above the lower border of the mandible	5
Stage 4b	Intracranial intradural extension	5

into the quadrangular space were located anterior to the anterolateral wall of cavernous sinus. Involvement of the cavernous sinus itself was quite rare and seen in only 6 cases. The most common segment of the ICA, which showed some tumor involvement was the paraclival ICA. Please refer to Table 5 for a listing of the involvement of various sites.

Residual and recurrent tumor

Out of the entire cohort of 242 cases, we observed 19 cases with residual disease and 22 recurrent cases Table 6. During the early phase of our surgical experience with endoscopic resections, we encountered residual and recurrent tumor most commonly located in the pterygoid wedge. A total of 10 such recurrences occurred in this

area. In the subsequent cases – which were performed after we had gained substantially more endoscopic experience – we drilled away the cancellous bone of the pterygoid wedge to ensure complete tumor removal, which allowed us to significantly reduce the incidence of residual and recurrent disease. As our surgical expertise evolved and more advanced tumors underwent endoscopic resections, tumor recurrences were noticed only in the superior orbital fissure, quadrangular space, inferior orbital fissure, and surrounding ICA.

The various sites of observed tumor recurrence are listed in Table 7.

Residual tumor was found in only 19/242 cases on the initial (36 hour) postoperative scan, and patients who showed residual tumor burden, underwent a second surgery for excision. The group with residual disease constituted 7.8% of the JNA cases of this series operated at our center.

Table 5: Involvement of the various sites in preoperative CT scan

Site	Number
Pterygoid wedge	241
Sphenoid sinus	240
Nasopharynx	239
Nasal cavity	232
Medial pterygopalatine Fossa	5
Complete pterygoalatine fossa	227
Infratemporal fossa	217
Cheek	27
Temporal fossa	2
Pterygoid fossa	65
Inferior orbital fissure	100
Orbit	61
Vidian canal	217
Lateral recess	237
Greater wing of sphenoid	110
Quadrangular space	73
Meckel's cave	11
Middle cranial fossa	28
Superior orbital fissure	39
Cavernous sinus	28
Internal carotid artery	11
Prestyloid parapharyngeal space above the lower border of mandible	5
Intracranial intradural extension	5

Staged operation

Seven patients underwent surgery that was planned as a two-step operation to begin with owing to the anticipated profound intraoperative blood loss during the primary surgery. There was a statistically significant correlation between the extent (stage) of the tumor on presurgical imaging and the need for staging the procedure into multiple operations. (fischer exact test $P < 0.001$) Please see Table 8 for details.

Intraoperative blood loss

Intraoperative blood loss is an important outcome of surgery and helps to evaluate efficacy of a surgical approach.[29] Blood loss was measured carefully by accounting for both the volume of blood that was aspirated during the surgery and for the amount of irrigation fluid that was used. Mean blood loss for each surgery according to the extent of disease and JSS stage was calculated [Table 9].

A clear progressive increase in intraoperative blood loss was observed with higher stages of disease/more advanced disease. The correlation of blood loss with extent of disease (stage) was studied for the newly proposed JSS as well as for other already existing staging systems; it became evident that blood loss correlated best with the stages in the JSS staging system when compared to others ($r = 0.92$ by Spearman rank correlation; Table 10). Intraoperative blood loss requiring blood transfusions was seen from stage 2c, and the amount of blood loss increased with more extensive disease stages. Staged operations were planned and performed for tumors of stages 4a and 4b in view of anticipated massive blood loss during the primary surgery and to give the patient some recuperation prior to complete tumor removal.

DISCUSSION

Owing to its dense vascularity and rather aggressive growth, JNA is a very challenging tumor – even for experienced surgeons. However, over the last years, a striking paradigm shift in surgical management of JNA has occurred with new endoscopic and endoscopic-assisted approaches performed by expert hands. With superior surgical instrumentation available, better endoscopic illumination techniques and substantially better direct vascular control methods, complete tumor removal can now be achieved for even very advanced cases of JNA, as seen in our stages 3a and above.

Table 6: Recurrence

	Stage 1 a	Stage 1 b	Stage 2 a	Stage 2 b	Stage 2 c	Stage 3 a	Stage 3b	Stage 4a	Stage 4b	Total
n	3	7	15	21	123	46	17	5	5	242
No recurrence	3	6	15	21	116	42	11	4	2	220
Recurrence	0	1	0	0	7	4	6	1	3	22
% of total recurrences	0.0	4.5	0.0	0.0	31.8	18.2	27.3	4.5	13.6	100

The primary objective of a clinically meaningful tumor staging system is to aid in determining the best management protocol as well as to prognosticate treatment outcome. After the introduction of the first classification system by Sessions et al. in 1981, a number of modifications were proposed.[2] Among these, the modification proposed by Radkowski et al. in 1996 is the most widely accepted classification.[2,10,24] Approximately a decade later, Onerci et al. developed another updated classification in 2006, which was based on advances made in imaging technology and the expanded use of endoscopes.[20] Shortly thereafter, in 2008, Carrilo et al. proposed yet another classification system in which tumor size was identified as an independent prognostic factor.[8] Snyderman et al. then proposed a staging system based on their retrospective review of endoscopic and open approaches. The authors concluded that two important factors (namely route of skull base extension and reduced vascularity after embolization) can be used to predict the prognosis in angiofibroma patients.[29]

Our staging system is predominantly pathoanatomical and classifies tumors based on their topographic extension, as seen on high-resolution preoperative imaging. It divides JNA into distinct subgroups that represent progressively more extensive tumor stages, and pairs each with a most suitable surgical approach for definite care. This system is based on the surgical principle of to distinct subgroups that represent progressively more extensive tumor stages, and pairs each with a most suitable surgical approach for definite care. This system is based on the surgical principle of "centripetal dissection" and sequential segmental resection.

The tailored approach evolved in our institution over time and its applicability can be seen in the analysis of this extensive cohort of 242 JNA patients who were operated strictly endoscopically or with endoscopically-assisted techniques at our center over the past 9 years.

A detailed preoperative CT scan analysis revealed the pterygoid wedge to be the most common site of residual tumor during the early phase of our surgical series. This observation was made on follow-up CT, and it was focally addressed endoscopically during the next cases as the surgical technique evolved and as we became more radical in our resection strategy. This knowledge was also applied to a small set of patients undergoing repeat surgeries. As we reinspected the pterygoid area, additional tumor could be identified at the pterygoid wedge, and more extensive "in depth" drilling was performed for all these cases. This led to no residual/recurrent tumor in this area on subsequent CT imaging. In three cases, we observed that JNA was limited to the pterygoid wedge and sphenoid on high-resolution CT without any nasopharyngeal soft tissue involvement at all on endoscopy. This observation was confirmed repeatedly in our growing series and with longer follow-up intervals, thereby revealing that the pterygoid wedge functions as the most likely site of origin of the tumor.

It is our impression that tumor growth occurs along certain tissue planes, which are those of least resistance. Another mode of spread appears to be along the vascular channels in the nose and skull base. The pathway of progressive growth and extension of tumor mass with bone destruction in JNA is more a "pushing" pattern of growth rather than one of malignant infiltration and this explains that the tumor – when spreading intracranially – respects the barrier formed by the dura.[5] We also analyzed the pattern of tumor spread into anatomically complex areas such as the greater wing of the sphenoid, the quadrangular space, the cavernous sinus, and along the ICA.

The tumor extension seen preoperatively on CT scan here was correlated to what we saw endoscopically, and both modes of observation appeared congruent in their findings.

Therefore, it was concluded that a designated preoperative CT protocol of high quality and thin cut technique for both bone and soft tissue windowing can help the surgeon to develop a clear strategy of how to approach this unique tumor in a stepwise manner. Once the tumor pattern and extent can be fully appreciated, the surgical team merely has to follow the proposed technical steps and principles.

Table 7: Recurrence sites

Recurrence in stage	n	Area
Stage 1b	1	Pterygoid wedge
Stage 2c	7	Pterygoid wedge, greater wing of sphenoid
Stage 3a	4	Superior orbital fissure, quadrangular space, infratemporal fossa
Stage 3b	6	Cavernous sinus, pterygoid fossa, superior orbital fissure
Stage 4a	1	Internal carotid artery
Stage 4b	3	Superior orbital fissure, pterygoid fossa, middle cranial fossa, internal carotid artery

Table 8: Staged operation

	Stage 1a	Stage 1b	Stage 2a	Stage 2b	Stage 2c	Stage 3a	Stage 3b	Stage 4a	Stage 4b	Total
N	3	7	15	21	123	46	17	5	5	242
Non-staged operation	3	7	15	21	123	46	17	3	0	235
Staged operations	0	0	0	0	0	0	4	2	5	7
% of total	0.0	0.0	0.0	0.0	0.0	0.0	0.0	30	70	100

Table 9: Intraoperative blood loss according to stage and blood transfusion

Stage	Number	Mean blood loss ml	Blood transfusion
Stage 1a	3	15.3	
Stage 1b	7	36.57	
Stage 2a	15	67.2	
Stage 2b	21	112.2	
Stage 2c	123	172.3	1-2
Stage 3a	46	293.1	1-4
Stage 3b	17	1348.3	4-14
Stage 4a and b	10	2919.1	4-16

Table 10: Spearman *R* value for correlation between intraoperative blood loss and stage

Staging system	*R* value
Janakiram *et al*.	0.92
Snyderman *et al*.	0.84
Onerci *et al*.	0.80
Rodkowski *et al*.	0.72
Andrews *et al*.	0.81
Chandler *et al*.	0.61
Sessions *et al*.	0.63

This image-based staging system emphasizes the necessity of an accurate preoperative assessment of the lesion to truly understand the extent of tumor infiltration. It also allows to pay tribute to extensions into difficult to reach anatomical areas, which then establishes the need to approach such extensive tumors via multiple surgical corridors or the rare need for a planned staged resection.

Blood loss is one of the most important outcome variables in JNA resections and a parameter which depends not only on surgical skill but largely on surgical strategies and stepwise surgical progress made intraoperatively.[2,29] preoperative anticipation of blood loss is a prerequisite in diligent surgical planning and can determine the need for possible staging of any procedure. In our analysis, intraoperative blood loss correlated best with the stages, as proposed by the JSS, and was more accurate in predicting blood loss than previous staging systems ($r = 0.92$) by Spearman rank correlation (from results correlation between stage and blood loss).

We found a consistent and positive correlation between the observed tumor stage and the amount of blood loss encountered across each of the stages of our staging system. However, this finding is not in agreement with the observation by Snyderman *et al*. who found no consistent correlation between some staging systems and the respective blood loss.[29] It was noted though that endoscopic staging systems had a better correlation to intraoperative blood loss than older classifications, such as the one employed by Radkowski.[25] One reason may be that almost all endoscopic staging systems will assign any area with intracranial high vascularity or with difficult access to a higher stage than other intracranial areas not bearing these features. This differential staging does not exist in older (nonendoscopic) staging systems, which may explain their rather poor correlation to intraoperative blood loss.

It is generally accepted that the pterygoid wedge represents a watershed zone for blood supply of JNA feeder vessels. This observation is reflected in our strategy of a segmental resection, which follows the principle that tumor feeding vessels anterior to the pterygoid wedge can be well controlled in a single step by direct visualization and ligation. That is also the reason that we did not pursue embolization preoperatively. This strategy will help avoid unwanted neurological sequelae that may be caused by embolization. The tumor posterior can be further resected in a staged approach depending on the blood loss encountered. We observed that, here again, blood loss can be managed well by direct surgical ligation without increasing the procedural morbidity and without the need for embolization.

Preoperative embolization has shown a reduction in intraoperative blood loss and a decrease in operative time in some studies, which will both facilitate complete excision.[7,11,13,14] However, a study by Lloyd *et al*.[12] and another by Borghei *et al*.[2] suggested that the risk of recurrence increases in cases with preoperative embolization.[2,11,12] This observation was later supported by Mann *et al*.,[2] and some authors have since suggested that embolization can lead to tumor being left behind at resection.[2,11]

Another aspect that should be taken into account is that preoperative embolization is not without complications. Some major complications may occur such as common iliac artery thrombosis, acute pulmonary edema, and cranial nerve deficits. Other minor complications such as sore throat, hemifacial pain, temporomandibular joint sourness, nasal alar necrosis, fever, and periorbital pain have also been reported.[18] At least three articles have also reported the debilitating complication of retinal artery occlusion and blindness following preoperative embolization for JNA.[21,25,30] The benefit of embolization should, therefore, be carefully balanced against the risk of neurological complications in an otherwise histologically benign tumor.

In a noteworthy study by Moulin *et al*., no significant difference was noted with respect to intraoperative bleeding in JNA cases when embolized and nonembolized groups were compared.[15]

At our center, JNA cases were surgically treated without embolization, and intraoperative bleeding was addressed and managed by a multipronged strategy. The

administration of hypotensive anesthesia was found to help in decreasing intraoperative blood loss. External carotid artery ligation can be performed in high-staged tumors. Intraoperatively, control over tumor feeding vessels was achieved by diligent visualization with direct identification and ligation, and those in close proximity of the ICA were cauterized using Kassam Bipolar forceps. Our surgical technique follows the principle of a "centripetal dissection," which enables the surgeon to clearly identify the feeder vessels. Other maneuvers such as optimal positioning of the patient, intraoperative warm saline irrigation, and the application of hemostatic agents also contributed to the control of blood loss.

The assignment to a high stage in our system correlated well with the need of multiple-staged operations and was found to be another robust variable. This aided significantly in surgical planning and was also a relevant aspect of presurgical patient counseling. Operations for extensive and high-staged tumors were then broken down into multiple procedures in view of anticipated excessive intraoperative blood loss in the primary surgery, and a second surgery was planned to achieve complete tumor excision. There was a statistically significant correlation between the stage of the tumor and the need to stage the operation as per the JSS ($P < 0.001$).

Surgical strategy is of paramount importance in managing JNA and significantly affects the prognosis of this disease. Surgical confidence has increased with better anatomical orientation skills and with increased experience in endoscopic skull base tumor resections. Irrespective of a particular surgical strategy or trajectory, the goal of all surgical approaches is to achieve wide exposure and good visibility for adequate vascular control and minimize morbidity.[7] Better visualization of JNA in cancellous bone, quadrangular space, cavernous sinus, and areas where the tumor is engulfing the ICA has enabled surgeons to adopt more aggressive approaches, even in complex areas, in hopes of complete excision with minimal morbidity and mortality. Our study shows that a proactive and extensive (not to say aggressive) surgical approach to JNA is feasible endoscopically, and that our approach results in excellent outcomes with minimal morbidity when performed by experienced hands.

The most important outcome, besides the patients' clinical status in the postoperative period, is the frequency of observed tumor recurrences, which are often due to inaccessible locations or under-resected tumor margins due to high vascularity.[29] By gaining more and more surgical experience with our cohort, we noticed a change in the location of possible residual and recurrent disease. Initially, we noted that the pterygoid wedge was the most common site. With increased understanding of the tumor spread topography and more extensive posterior pterygoid drilling, the sites for tumor recurrence (or small residuals)

changed to near to or in the quadrangular space, the inferior and superior orbital fissure, the middle cranial fossa, and the cavernous sinus. To further decrease these rates, surgical approaches were modified by widening the bony margins of, e.g., the inferior orbital fissure and with the diligent identification of a clean dissection plane that could be developed without the use of any cautery. This clearly improved our ability to follow the tumor into complex and deep structures. Even in experienced hands, we noted that, with more advanced and extensive tumor stages, the residual and recurrence rates were unavoidable. The stagewise recurrence is given in Table 11.

JNA has a high propensity for recurrence with rates reported as high as 32%.[2] According to Ramezani *et al.*, this can be as high as 50% if JNA is invading the infratemporal fossa, sphenoid sinus root of pterygoid, clivus, and cavernous sinus.[3,26]

Owing to this high recurrence rate seen in some JNA, a thorough and radical excision of the tumor with all its extension should be attempted. Boghani *et al.* stated in a comprehensive systematic review that, in purely endoscopic approaches, the recurrence rate ranges from only 0–23%. This number increases to 15–50% and 0–0% for endoscopic assisted and open approaches, respectively.[2] Pryor *et al.* reported no recurrences in 5 patients. Renkonen, however, had a 33.3% recurrence rate. In a comparatively larger series of 46 patients operated endoscopically, Nicolai *et al.* observed a recurrence rate of 8.7%.[17] Ardehali *et al.* reported, in their series of 47 patients, a recurrence rate of 19.1%.

As an endoscope provides a magnified and multiangled viewing opportunity, tumor extensions can be much better visualized than with a microscopic approach, and we think that this aspect is a key feature in explaining why the incidence of residual disease has been drastically reduced in well-done endoscopic cases.[5,16] However, at present the statistical analysis is limited by only small number of patients which were reported in these studies.[2] This is now corroborated by our series with a sizable patient cohort, in which a comparably low recurrence rate of only 9.1% was achieved.

In this article we have made a sincere effort to propose a clinically meaningful JNA staging system, which correlates to clear operative guidelines that show that most JNA can be managed endoscopically. Using these approaches and the currently available endoscopic

Table 11: Stagewise recurrence

Stage	Recurrence/ No. of patients
1	1/10
2	7/159
3	10/63
4	4/10

technology, we have been able to reach as far as the middle cranial fossa dura, parapharyngeal space, cheek, and temporal fossa. We believe that we have stretched the limits of minimal invasive resectability with such single or multicorridor endoscopic approaches. However, even in the most experienced hands, a few highly extensive tumors cannot be accessed endoscopically alone owing to their location and topography. For such tumors, we suggest to continue to employ external approaches, as recommended in the past.[5,4,8,16,22,23,27] Such tumors have hence been included as a separate standalone stage of our classification.

CONCLUSION

Surgical approaches in the endoscopic era have revolutionized the management of JNA and have improved surgical outcomes for extensive lesions. This study shows the importance of imaging in selecting the most suitable surgical approach with results in reducing morbidity and mortality in JNA surgery.

To this end we propose in this paper the JSS that is based on preoperative imaging characteristics obtained from data of one of the largest JNA case series to date. It reliably stratifies patients into treatment groups with definite surgical approaches, which redefine the achievable boundaries of endoscopic resection of JNA in complex areas such as Meckel's cave, cavernous sinus, and ICA. It also aids in predicting outcomes. It is of further value as it reports unique observations regarding presumed tumor origin and how this lesion spreads along preferred pathways.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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