



Surgical management of juvenile nasopharyngeal angiofibroma



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KEYWORDS

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Juvenile nasopharyngeal angiofibromas are benign yet aggressive anterior skull base tumors that occur almost exclusively in male adolescents. Diagnosis is typically made through radiographic findings and clinical characteristics; biopsy is not recommended due to the vascular nature of the disease. As with most tumors, there is a spectrum of tumor extent and invasion. In juvenile nasopharyngeal angiofibromas, one of the most important components of extent is the vascular supply. Once the vascular supply is identified, a systematic approach to resection can be planned. The majority of these tumors can be excised endoscopically, and those approaches are the focus of this article.

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Introduction

Juvenile nasopharyngeal angiofibromas (JNAs) are benign but locally aggressive tumors. They are challenging to treat surgically given their vascularity and proximity to critical structures. While historically addressed through an open approach, advances in endoscopic endonasal approaches have made this the primary treatment modality for all except the most advanced tumors.^{1–6} Case series and systematic reviews have found that outcomes after en-

doscopy endonasal resection for JNA reflect comparable rates of tumor control, but with reduced morbidity compared to open approaches.^{1–6}

JNAs arise in males and almost always in the peripubescent period. They have an interesting pathophysiology that is not fully understood. JNAs may originate from a remnant of the first branchial arch artery, and some consider them vascular malformations.^{7,8} Histologically they are encapsulated and consist of wide vascular channels lined by a single endothelial layer, rather than the typical vascular lining of both endothelium and a surrounding muscle layer.⁴ This incomplete architecture makes the vessels prone to rupture and hemorrhage. Grossly, JNAs appear pedunculated, lobulated, rubbery, and ranging in color from pink to tan or gray.

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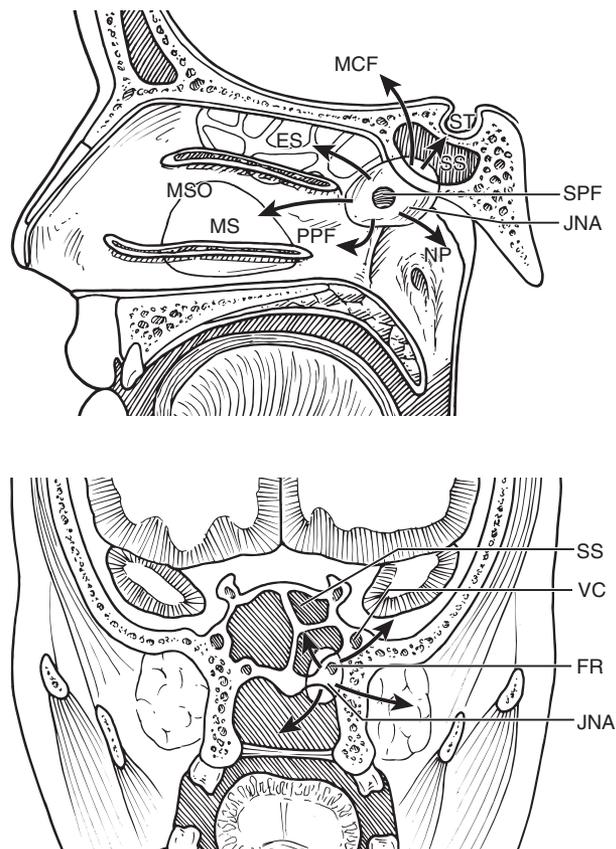


Figure 1 Common origin and spread patterns of juvenile nasopharyngeal angiofibroma from coronal and sagittal views. JNAs typically originate in the medial pterygopalatine foramen, at the lateral basisphenoid and near the sphenopalatine foramen. The tumor usually spreads through the sphenopalatine foramen into the nasal cavity as well as into/through the basisphenoid and vidian canal. The tumor can extend into the sinuses, orbit, and intracranially through multiple pathways.

The anatomical origin is consistent. These tumors arise from the lateral basisphenoid in the submucosa of the area around the sphenopalatine foramen (SPF). They characteristically spread by extending through and widening foramina and fissures (Figure 1). The classic Holman-Miller sign (anterior bowing of the posterior wall of the maxillary sinus, as seen on cross-sectional imaging), is due to tumor expansion in and lateral to the SPF. The very thin posterior maxillary wall is easily pushed forward by the growing JNA. Penetration through the SPF results in extension into the nasopharynx and paranasal sinuses. These tumors often extend into the infratemporal fossa through the pterygomaxillary fissure. JNAs also have the potential to extend into the orbit (through the infraorbital fissure) and intracranially (Figure 2). It is estimated that 10%-20% of JNAs have intracranial extension into either the anterior or middle cranial fossa.⁹ In many cases this is due to skull base erosion of the floor of the middle cranial fossa, the planum sphenoidale, or through the inferior orbital fissure, orbital apex, or superior orbital fissure, but dural invasion is very rare.



Figure 2 Axial CT image showing an advanced tumor with bilateral extent. Tumor extends into both left and right orbits as well as the middle cranial fossa.

The majority of JNAs are managed through endoscopic resection, which is the focus of this review. Historically, open resection through transpalatal, facial translocation, and open craniofacial approaches were utilized; however, experienced surgeons are now able to address both early and advanced staged tumors with an endoscopic endonasal approach.

Evaluation and workup

These tumors are often identified following epistaxis in a peripubescent patient, usually in combination with nasal obstruction, though some patients do not notice nasal obstruction as it develops slowly over time. Any adolescent male with epistaxis and unexplained nasal obstruction should raise suspicion for a JNA. While the vast majority of epistaxis will be from typical sources (the anterior septum) and due to dryness or trauma, any epistaxis that does not resolve promptly with medical management or anterior septum cauterization warrants further evaluation. Most adolescent males will tolerate nasal endoscopy in clinic with proper counseling, topical analgesia, and decongestion. If this is inadequate or not tolerated, imaging versus evaluation under anesthesia is a logical next step. If the patient is undergoing anesthesia for continued bleeding or a cauterization procedure, thorough endoscopy can be performed at that time. If not, a contrasted computed tomogra-

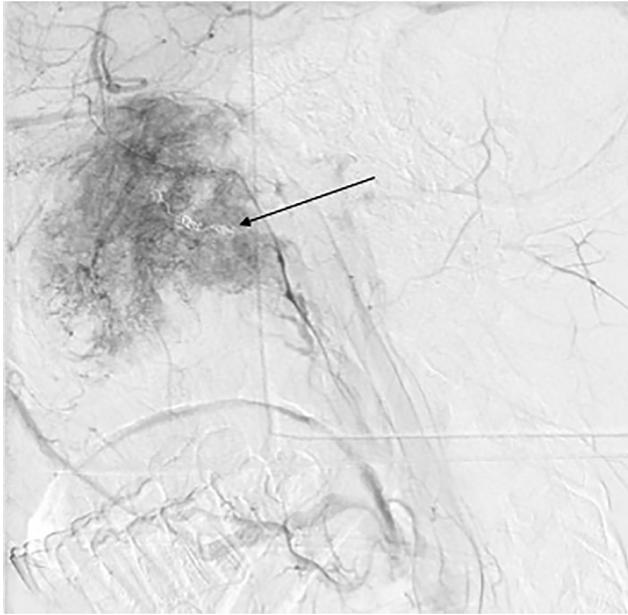


Figure 3 Embolization of JNA showing residual vascularity from ICA system following coiling.

phy (CT) or magnetic resonance imaging (MRI) should be obtained.

Once a presumptive diagnosis is established, precise evaluation of imaging is crucial for resection planning. Both CT and MRI are necessary to assess tumor extension and provide intraoperative image guidance. CT is superior for outlining bone landmarks and the carotid artery trajectory and bony covering.^{10,11} It will show the charac-

teristic Holman-Miller sign and erosion of the pterygoid base. The MRI better delineates tumor from retained sinus secretions and inflammation as well as orbital, intracranial, or cavernous sinus extension.^{10,11} Biopsy should not be performed as this will lead to excess bleeding. Diagnosis is made through characteristic imaging findings and demographics. Assessment of vascularity is important. Most JNAs are primarily supplied through the ipsilateral internal maxillary artery, though some can be supplied by internal carotid artery (ICA) branches and/or corresponding contralateral vessels.¹² Angiography (Figure 3) is the best method to determine supplying vasculature but is reserved until 24-48 hours prior to the planned resection to combine with embolization.^{13,19} This timing avoids unnecessary radiation exposure and risks from having 2 angiography procedures. In addition tumor re-vascularization, swelling, and necrosis is minimized when resection is performed soon after embolization.

Tumor staging

There are multiple staging systems employed for JNAs (Table 1). The Andrews¹⁴ and Radkowski¹⁵ systems have been the most widely used and are based on CT characteristics. The University of Pittsburgh Medical Center (UPMC) staging system is newer and accounts for vascularity of the tumor, particularly any intracranial circulation, as well as the route of intracranial extension.¹⁶ The UPMC staging system demonstrates stronger correlation with intraoperative blood loss and the need for multiple surgeries (staged, residual, or recurrent tumor).¹⁶ Examples

Table 1 UPMC, Andrews, and Radkowski staging systems

Stage	UPMC staging ¹⁶	Andrews staging ¹⁴	Radkowski staging ¹⁵
I	Nasal cavity, medial PPF. No residual vascularity*	Limited to nasopharynx and nasal cavity. Bone destruction negligible or limited to SPF	A: limited to nose or Nasopharynx B: limited to nose, Nasopharynx, and one or more sinus
II	Paranasal sinuses, lateral PPF. No residual vascularity*	Invading PPF or the maxillary, ethmoid, sphenoid sinus	A: minimal extension through SPF into medial PMF B: Full occupation of PMF, displacing posterior wall of maxilla forward, orbit erosion, displacement of maxillary artery branches C: Extension to ITF, cheek, posterior to pterygoid plate
III	Skull base, orbit, ITF. No residual vascularity*	A: Involving the ITF or orbital region without intracranial involvement B: Involving the ITF or orbit with intracranial extradural involvement	Erosion of skull base A: minimal intracranial extension B: extensive intracranial extension with or without cavernous sinus involvement
IV	Skull base, orbit, ITF. With residual vascularity*	Intracranial intradural tumor with cavernous sinus, pituitary or optic chiasm involvement	n/a
V	Intracranial extension: medial; lateral. With residual vascularity*	n/a	n/a

Abbreviations: ITF, infratemporal fossa; NP, nasopharynx; PMF, pterygomaxillary fossa; PPF, pterygopalatine fossa; SPF, sphenopalatine foramen; UPMC, University of Pittsburgh Medical Center.

* Refers to status of tumor vascularity after preoperative embolization of external carotid blood supply.

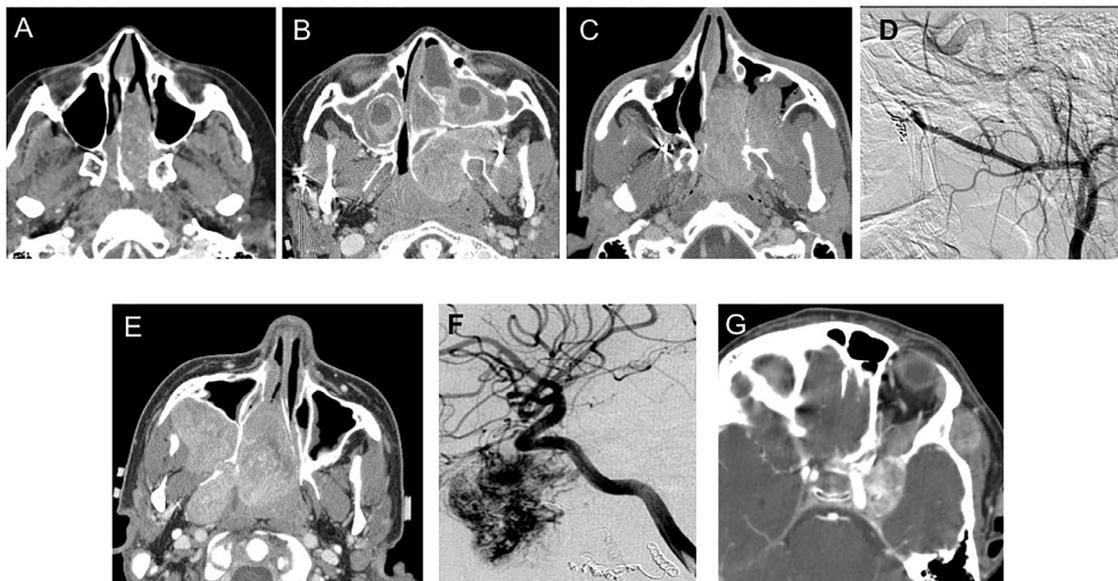


Figure 4 UPMC staging system. Axial CT scans and embolization images depicting tumors corresponding to each UPMC JNA tumor stage. (A) tumor confined to left nasal cavity and the medial pterygopalatine fossa (UPMC Stage I). (B) tumor involving left lateral pterygopalatine fossa and nasal cavity (UPMC Stage II). Inspissated secretions in bilateral maxillary sinuses. (C, D) CT and angiogram images from the same patient showing tumor involving left infratemporal fossa as well as an angiogram showing no residual vascularity following embolization of the external carotid artery supply (UPMC Stage III). (E, F) CT and angiogram images from the same patient showing tumor involving the infratemporal fossa as well as residual internal carotid artery vascularization following embolization of the external carotid artery tributaries (UPMC stage IV). (G) tumor is seen lateral to the left internal carotid artery (Stage V). Reproduced with permission from Snyderman CH et al. A New Endoscopic Staging System for Angiofibromas. *JAMA Otolaryngology* 2010; 588–94

of tumors corresponding to the UPMC stages are shown in [Figure 4](#).

Perioperative care

Because of the serious nature of this surgery, all patients should have an evaluation and clearance from their primary pediatrician. Preoperative labs including a complete blood count, coagulation assessment, and chemistry should be obtained. All patients should be typed and cross-matched for blood products. Often, 2 units of blood products are kept in the room in case rapid bleeding ensues. Coagulation factors such as fresh frozen plasma should also be available. In endoscopic endonasal surgery for advanced JNAs, the average blood loss is estimated to be 1300 mL.^{2,13,17} Considering the low intravascular volume of this patient population, intraoperative coagulopathy due to major blood loss is a significant concern. Consultation with a pediatric anesthesiologist is important to maximize preparation and safety in these operations. It is important to consider the smaller blood volume in younger and physically smaller patients and therefore the likelihood for decompensation. Patients and families should be prepared for staging of surgery in the event of excessive blood loss.

Typically, patients are admitted to the angiography suite for angiogram and embolization 24–48 hours prior to the planned procedure. It is very helpful for the surgeon to be present if possible to visualize the blood supply and the success of embolization. If not able to be present for

the procedure, consultation with the performing neurointerventionalist to review imaging and discuss findings is essential. Residual vascularity after embolization of the external carotid artery contribution is predictive of increased operative blood loss.^{15,18} Embolization of ICA feeders is not recommended due to the elevated risk of embolic complications (stroke, visual loss, facial paralysis, carotid dissection).^{20,21} Preoperative balloon occlusion testing of the ICA can be considered when the tumor extensively invades the cavernous sinus or encases the ICA, or the patient has been treated previously with multiple embolizations, surgery, or radiation therapy. This will assess the adequacy of the collateral circulation and the feasibility of carotid sacrifice, if necessary.

As mentioned above, a multidisciplinary approach to evaluation and care of these patients will maximize the best outcome. In addition to otolaryngologists and neurosurgeons, pediatricians, pediatric anesthesiologists, radiologists, and neurointerventionalists are key members of this group. Also, baseline visual acuity and assessment of ocular motility must be documented preoperatively; an ophthalmologist should be consulted if there are unusual visual changes preoperatively.

Surgical preparation

Advanced JNAs demand special anesthetic consideration. Prior adjuvant radiation therapy, angiographic embolization, or masticatory space surgical dissection, can

result in difficult intubation.²² With intracranial extension, increased intracranial pressure may be present.²³ Though very rare in JNA resection, a lower cranial nerve injury can increase risk of aspiration. Measures to be considered in this setting are: smooth induction of anesthesia, invasive monitoring of blood pressure, and promotion of moderate hyperventilation. Invasive hemodynamic monitoring will provide safe hypotensive anesthesia and optimal intravascular replacement strategies, if needed.

The patient is positioned supine in reverse Trendelenburg position with 15° elevation. This reduces venous pressure which decreases mucosal and tumor bleeding. The head is rotated towards the surgeons and secured in place with a Mayfield horse-shoe head holder. The intraoperative image guidance system is then registered. If the tumor has intracranial extension, neurophysiological monitoring is established: somatosensory evoked potentials monitor cortical function and electromyography can be used to monitor cranial nerves III, IV, VI, and V3.²⁴

The eyes should be examined, lubricated with ointment, and protected. Because intraorbital hematoma is a rare but potentially blinding complication of these surgeries, some surgeons prefer to keep the eyelids uncovered in order to be able to continuously monitor for sudden proptosis or pupillary changes. The face is prepped with 10% povidone-iodine solution and the nasal cavity is decongested with either oxymetazoline (0.05%) or epinephrine (1:10,000) soaked cottonoids. Preoperative antibiotic prophylaxis with a third generation cephalosporin with cerebrospinal fluid (CSF) penetration is administered in cases at risk for intradural exposure.

Surgical technique

The goals of surgery are as follows: (1) resect the tumor completely, with preservation of major neurovascular structures; (2) minimize morbidity; and (3) avoid the need for radiation therapy.²⁵ To accomplish these goals, a planned approach should be set based on imaging and vascularity. This is especially important in large tumors with extension into multiple areas. Generally speaking, the first step is identification of anatomical landmarks and creation of wide corridors to access the tumor. Defining the periphery of the tumor should then ensue, avoiding manipulation of the tumor or dissection into it. If possible, control and ligation of the blood supply prior to removing the tumor will minimize blood loss and improve visualization of the tumor. Surgery is best performed by a team of surgeons, allowing 2-handed dissection of the tumor and control of bleeding. This is especially important in the sphenoid region in proximity to critical neurovascular structures.

In order to create a wide corridor, the inferior portion of the middle turbinate is often removed. Wide maxillary antrostomy, ethmoidectomy, sphenoidotomy, and posterior septectomy is performed depending on access and tumor location. The tumor can usually be bluntly dissected from

the planum sphenoidale and medial wall of the orbit without disrupting the tumor.

Often the major vascular supply is from the internal maxillary artery. Therefore, an anterior transmaxillary approach (Caldwell-Luc) is performed first in many cases to facilitate ligation (if not embolized) and provide a lateral to medial approach to the tumor. A gingivobuccal incision is made, leaving a cuff of buccal mucosa for closure. Subperiosteal dissection exposes the anterior face of the maxilla to the infraorbital nerve. In younger patients with unerupted teeth, one must be careful to avoid injury to tooth buds. A safe point of entry is usually at the intersection of a transverse line at the level of the nasal floor and a vertical midpupillary line. Navigation can also be used to confirm tooth root location. Entry into the sinus with an osteotome or drill is followed by insertion of the scope to confirm location. The opening is then widened sufficiently to fit the endoscope and 2 instruments. The mucosa is removed from the posterior maxillary sinus wall followed by removal of the bone. The bone should be removed widely, from the pterygoid muscles to the SPF (Figure 4). The fat of the pterygopalatine fossa is carefully dissected until the internal maxillary artery is identified. Once identified it can be clipped, cauterized, and then divided. Evaluation of additional small vessels follows with bipolar cauterization and division. If additional exposure is needed, especially in advanced tumors, a medial maxillectomy can augment exposure and facilitate 2-handed dissection of the lateral aspect of the pterygopalatine fossa as well as the infratemporal fossa. The contents of the pterygopalatine space are displaced anteriorly by the tumor and must be dissected from the surface of the tumor in a medial to lateral direction to better define the margins of the tumor and preserve the descending palatine branch of the maxillary nerve (Figure 5).

The nasopharyngeal component should be addressed to identify the most inferior border of the tumor. The tumor often extends into the nasopharynx and fuses with the buccopharyngeal fascia. Incision of the nasopharyngeal mucosa with an extended needle-tip electrocautery provides an inferior margin of dissection and facilitates mobilization of the tumor into the oropharynx as it is dissected later in the case. This can be done transnasally or transorally depending on the posterior-inferior extent of the tumor.

Next, the sphenoid sinus and surrounding bone are addressed. Diligent dissection is needed to prevent inadvertent injury to any ICA feeders to the tumor. If any bone erosion over the carotid, optic nerve, or cavernous sinus is present, one must recognize this ahead of time through careful evaluation of the imaging. Within the sphenoid sinus, dissection in a plane between the tumor and the bony skull base will allow identification of important landmarks including the optico-carotid recess, sella turcica, and planum sphenoidale.

JNAs frequently extend into the base of pterygoid and pterygoid (vidian) canal and this can be a frequent site of residual tumor (Figure 6). If tumor is present in the ptery-

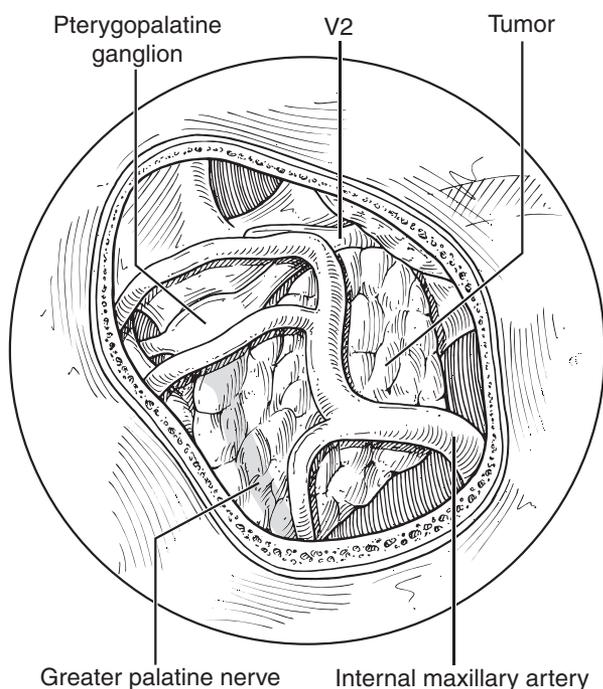


Figure 5 Anatomy of the pterygopalatine space as seen from a Caldwell-Luc approach showing the internal maxillary artery and its branches, V2 main trunk as well as the pterygopalatine ganglion and greater palatine nerve, and a frequent location of JNA tumor.

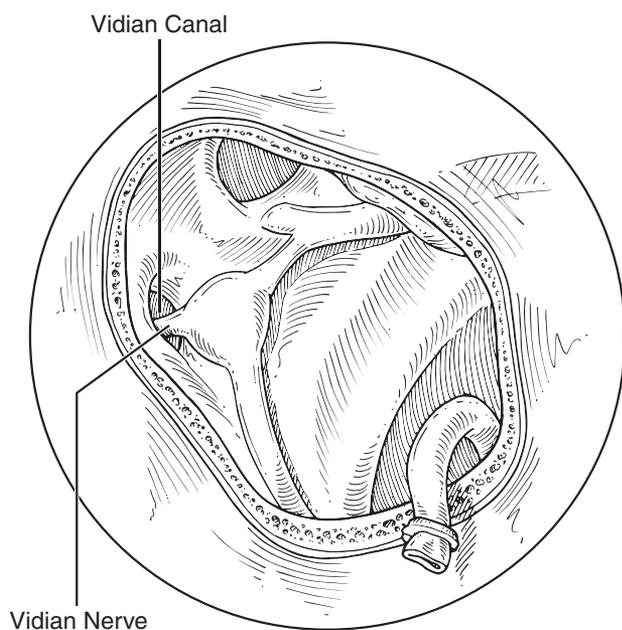


Figure 6 Anatomy of the basisphenoid, pterygoid plates, and vidian (AKA pterygopalatine) canal. Drilling of this bone is often necessary to remove tumor in this area and extending through the vidian canal.

goid canal, cavernous sinus, or intracranially, it is important to delineate and visualize the course of the carotid artery prior to dissection. Navigation and Doppler probe are helpful in localizing the ICA. The vidian artery is the most common ICA contributor and should be approached carefully and cauterized and divided. Descriptions of the vidian canal, contents, and anatomical relationships have been previously published.²⁶ After addressing the vidian artery, the bone of the basisphenoid and pterygoids is drilled to remove tumor from these areas. Hemostasis from venous oozing can be managed with Floseal, thrombin soaked gelfoam, or similar hemostatic agents.

Finally, any tumor extending into the orbit, Meckel's cave, and any intracranial component is dissected. The steps of resection will depend on the extension of the tumor. Often no reconstruction is necessary. If there is vessel exposure or dural exposure, an adipose graft is recommended for coverage. The muscle and adipose tissue in the masticator space may be covered with fibrin glue.

Management of residual tumor

If tumor in a critical neurovascular region cannot be resected, adjuvant options include observation and radiation. While it should not be relied upon, spontaneous regression of residual JNA has been reported.²⁷⁻³⁰ Because of the morbidity associated with radiation, especially in this young population, often residual will be closely monitored, following with serial imaging to determine if growth occurs. If growing, the next step is multidisciplinary consultation and discussion to weigh the risks and benefits of irradiation versus resection. Most residual/recurrent tumors are amenable to endoscopic resection.

Complications and morbidity

The most common morbidity is extensive blood loss and need for transfusion.³¹ This is not uncommon, especially in advanced tumors and those with multicomponent blood supply. The likely need for blood transfusion should be discussed with the patient and parents before surgery. Often the necessary extent of surgery will result in planned morbidity such as dry eye from loss of tearing due to vidian nerve or sphenopalatine ganglion resection.³² Hypoesthesia in the distribution of V2 or V3, trismus, and/or posterior septal defect may occur depending on extent of surgery. Complications congruent with all sinus and skull base surgeries are possible as well including but not limited to: extraocular muscle injury, vision loss, cerebrospinal fluid leak, postoperative epistaxis, sinusitis, hyposmia, or anosmia.

Staging of surgery

Advanced JNAs, especially those with ICA vascular supply are at risk for significant blood loss. Preoperative

discussion with anesthesia should set a blood loss limit and close communication should be ongoing throughout the procedure. It is recommended that this limit be no more than half of the intravascular volume. If that limit is neared, the surgeon should plan to cease surgery for that day. The patient and family should be prepared for staging of surgery if blood loss is excessive. A combination of cauterization and packing can be used for control of bleeding. Sometimes, multiple stages are necessary to achieve complete resection. The timing of additional stage(s) will depend on the stability of the patient; again, a multidisciplinary discussion is prudent.

Postoperative treatment

Patients are monitored in a pediatric intensive care unit or floor, depending on the amount of blood loss and extent of dissection. Significant blood loss or intracranial dissection warrant intensive care unit level monitoring. Length of packing will also be determined by blood loss and extent of dissection. Younger patients who did not tolerate nasal endoscopy preoperatively may need a scheduled postoperative debridement under anesthesia.

MRI is utilized for follow-up imaging as it can differentiate postoperative reparative processes and inflammation from tumor recurrence. Initial imaging is often between 1 and 3 months, knowing that residual inflammation may be present. This initial imaging not only evaluates for tumor but establishes a baseline for monitoring. MRI intervals are typically every 6 months for 12-18 months, followed by yearly scans for at least 5 years and through the duration of the pubescent period. Clinical evaluation with nasal endoscopy should be performed at similar intervals. Tumor recurrence is most likely due to incomplete resection of the primary tumor and usually occurs within 6-36 months.^{1,2,13,31}

Outcomes

Recurrence rates vary widely from 7% to 45%^{1,2,4,6,18,31,33,34} with increased recurrence rates in more advanced tumors. Blood loss also has similar variability with means ranging from approximately 500-1500 mL in systematic reviews.^{2-4,6,18} In advanced tumors (UPMC IV and V, Radowski IIIA and IIIB), staged surgery is needed in approximately 50% of patients, with 14%-33% having residual disease.^{1,2,6,16}

Disclosure

The authors reported no proprietary or commercial interest in any product mentioned or concept discussed in this article.

Conflict of interest

There are no conflicts of interest.

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