INTRODUCTION

A rare tumor that comprises only 0.5% of neoplasms in the head and neck (Herman 1999, Tewfik 1999), juvenile nasopharyngeal angiofibroma (JNA) is pathognomonically characterized as a benign vascular tumor located in the posterior nasopharynx of adolescent males. Although not a malignant process, JNA is known for its locally invasive spread with progressive growth that can attribute to a significant degree of morbidity commonly related to either intracranial extension or massive hemorrhage.

JNA was first described in conjunction with nasal polyps by Hippocrates in the 5th century BC (Babyn 2005), but it was Chelius who distinguished it as one associated with puberty in 1847. Initially regarded as a fibrous nasal polyp at that time, the term “angiofibroma” was not coined until Friedberg did so in 1940 (Gullane 1992).

DEMOGRAPHICS

There is a strong predilection for JNA to affect teenage males, typically between 14-15 years of age, although the reported age range spans between 10-25 years of age (Ardehali 2010). It exhibits a generally indolent course with symptoms commonly lasting for 6-12 months prior to diagnosis, with approximately 70% of individuals already demonstrating at least a stage II clinical presentation upon diagnosis (Radkowski 1996).

ORIGIN

The internal maxillary artery is the most common vascular source from which JNAs arise. Other known vessels include the ascending pharyngeal artery as well as the external, internal, and common carotid arteries. While not a frequent occurrence, JNAs have also been known to develop from blood supply contralateral to the side they form. The exact site that JNA originates from remains controversial although most accept the assertion that it involves the posterolateral nasal wall at the sphenopalatine foramen. However, there is a minority that believes JNA is related more to the vidian canal.
Similarly, the pathophysiology to JNA formation remains hotly contested. Given its typical location near the superior margin of the sphenopalatine foramen, there has been some postulation that the underlying mechanism derives from the embryologic chondrocartilage of the skull bones (Schiff 1959), particularly at the trifurcation of the palatine bone, horizontal ala of the vomer, and the root of the pterygoid process (Neel 1973, Bremer 1986).

Given its essential exclusivity to adolescent males, there has been some belief that JNA development is related to the pituitary androgen-estrogen axis (Schiff 1959), especially with the observation of androgen and estrogen receptors noted on some JNA cells (Montag 2006). While plausible, there has been no endocrinologic abnormality identified among individuals with JNA (Neel 1973, Sessions 1981, Shikani 1992). Other theories suggest a role for vascular endothelial growth factor receptor-2, transforming growth factor beta 1, or insulin-like growth factor 2 (Coutinho-Camillo 2008), while other ideas suspect that JNA is more of a vascular hamartoma (Girgis 1973) or inflammatory reaction.

**HISTOLOGY**

Histologically, JNA exhibits cells of myofibroblast origin surrounded by a fibrous pseudocapsule. There are multiple vascular channels dispersed within the neoplasm composed of abundant endothelial cells embedded in a collagenous tissue network. An important hallmark is the lack of a true muscular layer, and this absence precludes any form of vasoconstriction and is felt to contribute to the tumor’s high propensity for hemorrhage (Liu 2002).

**PRESENTATION**

The manner JNA conventionally declares itself is with unilateral nasal obstruction or recurrent epistaxis in an adolescent male. Physical examination will commonly reveal a smooth and lobulated, compressible purplish or reddish nasal mass. Surrounding structures in the nasopharynx may result in atypical symptoms including middle ear effusions and conductive hearing loss with blockage of the Eustachian tubes, rhinolalia, palatal deformity, hyposmia, or anosmia.

With more advanced tumors, anterior extension may impede the nasolacrimal duct and result in dacrocystitis. Further progression may manifest with a facial swelling or proptosis while encroachment toward the intracranial vault will lead to headaches or cranial neuropathies. Massive hemorrhage is typically affiliated with a large tumor burden.

**NATURAL HISTORY**

The key element of JNA behavior is submucosal extension toward the pterygomaxillary fossa, infratemporal fossa, or the superior orbital fissure (Radvkowski 1996, Enepekides 2004). Involvement of the superior orbital fissure facilitates invasion of the cavernous sinus or orbit. Intracranial extension occurs in 20-36% (Close 1989, Wiatrak 1993), typically with either the anterior or middle cranial fossae or the pituitary parasellar region. Despite the morbidity associated with intracranial spread in general, actual dural penetration is rare with JNA and is one reason some surgeons do not indiscriminately regard all such cases as unresectable.

Complete surgical extrication is vital to definitive treatment of JNA as an incomplete resection is the leading etiology for recurrence, estimated to occur in up to 46% depending on
surgical technique (Fagan 1997). The risk is higher for tumor extension to the sphenoid sinus, pterygoid base, and the clivus. Interestingly, spontaneous regression has been described in some cases, particularly in individuals older than 25 years of age leading to speculation that this phenomenon is related to post-pubertal hormonal changes (Tosun 2008). Others have contested this with the observation that regression is only possible for residual tumors that had undergone prior treatment (Neel 1973, Stansbie 1986, Mishra 1989).

DIFFERENTIAL DIAGNOSIS

A myriad of other neoplasms can masquerade with a similar appearance as JNA, which is an important consideration given its overall rarity. Pyogenic granulomas and hemangiopericytomas can present in the nasal passages and also be affiliated with a certain degree of epistaxis. Nasal polyps are other masses more commonly encountered in the nasal cavity, albeit with a lower propensity for hemorrhage. Other tumors involving the skull base can emulate a locally advanced JNA such as a craniopharyngioma, chordoma, chondrosarcoma, nasopharyngeal carcinoma, olfactory neuroblastoma, or rhabdomyosarcoma.

STAGING

The first classification scheme employed to better define JNA was introduced by Sessions in 1981, and there have been multiple modifications since then including those described by Fisch (1983), Chandler (1984), and Andrews (1989). The staging system introduced by Radkowski constitutes the most recent adaptation and focuses more on the tendency for JNA to extend posteriorly toward the pterygoid plates and also distinguishes the degree of skull base erosion present (Radkowski 1996). Table 1 presents this scheme below. Ultimately, however, no classification system has been universally accepted, and it is not uncommon for various articles to discuss their results using different systems.

<table>
<thead>
<tr>
<th>STAGE</th>
<th>FEATURES</th>
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<tbody>
<tr>
<td>IA</td>
<td>Limited to nose or nasopharynx</td>
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<tr>
<td>IB</td>
<td>Extension into at least one paranasal sinus</td>
</tr>
<tr>
<td>IIA</td>
<td>Minimal extension through sphenopalatine foramen, Includes minimal part of medial pterygomaxillary fossa</td>
</tr>
<tr>
<td>IIB</td>
<td>Full occupation of pterygomaxillary fossa with Holman-Miller sign, Lateral or anterior displacement of maxillary artery branches, May have superior extension with orbital bone erosion</td>
</tr>
<tr>
<td>IIC</td>
<td>Extension through pterygomaxillary fossa into cheek, temporal fossa, or posterior to pterygoids</td>
</tr>
<tr>
<td>IIIA</td>
<td>Skull base erosion with minimal intracranial extension</td>
</tr>
<tr>
<td>IIIB</td>
<td>Skull base erosion with extensive intracranial extension +/- cavernous sinus</td>
</tr>
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</table>

Table 1. Radkowski JNA Classification System
**RADIOLOGY**

JNA exhibits a characteristic appearance on roentgenology that often makes obtaining a biopsy redundant. Such a diagnostic approach is favorable given the potentially high risk for significant hemorrhage from such neoplasms. Key features to support a diagnosis of JNA include the presence of a vascular mass with an epicenter at the posterior nasal cavity near the medial pterygopalatine fossa, the presence of bony modeling—but not destruction—with tumor growth, and the lack of regional or distant metastasis (Amdur 2011). For atypical extension or unexpected rapid growth, a biopsy should be considered to assess for other neoplasms aside from JNA.

JNA will demonstrate an intense homogenous contrast enhancement on computed tomography (CT). An important advantage of CT imaging is its superiority in evaluating bony details compared to magnetic resonance imaging (MRI), and this is best exemplified with an anterior bowing to the posterior maxillary sinus wall that JNA is commonly associated with known as the Holman-Miller sign. Widening of the sphenopalatine foramen may also be observed.

Diffuse intense contrast enhancement is also noted with JNA on both T1- and T2-weighted MRI. The utility of MRI is demonstrated with its improved soft tissue differentiation compared to CT, as it is able to delineate mucosal inflammation versus sinus fluid and assist with accurate tumor staging. MRI is also crucial in assessing the degree of intracranial extension, and flow voids within the numerous tumor vessels have been described on MRI scans (John 2006).

**ANGIOGRAPHY**

JNA’s dependence on the carotid arterial system has understandably directed attention to evaluate the potential benefit of angiography. In addition to identifying the source vessel, angiography may serve as a vector for embolization prior to surgical excision. Furthermore, a balloon occlusion test of the carotid may be conducted to facilitate appropriate preoperative counseling (Danesi 2008). Despite its utility in managing JNA, angiography is not a required diagnostic endeavor and surgical excision may still be performed in the absence of it (Ahmad 2008).

Preoperative embolization is generally undertaken 24-72 hours prior to resection and often employs either gelfoam or polyvinyl alcohol foam. Gelfoam generally lasts for approximately two weeks while polyvinyl alcohol foam is more permanent. The rationale is that occluding the responsible artery from which the JNA originates will decrease intraoperative blood loss and even decrease the tumor size to augment resectability. Complications associated with embolization include the potential for cerebrovascular accident if one of the carotids is affected, blindness if the ophthalmic artery is embolized, and necrosis of skin and soft tissue depending on which vascular supply has been compromised. Facial paralysis has also been reported, but this was in conjunction with a preauricular approach for surgical excision and it is plausible that the facial palsy may be attributed more to the surgical excision as opposed to the embolization.

A number of studies support the role of embolization in reducing intraoperative blood loss (Moulin 1995, Li 1998, Liu 2002). However, Moulin reported statistical significance of this
occurrence only for larger staged tumors while Liu noted similar findings only for smaller ones limited to the nasal cavity or nasopharynx. Liu also compared embolization with carotid ligation and did not appreciate a difference between the two in regards to hemorrhage.

**SURGERY**

The primary treatment modality is surgical excision (Marshall 2006), and it remains a viable option in cases of intracranial extension (Bales 2002). While preoperative embolization is regarded as a beneficial adjuvant therapy, it can obscure tumor borders and complicate resection (Andrade 2007). Recurrence is highly related to incomplete removal, with most reports estimating that this occurs in 6-37.5% of surgeries (Fagan 1997, Hosseini 2005, Cansiz 2006, Hyun 2011) within six months postoperatively (Tyagi 2006). However, the surgical plan needs to consider that a more extensive resection in an attempt to prevent recurrence is inherently associated with a higher degree of morbidity. Areas of most concern include the pterygoid fossa, clivus, basisphenoid, sphenoid diploe, cavernous sinus, and intracranial vault.

A transpalatal approach involves splitting and retracting the soft palate to expose the hard palate. A portion of the palatine bone and inferior pterygoid plate is then removed to facilitate access to the nasopharynx from which the JNA can be removed. In general, the transpalatal approach is ideal for tumors limited to the sphenoid sinus as there tends to be limited lateral exposure, but Le Fort I osteotomies may permit access to the paranasal sinuses, pterygopalatine fossa, and infratemporal fossa (Yiotakis 2008). The major risks associated with this approach include palatal dehiscence and the formation of an oroantral fistula.

Creating a lateral rhinotomy incision provides an external approach to access more of the nasal cavities and nasopharynx, allowing for resection of larger tumors. A number of variations of this have been introduced that revolve around making a Weber-Fergusson incision with various extensions to customize the exposure necessary to remove a JNA. This includes combinations with a Lynch extension, lateral subciliary extension, and subciliary and supraciliary extensions. While exposure is greatly enhanced compared to a transpalatal approach, it comes with the caveat that a potentially unsightly scar may develop.

The midfacial degloving technique attempts to recreate the superior exposure afforded by a lateral rhinotomy but without the associated external incisions. In general, this involves creating a gingivobuccal incision coupled with intercartilaginous and transfixion incisions similar to those made in an external rhinoplasty. This is to essentially translocate the soft tissue of the midface off the bony midface of the skull, and access into the nasal passages is provided via Le Fort I osteotomies.

While cosmetically favorable, midfacial degloving is affiliated with a number of potential sequelae with nasal crusting being the most common. Others include epistaxis, nasal vestibular stenosis, nasolacrimal duct obstruction, facial paresthesia, and facial nerve palsy. An oroantral fistula could still arise, and carotid artery rupture is a rare but previously reported complication.

Historically, locally advanced JNAs were addressed with a large, extensive infratemporal fossa approach with possible craniotomy. As surgical techniques have progressively been refined, anterior access is now felt to be sufficient for most intracranially invading tumors and use of a craniotomy is less common. A transfacial, transmaxillary approach is generally utilized.
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for such situations (Elsharkawy 2010), and a medial maxillectomy is often believed to be required to access the medial infratemporal fossa, cavernous sinus, sphenoid sinus, or anterior skull base (Fagan 1997). There is growing sentiment that endoscopic access is feasible in select cases (Danesi 2008), and others have advocated a combined endoscopic and external approach (Douglas 2006).

Much interest has been invested in endoscopic resection of JNA given its generally positive results with avoidance of incisions. The general approach involves creating a middle meatus antrostomy with a middle turbinatectomy as needed for exposure. With a large enough antrostomy, the posterior maxillary sinus wall can then be removed to allow ligation of the sphenopalatine artery and any other vascular contributions in the area. Tumor resection from the pterygopalatine fossa can then proceed. Some disadvantages with endoscopic removal include the difficulty in employing simultaneous instrumentation (Wormald 2003), limited tumor mobilization inside the nasal cavity (Douglas 2006), and significantly impaired visualization with brisk hemorrhage (Yiotakis 2008).

One of the more common complications related to endoscopic tumor resection includes nasal synechia. Given the various neurovascular structures nearby, other possibilities include lacrimal duct stenosis, cheek paresthesia with damage to the maxillary nerve, and vision changes if cranial nerves III or IV are impacted. Sphenoid mucocele formation has been reported in addition to few accounts of cavernous sinus injury.

Acknowledging variations among institutions, stage I and II tumors have been felt to be best addressed with either transpalatal or endoscopic methods while a lateral rhinotomy or midfacial degloving was reserved for stage III tumors (Hosseini 2005). Others have generally followed suit, but there has been a shift favoring endoscopic removal of JNA (Mann 2004). The endoscopic approach was observed to manifest with less intraoperative blood loss, a shorter operative time, and a brief hospitalization as compared to either the transpalatal and midfacial degloving techniques for stage I and II tumors (Yiotakis 2008). Endoscopic removal has been deemed feasible for even stage IIIA tumors (Wormald 2003), and this is further augmented with decreased intraoperative and postoperative hemorrhage and a shorter hospitalization when combined with preoperative embolization (Ardehali 2010).

RADIATION

Originally reserved for unresectable or life-threatening tumors, radiotherapy (XRT) is an alternative treatment modality in managing JNA. Therapeutic results were appreciated with dose ranges between 30-46Gy (McAfee 2006, Chakraborty 2011), and primary XRT has been demonstrated to be just as effective as surgery with a 15% recurrence rate (Reddy 2001). The associated complication rate is low but more notable ones include temporal lobe necrosis (Lee 2002), cataracts (Amdur 2011), arrest of craniofacial growth, induction of future malignancies (Witt 1983) such as a fibrosacoma (Makek 1989), hypopituitarism, and osteoradionecrosis (Witt 1983).

XRT has historically been regarded to attain tumor control rates between 80-85% (Briant 1978, Cummings 1984, Reddy 2001), although Amdur reported control rates up to 90% and concluded that neoadjuvant XRT prior to a planned subtotal resection and adjuvant XRT for microscopically positive surgical margins were of minimal benefit. Furthermore, elective nodal...
irradiation was deemed unnecessary, and most recurrences after XRT would manifest by two years after treatment. The diagnosis of JNA should be questioned if there was a size decrease of less than 50% by one year post-treatment, and while there was no evidence to support the notion, there was concern that tumor hypoxia from preoperative embolization might impart radioresistance (Amdur 2011).

**MEDICAL AND OTHER THERAPY**

Chemotherapy has been investigated as treatment options in cases of JNA that had recurred after surgery and XRT, but a low therapeutic benefit coupled with poorly tolerated side effects has made this a rarely used endeavor (Lee 2002).

Given its sole demographic of adolescent males, hormonal therapy was hypothesized to decrease the size and vascularity to JNAs via estrogens or antiandrogens. The theory was that the reduced vascularity would support decreased intraoperative blood loss during surgical resection, and it was hoped that the antiandrogenic push would promote tumor regression. However, the physical and psychological side effects from such medications are understandably poorly tolerated in such young patients and serve as a significant impediment to their use, especially given the lack of efficacy with flutamide (Labra 2004).

Other treatment modalities that have been reportedly implemented to address JNA include coblation (Ruiz 2012), cryotherapy (Witt 1983, Spector 1988), electrocoagulation (Schiff 1959), gamma knife (Dare 2003, Park 2006), harmonic scalpel (Chen 2006), interstitial brachytherapy (Reddy 2001), KTP-laser embolization (Hazarika 2002), and sclerotherapy (Schiff 1959). However, further studies are warranted to further elucidate their role in the mainstay treatment of JNAs.

**CONCLUSION**

JNA is a rare vascular neoplasm localized to the posterolateral nasopharynx of adolescent males that typically presents with either nasal obstruction or recurrent epistaxis. Surgery and XRT constitute the primary treatment options, but given the rarity by which JNA occurs, it is important to evaluate for other neoplasms that may also manifest in the nasal cavity.

**REFERENCES**


