

TITLE: Juvenile Nasopharyngeal Angiofibroma
SOURCE: Grand Rounds Presentation, UTMB, Dept. of Otolaryngology
DATE: January 3, 2007
RESIDENT PHYSICIAN: Garrett Hauptman, MD
FACULTY PHYSICIAN: Seckin Ulualp, MD
SERIES EDITORS: Francis B. Quinn, Jr., MD and Matthew W. Ryan, MD

"This material was prepared by resident physicians in partial fulfillment of educational requirements established for the Postgraduate Training Program of the UTMB Department of Otolaryngology/Head and Neck Surgery and was not intended for clinical use in its present form. It was prepared for the purpose of stimulating group discussion in a conference setting. No warranties, either express or implied, are made with respect to its accuracy, completeness, or timeliness. The material does not necessarily reflect the current or past opinions of members of the UTMB faculty and should not be used for purposes of diagnosis or treatment without consulting appropriate literature sources and informed professional opinion."

Juvenile nasopharyngeal angiofibroma (JNA) is a rare, benign, vascular neoplasm that accounts for less than 0.5% of all head and neck tumors. JNAs occur almost exclusively in the nasopharynx of adolescent males. The site of origin of JNA remains controversial. Some believe that it takes origin from the superior lip of the sphenopalatine foramen at the junction of the pterygoid process of the sphenoid bone and the sphenoid process of the palatine bone. Others claim that it arises from the bone of the vidian canal. JNAs are slow growing and initially expand intranasally into the nasopharynx and nasal cavity and then into the pterygomaxillary space. Over time, JNAs will eventually erode bone and invade the infratemporal fossa, orbit, and middle cranial fossa. The blood supply to these benign tumors is most commonly from the internal maxillary artery, but may also be supplied by the external carotid artery, the internal carotid artery, the common carotid artery, or the ascending pharyngeal artery. Histologically, JNAs originate from myofibroblasts. The tumor lacks a capsule and spreads submucosally. It is composed of a fibrous abundance of single endothelial cell lined vascular spaces or channels. These channels are surrounded by a collagenous tissue network and lack a complete muscular layer.

As always, patient history and physical examination are of paramount importance in initiating patient evaluation. JNAs classically presents with unilateral nasal obstruction, epistaxis, and nasopharyngeal mass in adolescent males with an average age of onset of 15 years of age. Conductive hearing loss, dacryocystitis, rhinolalia, hard and soft palate deformity, and hyposmia or anosmia are not uncommon presentations. Advanced lesions may cause facial swelling, proptosis, cranial neuropathy, and massive hemorrhage. On physical examination, a smooth lobulated mass is often noted in the nasopharynx and/or lateral nasal wall. They have been described as pale, purplish, red-gray, and beefy red. JNAs are compressible. A patient presenting with the above described signs and symptoms should not undergo biopsy due to the risk of bleeding.

During initial evaluation, contrast tomography (CT) and magnetic resonance imaging (MRI) may be used to evaluate tumor extent. CT Scan is excellent for evaluation of bone detail and will enhance with contrast. Furthermore, the characteristic anterior bowing of the posterior maxillary wall due to the presence of a mass in the pterygomaxillary space known as the

Holman-Miller sign is a finding noted on CT Scan. MRI allows for examination of soft tissue and differentiation of tumor from mucosal inflammation and sinus fluid. Additionally, improved detail of the cribiform plate and the cavernous sinus is noted. Preoperative arteriography is helpful for the evaluation of feeding vessels and allows for embolization of JNAs.

There are a variety of staging criteria developed when evaluating JNAs which include those developed by Radkowski, Fisch, Andrews, and Sessions. The Radkowski criteria developed in 1996 is the most recently developed staging system and appears most commonly in recent literature on JNAs.

Treatment options for JNAs include surgery, radiation therapy, chemotherapy, and hormone therapy. Surgery is the gold standard of treatment and will be discussed further. External beam radiation is generally reserved for larger and/or unresectable tumors and tumors that are life threatening due to their location. The reason for limited use of radiation as a treatment modality is due to the potential carcinogenic side effects of radiation. Local control rates and recurrence rates are comparable to surgical results, however severe complications are encountered including growth retardation, temporal lobe radionecrosis, panhypopituitarism, cataracts, and radiation induced keratopathy. Tumor recurrence after radiation therapy may be very slow. Treatment regimens are variable- one proposed regimen used at the University of Florida is 30 to 35 Gy at 1.8 Gy per fraction. Chemotherapy is used when previous surgery and radiation have failed. Hormone therapy has been proposed due to the androgen receptors associated with JNAs in an attempt to decrease tumor size and vascularity. The rationale behind this treatment is that hormonal stimulation appears to play an important role with regards to growth of JNAs. Sex hormones have been used to attempt to induce regression. Estrogen has been shown to decrease size and vascularity of the tumor, but has feminizing side effects, variable response, and risk of cardiovascular complications. The use of flutamide, an androgen receptor blocker, has been found to have no distinct advantage in treatment of JNAs. Both serious side effects and unproven efficacy have resulted in hormone therapy falling out of favor as a treatment modality.

The treatment of choice in the vast majority of patients is surgical resection. Preoperative selective arterial embolization of feeding vessels from the external carotid artery has significantly decreased intraoperative blood loss and facilitated resection of larger tumors. Embolization is typically performed 24-72 hours prior to resection. Materials often used include gelfoam and polyvinyl alcohol foam. Gelfoam lasts approximately two weeks, while polyvinyl alcohol foam is more permanent. Studies have shown preoperative embolization to significantly reduce blood loss. Some complications encountered with the use of this procedure include brain and ophthalmic artery embolization, facial paralysis, and skin and soft tissue necrosis.

Traditional approaches for JNAs include transoral, transfacial, and combined craniofacial approaches (more specifically transpalatal, transantral, transnasal, lateral rhinotomy, midfacial degloving, LeFort 1 osteotomy, and infratemporal fossa approaches). Qualities shared by these approaches include oral and/or facial incisions and the need to remove or divide bone to gain access to the tumor. Advances in endoscopic sinonasal surgery and the ability to embolize these tumors preoperatively have made many of the resection amenable to endoscopic technique. The decision to perform JNA resection endoscopically should be based on the experience and skill of the surgeon as well as the extent of the tumor (ie. the lateral extent of the tumor must be

accessible endoscopically). The surgeon must also be willing and able to convert to an open approach if necessary. The morbidity of open approaches must be compared to the morbidity of incomplete tumor resection by performing the procedure via an endonasal approach. A study by Mann et al in 2004 examined tumor and surgical trends with regards to JNAs. Results showed no change in the staging distribution over the twenty year time period examined. There was a change in surgical technique which was a shift towards endoscopic resection in comparison to open resection. The extent of resection with endoscopic techniques is case dependent. Patient selection for endoscopic resection is of paramount importance for a successful outcome. It has been suggested that tumors involving the ethmoid, maxillary, or sphenoid sinus, the sphenopalatine foramen, nasopharynx, or pterygomaxillary fossa and have limited extension into the infratemporal fossa are amenable to endoscopic resection. JNAs that involve the orbit or middle cranial fossa are not ideal for endoscopic excision. The ability to convert to an open procedure is necessary whenever an endoscopic approach is entertained as the surgical approach. The advantages of performing endoscopic resection include improved cosmesis by avoiding external incisions and it is the most direct approach to the tumor. Several important points deserve discussion with regards to the endoscopic approach. Exposure is obviously necessary for successful tumor removal. A large maxillary antrostomy with wide visualization of the posterior maxillary wall enhances exposure. Additionally, a complete ethmoidectomy is helpful. Image guidance helps identify key structures.

Despite encouraging outcomes achieved with endoscopic resection of JNAs, it should not be considered the standard of care. Open approaches are favored by some surgeons and remain indicated for larger JNAs. The morbidity of open approaches must be weighed against the morbidity of incomplete tumor resection and continued tumor growth. Furthermore, all open approaches can be supplemented by the use of endoscopes. The illumination, magnification, and multi-angled view possibilities can facilitate open approaches.

JNAs have the potential to regress which usually occurs when the patient is 20-25 years old. Complete regression does not occur in all patients. Spontaneous regression is valuable for residual tumor following treatment. Recurrence rates have been reported between 30 and 50%. Since JNAs are benign and not multifocal, recurrence reflects incomplete initial resection and is more appropriately classified as persistent disease. Post-operative surveillance is performed by clinical evaluation including nasal endoscopy and imaging with CT and/or MRI. Timing of imaging is variable depending on the surgeon.

The major recent advancement in the treatment of JNAs has been the use of an endoscopic approach. When used for relatively small tumors, this technique can decrease morbidity substantially. Additionally, endoscopic technique can be used in conjunction with open approaches to improve visualization. The treatment of advanced lesions with intracranial extension is a challenging problem. Complete resection using the least morbid approach should be attempted whenever possible. Unresectable residual disease should be irradiated if the patient becomes symptomatic or if the tumor progresses on serial imaging. Primary radiation should be used when the morbidity of surgical resection is unacceptable.

Bibliography

Bremer JW, Neel HB III, De Santo LW, et al. Angiofibroma: Treatment trends in 150 patients during 40 years. *Laryngoscope* 1986; 96: 1321-1329.

Cansiz H, Guvenc MG, Sekecioglu N. Surgical approaches to juvenile nasopharyngeal angiofibroma. *J Craniomaxillofac Surg*. 2006 Jan;34(1):3-8. Epub 2005 Dec 15.

Cummings BJ, Blend R, Keane T, et al. Primary radiation therapy for juvenile nasopharyngeal angiofibroma. *Laryngoscope* 1984; 94: 1599-1605.

Douglas R, Wormald PJ. Endoscopic surgery for juvenile nasopharyngeal angiofibroma: where are the limits? *Curr Opin Otolaryngol Head Neck Surg*. 2006 Feb;14(1):1-5.

Enepekides DJ. Recent advances in the treatment of juvenile angiofibroma. *Curr Opin Otolaryngol Head Neck Surg*. 2004 Dec;12(6):495-499.

Hardillo JA, Vander Velden LA, Knecht PP. Denker operation is an effective surgical approach in managing juvenile nasopharyngeal angiofibroma. *Ann Otol Rhinol Laryngol*. 2004 Dec;113(12):946-950.

Herman F, Lot G, Chapot R, et al. Long term follow up of juvenile nasopharyngeal angiofibromas: Analysis of recurrences. *Laryngoscope* 1999; 109: 140-147.

Hosseini SM, Borghei P, Borghei SH, Ashtiani MT, Shirkhoda A. Angiofibroma: an outcome review of conventional surgical approaches. *Eur Arch Otorhinolaryngol*. 2005 Oct;262(10):807-812. Epub 2005 Mar 1.

Labra A, Chavolla-Magana R, Lopez-Ugalde A, Alanis-Calderon J, Huerta-Delgado A. Flutamide as a preoperative treatment in juvenile angiofibroma (JA) with intracranial invasion: report of 7 cases. *Otolaryngol Head Neck Surg*. 2004 Apr;130(4):466-469.

Lee JT, Chen P, Safa A, Juliard G, Calcaterra TC. The role of radiation in the treatment of advanced juvenile angiofibroma. *Laryngoscope*. 2002 Jul;112(7 Pt 1):1213-1220.

Liu L, Wang R, Huang D, Han D, Ferguson EJ, Shi H, Yang W. Analysis of intra-operative bleeding and recurrence of juvenile nasopharyngeal angiofibromas. *Clin Otolaryngol*. 2002; 27:536-540.

Mann WJ, Jecker P, Amedee RG. Juvenile angiofibromas: changing surgical concept over the last 20 years. *Laryngoscope*. 2004 Feb;114(2):291-293.

Pryor SG, Moore EJ, Kasperbauer JL. Endoscopic versus traditional approaches for excision of juvenile nasopharyngeal angiofibroma. *Laryngoscope*. 2005 Jul;115(7):1201-1207.

Radkowski D, McGill T, Healy GB, et al. Angiofibroma. *Archives of Otolaryngology*.

Volume 122(2), February 1996, pp 122-129

Reddy KA, Mendenhall WM, Amdur RJ, Stringer SP, Cassisi NJ. Long-term results of radiation therapy for juvenile nasopharyngeal angiofibroma. *Am J Otolaryngol.* 2001 May-Jun;22(3):172-175.

Schick B, Kahle G, Hassler R, Draf W. Chemotherapy of juvenile angiofibroma--an alternative? *HNO.* 1996 Mar;44(3):148-152. German.

Tosun F, Ozer C, Gerek M, Yetiser S. Surgical approaches for nasopharyngeal angiofibroma: comparative analysis and current trends. *J Craniofac Surg.* 2006 Jan;17(1):15-20.