Juvenile nasopharyngeal angiofibroma: current treatment modalities and future considerations

John M. Hodges · A. S. McDevitt · A. I. El-Sayed Ali · M. E. Sebelik

Abstract Juvenile angiofibroma (JNA) is a relatively uncommon, highly vascular and benign tumor that presents most commonly in adolescent males. Symptoms may persist from months to years and often times, these tumors are asymptomatic until they increase and encroach on critical structures. Because of technological advances both in surgery and radiology, management of JNA patients has been refined. With the advent of more sophisticated capabilities such as CT, MRI, intensity-modulated radiation therapy (IMRT), stereotactic guidance systems as well as advanced embolization techniques, these tumors can be diagnosed and managed more effectively.

Patients with juvenile angiofibroma (JNA) are typically silent for years and often present with epistaxis, nasal obstruction, facial numbness, rhinorrhea, ear popping, sinusitis, cheek swelling, visual changes and headaches. In addition to these symptoms, up to one-third of patients with this condition may present with proptosis or other orbital involvement, which are late symptoms and findings.

Most physicians agree that surgery is the primary treatment modality for the early-stage disease process. However, controversy arises regarding the best treatment

when a patient presents with more locally advanced disease involving widespread cranial-based extension or intracranial involvement which may necessitate a combination of treatment modalities including surgery and postoperative radiation.

With the advancement of endoscopic surgery, there have been a number of cases reporting the value of its use. The purpose of this review, however, will address not only endoscopic alternatives, but will discuss other treatment options as reported in the literature. Robotic surgery of the skull base for JNA is something to expect for the future.

Finally, with the advent of IMRT and an image-guided robotic radiotherapy delivery system, some researchers speculate that this will result in less objections for radiation in general and certainly less reservations for the use radiotherapy in certain circumstances, i.e. patient refusal of surgery or extensive non-resectable or recurrent JNA tumors.

Keywords Angiofibroma · Vascular tumor · Skull base · Endoscopic surgery · Image guided robotic radiotherapy · IMRT · Cyberknife · Embolization

J. M. Hodges¹ · A. S. McDevitt² · A. I. El-Sayed Ali³ · M. E. Sebelik⁴

¹Division of Otolaryngology, VA Medical Center - Memphis, University of Tennessee, Department of Otolaryngology Head and Neck Surgery, Memphis, TN, USA

²University of Memphis, Memphis, TN, USA.

³Zagazig University, Zagazig, Egypt

⁴Dept of Otolaryngology Head and Neck Surgery, VA Medical Center, Memphis, University of Tennessee, TN, USA

J. M. Hodges (✉)
E-mail: amcdevitt@att.net

Juvenile nasopharyngeal angiofibroma: current treatment modalities

Juvenile angiofibroma (JNA) is a benign, slowly growing, highly vascular and locally aggressive vasoformative neoplasm that presents most commonly in adolescent males with a median age of 14 years [1]. Although it is the most common benign neoplasm of the nasopharynx [2], it is a relatively rare, sporadic tumor and represents approximately 0.5% of all head and neck tumors [3]. The majority of these patients (75%) present with epistaxis and nasal obstruction with symptoms present from months to years. Often times,

these tumors are asymptomatic until they increase and encroach on critical structures.

Most surgeons agree that surgery is the primary treatment modality for the early-stage disease process. Complete surgical resection can provide cure for those patients without causing excessive morbidity [4]. However, controversy arises regarding the best approach to treatment when the patient presents with more advanced disease. Patients presenting with widespread cranial base extension or intracranial involvement pose difficulty for the surgeon to completely excise the tumor. In these dilemmas, a combination approach including surgery followed by postoperative radiation can be used, depending on the clinical scenario.

With the advent of endoscopic surgery, there have been a number of cases reporting the value of its use. This review, however, will cover all standard procedures that are reported in the literature, including the endoscopic removal of these vascular tumors, and report the use of image-guided radiotherapy (IMR), i.e. Cyberknife, which is a frameless radiotherapy device, as well as the gamma knife and intensity-modulated radiation therapy (IMRT).

Juvenile angiofibroma

Among theories concerning the etiology of juvenile angiofibroma, Chmielik et al. [5] define juvenile angiofibroma as an angioma with an extended fibrous component. In the development of the lesion, the participation of hormonal disorders of the pituitary gland-gonad axis is suggested as etiological. According to current opinions, juvenile angiofibroma is regarded as a developmental defect, affecting the embryonic vascular network surrounding the sphenoid bone [5].

Patients with JNA are typically silent sometimes for years and often present with epistaxis, nasal obstruction, facial numbness, rhinorrhea, ear popping, sinusitis, cheek swelling, visual changes and headaches. In addition to these symptoms, up to one-third of patients with this condition may present with proptosis or other orbital involvement, which are late symptoms and findings.

The exact site of origin of the tumor is subject to much speculation. The tumor originates from the superior margin of the sphenopalatine foramen, formed by the trifurcation of the palatine bone, the horizontal ala of the vomer, and the root of the pterygoid process [6]. The point of origin is important not only because it determines the pattern of tumor spread, but also because it influences decision-making for surgical access and extirpation. At the time of diagnosis, most tumors extend beyond the nasal cavity and nasopharynx or forward behind the wall of the maxillary sinus (Fig. 1).

Lateral growth can put the tumor in the pterygomaxillary fossa. Extension of the tumor can erode the pterygoid process of the sphenoid bone, and further lateral extension can fill the infratemporal fossa, thus producing classic bulging of the cheek. Tumor can also extend under the zygomatic arch which subsequently causes swelling above the arch. From the pterygomaxillary fossa, the angiofibroma can grow into the inferior and superior orbital fissures causing erosion of the greater wing of the sphenoid bone. Tumors can extend extradurally in the middle fossa near or adjacent to the cavernous sinus. Posterior extension of the tumor into the sphenoid sinus pushes upward and back to displace the pituitary and then can fill the sella turcica. In most cases, intracranial invasion ranges from 4.3% to 11%, but the tumor usually remains extrameningeal [6, 7]. Loss of vision can be the result of tumor in the sella or in the orbit. It should be

Fig. 1 A polypoidal nasopharyngeal angiofibroma occupying the nasal cavity [7]

noted that skull base erosion in JNA is different from malignant disease in that angiofibromas invade the skull base by expansion and bone resorption rather than by cellular infiltration. The similarity is the destruction of vital structures, i.e. the cranial nerves by pressure rather than cellular infiltration.

Spontaneous regression can occur, and clinical regression after incomplete removal or radiation therapy has been used as treatment. Recurrence rates were reported at 20% (range of 5–50%). Growth rate of these tumors is relatively slow.

Staging of nasopharyngeal angiofibromas

Different staging systems have been proposed to nasopharyngeal angiofibroma. The staging system proposed by Chandler [8] is based on the AJCC

classification for nasopharyngeal cancer and does not truly reflect the clinical behavior of JNA. Sessions' system of classification more accurately reflects the clinical behavior of JNA [9]. In 1996, Radkowski et al. [10] further modified Sessions' classification to include posterior extension to the pterygoid plates and the extent of skull base erosion, and the Andrews staging further defines the intracranial extensions. The four staging systems are shown in Table 1 for comparison. Currently, the standard classification for some surgeons is that of Andrews et al. [12]. New classifications are evolving as the extent of the disease is more clearly defined [13, 14].

Blood supply

The main blood supply is the internal maxillary artery. Other vessels can include the dural, sphenoidal and ophthalmic

Table 1 Staging system for JNA [11, 12]

Chandler	Sessions	Radkowski	Andrews
I Tumor confined to nasopharyngeal vault	IA Limited to nose and/or nasopharyngeal vault	IA Same	I Tumor limited to nasopharynx. Bone destruction is negligible or limited to sphenopalatine foramen
	IB Extension to one or more sinuses	IB Same	
II Tumor extending to nasal cavity or sphenoid sinus	IIA Minimal extension to PMF	IIA Same	II Tumor invading pterygopalatine fossa or maxillary, ethmoid, or sphenoid sinus with bone destruction
	IIB Full occupation of PMF with or without erosion of orbital bones	IIB Same	
	IIC Infratemporal fossa with/without cheek	IIC Or posterior to pterygoid plates	
III Tumor extending into antrum, ethmoid sinus, pterygopalatine maxillary fossa (PMF), ITF, orbit and/or cheek	III Intracranial extension	IIIA Erosion of skull base; minimal intracranial	IIIA Tumor invading infratemporal fossa or orbital region without intracranial involvement
		IIIB Erosion of skull base; extensive intracranial with/without cavernous sinus	IIIB Tumor invading infratemporal fossa or orbit with intracranial extradural (parasellar) involvement
IV Intracranial tumor			IVA Intracranial intradural tumor without infiltration of cavernous sinus, pituitary fossa or optic chiasma
			IVB Intracranial intradural tumor with infiltration of cavernous sinus, pituitary fossa or optic chiasma

branches of the internal carotid system. Because of the diverse arterial input, preliminary ligation of the external carotid artery is of little help in decreasing bleeding during excision. The vascularity of tumors varies, and the physician must differentiate between a vascular tumor versus a fibrous tumor. The bleeding potential of a given tumor is unpredictable at best, but the majority of tumors are vascular and must be critically respected for the bleeding potential. If possible, pre-emptive ligation of the sphenopalatine artery can be a useful adjunct in control of bleeding.

If the histological diagnosis is in doubt, a biopsy specimen can be taken only after the patient is anesthetized and has been prepped and draped for tumor removal because of the potential for profound bleeding in a non-controlled environment.

Management of JNA

Management of JNA has become more refined by more accurate diagnostic radiological tools such as CT and MRI. Improved embolization techniques preoperatively have also contributed to the successful management of JNA cases. Technological innovations such as image-guided robotic radiosurgery (IMR-Cyberknife), laser and gamma knife as well as improved anesthesia and increased familiarity with skull base surgical approaches have facilitated the management of these tumors.

Radiological evaluation of JNA

Various radiological methods have been employed in the diagnosis and treatment of juvenile angiofibroma. CT was and is essential in determining the precise location of the tumor (Fig. 2) [15]. Now MRI with and without gadolinium is the initial diagnostic method of choice. Flow voids and marked gadolinium enhancement of the mass is characteristic of JNA.

MRI has distinct advantages over traditional radiological techniques (Fig. 3). MRI provides multiplanar imaging with improved definition at the cribriform plate-planum sphenoidal and cavernous sinuses. MRI also provides improved differentiation of tumor from inflamed mucosa and mucous in the paranasal sinuses. MRI does not expose younger patients who will likely require serial follow-up studies to diagnostic radiation. MRI is especially advantageous at the skull base because intracranial involvement is the crucial factor on which operative morbidity and success rest. In the radiological evaluation of JNA, intracranial extension is usually extradural - destroying bone at the skull base, extending adjacent to the dura, but rarely invading the dura [16].

Fig. 2 Axial section of CT scan demonstrating a JNA extended into the posterior nasal cavity and nasopharyngeal vault. Minimal extension to the pterygomaxillary fossa [15]

Fig. 3 Coronal view of MRI of the same patient reported in Figure 2 [15]

Angiography and embolization of JNA

If a patient is a surgical candidate, preoperative carotid angiography is in order for the complete blood supply of the tumor to be demarcated (Fig. 4).

During embolization, the feeding vessels from the external carotid arteries-usually the internal maxillary artery and often the ascending pharyngeal artery are identified and embolized in one procedure (Fig. 5).

Fig. 4 Selective left common carotid injection shows hypervascular angiofibroma mainly supplied by the internal maxillary artery [14]

Fig. 5 Postembolization arteriogram shows occlusion of left internal maxillary artery and its branches supplying the tumor [14]

Polyvinyl alcohol (PVA) particles of the appropriate size (usually 300–500 μm) are used to embolize major feeding vessels. Balloon occlusion and assessment of collateral cerebral flow may occasionally be indicated when the internal carotid artery is involved by tumor or provides significant tumor blood supply.

Preoperative planning

Preoperative preparations aim to diminish the risk of complications associated with massive bleeding and blood transfusion. Hormonal therapy such as androgen or estrogen has been advocated in the past as a way to decrease the bulk and vascularity of JNA, but angiographic embolization makes hormonal therapy undesirable and unnecessary [16].

Ezri et al. [17] reported several techniques to decrease bleeding. Esthetic adjuncts such as hypotensive techniques and hypothermia have been recommended as well as rapid sequence induction. Extubation several hours after surgery is also recommended. The patient also should be placed in the reverse Trendelenburg position and deliberate hypotension induced (MAP 55–65 mmHg). Because of the potential of massive blood loss, multiple routes of access for blood replacement should be in place such as two large bore IV catheters.

Patients should undergo angiography to confirm vascularity of JNA, as this plays a major role in preoperative embolization. Embolization should be performed 24 hours preoperatively because JNA is known to achieve rapid revascularization [16].

It is reported that embolization increases the risk of incomplete excision, as a result of the reduced definition of the tumor border, especially when there is deep invasion of the sphenoid bone, but embolization is used by most reporting centers [18]. However, Andrade et al. reported not using embolization, even in advanced stage III and IV tumors, because he contends that complete resection is more difficult [19]. In spite of the reported risks of incomplete excision, embolization is the treatment of choice.

Surgical management of JNA

Surgery is the mainstay of treatment for JNA. The surgical approach is determined primarily on tumor location, extent and surgical expertise. The surgical technique used must take into account the effects of surgery on the young male craniofacial skeleton, which continues to grow until about 20 years of age [20]. Factors that may cause growth restriction of the midface include the elevation of soft tissue and periosteum from the midface, dissection of mucoperiosteum of the palate, ethmoidectomy, facial osteotomies and the use of metal plate fixation [21–24].

The surgical approaches can be inferior, lateral and anterior. Inferior approaches include transpalatal and transoral-transpharyngeal routes. Anterior approaches include transnasal, Le Fort I maxillotomy, medial maxillectomy and maxillary swing depending on the location. Lateral approach includes the infratemporal fossa approach.

The transpalatal and transoral-transpharyngeal routes are best suited for tumors localized in the nasal cavity and nasopharynx, but modified transpalatal approach with excision of pterygoid plates can access the pterygopalatine fossa (Fig. 6).

The transnasal approach can be used for tumors limited to the nasopharynx, nasal cavity and sphenoid sinus, but lateral exposure is very limited with this technique. According to Mann et al. [25] contraindications for the endonasal approach are stage IV angiofibromas and some stage III cases with major extension into the middle

cranial fossa. The Le Fort I maxillotomy approach affords access to tumors limited to the nasopharynx, nasal cavity, paranasal sinuses, pterygopalatine fossa, and to tumors with minor extensions in to the infratemporal fossa (Fig. 7) [26, 27].

The medial maxillotomy approach affords access to tumors in the nasopharynx, orbit, ethmoids, sphenoid sinus, pterygopalatine fossa, infratemporal fossa, and the medial part of the cavernous sinus - this can be performed through a lateral rhinotomy, or Weber-Ferguson approach, or by midfacial degloving, or modified midfacial degloving [27].

Fig. 6 Exposure of inferior aspect of the tumor in the pterygopalatine fossa after excision of pterygoid plates [16]

Fig. 7 Le Fort I osteotomy [26]

The infratemporal approach is best suited for tumors extending to the infratemporal fossa and for tumors involving the middle cranial fossa and the lateral part of the cavernous sinus. This approach permits ligation of the internal maxillary artery early in the dissection thus limiting intraoperative blood loss. The infratemporal fossa approach may be accomplished via a zygomatic osteotomy and subtemporal craniotomy combined with an anterior approach [27].

The block removal of the maxillary bone and reinsertion approach provides maximal exposure of the nasopharynx, sphenoid sinus, pterygopalatine fossa and cavernous sinus. However, it may affect facial growth due to extensive soft-tissue dissection and multiple osteotomies as shown in Fig. 8 [27, 28]. The frontotemporal craniotomy approach

is used in stage IVA tumors according to Andrew et al. classification [12, 29].

Extensive angiofibromas that invade intracranially and extend to the cavernous sinus may be resected safely through a combined approach. The temporal craniectomy provides excellent exposure to the carotid artery, cavernous sinus and superior orbital fissure, while the transfacial approach allows for complete removal of tumor in the nasopharynx, sphenoid sinus and medial cavernous sinus. Successful outcomes are ultimately determined by careful patient selection, imaging that clearly delineates the anatomic extend of tumor invasion, and preoperative embolization, and the collaboration of an experienced head and neck, skull-based and neurosurgical team [30].

Fig. 8 Maxillary bone removal and reinsertion [28]

Endoscopic surgery for JNA

Since advances in endoscopic technology, endoscopic approaches are used as an adjunct to combined approaches, and in some studies, endoscopic removal is the primary method of excision even with dural and cavernous sinus extensions of the tumor.

Most authors limit nasal endoscopic resection to those tumors restricted to the nasal cavity and paranasal sinuses, with minimal extension toward the pterygopalatine fossa (stage II) Rogers [31]. However, Carrau et al. [16] observed that when the pterygopalatine or infratemporal fossae are involved, the tumor may be treated exclusively via nasal endoscopy.

The surgeon needs free space to manipulate the surgical instruments and mobilize and/or retract the tumor in at least two planes. Thus, tumors that completely obliterate the nasal cavity and are not compressible are not amenable to customary endoscopic techniques. Partial resection of the tumor assists the surgeon in gaining space for instrumentation. This is most helpful when the tumor or a portion of the tumor is confined by rigid boundaries such as the nasal cavity and paranasal sinuses. The boundaries of the tumor can be easily identified and hemostasis can be achieved with cautery or packing against the bony walls. Conversely, juvenile angiofibroma in the pterygopalatine or infratemporal fossa is better preserved intact because this aids in the identification of its boundaries and aids in its dissection from the surrounding soft tissue.

Using endoscopy, successful treatment was obtained in a number of surgical cases where endoscopic and endoscopic assisted-surgery were used exclusively in 11 patients [16]. Rogers [31] reported 20 patients, using Radkowski staging – 4 patients (stage I), 7 patients (stage II) and 9 patients (stage IIIA). In addition to successful outcome in 20 patients, Rogers [31] suggested that highly vascular and extensive cases may leave residual tumor. Hazarika et al. [32] reported four cases, two of which underwent KTP/532 laser-assisted endoscopic excision alone, and the transpalatal approach was used with the endoscope and KTP/532 laser in another two cases successfully.

Andrade et al. [19] reported 12 patients, ranged in age from 9 to 22 years old. Eight patients were stage I, and 4 patients were stage II according to Andrew's classification, without preoperative embolization. Stages I, II and IIIA lesions were approached endoscopically, while the remaining 3 patients underwent open resection. There were no significant differences in mean operative time between the endoscopic and open groups (312 versus 365 minutes). In the endoscopic group, the intraoperative blood loss was almost half that of the open group (506 versus 934 cc) and the average length of hospital stay was 1 day less (3 versus 4 days). Blood loss and hospital length of stay were

important differences, giving credibility to endoscopic removal of JNA in his series.

Midilli et al. [34] reported 42 cases, 12 of whom were operated with endoscopic transnasal approach. They started tumor excision with partial resection of the middle turbinate and subperiosteal dissection of the septum and anterior sphenoidal wall. The middle turbinate and septum are sometimes directly associated with the tumor in cases of anterior spread. Starting the surgery with partial resection of the middle turbinate may facilitate the operation due to this relationship and better control of the sphenopalatine artery at the sphenopalatine foramen as shown in Fig. 9. The sphenopalatine artery should be endoscopically ligated if possible at the beginning of the procedure in all cases for better control of bleeding [35].

Endoscopic transnasal approach has advantages of no non-cosmetic sequela, less hemorrhage and no disruption in facial skeleton. The endoscopic approach allows better visualization of tumor contiguity, less hemorrhage, and enables dissection and ligation of vascular structures in JNA surgery [34].

Currently, more advanced tumors are more likely treated by using external approaches [35], but combining endoscopic surgery with external approaches is increasingly being used. The combination of endoscopic and open approaches for advanced tumors allows better visualization of the lesion and facilitates total removal [31, 36].

Ardehali et al. [38] studied 47 cases of JNA that were treated with nasal endoscopic surgery. According to Radowski et al. staging, 21 patients were stages IA–IIB, 22 were IIC, 3 were IIIA and 1 in IIIB. Five patients were embolized before surgery with a mean blood loss of 770 ml; whereas, in non-embolized patients, blood loss was 1,403.6 ml. In a follow-up period (mean 2.5 years), recurrence was noted in 9 patients and mean time of occurrence was 17 months after surgery. Two patients experienced rupture of the cavernous sinus with no mortality. The mean hospital stay was 3.1 days. Based on this study, endoscopic resection of JNA was found to be a safe and effective technique because of decreased blood loss, shorter hospitalization, and lower recurrent rates especially if tumors did not extend through intracranial space. Because of these findings and benefits of the procedure, endoscopic surgery is recommended as the first surgical step after embolization for tumors with stages I–IIIA of the Radowski staging system.

Based upon the recent findings in the literature, endonasal surgery is combined with a preoperative embolization of the arterial supply. There are some concerns about a higher recurrence rate with intracranial extension, but there is no contraindication to embolizing any size tumor because of other benefits [39].

Resection of type II and IIIa nasopharyngeal angiofibromas safely and effectively can be achieved endoscopically.

Fig. 9 Ligation of the sphenopalatine artery [37]

The advantage of this minimally invasive technique is the avoidance of external scars, shorter hospitalizations, and low morbidity. Of note, the intraoperative computer-assisted guidance systems provide substantial help in the removal of these tumors [40].

Adjunctive treatment with laser

There are several reports of treatment of JNA with laser. Using the KTP (potassium titanyl phosphate) laser, Scholtz et al. [41] reported decreased blood loss and reported 15% recurrence rate in his series. Also employing the KTP laser, Hazarika et al. [32] report nine cases in which removal of the tumor was accomplished endoscopically – 2 of the 9 cases underwent KTP/532 laser-assisted endoscopic excision.

Five cases of image-guided laser-assisted endoscopic excision were reported by Mair et al. [42]. In this series, the Nd:Yag laser as used under 4–10 watt of continuous power, in conjunction with a CT/MRI image guided navigational system. The laser was found to be extremely useful in debulking the core of the mass with no blood loss and in identifying the pedicle of the mass, which could be endoscopically avulsed [32].

Surgical team approach

Ideally, all intracranial extension of JNA must involve a team approach in order to effectively manage the patient. The team should include a neurosurgeon and an otolaryngologist/skull base surgeon work together with an interventional radiologist.

Radiotherapy for JNA

Patients with intracranial involvement, unresectable disease, religious preferences, or multiple recurrences may be good candidates for radiation treatment [43]. Liu et al. [44] reported 2 patients with stage IV incompletely resected tumors who were given 30 Gy and 40 Gy, respectively without recurrent at 1 and 6 years. This finding suggested that radiation may be an effective adjunctive therapy in recurrent or residual JNA. However, potential hazards associated with conventional radiation treatment should be considered. These side-effects include osteoradionecrosis, abnormal bone growth, as well as malignancy. In addition to these risks, panhypopituitarism, temporal lobe necrosis, cataracts and radiation keratopathy may be precipitated by conventional radiation treatment in patients in JNA. Recurrence rate of 20–30% can be expected with radiation treatment alone [1, 43, 46]. Harwood et al. [47] concluded that surgery and radiation carry comparable risks, but

that morbidity and mortality risks associated with surgery should be considered. However, most surgeons contend that surgery over radiation is the best choice.

Yang et al. [48] suggested that residual or recurrent disease can be managed with radical surgery rather than radiotherapy, as demonstrated in 15 cases which were successfully treated. Prior to Yang's report, however, the previous protocol of primary radiotherapy followed by surgery for residual disease was considered as the conventional approach to treatment of the disease process in some centers.

Once considered the treatment of choice, conventional radiation with 30–35 Gy for advanced, incomplete resected tumors and intracranial extension, this regimen is now considered controversial because of its adverse long-term effects. However, newer techniques in radiotherapy treatment such as intense-modulated conformal radiotherapy (IMRT) and gamma knife have great potential for future management of JNA. Good results were reported with three-dimensional IMRT, and others reported good results with gamma knife stereotactic radiosurgery [49]. Deguchi et al. [50] reported an image-guided, robotic radiotherapy (Cyberknife) to successfully treat a 12-year-old boy with JNA. Because of religious reasons, this patient's family refused surgery and received 2,400 cGy without regression of the tumor. He subsequently had three treatments with the Cyberknife (4,512 cGy with almost complete disappearance of the tumor [50]. Patient was free of tumor 8 years later [51].

Conclusion

Because of technological advances both in surgery and radiology, management of JNA patients has been refined. With the advent of more sophisticated diagnostic capabilities such as CT, MRI, IMRT, stereotactic guidance systems such as GE's navigation systems, gamma knife, and the robotic image-guided radiotherapy, JNA can be diagnosed and treated more accurately and effectively. Improvement in embolization preoperatively has also led to better management of JNA patients. In addition to technological breakthroughs, increased familiarity with skull base surgical approaches has been accomplished by more advanced training in this area for both otolaryngologists and neurosurgeons. In addition to better trained skull base surgeons, improved anesthesia has resulted in more effective management of JNA patients.

Over the past decade, additional technological advances in the care of JNA patients include use of image-guided robotic therapy, IMRT and improvement in laser technology.

Although there are various methods of managing the patient with JNA, surgery still remains the preferred treatment for these vascular tumors. Radiation is reserved for cases when surgery is contraindicated and rarely is indicated as a primary source of treatment.

Endoscopic surgery is rapidly becoming the method of choice and eventually may be replaced with robotic surgery which is in its infancy for treatment of skull base tumors. Finally, image-guided robotic radiotherapy could also be included in the future [52].

Although successful treatment has been seen early, the ultimate safety and long-term effects of robotic image-guided radiotherapy ultimately will be determined by its use and results when surgery is contraindicated, refused and is used for residual or recurrent JNA.

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