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The risk factors for residual juvenile nasopharyngeal angiofibroma and the usual residual sites

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ABSTRACT

Objective: Juvenile nasopharyngeal angiofibroma (JNA) is non-metastasizing but potentially locally destructive tumor of the nasopharynx. It can destroy the skull base and invade into the cerebrum. Surgical management is the primary standard but residual disease is always a risk factor. We aimed to determine the risk factors for residual disease and usual sites for these residual tumors.

Methods: The medical records of 131 patients (mean age 17.6 ± 6.8, range 9–71 years) with histologically proven JNA were retrospectively analyzed. The surgeries were all nasal endoscopic approaches, with or without assistant incision.

Results: The prevalence of residual disease was 16.8%. Risk factors associated with JNA recurrence included tumor stage, intraoperative bleeding, and the year in which the operation was performed. The pterygoid canal, pterygoid process, and pterygopalatine foramen were the most frequent locations for residual tumor.

Conclusion: Surgical management should take particular care for the pterygoid canal, petrygoid process, and pterygopalatine foramen. Contrast-enhanced CT and MRI are effective tools to evaluate complete JNA excision in the first two days after primary surgery. Careful exploration of these areas may be the key to avoid residual JNA.

1. Introduction

Juvenile nasopharyngeal angiofibroma (JNA) arises exclusively in adolescent males, and constitute 0.05–0.5% of all head and neck neoplasms [1]. It may arise from the sphenopalatine foramen, or opening to the pterygoid foramen or the pterygoid canal. The name JNA was given because of the belief that it arises in the nasopharynx. However, extensive surgical experience and CT studies indicated that these tumors arise in the pterygoid canal [2,3]. Although pathologically benign, JNA can invade to the nasal cavity, paranasal sinus, pterygopalatine fossa, infratemporal fossa, and even the skull base [4].

Although many therapies have been used in JNA, including estrogen, anti-androgens, steroids, or radiotherapy, surgery remains the standard treatment [5]. Despite significant advances in surgical techniques and instrumentation, surgery for JNA remains one of the most challenging tasks for otolaryngologists because of problems related to hemorrhage, surgical access, recurrence, and biologic behavior. Many surgical approaches have been used, such as the transpalatal, midfacial degloving, Le Fort I maxillotomy, transantral, lateral rhinotomy, and infratemporal approaches [6,7]. With minimum morbidity and better exposure, the endoscopic approach has become more widely utilized in the last two decades [8,9].

JNA is a benign tumor that does not metastasize, so recurrences are actually related to residual tumor growth. How to prevent leaving residual tumor behind at surgery is crucial for preventing “recurrence.” High residual rates and early recurrence have been reported for JNA, especially when the skull base is involved. Decreasing the rate of JNA recurrence depends on complete removal of the tumor and postoperative CT evaluation.

In this study, we retrospectively reviewed 131 patients who underwent endoscopic surgery in our department over the past 10 years. Factors including age, stage, surgical approach, early postoperative CT or MRI, intraoperative bleeding, and when the operation was performed, which may infect residual disease, were considered. We also studied the residual sites in cases where residual disease was identified. Careful management of these areas may be important for avoiding residual tumor.

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Table 1
Staging classification for JNA according to Radkowski et al. [4].

Radkowski stage	Definition	Number of patients
Ia	Limited to the nose and/or nasopharynx.	10
Ib	Same as Ia but with extension into one or more paranasal sinuses.	8
IIa	Minimal extension through the sphenopalatine foramen, into and including a minimal part of the medial-most part of the pterygomaxillary fossa.	26
IIb	Full occupation of the pterygomaxillary fossa, displacing the posterior wall of the maxillary antrum forward. Lateral and/or anterior displacement of branches of the maxillary artery. Superior extension may occur, eroding orbital bones.	16
IIc	Extension through the pterygomaxillary fossa into the cheek and temporal fossa or posterior to the pterygoid plates.	41
IIIa	Erosion of the skull base with minimal intracranial extension.	13
IIIb	Erosion of the skull base with extensive intracranial extension with or without cavernous sinus invasion.	17

2. Methods

2.1. Patients

A total of 131 patients with histologically proven JNA underwent surgery at the Eye, Ear, Nose, and Throat Hospital of Fudan University. Twenty-four of these patients had surgery at another hospital. Retrospective review of cases included patients presenting between 2006 and 2015. Patient age, tumor stage, and sites of residual disease were recorded. The follow-up period ranged from 21 to 135 (mean 78.4 ± 33.7) months.

The use of this data for research was approved by the Ethics Committee of the Eye, Ear, Nose, and Throat Hospital of Fudan University.

2.2. Staging

Preoperative paranasal and nasopharynx computed tomography (CT) was utilized to evaluate the extent of the tumor. Magnetic resonance imaging (MRI) was performed on patients when the CT scans showed skull base or cavernous sinus involvement. Tumor staging was based upon CT or MRI findings according to the classification of Radkowski [10].

2.3. Surgical treatment

None of the patients received preoperative drug or radiotherapy. Preoperative embolism was performed on patients whose tumor stages were IIb to IIIb, one to three days prior to surgery. All surgeries were performed under general anesthesia using the nasal endoscopic approach, with or without an assisted incision. Assisted incisions included sublabial and buccolabial incisions for JNA with extensive infratemporal fossa extension [5].

Early postoperative CT and MRI (within two days after surgery) were performed for detection of residual disease since September 2010 in this series of studies, when the surgeon was unsure about total excision of the tumor. Not all patients underwent early postoperative CT scan, considering its cost and potential harm of radiation. If the CT scan showed residual disease, revised surgery was performed approximately one week after the first surgery.

Long term residual disease was defined as clinical or imaging evidence of tumor presence in the nasopharynx and or neighboring structures, with symptoms including epistaxis or nasal obstruction after the first surgery. Radiographic studies were examined to determine if residual tumor existed in the following 12 locations: nasal cavity, nasopharynx, sphenoid sinus, maxillary sinus, ethmoid sinus, pterygoid canal, pterygopalatine foramen, pterygopalatine fossa, pterygoid process, infratemporal fossa, orbital apex, and skull base.

In this study, previous operations at the other hospital were not considered in the risk factor analysis, as data from these hospitals was not available. In the analysis of residual tumor sites, operations performed at the other hospital were included because the patient's residual tumor images were available at our hospital. We analyzed sites of residual disease based on CT and/or MRI images.

2.4. Statistical analysis

Independent variables analyzed included age, tumor stage, preoperative embolism, surgical approach, early postoperative CT or MRI, intraoperative bleeding, and the year in which the operation was performed. Statistical analysis was performed using the chi-square, Fisher exact and Kruskal-Wallis test. SPSS version 22 (IBM, Chicago, USA) was used for computations.

3. Results

One hundred and thirty-one patients (mean age 7.6 ± 6.8, range 9–71 years) with pathologically proven JNA presenting between 2006 and 2015 were reviewed. All patients underwent the endoscopic or endoscopic assisted approach. Table 1 shows the frequency of tumor stages, with the majority being stages IIa–IIb according to Radkowski stage.

Twenty-two patients required a second surgery due to residual disease. The total residual disease rate was 16.8%. Different factors that may have affected residual rates are shown in Table 2. Radkowski stage and intraoperative bleeding was significantly associated with high rates of residual disease ($p = 0.004$ and 0.001, respectively). Interestingly,

Table 2
Risk factors for residual disease.

Variable	Number of patients	Residual (%)	*p* value
Age (years)			
≤18	99	16 (16.2%)	0.909
> 18	32	6 (18.6%)	
Radkowski stage			
Ia	10	0 (0.00%)	0.004
Ib	8	1	
IIa	26	3	
IIb	16	2	
IIc	41	5	
IIIa	13	4	
IIIb	17	7	
Preoperative embolism			
Yes	70	11	0.724
No	61	11	
Surgical approach			
Endoscopic only	84	16	
Endoscopic assisted	47	6	0.467
Early postoperative CT OR MRI			
Yes	28	3 (10.7%)	0.332
No	103	19 (18.4%)	
Bleeding during operation			
≤800 ml	74	4 (5.4%)	0.001
> 800 ml	57	18 (31.6%)	
When operation were taken			
2006–2010	63	17 (27.0%)	0.003
2011–2015	68	5 (7.4%)	

Table 3
Frequency of residual sites for each of anatomic site (n = 43).

Anatomical site	No. patients	%
Nasal cavity	16	38.1%
Nasopharynx	27	64.3%
Sphenoid sinus	24	57.1%
Maxillary sinus	7	16.7%
Ethmoid sinus	11	26.2%
Pterygoid canal	35	83.3%
Pterygopalatine foramen	30	71.4%
Pterygopalatine fossa	24	57.1%
Pterygoid process	32	76.2%
Infratemporal fossa	21	50.0%
Orbital apex	19	45.2%
Skull base	19	45.2%

operations performed between 2011 and 2015 had significant low residual rates compared with those performed between 2006 and 2010 (p = 0.003). Patients who had early postoperative CT scans had lower residual rates, although this trend was not statistically significant.

The frequency of each involved anatomic site is shown in Table 3 with the residual sites shown on the CT scans (Fig. 1). The pterygoid canal and pterygoid process were the most frequent locations of residual disease.

4. Discussion

JNA is a rare vascular tumor of male adolescents and has a trend of high recurrence [11]. Previous studies on JNA have reported different recurrence rates, ranging from 5% to 55% [12]. In last two decades, the transnasal endoscopic approach has emerged as an alternative method to the open approach for the treatment of JNA. Our institute first performed the endoscopic approach in 2006; until now, more than two hundred patients have been treated in this way. Our total recurrence rate is 16.8%, similar to that of recent studies [3,13].

In our study, we found risk factors associated with JNA recurrence to be tumor stage and intraoperative bleeding, results which are consistent with previous studies [6,14]. A recent study found a significant association between tumor size and stage. Additionally, advanced stage tumors are supplied by a greater number of feeding vessels compared with early stage tumors [15]. Advanced stage, with more feeding vessels makes surgery dramatically harder and leads to a higher recurrence rate, especially when the tumor extends to the pterygoid process, orbital apex, and cavernous sinus [16].

Endoscopic surgery was first used for small JNAs limited to the nasopharynx or pterygopalatine fossa. Its indications were later expanded to larger tumors extending to the infratemporal fossa or even the cavernous sinus [17,18]. A recent systemic review showed that the purely endoscopic approach was associated with lower rate of recurrence compared to endoscopic-assisted surgery, while the latter method can increase the complexity of tumor resection [1]. In our study, the recurrence rate was no different between groups.

Analysis of residual sites of JNA showed that the pterygoid canal, pterygoid process, and pterygoid fossa are the most frequent locations of residual disease (Fig. 1). Tyagi et al. [16] found that extensions to the pterygoid fossa and basissphenoid, erosion of the clivus, intracranial extensions medial to the cavernous sinus, and invasion of the sphenoid diploe were risk factors associated with JNA recurrence. Interestingly, they also found that residual tumor regrowth was not observed from the infratemporal regions; but small evident residual tumors in the region of the pterygoid fossa, sphenoid sinus, clivus, and vidian canal had regrown substantially by this time. Our previous studies showed that the origin site should be more exactly in the pterygoid canal. From the pterygoid, the tumor can invade the sphenopalatine foramen, sphenoid sinus, and pterygopalatine fossa first, and then adjacent structures through these three locations [2]. Thus, in Tyagi's study recurrent tumors were all around the pterygoid canal. In a recent study by Thakar [3], it was shown that the pterygoid canal may harbor microscopic residual tumor after a seemingly complete excision, so attention towards this structure during surgery may reduce recurrence. Understanding the extensive pattern of JNA obviously benefits surgeons during excision.

Early postoperative CT and/or MRI scan (within two days after surgery) has been performed for detection of residual disease since September 2010 in this series, when the surgeon was unsure that the tumor had been completely excised. Although not statistically significant, patients who underwent early postoperative CT has lower residual rates (Fig. 2). Early postoperative CT and/or MRI can help find residual tumor, so that a second surgery can be formed within a week, prior to scar formation. However, long term follow-up with CT and/or MRI is still essential as tiny residual tumor may exist.

The surgeon's skill and experience is also relevant to patient outcomes. JNA is located very deep in the skull and tends to bleed severely, posing a challenge for the otolaryngologist. If the surgeon is not familiar with the anatomy rounding the sphenoid sinus and pterygoid process, complete removal of the JNA is very difficult. Surgical experience and competence affects recurrence rate in JNA patients. We demonstrated that surgeon experience is important in reducing recurrence rate by analyzing different recurrence rates between two phases, 2006 to 2010 and 2011 to 2015. The recurrence rate in the latter phase dramatically dropped from 27.0% to 7.4% (p = 0.003). With increasing efficiency and competence, the surgeon will have more adept skills to control bleeding intraoperatively and gain a clearer operative field. Moreover, familiarity with the anatomy of surrounding structures aids in the complete removal of the tumor.

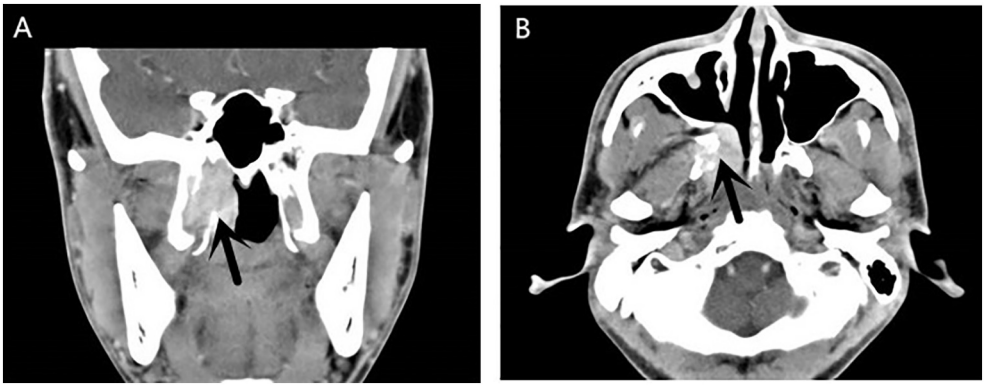

Fig. 1. Residual tumor located in the pterygoid canal, pterygoid process, and the pterygopalatine foramen (black arrow). A. Coronal contrast CT scan. B. Axial contrast CT scan.

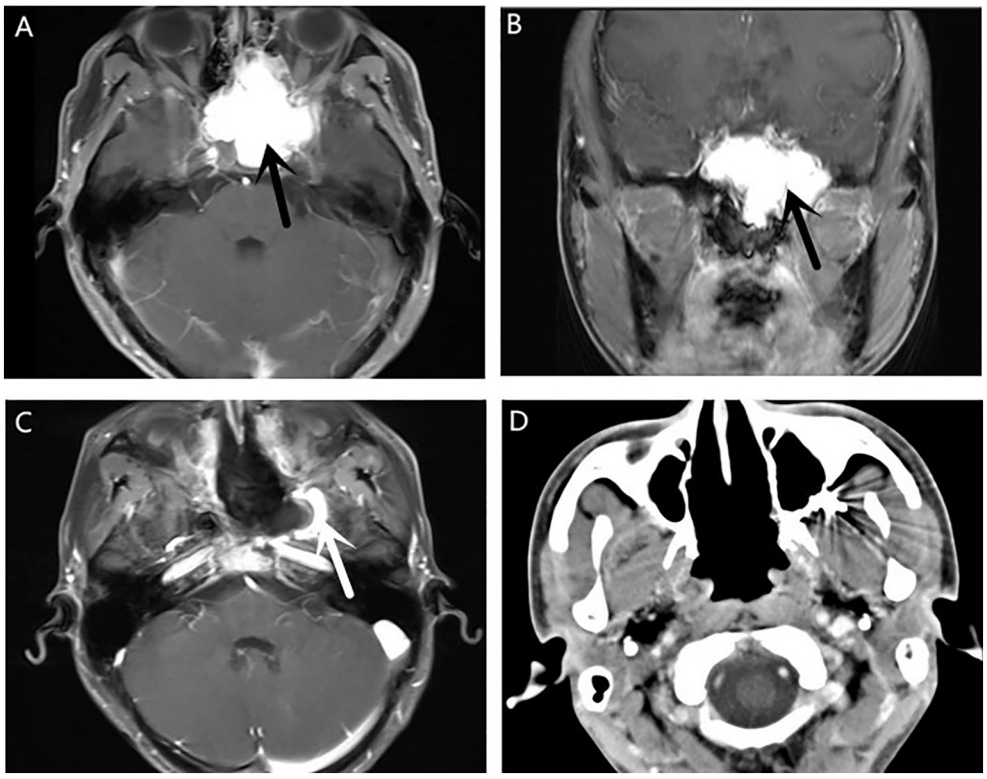

Fig. 2. A, B: Preoperative magnetic resonance imaging (MRI) show strong contrast enhancement of the tumor located in the sphenoid, pharynx, pterygopalatine fossa, orbital apex, and cavernous sinus. C: MRI performed two days after primary surgery, illustrating residual tumor in the region outside the left sphenoid sinus. D: Contrast CT shows no evidence of recurrent tumor one day after surgery.

5. Conclusions

The endoscopic approach, with or without assistant incision, is safe for patients undergoing JNA resection. Tumor stage and intraoperative bleeding are risk factors for JNA. Surgeon experience and competence also affects the recurrence rate in JNA. The pterygoid canal, pterygoid process, and pterygopalatine foramen are the most frequent locations for residual tumor. Careful exploration of this area and early postoperative CT scan is useful to reduce residual disease.

Compliance with ethical standards

This study was approved our local ethics committee. There are no conflicts of interest to declare.

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