Morbidity and Volumetric Progression in Juvenile Nasopharyngeal Angiofibroma in a Long-Term Follow-Up

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Abstract

Objective We compare the open and transnasal approaches for the excision of juvenile nasopharyngeal angiofibromas regarding the rate of morbidity, and residual tumor and its symptomatic recurrence over time. In addition, we present volumetric measurements of juvenile nasopharyngeal angiofibromas over time.

Methods All surgically treated patients of our institution were reviewed back to 1969 for type of surgery, residual tumor by magnetic resonance imaging (MRI)-based volumetry, recurrence, and morbidity. We performed a prospective clinical and radiological follow-up on reachable patients.

Results In total, 40 patients were retrievable from our records. We were able to follow up on 13 patients after a mean of 15.7 years since surgery (range: 1–47 years). Patients operated by the open approach had a higher rate of postoperative complications and thus a higher morbidity than endoscopic patients (4/4 vs 3/9; $p = 0.007$), although tumor sizes were equal among groups ($p = 0.12$). Persisting tumor was noted in 3/4 and 4/9 ($p = 0.56$) patients, respectively. The corresponding mean volumes of residual tumors were $16.2 \pm 14.4 \text{ cm}^3$ and $10.8 \pm 6.6 \text{ cm}^3$ ($p = 0.27$). No progression could be noted in endoscopically treated patients ($p = 0.24$, mean time between scans 2 years).

Conclusions Our analysis shows that the endoscopic approach results in less morbidity. The open approach does not guarantee freedom from persisting tumor tissue. Age seems to be a most important risk factor for the conversion of an asymptomatic persistence into a symptomatic recurrence.

Keywords

- angiofibroma
- follow-up
- morbidity
- endoscopic surgery
- infratemporal approach

Introduction

Juvenile nasopharyngeal angiofibroma (JNA) is a rare and benign vascular tumor accounting for up to 0.5% of all tumors in the head and neck region.¹ It typically has its origin in the epipharynx, with a close relationship with the sphenopalatine foramen. The painless mass usually becomes clinically apparent by nasal obstruction or recur-

rent unilateral epistaxis, which can be life-threatening. The tumor can expand into the nasal cavity and sphenoid, the pterygopalatine and infratemporal fossa, and shows a locally aggressive behavior by progressing even intracranially by bone remodeling and invasion.^{1,2} In the absence of any effective medical treatment, most cases are scheduled for surgery.

Today, visualization and removal of the tumor are performed endoscopically, endoscopically assisted, or in an open manner.^{1–3} Traditionally, endoscopic resection was

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reserved for smaller tumors (classes I and II in terms of the Fisch classification), whereas open surgery through an infratemporal approach or through facial translocation was performed in larger tumors (classes II and IIIa). Despite a reportedly high rate of morbidity following open procedures, they were the main standard of care for a long period of time.^{4,5} With the evolution of endoscopic techniques, it has now become possible to successfully resect also class III tumors less invasively.⁶ Various studies recently showed that the endoscopic technique seems to be superior not only regarding morbidity but also in visualization of persisting tumor tissue, blood loss, time spent in the hospital, and recurrences.^{7,8}

Although surgical techniques are evolved, the resection of JNA remains a demanding task that requires surgical expertise. This is because of the surrounding complex anatomical environment at risk for collateral damage and the potential of severe intraoperative bleeding despite improvements in preoperative superselective embolization.^{9,10} The main question therefore remains: whether radical resection is absolutely mandatory to prevent a symptomatic recurrence, and which approach produces better results concerning residual tumor and morbidity. In this study, we compare our cases operated by either open or endoscopic surgery in a long-term follow-up.

Material and Methods

Patient Recruitment and Data Acquisition

In this single-center study, we extracted the data of all patients who were treated for a JNA at our institution between January 1, 1969, and May 1, 2015, from our electronic patient system. The exclusion criteria were contraindication for magnetic resonance imaging (MRI), psychiatric or neurologic disease, and illicit drug or alcohol abuse. According to the decision of the cantonal ethics committee (KEK-ZH-No.2015-0056), only the patients who had shown up at the study-specific follow-up visit and signed an informed consent were included. The study was performed in accordance with the principles enunciated in the current version of the Declaration of Helsinki, the Essentials of Good Epidemiological Practice issued by Public Health Schweiz, and the Swiss Law and Swiss regulatory authority's requirements as applicable.

Patients Charts

We retrospectively acquired data from the patients charts, including type of surgery, prior embolization, reoperations, residual tumor (asymptomatic mass), recurrence (symptomatic tumor), postoperative complications, and demographic data including preoperative tumor classification according to Fisch (class I, tumor limited to the nasopharynx and nasal cavity; class II, tumor infiltrates the pterygopalatine fossa or maxillary sinus or ethmoidal sinus or sphenoid sinus with bone destruction; class IIIa, tumor infiltrates the infratemporal fossa or orbita without intracranial expansion; class IIIb, tumor infiltrates the infratemporal fossa or orbita with intracranial extradural expansion; class IVa, intracra-

nial intradural tumor without infiltration of the cavernous sinus, optic chiasm, or pituitary gland; class IVb, intracranial intradural tumor with infiltration of the cavernous sinus, optic chiasm, or pituitary gland). If available, tumor volume from immediate postoperative MRI scans was extracted. The determination of tumor volume was performed as described in the following.

Study Visit

In a study-specific visit, data regarding morbidity were prospectively assessed by a careful medical history, a physical examination, specifically of the cranial nerves, pure tone audiometry, forced-choice test of olfactory function (Sniffin Sticks Test, Burghart Messtechnik, ISO 13485, Wedel, Germany), questionnaires asking for problems in phonation or dysphagia, and subjective scar satisfaction. Hearing loss by pure tone audiometry was classified as follows: normal, 0 to 25 dB; mild, 25 to 40 dB; moderate, 40 to 70 dB; severe, 70 to 95 dB; profound, 95 to 100 dB; deafness > 100 dB (39).

Cranial Magnetic Resonance Imaging

For the detection of residual tumor, an MRI scan was performed in the same period as the study visit, and 3-mm-thick coronal and axial gadolinium-enhanced T1-weighted fat-saturated and T2-weighted images were acquired by a 3.0 Tesla Philips Healthcare or Siemens Skyra scanner. The tumor volume was extracted from the images by manual segmentation of the tumor in the coronal plane by a postprocessing software (3D Slicer, version 4.6, www.slicer.org) and rendering into a three-dimensional model (→ Fig. 1) based on the aforementioned images as well as the first postoperative MRI images retrieved from the radiological archives, if available.

Statistics

Statistical analysis was performed with the use of the IBM SPSS Statistics software for Mac OS X, version 23. Data are presented in a descriptive manner with means and standard deviations. Differences in mean tumor volume between

Fig. 1 Segmentation and three-dimensional model of tumor persistence.

groups was calculated by Student's *t*-test or the Wilcoxon test, as appropriate. Differences in statistical frequencies in the different groups were calculated by Pearson's chi-square and Fischer's exact tests. A *p*-value ≤ 0.05 was considered to be significant.

Results

Patients and Tumors

In total, 40 patients with a JNA could be retrieved from our electronic patient system. Of the 40 patients, 14 (35%) could be contacted, of which 13 (33%) met the inclusion criteria. All patients were male and had a mean age of 33.5 ± 13.2 years at the time of the study. They were operated at a mean age of 16.6 ± 3.2 years. Mean time to follow-up by our study was 15.7 years (range: 1–47 years). The preoperative tumor classification is presented in ▶Table 1. The tumors of the endoscopic and open surgery group did not differ according to the Fisch classification (*p* = 0.12).

Surgery

In nine (69%) patients, surgery was performed endoscopically, and in four (31%) patients, it was performed through an open approach (three infratemporal type C, one transpalatine). All patients operated in Zurich after 1979 received a superselective embolization with polyvinyl alcohol 24 to 72 hours prior to surgery.⁴ In our population, there were 12 of these patients (92.3%). There were no complications attributable to the embolization, such as paralysis of cranial nerves, amaurosis fugax, blindness, cerebrovascular insults, and necrosis of the tongue and face. All tumors, up to class IIIa, have been resected endoscopically since 2000.

Morbidity

No serious complications, such as damage to the meninges or the cavernous sinus, and cerebral abscesses, were recorded independently from the surgical technique and the class of the JNA. There were no fatalities. Patients operated by the open approach had a higher rate of postoperative complications and thus a higher morbidity (4/4 vs. 3/9; *p* = 0.007). Crossbite was the most common complication after open surgery (4/4), followed by a reduced or absent sensibility for the trigeminal branches V2 and V3 (3/4) and a moderate-to-severe conductive hearing loss (3/4). While the trigeminal cranial nerve impairments are inseparably inherent to the

open procedures, no other cranial nerve defects were reported in both approaches. In endoscopically operated patients, the major morbidity was due to mild conductive hearing loss (3/9), most probably caused by a dysfunction of the Eustachian tube. In two of these patients, a preoperative conductive hearing loss was already documented. In the endoscopic group, no other complications arose. No problems with swallowing or the sense of smell were found. Subjective satisfaction with the scars was fair in all four cases operated through the open approach. In all other cases, satisfaction was good.

Persistence/Recurrence

Residual tumor was noted in 3/4 and 4/9 after open surgery and endoscopic surgery in the follow-up MRI, respectively (*p* = 0.56). Symptomatic recurrence was only noted in three patients during puberty, of which two were operated through an open approach and one through an endoscopic approach. At the time of our follow-up visit, the mean volume of asymptomatic persisting tumors across all patients was 13.2 ± 11.0 cm³. Postoperative tumor volume was not influenced by preoperative tumor classification (*p* = 0.70). Residual tumors after open resection had a mean volume of 16.2 ± 14.4 cm³ compared with 10.8 ± 6.6 cm³ after endoscopic resection (*p* = 0.27). In the aforementioned patients, the persisting volume of the tumors directly after surgery was 10.3 ± 8.8 cm³. No progression could be noted from the immediate postoperative volume and the volume at our follow-up (*p* = 0.24, mean time between scans 2 years).

Discussion

This retrospective study on long-term follow-up of JNA treatment reports the following major findings:

- Morbidity is less frequent in endoscopically treated patients.
- The volume of asymptomatic persisting tumor tissue was equal for open and endoscopic surgery.
- A mean residual postoperative tumor volume of approximately 10 cm³ did not progress after endoscopic surgery in our adult patients. A progression into a symptomatic recurrence is most likely to occur only during puberty.

Given that patients usually are operated at a young age, the spectrum of possible morbidities has to be taken into account when the decision for a particular approach is made. According to this study, the morbidity caused by open approaches is high. All three patients operated through an infratemporal approach showed an anesthesia for the trigeminal branches V2 and V3, a crossbite, and a moderate-to-severe conductive hearing loss at long-term follow-up. Our results for the endoscopically operated patients are in line with other series showing low morbidity.⁷ In our series, dysfunction of the Eustachian tube and mild conductive hearing loss were the most common morbidities. However, most of these patients, as shown in this population, already have such a dysfunction before the

Table 1 Preoperative tumor classification

Fisch class	Number of patients operated endoscopically	Number of patients operated through open approach
I	1	0
II	2	1
IIIa	6	1
n/a	0	2

Abbreviation: n/a, not available.

operation due to the sheer mass effect of the tumor. Endonasal interventions bear the risk of olfactory impairment. In our study, however, no patients had a reduced sense of smell in the long run. This suggests that the risk is at least not higher than that after other transnasal procedures. Compared to open procedures, long-term cranial nerve deficiencies did not occur, neither in our series nor in others.^{7,11}

For the decision in favor of a specific resection method, it is important to know the differences in the rates of persisting tumor tissue and recurrence. The two different entities, persistence and recurrence, are used heterogeneously in the literature. In this study, a recurrence refers to a renewed symptomatic manifestation of the tumor after surgery, which needed further treatment. A mass alone, which was in contrast asymptomatic, was designated as a persistence. In seven (54%) patients, asymptomatic persisting tumor tissue was noted in our follow-up scan. None of them was symptomatic or needed further treatment. This reflects the overall low recurrence rate in endoscopically operated patients shown by others.¹ As there is a well-documented relationship between tumor size and recurrences, traditionally, tumors of class III or higher were operated through an open technique,^{1,5} for a complete resection would prevent a symptomatic reappearance of the tumor.^{3,10,12} The results of this study cannot support this rationale, as open surgery clearly does not warrant complete resection. The rate of persisting tumor tissue and its volumes were equal in the endoscopic and open surgery groups. The preoperative tumor sizes in both groups did not differ. Most importantly, our study shows that also in cases where no radical resection was performed, no progression could be noted after puberty in all endoscopic cases. This is in line with previous reports showing that persisting tumor not necessarily progresses or even shows involution at some point.^{2,10,13} A symptomatic recurrence occurred in three (23%) of our patients, all during puberty. Age seems to be an independent factor attributing to the risk of progression.¹⁴ The hormonal state during puberty seems to cause tumor tissue to have a tendency to grow, whereas involution occurs more frequently in the elderly population.^{15,16} In conclusion, the distinction between persisting tumor tissue and a progressing symptomatic recurrence is mandatory for the planning of further follow-up and other following therapies. Especially, the use of adjuvant radiotherapy, as it is argued by some authors,^{17,18} should be assessed very carefully in patients in this regard.

We are aware of the limitations of this study. One of them is its monocentric nature. Population sizes in studies assessing this rare disease are generally small, and from the 40 operated patients at our clinic, only 13 met the inclusion criteria and could be contacted. This makes the comparison of studies and the generalization of the results difficult. The long period of time during which patients were operated and the fact that recent patients were only operated endoscopically could cause a bias by improved medical treatments and rehabilitation not related to either the endoscopic or the open approach. On the other hand, the long period of

observation gives a comprehensive picture of long-term outcome.

Conclusion

Our analysis shows that the endoscopic approach results in less morbidity. The open approach does not guarantee freedom from asymptomatic persisting tumor tissue, and in case of endoscopic surgery, the tissue seems not to progress into a recurrence in adults. Age seems to be a most important risk factor for the conversion of an asymptomatic persistence into a symptomatic recurrence.

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