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Juvenile nasopharyngeal angiofibroma: a revised staging system*

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SUMMARY

***Objectives**: To discuss the shortcomings of current staging systems and to suggest modifications according to new surgical methods and data.*

***Study Design**: A retrospective chart review.*

***Methods**: The medical records of 36 patients, all of whom underwent resection of juvenile nasopharyngeal angiofibroma by external or endonasal approach between 1983 and 2002, were reviewed retrospectively. Follow-up period of patients ranged from 3 to 7 years (mean, 4.5 years). Tumour extent, sites and rate of persistent disease were analyzed and compared with the literature.*

***Results**: Persistent or recurrent disease was found in 12 of the 36 patients (33 %). The primary tumour of these 12 cases invaded one or more anatomic region beside nasopharynx: the base of the pterygoid process in 9 cases (75 %), the infratemporal fossa in 4 (33%), the pterygomaxillar fossa in 4 (33 %), and the sphenoid sinus in 2 cases (17 %). Involvement of the pterygoid process base was observed in only 3 of the 24 patients without persistent disease, whereas it was found 10 out of 12 patients with persistent disease.*

***Conclusions**: Advances in radiographic imaging, embolization, and surgical methods of treating angiofibromas have changed the sites associated with a high risk for persistent disease or morbidity. These changes have made it necessary for the authors to devise more appropriate classifications and, subsequently, several new staging systems were gradually introduced. Recent technological advances, particularly angled endoscopes, have resulted in improved exposure. In the light of all these recent advances, data from our series, and the literature, we suggested a new classification for determining the risk of persistent disease, choosing the appropriate surgical method, and for maintaining uniformity.*

Key words: angiofibroma, endoscopy, nasopharyngeal neoplasm, neoplasm staging, surgery

INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is a benign, highly vascular and locally aggressive tumour, which occurs primarily in adolescent males and accounts for 0.05% of all head and neck neoplasms. It may cause significant morbidity and occasional mortality. Although it is generally known as a neoplasm, recent theories have questioned whether it is a vascular malformation [1-3]. Since it was first described, the treatment of JNA has undergone an evolution. The introduction of endoscopes has made a significant improvement in the surgery of JNA. Preoperative tumour stage is very important in predicting the prognosis of JNA patients. The need for a uniform classification system has been expressed by other authors [4]. We analyzed our cases according to the extension of the tumour, the difficulties during surgery, and the localization of persistent disease, which has led us to suggest a new classification system. This proposed revision of the staging, which is based on both our experience and the literature, was devised to offer improved evaluation for the risk of tumour recurrence, as well as the capability for inter-institutional comparison of treatment results.

MATERIALS AND METHODS

Retrospective case studies were performed at a tertiary care centre.

Fifty-seven patients with JNA, who received treatment between 1983 and 2002, were analyzed. All the patients were male with a mean age of 16 years. Of all 57 patients, only 36 could be verified on files. These 36 patients made up our study group. The follow-up period of patients ranged from 3 to 7 years (mean, 4.5 years). Twelve patients had surgery, which was endoscopically or endoscopically assisted, and the other 24 patients had surgery with external surgical approaches. Medical

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records of the patients were analyzed based on the type of surgery, recurrences, and recurrence site. A new classification system was proposed according to these findings.

RESULTS

Residual disease was found in 12 of the 36 patients (33 %). Frequency of the residual disease was 17 % (2 of 12 cases) in the endoscopy group and 42 % (10 of 24 cases) in the externally approached group.

When all 12 patients with residual disease were considered, the residual tumour involved the sphenoid sinus in 2 patients (17%), the pterygomaxillar fossa in 4 patients (33%), the infratemporal fossa in 4 patients (33%) and the base of the pterygoid process in 9 patients (75%).

Involvement of the base of the pterygoid process by primary tumour was found in only 3 of 24 patients without residual disease, whereas it was observed in 10 of 12 patients who did have residual disease.

Both patients with residual tumour in the endoscopy group, had the residual tumour around the cavernous sinus on follow-up and in one of the cases, the base of pterygoid process was also involved.

In the externally approached group, persistent tumour involved the sphenoid sinus in 2 of the 10 patients, and the base of the pterygoid process in the remaining 8 patients. Among those 8 patients, tumour involvement extended to the pterygomaxillar fossa in 4 cases (50%) and to the infratemporal fossa in the other 4 (50%). In one of the cases in which persistent disease was found in the infratemporal fossa, the original tumour had a significant intracranial extension with a cephalic distension of the anterior cerebellar branch of the internal carotid artery. Interestingly, there was no persistent tumour in the intracranial cavity of this patient.

DISCUSSION

Preoperative tumour staging is a critical factor regarding prognosis. Staging systems were developed mainly to predict recurrence and to compare surgical results. They are based upon the behaviour of the tumour, the routes of spread, difficult areas for surgical exposure, and possible sites of recurrence. In 1981, Sessions et al. [5] suggested a staging system for JNA according to benign behaviour of the tumour. In 1984, Chandler [6] suggested another classification based on the system proposed for nasopharyngeal cancer by the American Joint Committee. However, this staging system does not reflect the benign behaviour of the tumour and does not differentiate extranasopharyngeal sites, except the sphenoid sinus and intracranial cavity. In 1989, Fisch [7, 8], proposed a new classification with special emphasis on dural involvement (Table 1). In 1996, Radkovski et al. [9] suggested a modification of the staging system of Sessions by stressing the importance of tumour extension posterior to the pterygoid plates (stage IIC). Radkovski et al. [9], differentiated between minimal (stage IIIA) and extensive intracranial tumour spread with possible tumour extension to the dural folds of cavernous sinus (stage IIIB). In the last decade, increased experience with advanced endoscopic and microscopic surgery and new techniques in embolization modified the surgical technique. Angled endoscopes gave surgeons enhanced exposure around the corners of compartments, enabling the removal of the tumour from these areas. Subsequently, the sites of recurrences changed. This change also brought the need for a new classification system.

Lloyd et al. [10] found pterygomaxillar fossa involvement in all of their 72 patients with JNA. The tumour was present in 100 percent of patients in both the pterygomaxillar fossa and the nasal cavity. Therefore, they suggested that angiofibroma arises in the pterygomaxillar fossa in the recess behind the sphenopalatine ganglion, at the exit aperture of the pterygoid canal. This is also consistent with our findings. Some degree of pterygomaxillary fossa involvement was always present in all tumours, even in very small ones. Therefore, partial involvement of the pterygomaxillary fossa should be classified as stage I. Most tumours show some degree of ethmoid or sphenoid sinus involvement. This does not affect the prognosis or surgical approach. Tumours confined to these sinuses have no adhesions to the sinus walls, so they can be removed without any difficulty. Figure 1 shows unilateral sphenoid sinus involvement and displacement of sphenoid sinus septum by a tumour in one of our patients. The tumour could have been dissected and removed endoscopically from the sphenoid sinus without any risk for leaving any remnants.

Two patients in our series, who had surgery by an external approach, had residual tumours involving the sphenoid sinus. In contrast, none of the patients in the endoscopic group showed any residual tumours in this area, even those with tumours that had arterial supply from the internal carotid artery (Figure 2). We believe that complete control of this area is possible with endoscopy. Therefore, ethmoid and sphenoid sinus involvement should also be classified as stage I. On the other hand, maxillary sinus involvement changes the surgical

Table 1. Fisch classification of nasopharyngeal angiofibroma (PMF: pterygomaxillary fossa, ITF: Infratemporal fossa).

Type	Description
I	Tumor limited to the nasopharynx and nasal cavity, bone destruction is negligible or limited to the sphenopalatine foramen.
II	Tumor invading the PMF or the maxillary, ethmoid, or sphenoid sinus with bone destruction.
IIIA	Tumor invading the ITF or orbital region without intracranial involvement.
IIIB	Tumor invading the ITF or orbit with intracranial extradural parasellar involvement.
IVA	Intracranial intradural tumor without infiltration of the cavernous sinus, pituitary fossa, or optic chiasm.
IVB	Intracranial intradural tumor with infiltration of the cavernous sinus, pituitary fossa, or optic chiasm.

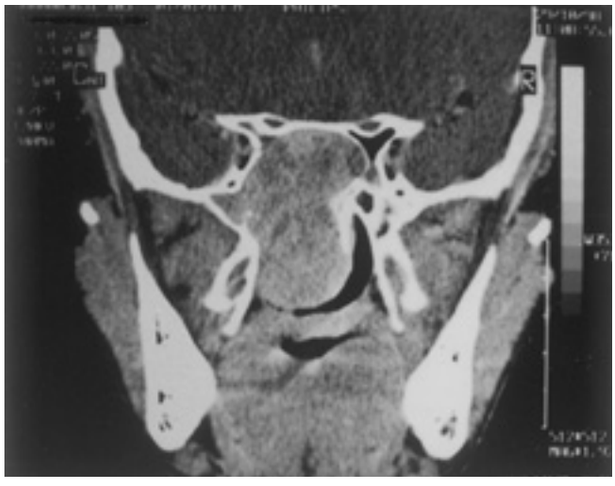

Figure 1. MRI scan shows unilateral sphenoid sinus involvement and displacement of sphenoid sinus septum by the tumour (Stage I).

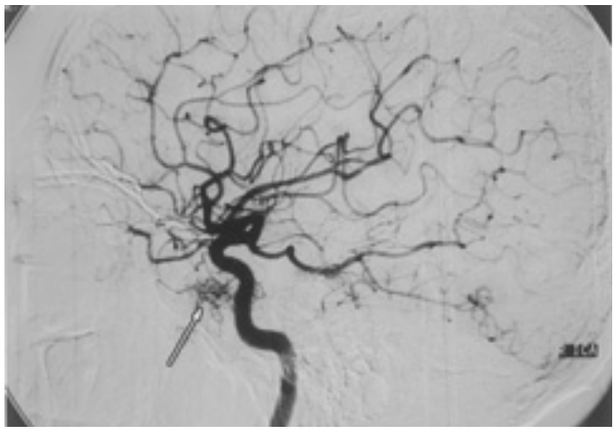

Figure 2. Selective angiography indicates a small portion of the tumour (arrow) in the sphenoid sinus has arterial supply from the internal carotid artery.

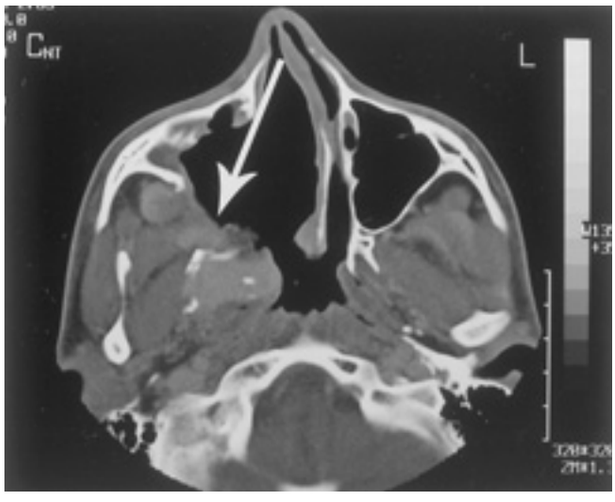

Figure 3. Postoperative CT scan shows excellent transnasal exposure (arrow), achieved by bone removal.

approach, denotes a bigger tumour, and therefore should be classified as stage II.

Fisch classified any pterygomaxillary fossa involvement as stage II [8]. Sessions [6] and Radkovski [9] classified minimal invasion of this region as stage IIA, and full occupation as stage IIB. Full occupation of the pterygomaxillary fossa indicates a more advanced tumour, and requires considerably more drilling of the anterior and medial bony structures of the fossa. For that reason, full occupation of the pterygomaxillary fossa was included in stage II. It is not an ominous sign for the tumour, since by drilling the posterior wall of the maxillary sinus and using angled endoscopes, this area can be completely cleaned. Postoperative CT scan of one of our patients shows that excellent exposure of this area is possible after drilling (Figure 3). A problem arises when there is invasion of the cancellous bone at the base of pterygoid plates. These tumours may even invade the greater wing of the sphenoid bone and this area is generally a source of recurrence. The extension into the cancellous bone, instead of simple pressure erosion at the pterygoid base, is indicative of the behaviour of the tumour (Figure 4). Lloyd et al. [11] found 93 % of their recurrences in patients with invasion and expansion of the cancellous bone at the base of pterygoid plates. Howard et al. [12] suggested drilling of the sphenoid bone after tumour removal appears to provide a lower rate of residual tumours. In our cases, 75% of the recurrences were found at the base of pterygoid plates. Endoscopic or microscopic surgery together with minimized bleeding by means of hypotensive anesthesia and preoperative embolization, provides better access to this region than conventional techniques. However, the increased ability to drill out the base of pterygoids and to remove tumour remnants does not guarantee complete excision. The risk of recurrence is still high for such tumours. This area also provides a route for middle cranial fossa invasion. Therefore, those patients should be carefully analyzed for middle fossa involvement with detailed imaging studies, since this will classify the

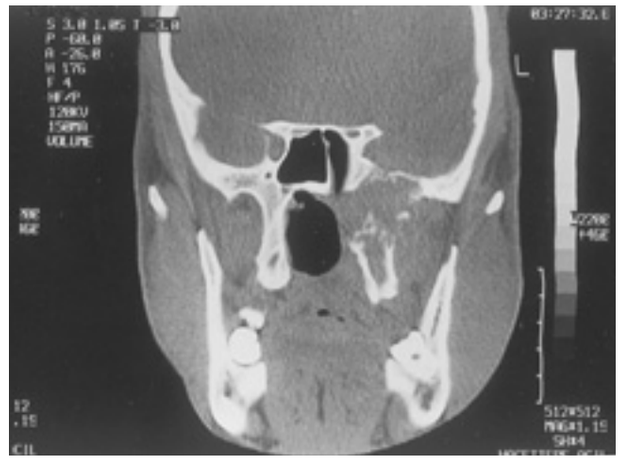

Figure 4. Deep extension into the cancellous bone at the base of the pterygoid and greater wing of the sphenoid (Stage III).

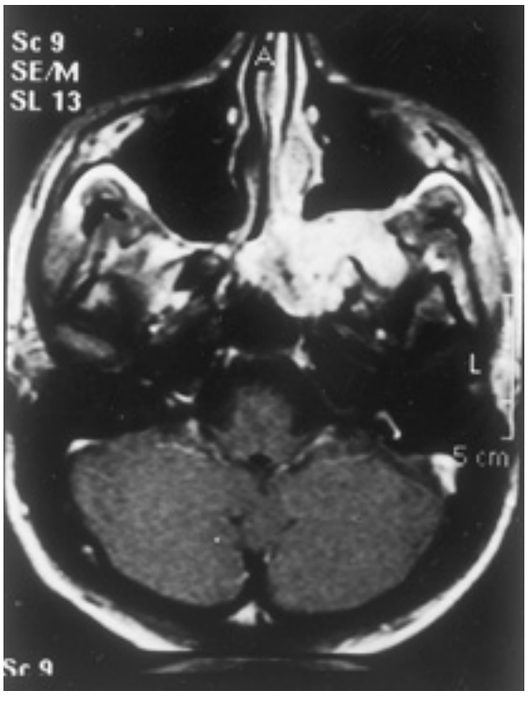

Figure 5. Limited infratemporal fossa extension (Stage II).

tumour as stage IV. In previous classification systems, the extension into the cancellous bone at the base of pterygoid plates had not been addressed. In the suggested classification, this extension is included in stage III, since the greatest number of recurrences occurs in this area.

Infratemporal fossa extension presents a challenge for the surgeon. The conventional techniques may be inadequate for complete removal, especially when the tumour reaches too far laterally. Infratemporal fossa involvement also brings the risk of intracranial extension via the foramen lacerum and foramen ovale. Significant lateral extension into the infratemporal fossa, in particular, towards the area of the cheek, is not readily accessible with endoscopes or midline approaches [13]. Even angled endoscopes and angulated instruments would not guarantee the complete removal of the tumour. Roger et al. [14] stressed the importance of the infratemporal fossa and the difficulty in resection due to the possible interdigitating penetration of the tumour. They reported that involvement of the base of the skull and, especially, the roof of the infratemporal fossa, the cavernous sinus, and the body of the sphenoid are all associated with an increased rate of relapse. Herrman et al. [13] also found that infratemporal fossa involvement was associated with an increased risk of recurrence, although they attributed this to the choice of anterior approaches in their cases. In 33% of our recurrent patients, there were extensive tumours in the infratemporal fossa. Extension posterior to the pterygoid plates into the medial and lateral pterygoid muscle region presents another challenge for the surgeon. Generally, tumours in this area are missed. Therefore, these tumours should be considered as stage III. On the other hand, no recurrences were observed in our endoscopic group with limited posterior and infratemporal fossa extension (Figure 5). If the tumour does not reach beyond the lateral border of the posterior maxillary sinus wall (limited infratemporal fossa extension), it can be removed by drilling out the posterior maxillary sinus wall (Figure 3). Although, transnasal removal of some extensive lateral extensions is possible in the absence of skull base penetration and infiltration (Figure 6), complete removal is not guaranteed. Therefore, we should differentiate limited (stage II) and extensive (stage III) infratemporal fossa extension, since this has a very close relationship with the risk of residual disease and surgical access.

Radkowski classified minimal intracranial extension as stage IIIA and extensive extension as IIIB, regardless of the localization of involvement [9]. Fisch classification stresses only the

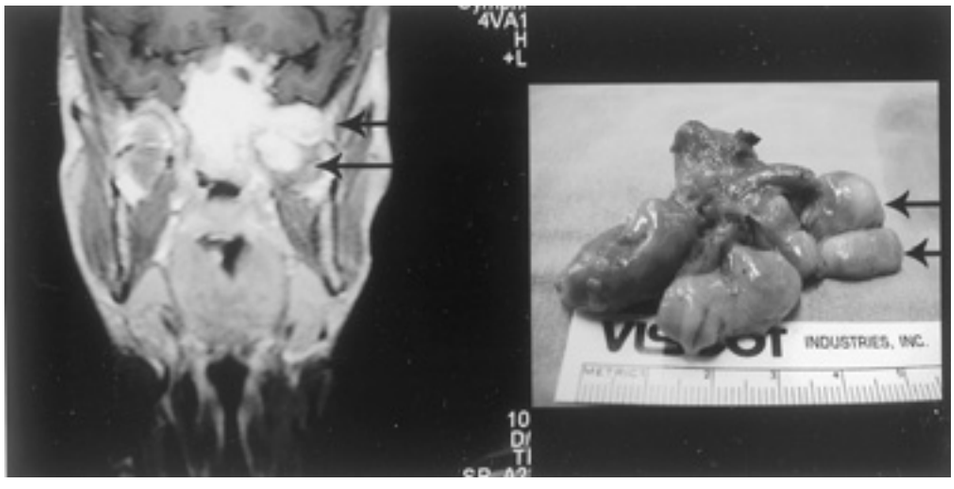

Figure 6. Complete endoscopic removal of lateral tumour expansions in the absence of infiltration. Tumour lobules in MRI scan and specimen (arrows) show comparable match.

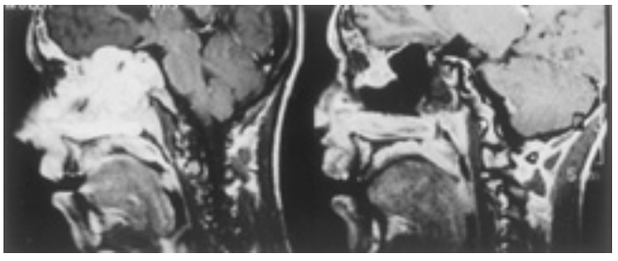

Figure 7. Anterior cranial fossa extension removed by the endoscopic approach. Preoperative and postoperative sagital MRI scans are seen on the left and right, respectively (Stage II).

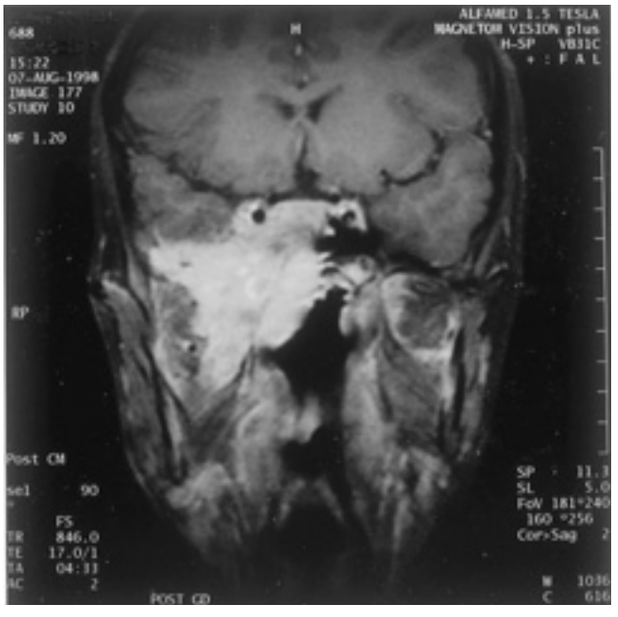

Figure 8. MRI scan of a large tumour shows middle cranial fossa involvement and cavernous sinus obliteration.

involvement of the cavernous sinus, pituitary fossa, or optic chiasm, but it does not take into consideration other intracranial sites [8]. Yet, both the site and degree of the intracranial extension played a major role in recurrence in our patients. Anterior fossa extension does not present any difficulty in endonasally removing the tumour from this area (Figure 7). In contrast, middle fossa involvement was correlated with an increased risk of recurrence (Figure 8) due to unresected tumour extensions in this area and also to the larger size of such tumours. Therefore, anterior and middle cranial fossa extension is differentiated in our revised classification system (anterior fossa involvement as stage II, middle fossa involvement as stage IV).

The main contribution of Fisch classification is dural involvement [8]. According to Fisch [8], an extradural tumour is stage IIIB, and an intradural tumour is stage IVA. Infiltration of the cavernous sinus, pituitary fossa, and optic chiasm makes it stage IVB. This Fisch classification system mainly reflects a lateral approach policy. However, cavernous sinus involvement is not always a poor prognostic indicator, because the tumour never invades the sinus by cellular infiltration, as do malignant carcinomas. Actual, dural penetration is unlikely and some lesions obliterating the cavernous sinus can often be removed through the nose, which does not present any problem, except for some venous bleeding after resection. Even large intracranial extensions, which may become adherent to the dura, can be dissected. Although the possibility of intradural extension cannot be denied, to prove this, the tumour should be seen intradurally from an initial neurosurgical approach, or the tumour transgressing the dura should be shown histopathologically. To the best of our knowledge, there is only one documented case in the literature that fulfilled these criteria [4,15,16]. We did not find any intradural tumour involvement in any of our cases, even in the presence of intracranial extension. On the other hand, the staging systems are based on the radiological appearance of the tumour before surgery. It is often not possible to radiologically distinguish whether the tumour extends intradurally or not [4]. Therefore, in the revised classification system dural involvement was not taken into consideration.

Instead of dural involvement alone, the site and extent of intracranial involvement was found to be more important to us. Cavernous sinus obliteration in preoperative MRI scanning is a challenge for surgeons (Figure 8). Although bleeding might result in incomplete tumour resection in some larger tumours, complete transnasal removal can be achieved in some cases. Even in some patients with residual tumour, postoperative radiological appearances of small tumour remnants remain stabilized without any radiological and clinical progress [17].

Intracranial tumour extension between the pituitary gland and internal carotid artery, and posterolateral to the internal carotid artery presents difficulty in surgical resection and may result in severe hemorrhage [18] (Figure 9). Normally, tumours filling

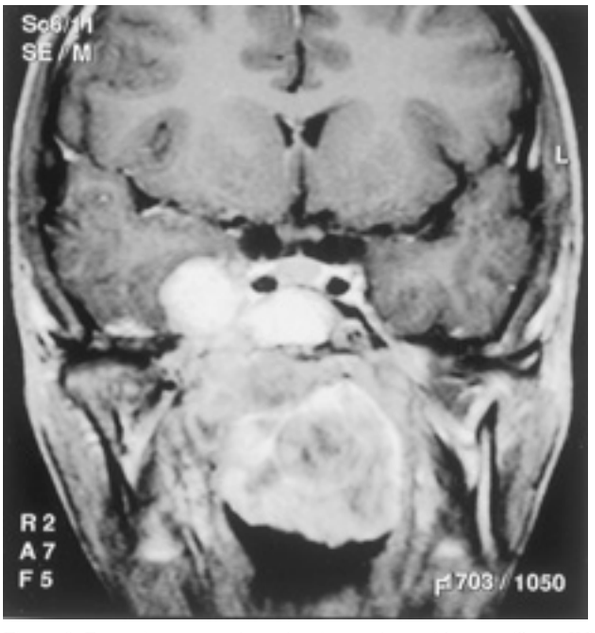

Figure 9. Extension posterolateral to internal carotid artery (Stage IV).

Table 2. Revised staging system for juvenile nasopharyngeal angiofibroma (PMF: pterygomaxillary fossa, ITF: Infratemporal fossa).

Stage	Site
I	Extension to the nose, nasopharyngeal vault, and sphenoid sinus.
II	Extension to the maxillary sinus or the anterior cranial fossa, full occupation of the PMF, limited extension to the ITF, or the pterygoid plates posteriorly.
III	Deep extension into the cancellous bone at the base of the pterygoid or the body and the greater wing of the sphenoid, significant extension to the ITF or pterygoid plates posteriorly or orbital region, and obliteration of cavernous sinus.
IV	Intracranial extension between the pituitary gland and internal carotid artery, tumor extension posterolateral to the internal carotid artery, and extensive intracranial extension.

the sphenoid sinus can be removed without any difficulty. However, resection will be difficult or be accompanied by high risk, when the tumour spreads intracranially between the internal carotid artery and pituitary gland, or lateral and posterior to the internal carotid artery. Therefore, these cases should be classified as stage IV.

As a result, the following points should be taken into consideration of the classification system:

1. Ethmoid and sphenoid sinus invasion has no effect on persistent disease and can be completely removed endoscopically and should be classified as stage I.
2. Minimal extension to the pterygomaxillary fossa should be classified as stage I, since all tumours show minimal extension from the site of origin to this fossa.
3. Maxillary sinus invasion and full occupation of the pterygomaxillary fossa should be placed in stage II, because it denotes a bigger tumour and a more extensive approach, but can still be removed completely.
4. If the tumour does not reach beyond the lateral border of the posterior maxillary sinus wall, it can be removed by drilling out the posterior maxillary sinus wall. Therefore, we should differentiate limited infratemporal fossa extension from significant infratemporal fossa extension. Significant infratemporal fossa extension and extension posterior to pterygoid

Table 3. Staging Systems for juvenile nasopharyngeal angiofibroma (PMF: pterygomaxillary fossa, ITF: Infratemporal fossa).

Stage		**Chandler et al 1984**	**Sessions et al. 1981**	**Radkowski et al. 1996**	**Revised**
I	A	Tumor confined to the nasopharyngeal vault	Limited to the nose or nasopharyngeal vault	Same as in Sessions'	Nose, nasopharyngeal vault, ethmoidal-sphenoidal sinuses, or minimal extension to PMF
	B		Extension into one or more sinus	Same as in Sessions'	
II	A	Tumor extending into the nasal cavity or sphenoid sinus	Minimal extension to PMF Full occupation of PMF	Same as in Sessions'	Maxillary sinus, full occupation of PMF, extension to the anterior cranial fossa, and limited extension to the infratemporal fossa
	B		with or without erosion of orbital bones	Same as in Sessions'	
	C		Infratemporal fossa with or without cheek	Or posterior to the pterygoid plates	
III	A	Tumor extending into antrum, ethmoid sinus, PMF, ITF, orbit, and/or cheek	Intracranial extension	Erosion of skull base minimal intracranial	Deep extension into the cancellous bone at the base of the pterygoid or the body and the greater wing of the sphenoid, significant lateral extension to the infratemporal fossa or to the pterygoid plates posteriorly or orbital region, cavernous sinus obliteration
	B			Erosion of skull base extensive intracranial with/without cavernous sinus	
IV		Intracranial tumor			Intracranial extension between the pituitary gland and internal carotid artery, tumor localization lateral to internal carotid artery, middle fossa extension, and extensive intracranial extension

plates has a higher risk of persistent disease and should be classified as stage III, whereas limited infratemporal fossa extension should be classified as stage II (Figure 5).

5. Deep extension into the cancellous bone at the base of the pterygoid, corpus, and greater wing of the sphenoid has a high risk of persistent disease. Therefore they should be included in stage III (Figure 4).
6. Anterior cranial fossa involvement is not a main cause of recurrences, and should be differentiated from middle fossa or extensive intracranial extension (Stage II versus Stage IV; Figure 7, 8).
7. Cavernous sinus obliteration in MRI is a challenge for surgeons, but complete tumour removal is more likely than in other types of extensive middle fossa invasion lateral to the internal carotid artery, or through the space between internal carotid artery and pituitary gland (Stage III versus Stage IV; Figure 9).

This new classification with 4 stages, maintains simplicity without sacrificing the predictability of the risk of persistent disease or the appropriate choice of surgical method. Stage I indicates low possibility of persistent disease by endonasal endoscopic/microscopic approach. Stage II indicates low possibility of persistent disease, but denotes a larger tumour, which requires more extensive surgery, such as combining Caldwell-Luc or additional endonasal drilling. Stage III represents a high possibility of persistent disease and more extensive surgery. Stage IV is indicative of a very high possibility of persistent disease and morbidity or an unresectable tumour, and combined extensive (intracranial) surgery should be considered.

CONCLUSIONS

The classification systems of Radkowski (modification of Session Classification) and of Fisch do not cover all aspects of tumour extension and recurrence. We suggest classifying stage II A in Sessions classification as stage I, since all JNA originate from this area. All stage I tumours can be completely removed with very low risk of recurrence. Stage II is associated with low risk of recurrence when proper surgical techniques are used. Stage III tumours have a higher risk of recurrence and the degree of the intracranial extension must be determined carefully. Stage IV tumours always required a combined approach and complete resection may not be possible. Full occupation of the pterygomaxillary fossa, which is stage II B in Sessions' classification, is considered stage II in our classification system, since this area is now afforded better access. To stress the importance of deep cancellous bone invasion and to include these patients in the staging system these cases were classified as stage III, indicating a more advanced stage than mere pterygomaxillary fossa extension. To differentiate limited and extensive lateral extension in the infratemporal fossa and posterior to the pterygoid plates, limited lesions were classified as stage II and extensive lesions as stage III. The tumour can be dissected from the cavernous sinus, but it is more difficult to remove the tumour when it spreads to the intracranial cavity between the pituitary gland and internal carotid artery, or laterally to the internal carotid artery (Stage III versus IV). To clarify the difference between anterior and middle fossa involvement, anterior cranial fossa involvement is classified as stage II, and middle fossa invasion as stage IV (Table 2, 3).

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