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Juvenile nasopharyngeal angiofibroma: the routes of invasion*

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SUMMARY *The juvenile nasopharyngeal angiofibroma has a characteristic growth in all directions from its origin. However, the extensions of the tumor seem to be independent, each one with distinct behavior. The aim of this study is to analyze the preferential direction and routes of JNA growth, as well as its correlation with the patient's age. We analyzed 33 patients without any previous treatment, attempting to the extension and routes of tumor's growth (CT scan), and its correlation with the patient's age. The sphenopalatine foramen region was affected in all cases. From this point, a growth towards several routes with a different rhythm was noted, determining variable configurations to the tumor. The lateral and superior growths were the most frequent. The expansion into the pterygopalatine fossa was very frequent and could involve important anatomical structures, determining higher morbidity. Three sites were invaded through more than one route: pterygoid fossa, middle cranial fossa and maxillary sinus. There was no significant correlation between invasion route and patient's age. However, considering the age, there was a concomitance between tumor development and facial growth by "displacement". We discuss this condition, suggesting an explanation to the tumor invasion and expansion inside the pterygopalatine fossa.*

Key words: angiofibroma, skull base tumors, facial growth, pterygopalatine fossa, nasopharyngeal tumors

INTRODUCTION

Although the juvenile nasopharyngeal angiofibroma (JNA) is a benign tumor, its behavior is often aggressive. From its origin in the sphenopalatine foramen region, the tumor grows in all directions through multiple projections. However, these projections have distinct rates of development. Some tumors show preference to grow laterally, while others toward a posterior, medial, anterior or superior direction. The explanation to this fact is still unknown.

Another controversial characteristic is its tendency to grow through high resistance ways between the bones, instead of only occupying space. The best example is the invasion of the pterygopalatine fossa through the narrow pterygomaxillary fissure, which is considered the most important event to the tumor development (Weprin and Siemers, 1991). A similar question remains about its preference to invade the cranial fossa by a parasellar route (lateral to the sphenoid sinus) rather than through the sphenoid itself, which represents an easier route.

Also, some authors believe that the tumor aggressiveness is related to the patient's age, observing that both intracranial and infratemporal invasion usually occur in younger patients (Jafek et al., 1979). However, others did not find this correlation and consider these extensions as a result of anatomic peculiarities (Bremer et al., 1986).

The aim of this study is to analyze the preferential direction and routes of JNA growth, as well as its correlation with the patient's age.

MATERIAL AND METHODS

Thirty-three untreated patients with histological diagnosis of JNA were studied in the Otolaryngology Department of the University of São Paulo. All patients were white males and the age ranged from 9 to 25 years (mean 15.66; median 16 years).

The extension of the tumor was evaluated on CT scans (iodine-contrasted coronal and axial 5mm cuts) and they were classified according to Sessions et al. (1981). The route of invasion of each craniofacial site was deduced by the dislocation

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and/or erosion of the bony wall. A synthesis of the routes of growth in each projection of the tumor was plotted in standard axial and coronal schemes.

From the sphenopalatine foramen, the anatomical sites were classified according to the direction of growth: anterior (nasal cavity and maxillary sinus); posterior (pharyngeal recess, pterygoid fossa and parapharyngeal space); lateral (pterygopalatine, infratemporal and temporal fossa); superior (sphenoid sinus, orbitary cavity and cranial fossa) and medial (nasopharynx and contralateral sites).

Table 1. Distribution of the patients according to the tumor stage (Sessions classification).

Stage	Patient n.	%	Mean age* (years)
IA	1	3.03	11
IB	5	15.15	15.6
IIA	4	12.12	17.25
IIB	9	27.27	16.55
IIC	3	9.09	17
III	11	33.33	15

* Kruskal-Wallis anova by ranks and median test (p=[illegible])

Table 2. Frequency of invasion of each anatomical site and the correlation between the direction of growth and the patient's age.

Anatomical site	Invasion n	%	Direction of growth
Nasal cavity	33	100.00	Anterior
Maxillary sinus	25	[illegible]	
Pharyngeal recess	10	30.30	
Pterygoid fossa	8	24.24	Posterior
Parapharyngeal space	3	[illegible]	
Sphenoid sinus	27	81.81	
Orbitary cavity	16	48.48	Superior
Middle cranial fossa	11	33.33	
Pterygopalatine fossa	27	81.81	
Infratemporal fossa	19	[illegible]	Lateral
Temporal fossa	4	12.12	
Nasopharynx	33	100.00	Medial
Contralateral sites	18	54.54	

* [illegible] R non-parametric studies

The patient's age at the time of the radiological study was correlated to the JNA stage, preferential direction of tumor growth and to the routes of invasion of these sites. These correlations were statistically analyzed by Kruskal-Wallis Anova by ranks and median test, Spearman R non-parametric test and Mann-Whitney non-parametric test, respectively.

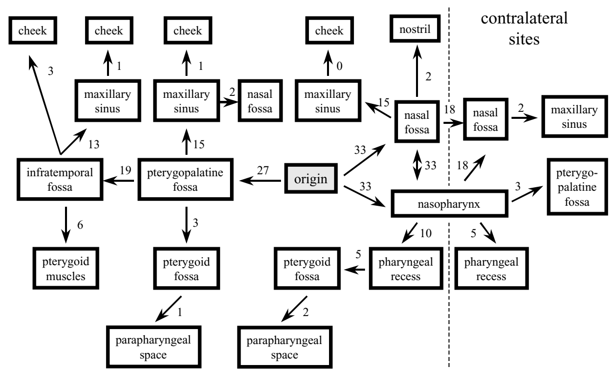

Figure 1. Schematic representation of the routes of invasion of the juvenile nasopharyngeal angiofibroma from its origin toward each anatomical site in the axial plane and the frequency of occurrence.

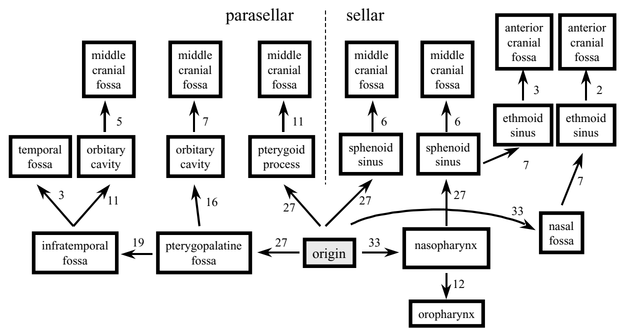

Figure 2. Schematic representation of the routes of invasion of the juvenile nasopharyngeal angiofibroma from its origin toward each anatomical site in the coronal plane and the frequency of occurrence.

Table 3. Frequency of invasion of the three sides invaded by two different routes and its correlation to the patient's age.

Anatomical site	Routes of invasion	Invasion (n. cases)	Age vs Route of invasion*
Maxillary sinus (n=25)	Through nasal fossa	8	
	Through pterygopalatine fossa	8	p = 0.37 (n.s.)
	Both	[illegible]	
Pterygoid fossa (n=8)	Through nasopharynx	5	
	Through pterygopalatine fossa	3	p = 0.40 (n.s.)
	Both	0	
Middle cranial fossa (n=11)	Through sphenoid sinus	[illegible]	
	Through pterygopalatine fossa	6	p = 0.55 (n.s.)
	Both	5	

* Mann-Whitney non-parametric test

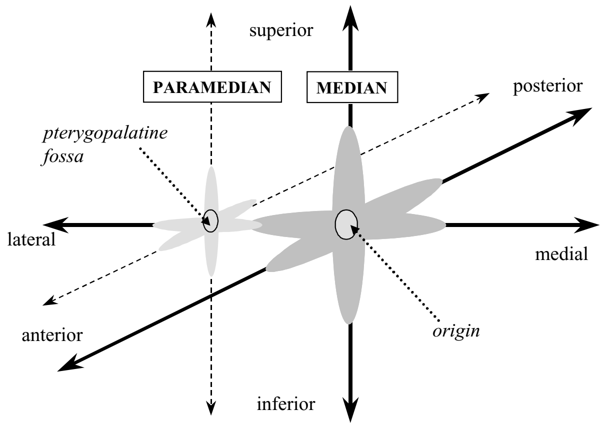

Figure 3. Schematic representation of the multiple directional growth of the juvenile nasopharyngeal angiofibroma from 2 different points: a) the origin in the sphenopalatine foramen (median expansion); b) the pterygopalatine fossa (paramedian expansion).

RESULTS

The classification of JNA based on Session's stage is represented in Table 1. Seventy percent of the patients were in advanced stages (IIb, IIc and III). There was no significant correlation between the patient's mean age and the tumor stage (p=0.86). The frequency of involvement of each anatomical site is represented in Table 2 and the routes of invasion can be observed in the axial and coronal schemes (Figure 1 and 2).

The sphenopalatine foramen region was involved in all cases and was considered the JNA origin. From this point, the tumor involved the nasopharynx and posterior nasal fossa in 100% of the cases and the sphenoid sinus and pterygopalatine fossa in 82%, demonstrating a multidirectional growth toward anterior, medial, lateral and superior directions in more than 80% of cases. The correlation between each direction of growth and the patient's age was not significant.

Once inside the pterygopalatine fossa, the JNA also presented a multidirectional growth, invading the infratemporal fossa and cheek (lateral direction), maxillary sinus (anterior direction), orbitary cavity and cranial fossa (superior direction) and pterygoid fossa (posterior direction).

Three sites were invaded by more than one route: maxillary sinus, pterygoid fossa and middle cranial fossa. There was no significant relation between the route of invasion and the patient's age (Table 3).

DISCUSSION

The JNA preferentially involves adolescents and young males. Although there was a prevalence of advanced tumors in this series (70% of cases were stage IIB, IIC or III based on Sessions classification), the patient's average was between 15 and 16 years. Many studies published in Europe and United States (Bremer et al., 1986; Spector, 1988; Lund et al., 1989; McCombe et al., 1990; Ungkanont et al., 1996) referred patients with earlier tumors, but the average age was always similar to ours. Besides, there was no relation between the patient's age and the parameters of tumor extension as stage, preferential direction of growth or routes of invasion. So, these findings support that the tumor aggressiveness is not related to the patient's age, although observed by others (Jafek et al., 1979).

The sphenopalatine foramen region was involved in all cases and is considered the point of origin of the JNA according to many authors (Bremer et al., 1986; Spector, 1988; Lund et al., 1989; Lloyd et al., 1999). From this point the tumor grows in all directions through multiple projections (Neel et al., 1973; Lloyd et al., 2000). The lateral and superior regions offer higher resistance to the JNA growth and were supposed to be avoided by the tumor. However, they were almost as invaded as the anterior and medial sites, which are empty cavities with lower resistance.

The lateral invasion into pterygopalatine fossa is considered the most important event of JNA expansion (Weprin and Siemers, 1991). It occurred in 81.81% of the cases in this study, always through the pterygomaxillary fissure. This was the

Figure 4A. Invasion of the maxillary sinus through the medial wall by tumor expansion in nasal fossa (arrow).

Figure 4B. Invasion of the maxillary sinus through the posterior wall by tumor expansion in pterygopalatine and infratemporal fossa (arrow).

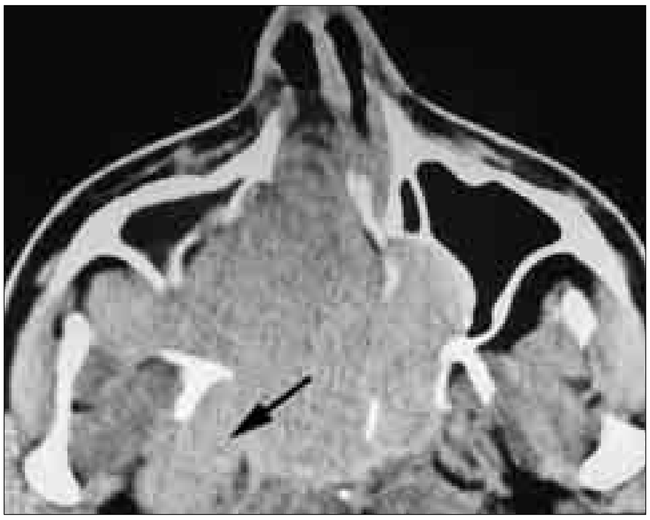

Figure 5A. Invasion of the pterygoid fossa and parapharyngeal space by tumor expansion in nasopharynx (arrow).

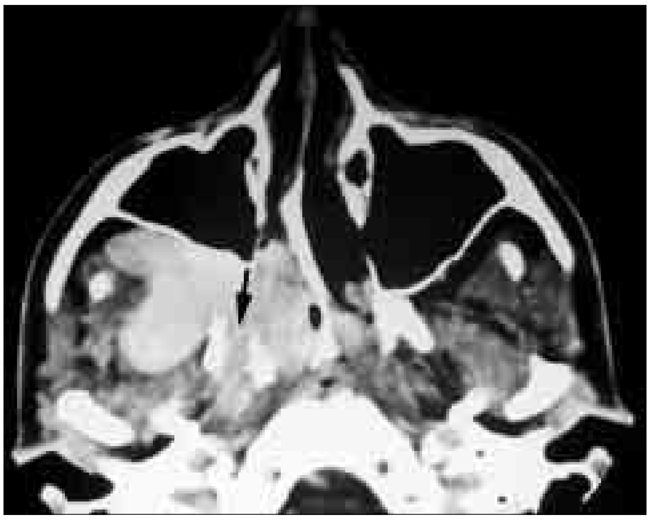

Figure 5B. Invasion of the pterygoid fossa and parapharyngeal space by tumor expansion in pterygopalatine fossa (arrow).

exclusive route of invasion into infratemporal fossa, cheek and orbitary cavity, the main route to middle cranial fossa (90%) and maxillary sinus invasion (65.2%), and a secondary route to the pterygoid fossa invasion (37.5%). So, the pterygopalatine fossa invasion also allowed the JNA to get into sites classified as anterior, lateral, posterior and superior in relation to its origin. However, this invasion resulted from a paramedian rather than a median expansion of the tumor (Figure 3). This paramedian growth is related to a higher morbidity due to many important anatomical structures. It may promote facial asymmetry, exophthalmia, intracranial and cavernous sinus invasion, dysfunction of cranial nerves and frequent recurrences (Achouche et al., 1992; Herman et al., 1999; Lloyd et al., 2000).

All cases presented expansion to anterior and medial sites. Although they did not offer resistance to the tumor growth, it usually preferred other directions, suggesting a stronger biological control rather than a physical one. These sites are also related with less morbidity, even in large involvement. There are spaces to be occupied and few anatomical structures to lead to other symptoms besides nasal obstruction and palatal dysfunction (with voice and swallowing alteration). Facial asymmetry could be present in larger maxillary involvement.

Superior expansion to the sphenoidal sinus was observed in 27 cases, and six of them promoted dural exposition. However, 5 of these 6 cases were advanced tumors with larger cranial invasion through the parasellar route. Again, the expected morbidity related to trans-sphenoidal cranial invasion is much lower than the parasellar one, considering the compression of anatomical structures, difficulty in surgical resection and recurrences (Lloyd et al., 1999).

From the pterygopalatine fossa, JNA can invade the medial cranial fossa eroding the base of pterygoid process, invading the pterygoid canal or enlarging the inferior and superior orbitary fissure (Lloyd et al., 2000). Usually JNA does not invade the meninges (Jones et al., 1986; Spector, 1988),

Figure 6A. Invasion of the middle cranial fossa by tumor expansion in sphenoid sinus (arrow).

Figure 6B. Invasion of the middle cranial fossa by tumor expansion in pterygopalatine fossa (arrow).

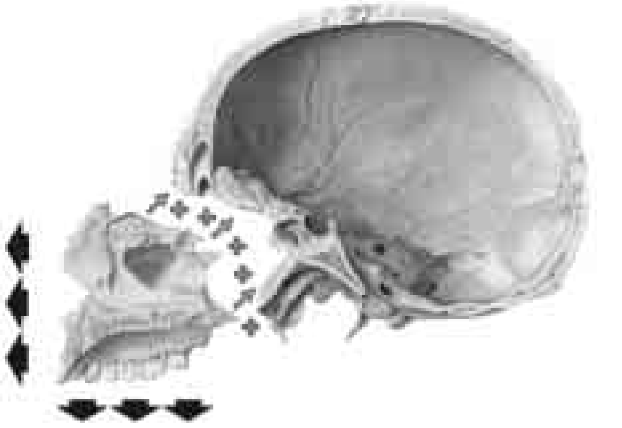

Figure 7A. Facial growth by "displacement", representing the normal growth of the nasomaxillary complex by traction of the soft tissue toward anterior and inferior directions (large arrows), with the tendency to keep bone contact (small arrows), resulting in osteogenic stimulus (+).

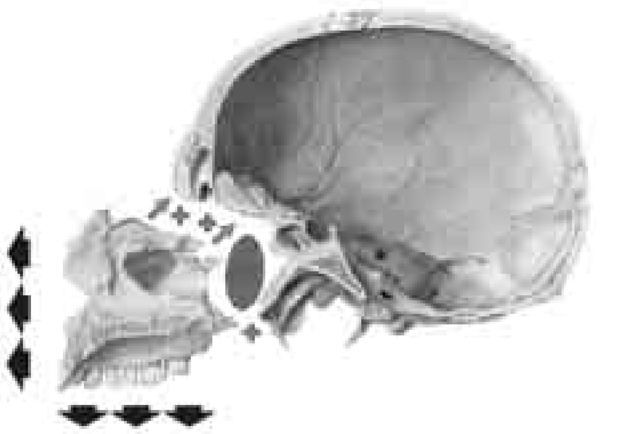

Figure 7B. The presence of the tumor (black ellipse) between the maxillary and the sphenoid bones inhibits the osteogenesis (+), promoting the widening of this fissure during the traction of the soft tissue (large arrows).

although dural invasion may occur in a few cases, especially in recurrence (Butugan et al., 1995; Dannesi et al., 2000). Among the 11 cases with meningeal exposition, just 1 showed invasion and transposition of the dura, without invasion of the brain.

The expansion of JNA from its origin to posterior sites could also represent a paramedian development, and be related to higher morbidity and to greater surgical difficulties because of the involvement of important anatomical structures. The tumor grows into pharyngeal recess, posteriorly to the medial pterygoid plate, resulting in invasion of the pterygoid fossa and parapharyngeal space. This expansion is related to the lacerum foramen (Radkowski et al., 1996), which has a relation with important anatomical structures and represents increased potential morbidity.

We identified 3 sites invaded by more than one route: the maxillary sinus (through the posterior wall and/or lateral wall) (Figure 4); the pterygoid fossa and parapharyngeal space (through the nasopharynx or pterygopalatine fossa) (Figure 5); and the middle cranial fossa (through the trans-sphenoidal route and/or parasellar route) (Figure 6). In all cases, one of the routes was from the pterygopalatine fossa. Although it represents a high resistance way, it was the most frequent route, except for the pterygoid fossa. The challenge of this finding is to understand the pterygopalatine fossa invasion.

Indeed, the walls of the pterygopalatine fossa are not rigid bony structures during the puberty. In males, the craniofacial growth occurs up to 18 years of age, especially between 12 and 14 years. The growth of the nasomaxillary complex occurs through a "displacement" mechanism (Enlow and Hans, 1996), in which the bony structures are displaced anteriorly and inferiorly by the traction of facial soft tissues in expansive growth. In this process, the nasomaxillary complex tends to be separated from the skull base, especially from the sphenoid bone. It stimulates osteogenesis between the maxilla and skull base, promoting simultaneous and proportional bone deposition to keep contact between them (Figure 7a). According to the authors, the interposition of foreign material between these bones would cause the disappearance of the osteogenic stimulus. With the maintenance of traction by the soft tissues in expansion, a passive separation of these articulated bones would occur (Figure 7b).

The most accepted theory for JNA genesis is related to microhemorrhages and fibrous repair. Repeated episodes create a tumor mass that would grow progressively (Beham et al., 1997; Beham et al., 2000; Liang et al., 2000). This process tends to worsen in the presence of vasodilatation and increased local blood flow, especially if the capillaries were malformed. The sphenopalatine foramen region is rich in vascular erectly tissue, which is sensitive to sexual hormones. (Brentani et al., 1989; Nagai et al., 1996). There is a chronological concurrence of sexual development, facial growth and JNA genesis. The adolescence period would create at least two favorable conditions for the development of JNA inside the pterygopalatine fossa: 1) an exacerbated blood flow due to hormonal stimulus and osteogenesis, predisposing to microhemorrhages and fibrous repair; 2) unconsolidated bones in an osteogenic process, especially in the maxillary-sphenoidal interface. With the JNA interposition between these bones, the osteogenesis stimulus disappears with progressive separation of bones, enlarging the pterygomaxillary and maxillo-sphenoidal fissures (inferior orbital fissure) and the pterygopalatine fossa. Thus, a favorable ground for tumoral expansion to the infratemporal fossa (laterally), orbit and cranial cavity (superiorly) would be created.

The tumor size was related to the number of sites involved. However, the preferential direction of growth was not related to its size. For instance, a large tumor with exteriorization through the nostril presented a small lateral projection. The same occurred to the routes of invasion. A tumor with very large extensions in lateral (infratemporal and cheek invasion) and superior (orbitary and cranial fossa invasion) directions preserved the pterygoid fossa and parapharyngeal space. There were also some large tumors that presented a globoid growth, dislocating centripetally the bone structures from its origin, whereas other tumors showed a complex growth with multiple ramifications through the narrow bone fissures.

Although our study revealed many interesting characteristics of JNA growth, several aspects about this very peculiar tumor still need to be elucidated.

CONCLUSION

The expansion of JNA inside pterygopalatine fossa is related to important anatomical structures, promoting potential morbidity and higher surgical difficulties. Although there was no relation between the tumor extension and the patient's age, the concomitance between tumor and facial development could explain the invasion of pterygopalatine fossa, which is one of the greatest challenges to explain the JNA growth.

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