Case Report

Juvenile nasopharyngeal angiofibroma

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Abstract

Juvenile nasopharyngeal angiofibroma (JNA) is a rare benign tumor arising predominantly in the nasopharynx of adolescent males. It is an aggressive neoplasm and shows a propensity for destructive local spread often extending to the base of the skull and into the cranium. Clinically, however, it is obscure with painless, progressive unilateral nasal obstruction being the common presenting symptom with or without epistaxis and rhinorrhea. Diagnosis of JNA is made by complete history, clinical examination, radiography, nasal endoscopy and by using specialized imaging techniques such as arteriography, computer tomography and magnetic resonance imaging. Histopathology reveals a fibrocellular stroma with spindle cells and haphazard arrangement of collagen interspersed with an irregular vascular pattern. A case report of JNA with rare intra-oral manifestation in a 17-year-old male patient is presented in the article. JNA being an aggressive tumor may recur posttreatment. Thus, early diagnosis, accurate staging, and adequate treatment are essential in the management of this lesion.

Key Words: Androgen receptor, juvenile angiofiborma, nasopharyngeal angiofibroma

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INTRODUCTION

Juvenile nasopharyngeal angiofibroma (JNA) is a benign neoplasm of the nasopharynx. It accounts for 0.5% of all head and neck tumors occurring in 1 of 150,000 individuals. Adolescents and young adults between 14 and 25 years are affected, and there is a distinct male predominance.[1] Recent reports suggest that the tumor is more common in the Indian subcontinent than in the West.[2]

Hippocrates first described this tumor in the 5th century B.C. In 1940, Friedberg called it juvenile angiofibroma.[3] The term juvenile is debatable as JNA may occur in older patients as well. However, since a vast majority of the cases do occur between 14 and 25 years of age, this term is retained. The prevalence in males may be explained by high androgen receptor (AR) expression suggesting that JNA is androgen dependent.[3]

Based on the clinical and radiological features, JNA is classified into three types. Type I includes lesions fundamentally localized to the nasal cavity, paranasal sinus, nasopharynx, or pterygopalatine fossa. Type II is a JNA extending into the infratemporal fossa, buccal region, or orbital cavity with anterior and/or minimal middle cranial fossa extension but intact dura mater. Type III is a calabash-like massive tumor lobe in the middle cranial fossa.[4]

The origin and development of JNA is not fully understood. Current debate involves the hamartoma and vascular

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malformation theories.[5] Occasional cases are known to regress like hamartomas.

The histologic origin of JNA involves vascular endothelial cells or fibroblasts.[6] Whether both components proliferate and grow together or one component is responsible for the growth and other merely a bystander is also debated. Recent immunohistochemical and genetic studies throw some light on this topic.

Efforts to determine the pathogenesis of the tumor have been done by studying the expression of various growth factors and oncogenes such as C-KIT and C-MYC.[7] Significantly higher immune staining with CD34, vascular endothelial growth factor, flt-1 and flk-1 in JNF, when compared to orbital cavernous hemangiomas, indicates its vasoproliferative nature. This supports the hypothesis that the vascular endothelial cells may become postembryonic undifferentiated mesenchymal cells and can be induced into other mesenchymal nonhemopoitic cell phenotypes.[5] The GSTM 1 gene has been implicated in the formation of JNA. Loss of expression of GSTM 1 (null genotype) is seen in this tumor.[8]

JNA's sex selectivity and the relatively young age at diagnosis suggest that its development is hormone dependent. Several authors studied ARs, progesterone receptors, and estrogen receptors (ERs) in JNA with discrepancies in the results. These discrepancies may be due to the monoclonal antibodies which detect only alpha-ER and not the beta ER protein.[9]

In spite of the reports of hormonal disorders in patients with JNA and the presence of AR and/or ERs in tumor tissues, no apparent alterations of serum hormone levels are observed. The hormonal influence in JNA remains controversial.[1]

CASE REPORT

A 17-year-old male patient presented with a painless, progressive swelling in the upper jaw since 2 weeks. He also complained of difficulty in breathing since 6–7 months. He had no noteworthy family history or past medical history. Extraoral examination revealed normal appearing overlying skin. Intraoral swelling was diffuse, obliterating the vestibule and extending from the lateral incisor anteriorly till the pharynx posteriorly [Figure 1]. Overlying mucosa appeared normal. On palpation, the swelling was firm and nontender.

Computed tomography (CT) scan showed the presence of a soft tissue mass involving the maxillary sinus, nasal cavity, and nasopharynx. The mass extended superiorly from the skull base till the maxillary tuberosity and anteroposteriorly from nasal cavity till posterior wall of maxillary sinus [Figures 2 and 3].

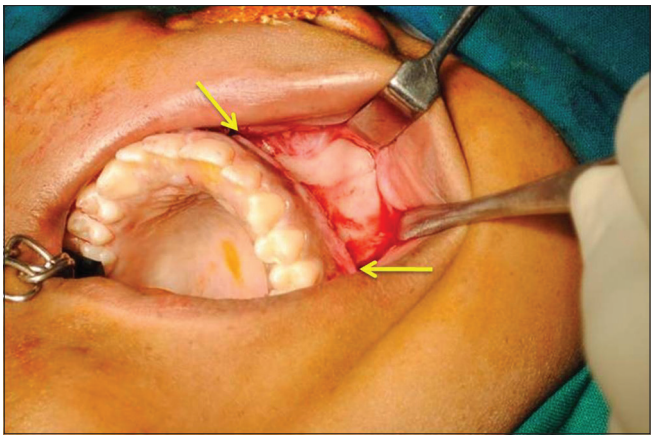

Figure 1: Intraoral view showing swelling on the upper left side of the maxilla and obliteration of the vestibule

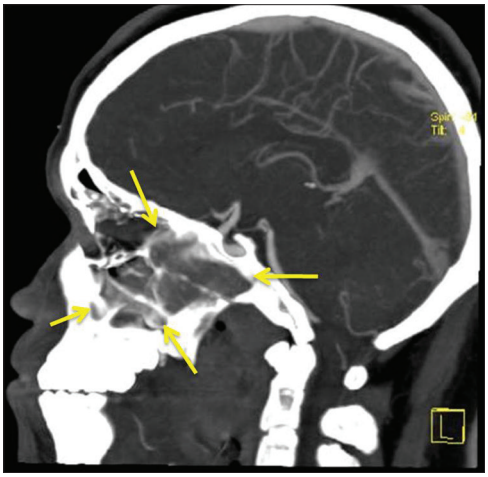

Figure 2: Sagittal section in computed tomography scans showing site and extent of the lesion

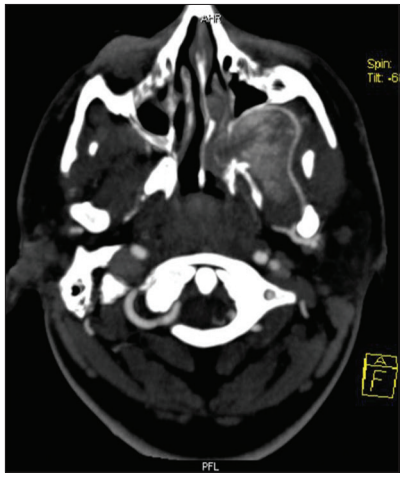

Figure 3: Axial section in computed tomography demonstrating obliteration of the nasal cavity and maxillary sinus

Provisional diagnosis of nasopharyngeal angiofibroma, soft tissue tumor, nasopharyngeal polyp or vascular tumor was

made. Surgical excision was done with moderate intraoperative bleeding. The excised gross specimen was soft to firm in consistency, white to yellow with darker vascular areas. No encapsulation was noted [Figure 4].

Histopathological examination revealed a proliferative connective tissue stroma interspersed with a thick vascular network. Numerous blood vessels with irregular size and shape were seen with a single lining endothelial cell layer. Blood vessels were seen in large number at the periphery of the lesion [Figure 5]. Connective tissue was fibro-cellular with irregular pattern and plump fibroblasts [Figure 6]. Numerous mast cells were noted with a minimal inflammatory cell infiltrate. Figure 7 shows mast cells in toluidine blue stain.

DISCUSSION

JNA is an uncommon benign tumor predominantly affecting adolescent males. Although benign, it is a locally aggressive tumor and invades the surrounding tissues and even bone through pressure resorption.

This tumor originates in the lateral wall of the nasal cavity, close to the superior border of the sphenopalatine foramen.[10] The growth initiates in the submucosa of the floor of the nasopharynx extend to the nasal septum and the posterior space of the nose and causes airway obstruction. Continuous growth involves the sphenoidal sinus, nasal fossa and middle turbinate, pterygomaxillary fossa and the posterior wall of the maxillary sinus as seen in the present case. Eventually, the tumor may invade the infratemporal fossa and the middle cranial fossa.

Isolated case reports of angiofibromas arising outside the nasopharynx are noted, most commonly in the maxillary sinus (32%) and ethmoid sinus (10%).[11] These tumors are clinically distinct from nasopharyngeal angiofibromas. They develop at a slightly older age and occur more commonly in women.

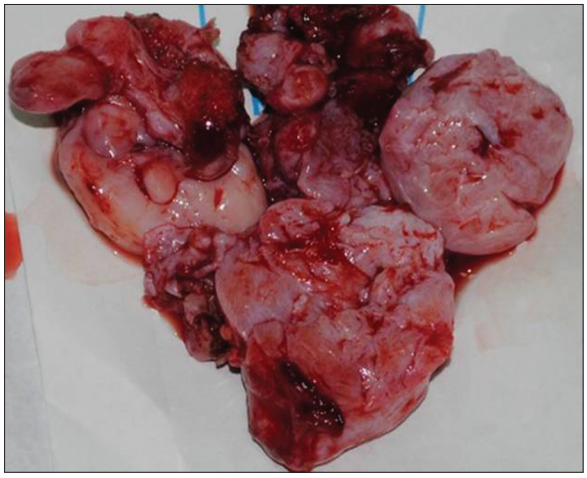

Figure 4: Gross specimen showing tumor mass with vascular areas

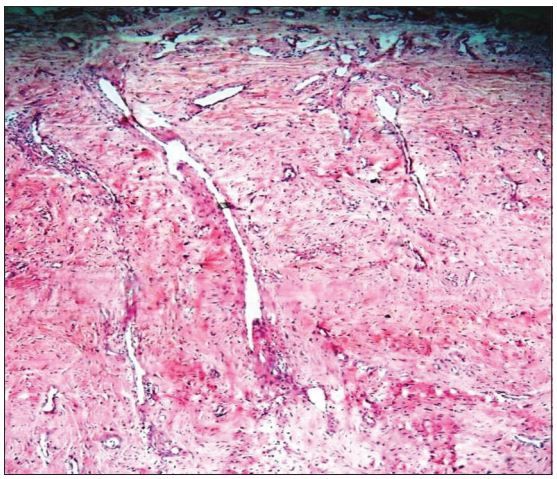

Figure 5: Photomicrograph showing fibrocellular stroma and numerous blood vessels at the periphery (H&E stain, ×40)

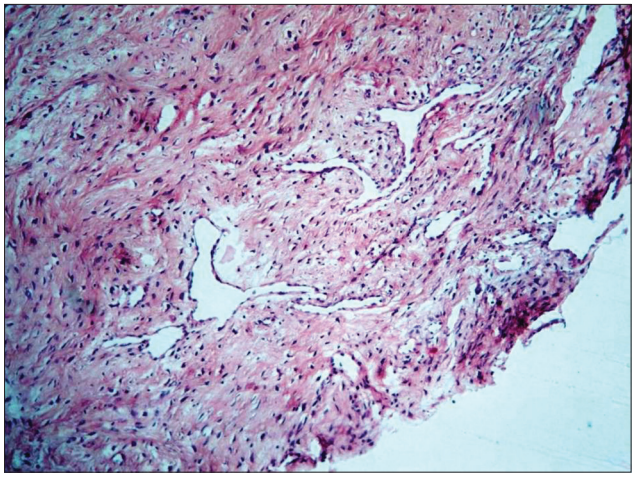

Figure 6: Photomicrograph showing a staghorn appearance of the blood vessels (H&E stain, ×100)

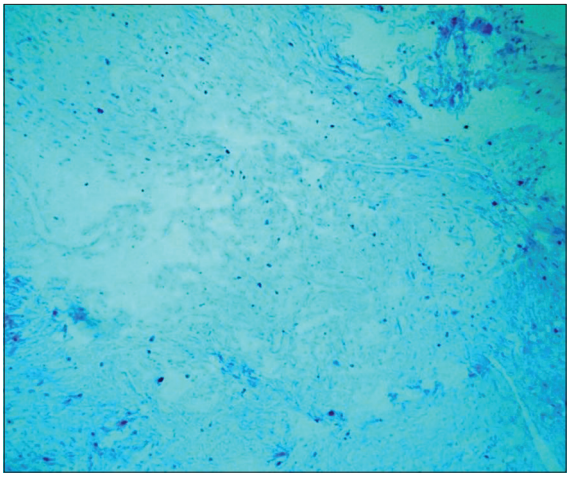

Figure 7: Distribution of mast cells in the lesion (Toluidine blue stain, ×40)

JNA is benign but locally destructive. This may be attributed to a rich vasculature and lack of encapsulation. It impinges on adjacent structures and causes pressure erosion of bone. This invasiveness and extensiveness lead to high recurrence rates of 0–57%.[1]

Chandler *et al*. have proposed several staging systems for JNA.[12] This helps to determine the tumor site and extent. Fisch classification, however, is currently accepted. JNA is classified as Type I when the tumor is restricted to the nasal cavity and the nasopharynx without bone destruction, Type II when the tumor invades the pterygomaxillary fossa and maxillary, sphenoidal and ethmoid sinuses with bone destruction, Type III when the tumor invades the infratemporal fossa, the orbit, and the parasellar region but remains lateral to the cavernous sinus and Type IV when the tumor invades the cavernous sinus, the optic chiasma and the pituitary fossa.[13]

JNA classically presents as a painless, progressive unilateral nasal obstruction. Epistaxis, rhinorrhea and pain may also be seen. Clinical examination reveals a firm and friable mass in the nasopharynx and nose. As this tumor is aggressive and expansile, it invades adjacent structures causing further symptoms. Impaired Eustachian tube function, facial deformity, proptosis and changes in visual acuity may be seen. Invasion of the intracranial region may lead to cranial nerve palsy. Angiofibromas originating outside the nasopharynx may appear as an intraoral mass in the retromolar or buccal space area.[11] Present case did show an intraoral swelling even though it originated in the nasopharynx.

Diagnosis of JNA is made by complete history, clinical examination, radiography, nasal endoscopy; and specialized imaging techniques such as arteriography, CT, and magnetic resonance imaging (MRI). These techniques help to establish the exact site, extension and relation of the tumor to the adjacent structures such as blood vessels and nerves. This makes it possible to precisely stage JNA.[14]

CT images show a heterodense mass that is centered in the sphenopalatine foramen. Avid enhancement is noted on contrast-enhanced CT. At the time of diagnosis, the mass classically involves the pterygopalatine fossa. In this location, it produces widening of the pterygopalatine fossa, inferior orbital and pterygomaxillary fissures and bowing of the posterior wall of the maxillary antrum. Bony erosion of the nasal cavity, hard palate and pterygoid plates is also common. Anterior bowing of the posterior maxillary wall, due to invasion of the pterygomaxillary space on axial CT, known as the Holman-Miller sign is one of the characteristic findings.[15] Coronal CT images show the relationship between the tumor and surrounding structures based on which the staging can be done. Accordingly, the treatment options, operative approach and prognosis can be determined.

MRI is superior to CT for detecting soft tissue extension of the tumor intracranially.[16] The lesion shows low signal intensity in T1-weighted images but heterogeneous intermediate signal intensity in T2-weighted images. Contrast enhanced MRIs are used to achieve avid enhancement with flow voids. These features along with the specific age and sex predilection can help in differentiating JNA from other nasopharyngeal lesions. MRI is used posttreatment to detect residual or recurrent tumor mass and to monitor the effects of radiotherapy.

Angiography is a useful adjunct in the diagnosis of vascular tumors. The location and size of the tumor and feeding vessels are clearly demonstrated by this technique. The vascular supply to JNAs is primarily from distal internal maxillary artery branches, particularly the sphenopalatine, descending palatine and posterior superior alveolar branches.[17] JNAs may also be supplied by the ascending pharyngeal artery.

The main clinical presentation of JNA is unilateral nasal obstruction with or without epistaxis. Any lesion with this presentation may be confused with JNA. These lesions include inflammatory polyps, angiomatous polyps, nasopharyngeal cysts and carcinomas, soft tissue neoplasms such as papilloma, lymphoma, neurofibroma, maxillary malignancies, nasal fossa esthesioneuroblastoma, adenoid hypertrophy, cervical vertebrae cordomas and retropharyngeal ganglia tuberculosis.[18] A careful history noting, age, sex and location of the lesion may help to differentiate JNA from other lesions. Further CT scan and MRI may also help in arriving at a diagnosis. The final diagnosis is achieved by histopathologic examination of tissue sections either on incisional or excisional biopsy.

Macroscopically this tumor appears as a rounded, circumscribed, noncapsulated mucosa covered mass. The color depends on the vascular component and may vary from pale white in less vascular lesions to a pink and wine colored mass in highly vascularized ones.

Histopathologically JNA shows a fibrocellular stroma with spindle cells and haphazardly arranged collagen interspersed with an irregular vascular pattern. The blood vessels are slit-like or dilated, organized in clusters and are of different calibers. A higher density toward the periphery is noted, which was seen in the present case too. The muscular lining of the blood vessel is absent in small and incomplete in larger vessels. A typical staghorn type appearance is seen.

Mitosis is rare.[5] Beham *et al.* in 1997 proved the spindle cells of JNA to be fibroblasts and not myofibroblasts.[18] However, myxoid areas were not present in our case, they can be seen interspersed within the tumor. Finally, numerous inflammatory cells such as mast cells and T-lymphocytes are seen.[19]

Early diagnosis and treatment are required for a good prognosis in JNA. Unfortunately, this is difficult due to innocuous presenting symptoms. Advanced lesions with orbital and intracranial extension are difficult to treat and may recur often. When diagnosed early the patients are treated with a combination of preoperative embolization and surgical resection providing a good prognosis. Advanced JNA is much more difficult to treat.[4] Recurrent tumors must be managed individually taking into account location, age, complications and the possibility of spontaneous resolution. This would better define the treatment strategy.

Several reports suggest that JNA regresses over time. A wait and watch policy with periodic imaging may thus postpone or eliminate the need for surgery and reduce morbidity.[20] Recurrence rates depend on the clinical stage of the tumor but are generally higher in patients with anterior and/or posterior lateral extension than in patients with anterior lateral extension only.[21]

CONCLUSION

JNA is an uncommon, highly vascular, locally invasive, unencapsulated tumor with a distinct predilection for an origin in the nasopharynx of adolescent males. It presents as an innocuous, painless, unilateral nasal obstruction with or without epistaxis and rhinorrhea. Diagnosis is arrived at by clinical examination, radiography, nasal endoscopy and specialized imaging techniques such as CT scan and MRI. The classification and clinical staging is relatively easy and helps to plan treatment and determine prognosis.

Arteriography followed by preoperative embolization and surgical resection is the treatment of choice. JNA being an aggressive tumor may recur posttreatment. Thus, early diagnosis, accurate staging and adequate treatment are essential in the management of this lesion.

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Conflicts of interest
There are no conflicts of interest.

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