Bilateral juvenile nasopharyngeal angiofibroma: A rare case report

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ABSTRACT
Juvenile nasopharyngeal angiofibroma (JNA) is a benign, vascular tumour primarily occurring in adolescent males. Juvenile nasopharyngeal angiofibroma is normally unilateral, originating from the sphenopalatine artery. Two separate masses arising from both sides are exceedingly rare. We report a case of a 29-year-old male presented with increasing nasal obstruction, recurrent epistaxis, and a mass on his left buccal. Computed tomography and magnetic resonance imaging revealed non-contiguous tumours on the right nasopharynx and on the left buccal. Angiography showed independent vascular supplies from each side with no bilateral supply noted. Preoperative embolization on both vascular supplies was done, followed by surgical removal of the tumours with no major complication. Histopathological examination showed both are JNA. No major complications were noted. This case discusses how suspecting bilateral juvenile angiofibroma in a patient with two non-contiguous masses in head and neck region is recommended. Proper diagnosis of bilateral JNA can lead to better management and results.

Introduc

Juvenile nasopharyngeal angiofibroma (JNA) is a rare, highly vascular benign tumour that was first described by Chaveau in 1906. They account for less than 0.5% of all head and neck tumours and the vast majority of cases manifest in males aged 10–24 years [1]. The site of the origin tumour is most likely at the superior margin of the sphenopalatine foramen and spreads into the submucosal plane. Over 98% of the tumours primarily involve the nasopharynx and thus called juvenile nasopharyngeal angiofibroma. Nevertheless, it can occur outside the nasopharynx as reported in some cases. Although benign, JNA can cause morbidity because of their highly vascular nature and local invasion through extensive bone destruction and remodelling [1]. The tumour can extend into the contralateral side of the nasopharynx, giving a false bilateral appearance. A true bilateral mass (two separate mass arising from both sides simultaneously) are extremely rare and to best of our knowledge only four cases was reported and ours is the most exten

Case report

A 29-year-old male complained of worsening nasal obstruction on his right nose following his left nose since 11 years ago, with a history of moderate to severe epistaxis 5 years ago. Another complaint includes enlarged mass on his left cheek for 5 years. History of doubled vision and lump on the neck were denied with no similar family history. On physical examination, a smooth-surfaced mass was causing complete obstruction on the right nose. A fixed, solid mass on the left buccal sized $7 \times 6 \times 5$ cm was found, with wide oropharyngeal space and no destruction on the hard palate (Figure 1). Fibre optic rhinopharyngolaryngoscopy showed a large, smooth-surfaced mass filling the right posterior nasal cavity and nasopharynx, with extension to the left choana causing a partial obstruction in the left nose. The rest of the head and neck examination and laboratory findings were within normal limits.

Biopsy taken from the right nasal cavity showed that the histopathological features can be matched to telangiectasis (vascular malformations). Fine needle
biopsy performed on the left buccal gives negative results since there was no suspicion of angiofibroma. Difficulty in inserting the needle gives the possibility of the tissue not being representative.

Computed tomography (CT) and magnetic resonance Imaging (MRI) scan demonstrated a solid mass enhanced with contrast administration, suggesting hypervascularization on the left buccal sized 6.1 × 4.5 × 8.9 cm, with expansion to the left masticator space, left orbital floor, with erosion posterior and lateral wall of left maxillary sinus, left parapharyngeal space with involvement of the lateral and medial pterygoid muscle and left temporal muscle with pterygomaxillary fossa around 13 mm. Right nasal cavity sized 6.5 × 4.7 × 5.3 cm dilate right pterygopalatine fossa, destroying the lateral and medial pterygoid plates, involving vidian canal, extended to choana, nasopharyngeal cavity, attached to the soft palate, destructed the base of sphenoid and ethmoid sinuses.

Both mass suggestive of angiofibroma. According to the staging system of Radkowski [6], left sided tumour was staged as IIC and right sided one as IIA (Figure 2).

Digital subtraction angiography showed hypervascular lesions on the right side fed by branches of the right internal carotid artery, right internal maxillary artery, and ascendat pharyngeal arteries (dominant from the right internal maxillary artery) and

Figure 1. Enlarged mass on left cheek.

Figure 2. Hypervascular on the left buccal sized 6.1 × 4.5 × 8.9 cm, with expansion to the left masticator space, left orbital floor, with erosion posterior and lateral wall of left maxillary sinus, left parapharyngeal space with involvement of the lateral and medial pterygoid muscle and left temporal muscle with pterygomaxillary fossa around 13 mm. Right nasal cavity sized 6.5 × 4.7 × 5.3 cm dilate right pterygopalatine fossa, destroying the lateral and medial pterygoid plates, involving vidian canal, extended to choana, nasopharyngeal cavity, attached to the soft palate, destructed the base of sphenoid and ethmoid sinuses.
hypervascular lesions on the left side fed by arterial branches of left maxillary artery with no vascular relationship between the lesions on the right side and the left side (Figure 3).

Preoperative embolization of hypervascular lesions in right-sided nasopharyngeal projections was performed using polyvinyl alcohol and gel foam, with feeding of distal branches of the right internal maxillary artery. Embolization was also done in the left buccal maxillary projection with feeding from the distal branches of the left internal maxillary artery (Figure 3).

Both tumours were successfully excised with midfacial degloving approach with total perioperative blood of 1.000 ml (Figure 4). The patient was given 500 ml blood transfusion and nasal packing was inserted to the right nasal cavity which was removed after 3 days. The post-operative course was uncomplicated. Patient was discharged a day after nasal packing removal.

Histopathology examination on both masses showed variable admixture of blood vessels and fibrous tissue. The vascular channel lacks the surrounding smooth muscle and innervation of normal blood vessels while the fibrous component consisted of stellate-shaped cells embedded in a rich collagen matrix that was concluded to be angiofibroma (Figure 5).

On one-month post-surgery, patient had no complaint except numbness on his left cheek. There were

Figure 3. Preembolization (left): hypervascular lesions on the right side fed by branches of the right internal carotid artery, right internal maxillary artery, and ascendens pharyngeal arteries (dominant from the right internal maxillary artery) and hypervascular lesions on the left side fed by arterial branches of left maxillary artery with no vascular relationship between the lesions on the right side and the left side. Post embolization (right): There were no hypervascularization lesions fed by right external carotid artery branches and minimum vascularization lesions fed by small branches of right internal carotid artery, (left): There was no hypervascularization on the left lesion fed by left maxillary internal artery.

Figure 4. Tumour mass excised from midfacial degloving procedure. Left: mass from the left buccal. Right: mass from the right nasal cavity.
no signs of recurrence upon nasal fibre optic endoscopy (Figure 6).

Ten months post-surgery, the patient came for regular visit with no complaints of nasal obstruction nor epistaxis. MRI of the nasopharynx with contrast were performed which showed there was still a mass on posterolateral sphenoid sinus infiltrating left and right sphenoid wings and also a mass on the left masticator space infiltrating left maxillary sinus, suspected of recidive or residual tumour (Figure 7).

Discussion

Although the vast majority of nasopharyngeal angiofibroma cases manifest in males aged 10–24 years, some deviations of this classic presentation have been reported [4]. In this case, we present a case of juvenile nasopharyngeal angiofibroma in a 29-year-old male patient. Juvenile nasopharyngeal angiofibroma may be misdiagnosed initially, especially in cases of bilateral JNA. The current case is the fourth reported case of bilateral juvenile angiofibroma in the literature. The patient has experienced the symptoms since 11 years ago when he was 18 years old. The delay of treatment was due to financial problems. Five years later the epistaxis episode decreased and then was ceased. Schick’s newest findings show elevated levels of all androgen receptor tested, except beta-estrogen and progesterone receptors. Elevated receptors include alpha-estrogen receptor, FSHR, and LHR when

![Figure 5. Left: mass from the buccal shows more fibrous component which have spindle shaped to stellate to plump nuclei with variable collagen stroma (magnification 100 times). Right: mass from the right nasal cavity shows more vascular component which consist of thin-walled, complex vascular arrangement of blood vessels that vary in size and appearance from stellate or staghorn (magnification 100 times).](image1)

![Figure 6. Follow up of patient 1 month post-surgery.](image2)
compared to nasal mucosa stroma. These receptor expression and age-related physiological hormone changes in male, postulated to stimulate the proliferation of angiofibroma. These findings may relate to the peak of symptoms and epidemiology in adolescent male [7].

The exact site of origin of JNA is controversial. The majority supports its origin from the upper lip of the pterygopalatine foramen, while others stated it arises from the distal bony vidian canal. The mass can expand laterally from sphenopalatine foramen to pterygopalatine fossa, pterygomaxillary fissure, infra-temporal fossa and also cheek, making a dumbbell appearance [8]. In this case, the mass on the right nasal cavity dilate the pterygopalatine fossa, destroying the lateral and medial pterygoid plates, and also involving vidian canal. However, the mass on the left buccal did not expand to nasopharynx region but instead into pterygopalatine fossa, pterygomaxillary fissure, into the buccal. The reason for a bilateral occurrence is not known.

The etiology of JNA itself remain elusive. Because of the tumour’s vascularity, early studies of JNA hypothesized a vascular etiology due to incomplete regression of the first branchial artery which remnants at the superior margin of the sphenopalatine foramen. However, rare cases of extranasopharyngeal angiofibroma have been reported, so a multicentric origin can be considered [9]. Occurring predominantly in adolescent males, several researches have been conducted in determined the relationship between JNA and sex chromosomes. Chromosomal studies of JNA using the comparative genomic hybridization showed a number of chromosomal abnormalities in the JNA. DNA gains are more common than DNA losses with the exception of the frequent loss of chromosome Y. Vascular endothelial growth factor (VEGF) as well as vascular endothelial growth factor receptor-2 (VEGFR-2) and platelet-derived growth factor (PDGF) have also been described and associated with vessel density in JNA [10]. The role of viral infections and immunity has turned to further investigation about the role of the immune system in the development of JNA. The discovery of mast cells and lymphocytes in tumour samples leads to further investigation of evidence of a chronic inflammatory process and expression of a specific Toll-like receptor (TLR-3) was found to correlate with tumour stage [1].

Mishra [2] reported an alternative etiology of neo-emergence of JNA (at a different site) that may be possible for the circulating levels of angiogenic factors to increase following excision of the tumour mass. It may exert their expression on some other vascular nidus (hemangiomatous, hamartomatous or vascular malfunction) resulting in a ‘new JNA’. However, that etiology may not apply in this case which both of tumours appears before surgery interventions and was vascularized separately.

The triad clinical presentation of JNA are unilateral nasal obstruction, recurrent epistaxis and nasal discharge. In this case, patient experienced all the symptoms and also felt a mass on his left cheek. MRI dan CT imaging shows both were hypervascular mass.
suggesting an angiofibroma, in which right mass is more contrast-enhanced than the left one. Histologically, angiofibroma is composed of fibrocollagenous stromal proliferation with an admixture of variably vascular space. Vascular component is comprised of thin-walled, small to large vessels varying on appearance from stellate to staghorn to barely conspicuous, owing to mark compression by stromal fibrous tissue. Stroma is composed of fibrous tissue with fine or coarse collagen fibers whereas its cells are spindle shaped and stellate with plump nuclei, and tend to radiate around vessels [11]. In this case, histologic examination also showed us that both masses showed similar picture: vascular channels lack the surrounding smooth muscle, innervation of normal blood vessels, and stromal fibrous from spindle to stellate shaped which was concluded to be angiofibroma.

However, the mass on the left side shows more fibrous stoma tissue and less vascular component rather that the right one and vice versa. 

This is an unusual presentation of JNA, which mostly reports as unilateral [3]. The mass on his left buccal/cheek originated from the sphenopalatine foramen and exited through the buccal region from pterygomaxillary fissure with no extension to the nasopharyngeal nor to the nasal cavity. The mass on the right nasal cavity dilate the pterygopalatine fossa, destroying the lateral and medial pterygoid plates, and also involving vidian canal, extended to choana, nasopharyngeal cavity, attached to the soft palate, destructed the base of sphenoid and ethmoid sinuses. 

Demonstration of the anterior bowing of the posterior maxillary wall due to the presence of a mass in the pterygomaxillary space on axial CT slices known as the Holman–Miller sign, is a characteristic finding in JNA [3]. This presentation was also found in the patient. Computed tomography with full extension through the base of the maxilla provides information about the extent of bone erosion, in particular, the depth of invasion into the bone of the sphenoid sinus, a main predictor of recurrence, and enlargement of the sphenopalatine foramen in JNA cases. On the other hand, MRI with contrast provides clarity in determining the extension of JNA, border between tumour and the surrounding soft tissues, intracranial and critical structures, such as the internal carotid artery, cavernous sinus, and pituitary gland. Recurrence and residual tumours are best evaluated on MRI [12].

Biopsy was taken from the right nasal cavity with preparation of the risk of bleeding due to its atypical presentation of JNA which usually is a red, hypervascular mass. This could be because the component of the mass is a mixture of blood vessels and fibrous stroma. In some literature, JNA consisted of more stromal components than blood vessels in older patients.

Preoperative identification of the blood supply is essential in planning the surgical approach. Digital subtracted angiography performed in this patient revealed bilateral supply from these two non-contiguous masses, which is rare. Bilateral vascular supply of the mass was reported to be very common by Wu et al. [13] so angiography of bilateral carotid systems should be routinely done preoperatively. The blood supply typically arises from the internal maxillary artery. With the continuing growth of a juvenile nasopharyngeal angiofibroma, an additional blood supply is also induced from the internal carotid system, as was the case for the right-sided juvenile nasopharyngeal angiofibroma in our patient [3].

Preoperative embolization, considered as standard treatment nowadays, has shown to minimize the blood loss. Retrospective study conducted by Pei et al. [14] shown that mean volume of intraoperative blood loss in patients with preoperative embolization was significantly lower than in the patients without preoperative arterial embolization (385.3 ml vs 1215.0 ml, \( p < .001 \)). Study suggested that tumour above Andrew stage IIIb or University of Pittsburgh (UPMC) stage III should undergo bilateral angiography for embolic evaluation due to their significance contribution to increased operative blood loss [15]. The UPMC JNA staging systems account for both route of skull base extension and tumour vascularity, which are two important tumour attributes in the age of preoperative embolization and endoscopic endonasal surgery.

Embolic agent that can be used are liquid and particulate agents. Liquid embolic agents, such as Ethanol or Acrylic, and powdered particulate materials can penetrate into the smallest blood vessels of the tumour but need to be used very selectively because they can also cause the most damage to adjacent normal tissues. Relatively large particulate agents, such as polyvinyl alcohol (PVA) and gelfoam, do not penetrate into the tumour as deeply but are also less likely to damage adjacent normal tissues [16].

In this case, a bilateral embolization with PVA and gelfoam was done, which ultimately reduced the risk of heavy bleeding. Wu et al.[5] stated if the surgeon performed a simultaneous procedure in symptomatic true bilateral JNA, a staged procedure should be prepared due to the possibility of massive bleedings from two simultaneous surgical sites and increased...
operative times. In this case, both tumours were successfully extracted with moderate blood loss volume.

Thakar [17] investigate the use of flutamide, an antiandrogen agent, preoperatively in patients with JNA (Radkowski stage IIB-IIIB). From his study, the use of flutamide 10 mg/kg BW orally 6 weeks prior to admission, succeeded in reducing tumour volumes (mean 16.5%) which confirmed by MRI as well as testosterone level production. However, these results were only significant in postpubertal cases, while prepubertal cases had inconsistent and minimal responses. No significant toxicity was noted, with the exception of transient breast tenderness.

In this case, we did not use flutamide as an adjuvant therapy. Open surgery with midfacial degloving approach was done to the patient. Surgeon’s experience influences surgical approach taken, endoscopic surgery may lessen blood loss intraoperatively, but due to the tumour extension to lateral parapharyngeal space, open surgery approach was taken [11]. Recurrence rates tend to relate more closely to tumour stage than to resection method. Therefore, tumours that infiltrate the infratemporal fossa, sphenoid sinus, base of the pterygoid, cavernous sinus, foramen lacerum, optic canal, and anterior fossa are at higher risk for recurrence. The decision in choosing open surgery is based on the stage and infiltration of the tumours. Midfacial degloving approach was chosen due to no external surgical incisions. In addition, Howard et al. [18], treated 19 cases of JNA with the midfacial degloving approach and reported no recurrences with 6 months to 3 years of follow-up. Recurrence rates for JNA range from 13% to 46% and it was mainly depend on stage of tumour and extent of surgical removal [19]. The recurrence of the tumour usually occurs in 3 to 4 months post operatively. Recurrence rates also correlate with the extent of the tumour and, specifically, the involvement of the skull base: tumour involving the infratemporal fossa, sphenoid sinus, base of pterygoids, clivus, cavernous sinus, and foramen lacerum. The base of the sphenoid, in particular the removal of the cancellous bone of the base of the sphenoid, has been associated with decreased recurrence rates in several studies [10]. In this case, the patient could not come in a monthly basis due to financial problems. The patient came 10 months post-surgery, whether the mass shown in MRI post operatively is a recurrence or residual tumour, could not be specifically known. Although according to the staging system of Radkowski [6] the left sided tumour was staged as IIC and right sided one as IIA, bilateral mass has its own challenges and difficulties including the potential of bleeding and also the big size of the masses in this case (left buccal sized 6.1 x 4.5 x 8.9 cm and right nasal cavity sized 6.5 x 4.7 x 5.3 cm). Apart from that, from the preoperative CT scan and MRI we know that the mass on posterolateral sphenoid sinus infiltrate left and right sphenoid wing. The study conducted by Szymanska [20] showed that the recurrence rate in patients with anterior and/or posterior lateral extension is significantly higher than in patients with anterior lateral extension only.

Follow up of JNA post-operatively to detect recurrence of the tumour cannot solely be based on symptoms and physical examination, especially in previously treated advanced tumours. Serial radiographic imaging with contrast-enhanced CT or MRI, or both, is the choice for follow-up. MRI is particularly sensitive for residual disease. If it shows residual disease, patient should be monitored with follow-up imaging in 4 to 6 months. If there is further growth of the residual disease and it is relatively easy to remove, repeat surgery (open or endoscopic) is the best option. If there is no growth or involution, monitoring of this finding can continue with serial imaging studies. The average time to recurrence is 21 months after initial procedure [1]. in this patient, there were no symptoms of nasal obstruction nor epistaxis 10 months after surgery, so we plan to follow up the residual or recurrence mass by serial MRI. Surgical management of recurrent and, especially, extensive recurrent tumours is complex, because additional collateral blood flow develops, especially from the internal circulation. Radiation therapy should be reserved for circumstances in which repeat surgery would involve high risk for morbidity [1].

Conclusion

Occurring almost exclusively in adolescent males, juvenile nasopharyngeal angiofibroma is a benign fibrovascular tumour. The expression of sex hormone receptors helps explain its sex and age predilection. At present, preoperative embolization is recommended to minimize surgical blood loss. Surgery remains the standard of care. Both endoscopic and open approaches offer effective treatment of JNA with
similar rates of recurrence. This case showed complete separate bilateral tumours with separate blood supply. Suspecting bilateral juvenile angiofibroma in patient with two non-contiguous mass in head and neck region is a must. Proper diagnosis of bilateral JNA is helpful in guiding management and lead to good results.

Informed consent statement

The patients participating in this report have given the author their permission to be the subject of this case-report and to be photographed in a written consent.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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