SUNTEXT REVIEWS

SunText Review of Case Reports & Images
ISSN: 2766-4589

Open Access
Case Report
Volume 1:1

Nasopharyngeal Carcinoma Mimicking Juvenile Nasopharyngeal Angiofibroma, A Literature Review and Treatment Implications

Manton T[1] and Ha JF[1,2,*]

[1]*Department of Paediatrics Otolaryngology Head & Neck Surgery, University of Michigan Health System, USA*
[2]*Department of Paediatrics Otolaryngology Head & Neck Surgery, Perth Children's Hospital, Western Australia; Murdoch ENT, Wexford Medical Centre, St John of God Hospital (Murdoch), Western Australia; School of Surgery, University of Western Australia, Western Australia; St John of God Hospital (Murdoch), Wexford Medical Center, Western Australia*

[*]**Corresponding author:** Jennifer Ha, St John of God Hospital (Murdoch), Wexford Medical Center, Suite 17-18, Level 1, 3 Barry Marshall Parade, Murdoch 6150, Western Australia; Tel: +61863326868; Fax: +61863326800; E-mail: drjennha [at] yahoo [dot] com [dot] au

Received date: 21 August 2020; **Accepted date:** 30 August 2020; **Published date:** 07 September 2020

Citation: Manton T, Ha JF (2020). Nasopharyngeal Carcinoma Mimicking Juvenile Nasopharyngeal Angiofibroma, A Literature Review and Treatment Implications. SunText Rev Case Rep Image 1(1): 102.

DOI: https://doi.org/10.51737/2766-4589.2020.002

Abstract

Introduction: Nasopharyngeal tumors in the pediatric population are rare. Accurate diagnosis is vital as there are significant differences in treatment algorithms based on the characteristics of the tumor ranging from observation, surgical excision, chemo-radiation, or multimodality treatment. We present a case in which the pre-operative workup of a nasopharyngeal mass was consistent with Juvenile Nasopharyngeal Angiofibroma (JNA). However the final histopathologic diagnosis following surgical excision revealed Nasopharyngeal Carcinoma (NPC).

Case: A 13 year-old male was referred to our department for a suspected right JNA. His presenting symptoms included intermittent right anterior epistaxis, nasal congestion, facial fullness as well as persistent right otalgia, headache and neck pain following a recent facial trauma. MRI revealed a 4.5 x 4.3cm mass originating from the posterolateral nasal sidewall extending into the pterygopalatine fossa. Flexible nasendoscopy revealed a large hypervascular posterior nasal mass. Pre-operative embolization of the feeding vessels was performed prior to surgery. The preliminary pathology was concerning for sarcoma, therefore a right jugulodigastric lymph node was biopsied. This was consistent with NPC. He underwent definitive concurrent chemo-radiation therapy. A review of the literature reveals additional case reports of pre-operative clinical and radiographic suspicion for JNA with a differing histologic diagnosis.

Conclusion: Nasopharyngeal tumors often have similar presenting symptoms. Imaging can often help to delineate the diagnosis. Whilst endoscopic biopsy is usually performed, in the setting of a possible JNA, it is not advised due to the risk of hemorrhage. We advocate the use of selected biopsy in diagnosing some nasopharyngeal masses prior to surgical excision.

Keywords: Juvenile nasopharyngeal angiofibroma; Nasopharyngeal cancer; Management; Differential

Introduction

Nasopharyngeal masses in the pediatric population are rare, the majority of which are benign. The differential diagnosis is diverse and include inflammatory lesions, vascular lesions, nasopharyngeal cysts, congenital lesions, benign and malignant tumors, adenoid hypertrophy, chordomas, and retropharyngeal ganglia tuberculosis [1]. The most common abnormality in the pediatric population is benign adenoidal hypertrophy [2]. Given the anatomic complexity of the nasopharynx and close proximity to vital structures (orbit and skull base), a thorough workup with radiographic imaging is often necessary. In the juvenile male population, one must have a high index of suspicion for Juvenile

Nasopharyngeal Angiofibroma (JNA) when a patient presents with a vascular posterior nasal mass, since this is the most common benign nasopharyngeal tumor in this population [3]. The definitive treatment is usually surgical excision with varying surgical approaches based on the anatomic pattern of involvement. JNA has characteristic clinical and radiographic findings, thus biopsy is not usually indicated. In addition, there is also a risk for significant hemorrhage following endoscopic biopsy.

Case

A 13-year-old male was referred to our Paediatric Otolaryngology department for a suspected right JNA. This was discovered incidentally when he had a magnetic resonance imaging (MRI) (Figure 1) to investigate his persistent right-sided otalgia, headache and neck pain following a basketball injury to his right mandible. He reported intermittent spontaneous right anterior epistaxis that resolves with pressure. He attributed this, as well as nasal congestion and facial fullness to the cold weather.

Figure 1: *T2 weighted axial MRI demonstrating the lesion filling the right choanae, extending anteriorly suspicious for JNA*

His flexible nasendoscopy (FNE) revealed a hypervascular mass suspicious for a right JNA (Figure 2). Surgical excision was recommended. He was referred to the interventional radiologist for pre-operative embolization. This 4.5 x 4.3cm mass was supplied by arterial branches from the sphenopalatine, distal internal maxillary and anterior divisions of ascending pharyngeal arteries. Embolization was performed successfully with Onyx. There was complete devascularisation of the mass on the angiography. He had an endoscopic approach to the tumor resection, combined with Caldwell Luc to remove the portion extending laterally beyond the pterygopalatine fossa.

Figure 2: *FNE showing a hypervascular mass arising from the right lateral nasal wall filling the posterior choanae.*

The initial histopathology was suspicious for sarcoma. However, as the material was too necrotic, he underwent an excisional biopsy of his right jugulodigastric lymph node. This was diagnosed as nasopharyngeal carcinoma (NPC). It was re-staged as a right stage 4a (T4N2M0) EBER positive NPC. He was enrolled in the Children's Oncology Group protocol ARAR0331 and completed his concurrent chemoradiotherapy (cisplatin and 5-FU chemotherapy; 70.2 gray to the gross disease and 45 gray to bilateral cervical nodes delivered with 7 field 6 MV intensity modulated radiotherapy). This was completed in November 2011. His follow up positron emission tomography (PET) demonstrated no enhancement. His follow up FNE (Figure 3) also did not demonstrate any recurrence.

Figure 3: *Follow up FNE in 2012 demonstrating no recurrence.*

His follow up PET 17 months later was suspicious for metastatic lesions to his liver and spleen. This was confirmed on MRI and biopsy. He was enrolled in the Texas Children's Phase II Carbo/Docetaxel followed by EBV CTL protocol (5 cycles of chemotherapy, followed by cytotoxic T cell infusions), completed in the following 7 months. However, there was evidence of progression on the follow up imaging, so he underwent salvage chemotherapy (12 cycles of Gemcitabine and Vinorelbine) in the following 9 months. Unfortunately imaging three months after the salvage chemotherapy was concerning for persistent disease. He was resumed on chemotherapy with Vinorelbine and Gemcitabine (6 cycles), which was completed in the following 6 months. He then underwent 2 treatments of TGF beta resistant cytotoxic T lymphocyters therapy, completed a month later. He continued to have progressive disease and elected to pursue alternative therapies in addition to the recommended chemotherapy with Cyclophosphamide and Topotecan in California. He has since relocated there.

Discussion

JNA is a highly vascular benign but locally invasive tumor, which represents about 0.05% of all head and neck tumors [4]. They arise almost exclusively in adolescent males. Presenting symptoms include unilateral nasal congestion, epistaxis, hyposmia, rhinorrhea, and facial pain. Less commonly, the expansile bony changes may result in facial deformity, vision changes or cranial nerve palsy. These tumors can extend through the sphenopalatine foramen into the pteryopalatine fossa with subsequent expansion and displacement of the surrounding anatomic structures [5]. The blood supply is most commonly from the branches of the internal maxillary artery, but may also be from the external carotid artery, internal carotid artery, common carotid artery, or ascending pharyngeal artery [6]. FNE often reveals a pink/red, lobulated submucosal mass seated in the posterior nasal cavity. Typical computed tomographic (CT) findings include an enhancing mass emanating from the posterolateral wall of the nasal cavity, involving the sphenopalatine foramen and pterygomaxillary fossa. The Holman-Miller sign is a pathognomonic CT finding which includes anterior bowing of the posterior maxillary wall from the expansile pressure exerted by the tumor [4].

Preoperative biopsy is usually discouraged due to the risk of significant, even life-threatening hemorrhage. A probable diagnosis of JNA is often thought to be sufficient based on the characteristic clinical and radiographic findings [7-9]. The definitive treatment is embolization followed by surgery. Other treatment options include radiotherapy, chemotherapy, and or hormone therapy [6].

NPC is a rare aggressive malignancy often diagnosed in the setting of advance locoregional disease and distant metastasis. NPC represents approximately 1% of all childhood cancers in the U.S. and Europe, and as high as 10-20% in Southeast Asia and Africa [10]. They account for 40-50% of childhood malignancies isolated to the nasopharynx [11]. Similarities in etiology have been shown between juvenile and adult NPC with its frequent concomitant infection with EBV, association with consumption of salted fish containing volatile nitrosamines and male predominance (1.8:1) [12,13]. The World Health Organization has classified NPC into three subtypes: Type I includes keratinising squamous cell carcinoma, Type II includes non-keratinizing epidermoid carcinoma and Type III includes undifferentiated carcinoma. The most common histologic type of NPC found in the juvenile population is the WHO Type III form which is classically associated with more advanced locoregional disease and distant metastasis [13]. The most common presenting symptoms include a painless neck mass, nasal obstruction, epistaxis, conductive hearing loss or serous otitis media caused by eustachian tube obstruction. The invasive nature of these tumors can lead to cranial nerve palsies from skull base extension.

Diagnosis is obtained by a combination of physical examination, FNE and radiographic imaging studies. On FNE, it is typically a submucosal pink, friable lesion emanating most commonly from the fossa of Rosenmuller. Workup often includes MRI to further detail the characteristics of the tumor as well as the extent of invasion. On MRI, it has a heterogeneous intermediate signal intensity on T2-weighted images and moderate contrast enhancement (less than that of normal mucosa) on T1-weighted images with or without infiltration outside of the nasopharynx.

The mainstay of treatment for NPC includes concomitant chemo-radiotherapy [12]. Undifferentiated NPC is particularly radiosensitive. Salvage neck dissection is limited to the setting of persistent nodal disease following systemic therapy. Despite apparent local tumor control after high-dose radiotherapy, treatment commonly fails due to locoregional recurrence or development of distant metastatic disease. Most recurrences occur within two years (median 8 months) and over 50% of these patients develop distant metastatic disease [10,14]. This was the case in our patient. With radiotherapy alone, 5-year survival rates have been reported as low as 20-60% [10,14]. With the addition of neoadjuvant or concurrent chemotherapy to standard high dose radiotherapy regimens, there has been a significantly decreased risk of developing distant metastasis as well as increased disease-free survival [14- 16]. Wolden et al reported improved metastasis-free survival (16% vs 57% p=0.01) as well as 10-year disease-free survival (84% vs 35%, p<0.01) with the addition of chemotherapy versus radiation alone in pediatric patients with ages ranging from 12-20 years [15]. Targeted therapies addressing the pathogenic role of EBV have been developed with promising results including interferon-beta administration as well as EBV-specific cytotoxic T-lymphocytes [17]. The risks of long-term, treatment-

related toxicity can be quite significant in the juvenile population: growth retardation, dental pathologies, life-long xerostomia, endocrine derangements, ototoxicity and development of secondary malignancies (relating to high-dose radiotherapy) [3].

A review of the English literature was conducted to identify other cases similar to our patient. There were a total of 5 reports, which are summarised in (Table 1). We included a description of the pre-operative finding as the images were unavailable.

Table 1: *Case report summary of nasal masses presenting as JNA.*

Case	Pre-Op Image	Pre-Op Radiology	Tumor Location	Pathology	Follow Up
Mani et al [18]	Anterior 2/3 of NP filled with a bilobular reddish-grey, firm mass	X-ray: Nasopharyngeal (NP) mass & Homan miller sign Angio: Arterial supply from ascending pharyngeal and maxillary arteries	Left spheno-ethmoidal recess, anterior bowing of posterior maxillary sinus wall on exam/imaging. Actual from Left posterior septum at time of surgery	Embryonal rhabdomyosarcoma	Recurrence at 1 yr follow up requiring subtotal palatectomy; 3mo later recurrence at R anterior torus palatine requiring cryosurgery and XRT
Harrison DF [19]	No description available	X-ray: NP mass with erosion of lateral pterygoid plate CT: Erosion of sphenopalatine foramen with extension into the pterygopalatine fossa MRI: Extension through infratemporal fossa	Musculature of the right lateral pterygoid	Embryonal rhabdomyosarcoma	Information unavailable
Shaffer et al [20]	Tan lobulated mass in the nasopharynx	Xray: NP mass with erosion of sphenoid sinus & Homan Miller sign Angio: Arterial supply by internal maxillary artery	Nasopharynx with extension into the pterogomaxillary space and infratemporal fossa	Lymphoepithelioma	Information unavailable
Burkey et al [16]	Deep red submucosal NP mass	CT: NP mass with widening of pterygopalatine fossa, erosion of posterior maxillary wall and base of pterygoid bone, fills masticator space, extends into nasopharynx & middle cranial fossa Angio: Arterial supply from ascending pharyngeal & internal maxillary arteries MRI: Extension through foramen ovale, L inferior orbital fissure and orbital apex as well as cavernous sinus	Per pre-op radiology	Embryonal rhabdomyosarcoma	Information unavvailable

Mani et al published the first case report of a malignant nasopharyngeal mass misdiagnosed as a JNA. Final surgical histopathology revealed embryonal rhabdomyosarcoma [18]. Harrison reported his personal experience of 44 patients treated surgically for presumed JNA, one of which was an embryonal rhabdomyosarcoma on final histopathologic review [19]. Shaffer

et al. reported cases suspicious for JNA on angiography, which were later found to be lymphoepithelioma and fibrous dysplasia following surgical excisions [20]. Burkey et al from our own institution presented a case in 1990 with clinical and radiographic findings consistent with JNA. However, their team had concern for malignancy given the extent of disease and young age of the patient thus endoscopic biopsy was performed under a general anesthetic following pre-operative embolization. Histopathology revealed embryonal rhabdomyosarcoma [16].

There may be a role for performing endoscopic biopsy under a general anesthetic in lesions probable for JNA, but with atypical presenting signs and symptoms. The risk of post-operative hemorrhage is significantly reduced with the advent of pre-operative embolization. While this does lead to the patient undergoing an additional general anesthetic, we feel that in a healthy patient population these risks are acceptable as the definitive histopathologic diagnosis may have the potential to change the management. Alternatively, a frozen section can be obtained to confirm the pathology prior to proceeding with the definitive surgery.

Conclusion

Our present case and the review of cases in the literature suggest that there may be a role for performing endoscopic biopsy under a general anesthetic in lesions probable for JNA, but with atypical presenting signs and symptoms. The ultimate goal is to prevent inappropriate surgical intervention in patients with malignant and potentially metastatic disease.

References

1. Alves FR, Granato L, Maia MS, Lambert E. Surgical approaches to juvenile nasopharyngeal angiofibroma - case report and literature review. Int Arch Otorhinolaryngol. 2006; 10:162-166.
2. Stambuk HE, Patel SG, Mosier KM, Wolden SL, Holodny AI. Nasopharyngeal carcinoma: recognizing the radiographic features in children. Am J Neuroradiol. 2005; 26: 1575-1579.
3. Waldman SR, Levine HL, Astor F, Wood BG, Weinstein M, Tucker HM. Surgical experience with nasopharyngeal angiofibroma. Arch Otolaryngology. 1981; 107: 677-682.
4. Bakshi SS, Bhattacharjee S. Juvenile nasopharyngeal angiofibroma. J Pediatric Hematol Oncol. 2016; 38: 491-492.
5. Neel III HB, Whicker JH, Devine KD, Weiland LH. Juvenile angiofibroma: review of 120 cases. Am J Surg. 1973; 126: 547-556.
6. Wu AW, Mowry SE, Vinuela F, Abemayor E, Wang MB. Bilateral vascular supply in juvenile nasopharyngeal angiofibromas. Laryngoscope. 2011; 121: 639-643.
7. Doyle PJ, Riding K, Kahn K. Management of nasopharyngeal angiofibroma. J Otolaryngol. 1977; 6: 224-232.
8. Gullane PJ, Havas TE. Nasopharyngeal Angiofibroma. Current therapy in Otolaryngology-Head and Neck Surgery, B.C. Decker, Toronto. 1987; 178-181.
9. Spector JG. Management of Juvenile Angiofibroma. Laryngoscope. 1988; 98: 1016-1026.
10. R Mertens R, B Granzen B, L Lassay L, Gademann G, Hess CF, Heimann G. Nasopharyngeal carcinoma in childhood and adolescence. Cancer. 1997; 80: 951-959.
11. Afqir S, Ismaili N, Alaoui K, Ahid S, Lotz JP, Horn E, et al. Nasopharyngeal carcinoma in adolescents: a retrospective review of 42 patients. Eur Arch Otorhinolaryngology. 2009; 266: 1767-1773.
12. Downing NL, Wolden S, Wong P, Petrik DW, Hara W, Le QT. Comparison of treatment results between adult and juvenile nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys. 2009; 75: 1064-1070.
13. Ayan I, Altun M. Nasopharyngeal carcinoma in children: retrospective review of 50 patients. Int J Radiat Oncol Biol Phys. 1996; 35: 485-492.
14. Serin M, Erkal HS, Elhan AH, Cakmak A. Nasopharyngeal carcinoma in childhood and adolescence. Med Pediatric Oncol. 1998; 31: 498-505.
15. Wolden SL, Steinherz PG, Kraus DH, Zelefsky MJ, Pfister DG, Wollner N. Improved long-term survival with combined modality therapy for pediatric nasopharynx cancer. Int J Radiat Oncol Biol Phys. 2000; 46: 859-864.
16. Burkey B, Koopmann CF, Brunberg J. The use of biopsy in the evaluation of pediatric nasopharyngeal masses. Int J Pediatric Otorhinolaryngol. 1990; 20: 169-179.
17. Gioacchini FM, Tulli M, Kaleci S, Magliulo G, Re M. Prognostic aspects in the treatment of juvenile nasopharyngeal carcinoma: a systematic review. Euro Arch Oto-Rhino-Laryngol. 2016; 274: 1205-1214.
18. Mani RL, Smith MF. Rhabdomyosarcoma simulating nasopharygeal angiofibroma. Oncology. 1968; 22: 74-80.
19. Harrison DFN. The natural history, pathogenesis, and treatment of juvenile angiofibroma. Arch. Otolaryngol. Head Neck Surg. 1987; 113: 936-942.
20. Shaffer K, Haughton V, Farley G, Freidman J. Pitfalls in the radiographic diagnosis of angiofibroma. Radiology. 1978; 127: 425-428.