Atypical Presentations of Nasopharyngeal Masses: A Case Series

Archana R Pillai¹, A M Aneesa², K B Rajamma³

¹Assistant Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ²Resident, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ³Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ³Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ³Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ³Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala, ³Professor, Department of ENT, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala

Abstract

Among all the tumors presenting in the head and neck region, nasopharyngeal masses shows a broad range of benign and malignant tumors, fungal infections, granulomatous inflammation, autoimmune diseases and congenital lesions in children as well as adults. The commonly encountered masses are nasopharyngeal cancer, Juvenile nasopharyngeal angiofibroma, lymphomas (2.5% of head and neck tumors), papilloma (0.5-4% of nasal tumors). Nasopharyngeal cancer shows a unique geographical variation in its incidence. Our study is an attempt to analyse in detail regarding the rare and interesting presentations of nasopharyngeal masses. We have chosen five cases which were the most interesting including an olfactory neuroblastoma and primary tuberculosis of adenoids in an immunocompetent patient and done a review of literature to give a comprehensive picture.

Key words: Inverted papilloma, Nasopharyngeal mass, Non-Hodgkin's lymphoma, Olfactory neuroblastoma, Primary nasopharyngeal tuberculosis

INTRODUCTION

Nasopharyngeal lesions have plethora of differential diagnosis which includes malignancy (squamous cell carcinoma and lymphoma), fungal infection (aspergillosis, mucormycosis) granulomatous inflammation (sarcoidosis, leprosy, syphilis, tuberculosis) and autoimmune disease (polyarthritis nodosa, Churg-Strauss and Wegener's granulomatosis).¹

Apart from these, some rare tumors that presented as nasopharyngeal masses in our hospital includes olfactory neuroblastoma and primary tuberculosis of nasopharynx in an immunocompetent patient. We are highlighting the need for a high index of suspicion for the successful recognition of early lesions as the management of each case is unique and challenging to achieve a good outcome.

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Case No 1

A 70-year-old hypertensive, smoker, and non-alcoholic male patient presented with the complaints of nasal obstruction and decreased sense of smell for the past 4 years. Diagnostic nasal endoscopy revealed a pale-pinkish polypoidal mass seen attached to the middle turbinate on left side occupying both nasopharynxes (Figure 1). Mass is non-friable and does not bleed on touch. Mass extends beyond the choana and is filling the nasopharynx. There is no cervical lymph node enlargement. Conventional X-ray paranasal sinuses and computed tomography (CT) revealed soft-tissue opacity in the left nasal cavity and left maxillary sinuses. Lesion was extending posterior nasal cavity, upper part of posterior nasal septum, and nasopharynx. Magnetic resonance (MR) angiogram showed no increased vascularity or extension into brain. However, deossification of intervening bone is seen. Microscopic examination of the excision biopsy mass suggested inverted papilloma.

The patient was thoroughly evaluated and endoscopic removal of mass from the nasal cavity, maxillary ethmoidal, sphenoidal, and frontal sinuses was done. No adjuvant treatment was given. The patient became asymptomatic after surgery and during follow-up.

Corresponding Author: Dr. Archana R Pillai, Assistant Professor, Sree Gokulam Medical College and Research Foundation, Venjaramoodu, Trivandrum, Kerala. E-mail id: drarchanapillai@gmail.com

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Case No 2

A 70-year-old hypertensive, diabetic, and smoker male patient presented with recurrent episodes of epistaxis. Each episode required bilateral anterior and posterior nasal packing.

Diagnostic nasal endoscopy revealed a mass arising from the nasopharynx attached to the inferior turbinate and soft palate. CT scan revealed a mass filling the left sphenoid, ethmoid sinuses and left nasal cavity with erosion of the nasal septum, turbinates and cribriform plate, ethmoid air cells, lamina papyracea, and root of sphenoid sinus on left side (Figure 2). The patient underwent excision biopsy and histopathology report came out to be olfactory neuroblastoma (ONB) which was confirmed with an IHC study.

Case No 3

A 36-year-old woman presented to our Outpatient Department (OPD) with complaints of nose block and mild pain mainly on right side foreign vague discomfort in the nasopharynx and thick scanty post-nasal discharge and a sense of ill-being and tiredness. On examination, she had a gross DNS to the right side with turbinate hypertrophy and was taken up for septoplasty. There was a raised erythrocyte sedimentation rate. There was no cervical lymphadenopathy and mild splenomegaly.

Pre-operatively, a diagnostic nasal endoscopy (DNE) was also done and a mass was seen in the nasopharynx almost completely filling the choana. Histopathology slides showed respiratory epithelium, multiple granulomas filled with Langerhan's giant cells and epithelial cells and a highly vascular stroma which was reported as tuberculosis. AFB staining of the slides did not reveal acid-fast bacilli. Hence, the patient was evaluated further for tuberculosis post-operatively. Mantoux test and sputum AFB were negative. A pulmonology evaluation showed no signs of pulmonary tuberculosis. She was treated as primary case of extra pulmonary tuberculosis with antituberculosis treatment category 1 for 6 months. After 1 month of treatment, the patient was reassessed with DNE and the size of mass was found to be considerably reduced. She also reported considerable relief of foreign body sensation. Another DNE done after 6 months of treatment, a repeat biopsy was taken and found to be normal.

Case No 4

A 53-year-old hypertensive male patient came with complaints of nasal obstruction, ear block, and snoring for 4 years. Clinical examination including nasal endoscopy revealed a pale pink mass completely filling the nasopharynx (Figure 3). It was rubbery in consistency and non-friable mass extending up to upper part of soft palate with minimal airway. There was no cervical lymphadenopathy. CT examination revealed a mass filling the nasopharynx. The patient underwent excision biopsy of the mass. Histopathological study revealed non-Hodgkin's lymphoma. The patient was referred for radiotherapy.

Case No 5

A 58-year-old male diabetic and COPD patient with no addictions presented with recurrent episodes of nasal bleed for 2 months. Bleeding was in moderate amount which subsided itself. Clinical examination and nasal endoscopy showed a reddish mass above the Eustachian tube orifice in the nasopharynx. Mass was friable. Conventional CT revealed a small irregularity in the nasopharyngeal region. Microscopic examination of the incision biopsy showed abnormal lymphoid hyperplasia pointing toward a diagnosis of lymphoma. IHC was DNE and the patient referred for chemoradiation.

Case No 6

A 45-year-old hypertensive male patient presented with complaints of nasal obstruction for 3 months which was progressive in nature. He underwent surgery 6 times for recurrence of rhinosporidiosis for 25 years. Clinical examination and diagnostic nasal endoscopy showed a rhinosporidial mass attached to the nasopharynx, Eustachian tube orifice, and soft palate. Part of cartilaginous and most of bony septum, inferior turbinate, and middle turbinate are partly destroyed. The patient underwent surgery and histopathology report came out to be rhinosporidiosis.

DISCUSSION

Inverted Papilloma

Sinonasal papillomas account for 0.5-4% of all nasal tumors² inverted papillomas (IP) and exophytic papillomas are the most commonly diagnosed subtypes (50% each) and oncocytic papillomas (OSP) are the rarest type (3-5%).^{3,4} An average age of 44 years being more likely to have an exophytic papilloma, and patients one decade older were more likely to show one of the remaining two types.⁵⁻⁹

IPs tended to arise from the maxillary, ethmoid and sphenoid sinuses, and lateral nasal wall. Exophytic papillomas were most common within the nasal cavity on the nasal septum and within the vestibule. OSP exhibited a predilection for the ethmoid sinuses. The mechanism by which IP causes the bony reactions like osteitis may be secondary to the secretion of the bone morphogenic peptide tumour cells.¹⁰ CT findings highly suggestive of papilloma include a contiguous nasal cavity and sinus mass with heterogeneous contrast enhancement and unilateral sinus opacification.^{4,6,7} Thinning or bowing of adjacent bone is seen, most commonly the medial wall of the maxillary sinus and the lamina papyracea. When bony erosion or destruction is seen, associated malignancy must be considered. Focal hyperostosis and osteitis within the opacified sinus has been shown to predict the site of origin of IP.^{2,6,11} MR imaging (MRI) can be useful in defining the extent of the tumor and differentiating the tumor mass from inspissated mucus and for detecting intracranial and intraorbital extension of tumor.

The human papilloma virus (HPV) types 6, 11, 16, and 18 have been implicated as a leading factor. The differential expression of certain cell cycle proteins may significantly contribute to the transformation process.¹² Chronic inflammation of sinuses has also been hypothesized as a precursor for the development of sinonasal papillomas.^{8,9,13} Other potential risk factors, including alcohol use, tobacco use, and history of prior sinus surgery, failed to show a significant association with any subtype of papilloma in the study by Vorasubin *et al.* 5-15% of cases of IP can be associated with malignancy and 4-17% of cases of OSP have been associated with malignancy.^{3,13,14}

Infection with HPV16 and 18 may occur early in the process of tumorigenesis with several other insults required to transform benign IP to dysplasia or malignancy.⁶

On gross analysis, IP usually appears large, firm, and gray in color with a multinodular, polypoid, uneven surface.⁶ Exophyticpapillomas grossly appear as gray-tan, exophytic, mushroom-shaped verrucous papillary proliferations classically arise from the anterior nasal septumttached to the underlying mucosa by a narrow stalk.^{27,15} Histologically, markedly thick inverted or endophytic growth of nonkeratinizing transitional cells is seen. The thick epithelium undergoes squamous maturation and inverts into the stroma with a distinct basement membrane that separates the epithelium from the underlying connective tissue stroma (Figure 4). Surface keratinization and a granular cell layer are uncommon; numerous intraepithelial microcysts containing cell debris, macrophages, and mucin are present.

Treatment

Although external approaches were once exclusively used, endoscopic resection has been gaining popularity because of decreased morbidity without compromising recurrence rates. Ultimately, the type of approach depends on the site of tumor attachment and extension.^{6,16-20}

The site of tumor attachment is crucial to identify to ensure complete resection, which involves complete removal



Figure 1: Pale pink mass attached medial to middle turbinate in left nostril and filling the nasopharynx



Figure 2: CT scan showing mass in left nasal cavity and bony erosions



Figure 3: Pink rubbery mass completely filling the nasopharynx

of the affected mucosa and mucoperiosteum, because incomplete or limited resections are thought to be the leading cause of recurrence.²¹

Microscopic foci of residual papilloma can be concealed within the bone at the attachment site. Therefore, drilling the bone at the site of attachment can further reduce the risk of recurrence.²² Some reports suggest the use of radiation therapy for locally advanced papillomas or papillomas with multiple recurrences.^{4,18}

About 5-60% of IP cases can recur, shown to increase the risk of recurrence for IP including tobacco exposure, increased tumor size, increased hyperkeratosis, squamous epithelial hyperplasia, increased number of mitoses, bilaterality, and the lack of inflammatory polyps.^{5,6,23-25} In addition, IP originating from the frontal sinus tends to have multiple recurrences, likely because of technical difficulties operating in this location.^{6,24} Most recurrences usually occur within the first 3 years.

ONB

ONB is an uncommon malignant neuroectodermal nasal tumor comprising about 2% of all sinonasal tract tumors



Figure 4: Squamous matured epithelium inverted into the stroma



Figure 5: Small round blue cells slightly larger than mature lymphocytes

with an incidence of approximately 0.4 per million population. ONB are thought to arise from the specialized sensory neuroepithelial olfactory cells that are found in the upper part of the nasal cavity. Specifically, Jacobson's vomeronasal organ, sphenopalatine ganglion, ectodermal olfactory placode, ganglion of Loci (nervus terminalis), autonomic ganglia of the nasal mucosa, and the olfactory neuroepithelium (cribriform plate and superomedial surface of the superior turbinate) are all sites of origination for this malignant neural crest derived neoplasm.

A bimodal age distribution in the 2nd and 6th decades of life is seen without a gender predilection, usually presenting with unilateral nasal obstruction (70%) and epistaxis (50%), less commonly headaches, pain, excessive lacrimation, rhinorrhea, anosmia, and visual disturbances. Even though the tumor arises from the olfactory neuroepithelium, anosmia is not a common complaint (5%). The tumors tend to be locally aggressive, involving adjacent structures (orbit and cranial cavity).



Figure 6: Rosette arrangements of cells in neuroblastoma



Figure 7: Mature small round lymphocyte cells seen in low power



Figure 8: lymphocytes seen in high power



Figure 9: Submucosa showing sporangiospores of rhinosporidium

A "dumbbell-shaped" mass extending across the cribriform plate is one of the most characteristic imaging finding, similar to our case. The upper part in the intracranial fossa, while the lower part in the nasal cavity, with the "waist" at the cribriform plate. CT will show speckled calcifications and bone erosion. Contrast-enhanced CT will show homogenously enhancing mass, with non-enhancing areas suggesting regions of necrosis. T2-weighted images may show hyperintense regions which correlate to the cystic regions at the advancing edge. There is often marked tumor enhancement after gadolinium. ONB may rarely present with only an intracranial (frontal lobe) mass. Ectopic tumors within the paranasal sinuses (not ethmoid) are vanishingly rare, except in recurrent tumors.

Histologically, a lobular architecture comprised "primitive" neuroblastoma cells. The tumor cells are "small, round, and blue" cells slightly larger than mature lymphocytes, with a very high nuclear to cytoplasmic ratio (Figures 5 and 6).

Two types of rosettes are recognized: The delicate, neurofibrillary, and edematous stroma forming the center of a cuffing or palisaded arrangement of cells in Homer–Wright pseudorosettes (30%) while a "gland-like" tight annular arrangement is seen in Flexner–Wintersteiner rosettes (5%). Special stains like silver stains such as Bodian, Grimelius, and Churukian-Schenk may highlight the neurosecretory granules but immunohistochemistry is the more popular diagnostic tool.

Management

The Kadish *et al.* proposed staging system from 1976 is still used, even though Dulguerov and Calcaterra have proposed a tumor, node, and metastasis-type classification. The Kadish system includes: A - tumor limited to nasal cavity; B - nasal cavity and paranasal sinuses; and C - beyond nasal cavity and sinuses. Most tumors are in Stage C (about 50%), survival rates are 75-91% for Stage A, 68-71% for Stage B, and 41-47% for Stage C. Overall, there is a 60-80% 5-year survival. Low-grade tumors have an 80% 5-year survival while high-grade tumors have a 40% of survival.

Due to potentially significant bleeding, biopsy should be used with caution. Complete surgical elimination frequently requires a bicranial-facial approach (trephination) which removes the cribriform plate and is usually followed by a course of radiotherapy as the treatment of choice to achieve the best long-term outcome. An elective neck dissection is not warranted. Palliation with chemotherapy is achieved for advanced unresectable tumors or for disseminated disease. Autologous bone marrow transplantation has achieved long-term survival in limited cases.

Recurrences develop in about 30% of patients (range 15-70%), usually within the first 2 years after initial management. Cervical lymph node metastasis (up to 25%) or distant metastases (approximately 10%) develop irrespective of the grade of the tumor, the most frequent sites being lungs and bones. Overall survival is adversely affected by female gender, age <20 or more than 50 years at initial presentation, high tumor grade, extensive intracranial spread, distant metastases, tumor recurrence, a high proliferation index, and polyploidy/aneuploidy.²⁶

Primary Tuberculosis of Nasopharynx

Nasopharyngeal tuberculosis comprises only <1% of extrapulmonary tuberculosis found in the upper respiratory tract. According to Rohwedder,²⁷ only 0.1% of nasopharyngeal involvement were detected in primary active pulmonary tuberculosis patients. However, the nasopharynx is a relatively silent region, and the disease may be more common than suspected,^{28,29} especially in endemic areas and with an increase in HIV, but in our case, the patient was immune competent. Nasopharyngeal

tuberculosis is seen most commonly in women and in $5-6^{\text{th}}$ decades.³⁰⁻³²

Cervical lymphadenopathy, nasal obstruction, rhinorrhea, epistaxis, serous otitis media, and hearing loss are the most common clinical symptoms.^{33,34} Tuberculosis can involve the nasopharynx primarily without affecting any other system or secondary to pulmonary or extra pulmonary involvement.³⁵ Many a times, tuberculosis of nasopharynx is underdiagnosed due to less obvious signs and symptoms in all the cases.³⁶ Atypical presentations with diplopia and sleep apnea have also been reported.^{37,38}

Endoscopic examination may reveal a polypoidal mass, ulceration, plaque, or diffuse mucosal thickening of the nasopharynx.³⁹⁻⁴¹ For definitive diagnosis, repeated biopsies should be done. Epithelioid giant cells and granulomatous inflammation that was characterized by caseous necrosis are the usual pathological findings. Isolation of acid-phase bacilli and produce Mycobacterium tuberculosis in the culture is very difficult procedure in the nasopharyngeal tuberculosis.42 As acid-fast bacilli are found in only 10% of tuberculosis specimens by direct examination,¹ Arnold et al.⁴³ investigated the use of tuberculostearic acid in formalin fixed, paraffin wax embedded tissue specimens and found it useful for rapid diagnosis. Furthermore, MRI and positron emission tomography (PET) may be useful for differentiating nasopharynx cancer from tuberculosis but false positives are quite high as per the study by Kim.44

The treatment of extrapulmonary tuberculosis is same as that of pulmonary tuberculosis.⁴⁵ Patients are 2-month treated with 4 drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol), followed by 4-month treated with two drugs (isoniazid and rifampicin) as done with our case which gave good response.

Non-Hodgkin's Lymphoma

The head and neck is the second most common region for extranodal lymphoma after gastrointestinal tract. Among various head and neck sites, Waldeyer's ring, which is an area encompassed by the nasopharynx, tonsil, and base of the tongue, is most often involved by non-Hodgkin's lymphoma (NHL).⁴⁶ Patients of any age group can be affected. However, most patients are middle-to-older age with male preponderance. Death in these patients is due to sepsis or due to compression of the vital organs by the enlarged lymph nodes.⁴⁷ A substantial percentage of NHL arise from tissue other than lymph nodes and even from sites which normally contain no lymphoid tissue.⁴⁸ Certain workers such as pesticide applicators, workers in the petroleum, organic chemicals, food preservatives, and plastic and synthetic industries have slight increased risk of NHL.⁴⁹ The most common chromosomal abnormality associated with NHL is the t (14; 18) (Q32; Q21) translocation that is found in 85% of follicular lymphomas and 25-30% of intermediate grade of NHL.⁵⁰ Clinically, lymphadenopathy (most common), fever, night sweat, weight loss, spleen involvement (20%), and involvement of liver (advance disease).^{50,51}

Usually, hematologic and biochemical profiles of the patients are normal. Histologically seen as small round tumor cells (Figures 7 and 8) MRI of the head and neck, chest, abdomen, and pelvis is the mainstay for staging of NHL. However, concurrent PET with 18F-fluorodeoxyglucose and CT (PET/CT) is also a useful method for staging and assessment of the therapeutic response. Positive staining for leukocyte common antigen in histological specimen distinguishes malignant lymphoma from non-lymphoid neoplasm. However, diffuse large B-cell lymphomas are commonly positive for CD20 immunohistochemical stains.

The WHO modification of the revised European-American lymphoma classification recognizes three major categories of lymphoid malignancies as B-cell neoplasm, T-cell natural killer cell neoplasm, and Hodgkin's lymphoma. The NHL can be divided into two prognostic groups: (1) Indolent NHL types have a relatively good prognosis, with median survival of 10 years, but they are not curable in advanced clinical stages⁴⁹ and (2) the aggressive lymphomas have a poor prognosis, with a median survival of 2-3 years.

In general, the standard treatment for patients with diffuse large B-cell lymphoma is chemotherapy followed by involved field radiotherapy as this would prevent the spread of the disease and reduce the radiation field and radiation in most of the cases. RCHOP chemotherapy regimen is considered as a standard treatment for patients with advanced stage of diffuse large B-cell lymphoma.⁵²

Rhinosporidiosis

Rhinosporidiosis is a chronic and localized infection of the mucus membranes and the lesions present clinically as polypoid, soft masses (sometimes pedunculated) of the nose, throat, ear, and even the genitalia in both sexes. The presumed mode of infection from the natural aquatic habitat of *Rhinosporidium seeberi* is through the traumatized epithelium "transepithelial infection" most commonly in nasal sites.⁵³

The etiological agent is *R. seeberi*, the microbe has been considered a fungus by most microbiologists, although its taxonomy has been debated.^{54,55} The infectious agent forms round and thick-walled sporangia in the submucosa of the affected site, varying from 10 to 200 mm in size, which are visible as white dots in the mucosa containing smaller

"daughter cells" (called "sporangiospores") (Figure 9). It can be visualized with fungal stains such as Gomori methenamine silver and periodic acid-Schiff as well as with standard hematoxylin and eosin staining.⁵⁶

Treatment

The only curative approach is the surgical excision combined with electrocoagulation. Recurrence, dissemination in anatomically close sites, and local secondary bacterial infection are the most frequent complications.

CONCLUSION

This study mainly aims to enlighten the most interesting and rare presentations that can occur in the nasopharyngeal area along with the newer diagnostic and therapeutic advances. Squamous cell carcinoma, sinonasal undifferentiated carcinoma, extranodal NK/T-cell lymphoma, nasal type, rhabdomyosarcoma, Ewing/PNET, mucosal malignant melanoma, and neuroendocrine carcinomas could be the various differential diagnosis. An ENT surgeon has to keep an open mind to consider all these differential diagnosis in a case of nasopharyngeal mass. This will improve the accuracy of diagnosis and therapeutic outcome, especially in cases where early diagnosis can improve the chance of survival.

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