To study the immunohistochemical profile of sinonasal and nasopharyngeal masses

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ABSTRACT

Introduction: Sinonasal and nasopharyngeal tract masses can be difficult to diagnose as they have unusual diverse morphology and histopathology with anatomic and embryonic distinction and immunohistochemistry (ICH) becomes mandatory for diagnosis. Aims and Objectives: A retrospective observational study of 5 years from 2011 to 2016 till date was conducted at a tertiary care center. Total analyses of 200 cases were done to study the clinical presentation and histomorphology of all sinonasal and nasopharyngeal masses with gender and age distribution and highlighting the entities with rare clinicopathological and histological presentation and study of ICH in these lesions. Results: Out of total 200 cases, 148 (74%) were inflammatory or infective non-tumorous masses and 52 (26%) were neoplastic, out of which 27 (13.5%) were benign and 25 (12.5%), were proven to be of malignant etiology. In benign neoplastic category, unusual entities were juvenile angiofibroma, meningioma, and hemangioma. Among the cases with atypical clinicopathological presentation and unusual entities which required ICH for diagnosis were chordoma, diffuse large B-cell lymphoma, esthesioneuroblastoma, sinonasal adenocarcinoma, adenoid cystic carcinoma, and nasopharyngeal carcinomas. Conclusion: Sinonasal and nasopharyngeal masses are having diverse clinical presentations at different sites having unusual clinical presentation and varied histopathology and the unusual varieties also occur which rare to these locations and should be promptly diagnosed with ICH for early, accurate and optimal treatment.

Key words: Immunohistochemistry, Nasopharyngeal mass, Sinonasal mass

Introduction

The sinonasal tract and nasopharynx are in close proximity to the vital structures such as the orbit, brain and the cavernous region, and early detection of lesions in these areas are vital for favorable outcome. With routine diagnostic nasal endoscopy, better imaging and biopsy of suspicious lesions have changed the outlook to sinonasal and nasopharyngeal masses. The nasal cavities and all the paranasal sinuses are collectively called sinonasal tract.¹² The sinonasal tract is anatomically and embryologically distinct from the nasopharynx. Although both are lined by identical appearing ciliated respiratory epithelium, the epithelium of the sinonasal tract is ectodermally derived whereas that of the nasopharynx is endodermally derived. This embryologic difference may be a factor in the varied development of epithelial lesions at the two sites, e.g., scheiderian papillomas and nasopharyngeal carcinomas.³⁴ Despite the anatomical differences in both the areas, they also present with identical type of lesions due to the presence of similar structures such as minor salivary glands and connective tissues. With the vast forms of lesions presenting in these areas, it is essential to resort to immunohistochemistry (ICH) for exact lineage of the diverse histological presentations.

This is a retrospective observational study which is done to analyze the varied histomorphology of sinonasal and nasopharyngeal masses and role of ICH to diagnose these tumors early and accurately.

Aims and objectives

The aim of the study was to assess the occurrence of various masses arising from the sinonasal tract and nasopharynx and analyze, the role of IHC in differentiating these tumors.

Materials and Methods

This is a retrospective observational study of lesions and masses of sinonasal tract and nasopharynx which were received after incisional biopsy or surgical excision. The duration was from May 2011 to April 2016 a total of 5 years. The patients were evaluated on the basis of their chief complaints. Complete ENT examination which included nasal endoscopy and radiological evaluation was done. The study was carried out in collaboration with ENT and oncopathology department. Patient's feedback, clinical history and follow-up were done. Histopathology, microbiological culture, and isolates were also studied. Hematoxylin and eosin (H and E) sections were studied for histopathological review and lesions were subgrouped into non-neoplastic lesion, benign neoplasm, and malignant neoplasm categories. Depending on the morphology
and histopathology, the sections were subjected to special stains periodic acid-schiff, Grocott, Congo red, gram stain for the demonstration of bacterial or fungal organisms. The tumors when suspected to be lymphomas, esthesioneuroblastoma or poorly differentiated carcinomas were subjected to ICH methods using Dako antibodies Pancytokeratin (CK), AE1AE3, MNF116, epithelial membrane antigen, leukocyte common antigen (LCA), CD20, CD3, synaptophysin and other immunohistochemical panel as and when needed to arrive to a final diagnosis.

Results

A total of 200 cases of sinonasal and nasopharyngeal lesions were studied retrospectively. 148 non-neoplastic lesions, 27 benign neoplasms, and 25 malignant neoplasms were found. Non-neoplastic masses were in 89 males of age group 15–66 years and 59 in females in age group of 20–65 years. The benign neoplastic masses were total 27 with 16 in males in age group 11–52 years and 11 in females in age group 21–68 years, and malignant masses were 25 of which 16 were in males in age group 42–68 years and 9 in females in age group 44–58 years. A male predominance was seen in both benign and malignant neoplastic categories except for fungal ball which was seen predominantly in females, in ratio of 1.5:1 (female: male).

Non-neoplastic masses were total 148, of which 82 patients were identified with fungal rhinosinusitis, in whom the mean patient age was 60 years (range 18–90 years) with a male to female ratio of 1.5:1. The most common symptoms present in non-neoplastic lesions were nasal obstruction (90.5%) and rhinorrhea (88.5%) while the least common symptom was epistaxis (0.04%) mostly related to chronic invasive fungal rhinosinusitis and rhinosporidiosis. 55% of cases were unilateral with 19.5% cases with intraorbital and intracranial extension seen in cases of allergic fungal rhinosinusitis (AFRS) and invasive fungal rhinosinusitis. Of all the cases of fungal rhinosinusitis, 72 (88%) had non-invasive fungal disease while 10 (12%) had invasive disease. In the non-invasive fungal disease, 16 patients had fungal ball (11 involving maxillary sinus, 3 in sphenoid and the remainder 2 in ethmoid sinuses). The diagnosis was made by diagnostic nasal endoscopy and computerized tomography scan which showed single sinus heterogeneously enhancing lesion with sclerosis of the sinus walls. The fungal ball isolated was identified histologically in H and E stains, with loads of fungal hyphae and yeast forms with no tissue invasion. The 54 cases of AFRS all were evaluated and diagnosed based on Bent and Kuhns criteria. In these patients of AFRS was seen with pink staining lamellated mucin with eosinophilic debris and fungal hyphae or mucin without fungi and with 40 cases yielding positive culture for fungal growth. Aspergillus sp. with acute angled branching septate fungal hyphae was seen in 49% of cases of non-invasive fungal infection and in 22% sections and fungal isolates grew bipolaris which were confirmed to be fungal culture. 10 (12% of fungal rhinosinusitis) patients were classified as having invasive fungal rhinosinusitis. In these 8 cases where acute invasive fungal rhinosinusitis, 5 patients were immunocompromised either due to immunosuppressive therapy/HIV and 3 patients were diabetic as per the clinical notes. Hyphal forms with acute angled septate branching Aspergillus sp. was seen in the sections in 4 cases and broad hyphae of mucor with 90-degree branching seen in 4 cases with evidence of invasiveness and blood vessel invasion. 2 cases were of chronic granulomatous invasive fungal infection diagnosed in immunocompetent individuals with involvement of maxillary sinus and orbit. Both the cases were managed with surgeries and 6 months of oral antifungal therapies.

Rhinosporidiosis is seen in 7 cases out of which 3 were recurrent cases, 3 had undergone surgery with dapsone therapy without recurrence in 2 years follow-up and 1 had loss to follow-up post-surgery. 1 case was rhinoscleroma with the presence of foamy Mikulicz cells and Klebsiella was isolated on culture. 52 cases were allergic polyps with classical histopathology of a polypoidal lesion lined by epithelium and underlying stroma with edema and inflammatory cells associated clinically with chronic rhinosinusitis. 19 cases were antrochoanal type, 1 was sphenocoanal type and 32 cases of pan-sinus involvement. 10 were revision cases out of which 3 had a history of aspirin sensitivity.

Among 27 cases of benign neoplasms, the most common symptoms were nasal obstruction (85.2%), epistaxis (66.6%), and 92.5% cases were with unilateral nasal disease. 13 were cases of inverted papilloma with a characteristic histology of proliferation of squamous epithelium in downward trajectory into the underlying stroma in the age range of 43-66 years with 12 males and 1 female. There were 7 arising from maxillary sinus, 5 from the lateral wall of nose and 1 from the sphenoid sinus. 5 cavernous hemangioma, 2 hamartoma in 25–28 years male, 5 cases of juvenile angiofibroma in age group 11–17 years in males. 2 meningioma of the meningotheial type in 54 years male which was extracranial meningiomais arising from the sinonasal tract without any evidence of an association with an intracranial tumor (also called heterotopic, ectopic, or extra calvarial) and this is a rare clinical presentation. In our study, sinonasal tract meningiomas were common in males although the literature supports a slight female predominance, 1:1.2, or approximately 55%.

Of the total 25 cases of malignant masses, 2 nasopharyngeal chordomas in 68 years female and 65 years males with characteristic physaliphorous cells [Figure 1], chordoma are considered potentially malignant because they are slow they can invade other tissues, frequently recur after removal and have potential to metastasize. Primary chordoma in the nasal cavity and nasopharynx is an extremely rare tumor in the extrasosseous axial skeleton. Lesions in these sites primarily present as a soft tissue polypoidal mass without the involvement of the skull base bone (clivus), so the preoperative diagnosis of the tumor is possibly difficult.
About 1 case of squamous cell carcinoma of the lateral wall of nose, 2 cases of esthesio (olfactory) neuroblastoma which was positive for NSE, chromogranin and synaptophysin positivity [Figure 2] and the IHC of olfactory neuroblastoma is tabulated in form of Table 2. One was arising from cribriform area, and the other from lateral wall of nose and the differential diagnosis considered were sinonasal small cell neuroendocrine carcinoma which was negated by the presence of high mitotic rate and necrosis is prominent. Neurofibrillary stroma and S-100 positive cells are lacking. There may be diffuse CK positivity, sinonasal undifferentiated carcinoma, non-keratinizing nasopharyngeal carcinoma, alveolar rhabdomyosarcoma: Negative for neuroendocrine markers and S-100 but positive for desmin and actin, melanoma, small cell variant which show more pleomorphism and are negative for neuroendocrine markers but diffusely positive for S-100, teratocarcinosarcoma, pituitary adenoma: Express CK and specific pituitary hormones and lymphomas with characteristic ICH.

Ewing sarcoma/PNET, 2 cases each of sinonasal adenocarcinoma, 1 case of adenoid cystic carcinoma, and 2 case of non-Hodgkins lymphoma which was of diffuse large B-cell type. Primary non-Hodgkin’s lymphoma (NHL) of the nasal cavity is an extranodal form of NHL characterized by association with Epstein-Barr virus (EBV) infection, predominance of T-cell phenotype and a worse prognosis compared to nodal lymphoma.

15 cases of nasopharyngeal carcinoma undifferentiated with wide spread CNS metastases which are a rare clinical presentation. And in which the lymphoma and carcinoma panel ICH was done with LCA, CK, CD 20, CD3 and MIB1 to assess the proliferative index or mitosis. All the cases of neoplasms were evaluated with endoscopy and imaging, but biopsy confirmed the diagnosis for the definitive treatment.

**Discussion**

The sinonasal and nasopharyngeal masses are having varied histomorphology\(^{[3,4]}\) and it is important to differentiate non-neoplastic, benign and malignant lesions with recognition of unusual lesions as early diagnosis and treatment are lifesaving.

In our retrospective study, the overall mean patient age was 60 years (range 18–90 years) with a male to female ratio of 1.5:1. 88% had non-invasive disease with 20% having fungal ball, 66% AFRS, 2% combined fungal ball and rhinosinusitis and 12% had invasive disease. In 16 patients, fungal ball was identified histologically in H and E stains in all adult patients with mean age of 50 years (range 35–55 years) with female preponderance with F: M ratio 1.5:1, with loads of fungal hyphae and yeast forms with no tissue invasion. This was distinguished from saprophytic fungal infestation with spores in crusts and mucus in the nose. Treatment done was surgical removal of the fungal ball under endoscopic guidance. In 54 patients of AFRS was seen with pink staining lamellated mucin with eosinophilic debris and fungal hyphae or mucin without fungi and with or without culture growing fungus. The diagnostic nasal endoscopy was done in all cases and diagnosis was based of Bent and Kuhn diagnostic criteria\(^{[5]}\) for AFRS. Treatment done was surgical removal of eosinophilic mucin and diseased mucosa to establish ventilation of sinuses and long-term oral/nasal steroid therapy.

Study by Granville *et al.* showed in 23% patients *Aspergillus* fungal ball, and 2.1% cases acute rhinosinusitis and 3.1% with

### Table 1: The prevalence data of all sinonasal lesions

<table>
<thead>
<tr>
<th>Sinonasal lesions</th>
<th>Number of cases</th>
<th>Males</th>
<th>Age range in males (years)</th>
<th>Females</th>
<th>Age range in females (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non neoplastic lesions</td>
<td>148</td>
<td>89</td>
<td>15-66</td>
<td>59</td>
<td>20-65</td>
</tr>
<tr>
<td>Benign tumors</td>
<td>27</td>
<td>16</td>
<td>11-52</td>
<td>11</td>
<td>21-68</td>
</tr>
<tr>
<td>Malignant tumors</td>
<td>25</td>
<td>16</td>
<td>42-68</td>
<td>9</td>
<td>44-58</td>
</tr>
</tbody>
</table>
In Sinonasal and nasopharyngeal region, both benign and malignant masses are common. Among 27 cases of benign neoplasms, 13 cases of inverted papilloma were present with characteristic inward trajectory of hyperplastic metaplastic squamous epithelium with underlying edematous stroma. Buchwald et al. studied 82 patients with sinonasal papillomas diagnosed from 1975 to 1993 histologically and showed 58 cases of inverted papillomas.

About 5 lobular capillary hemangiomas in patients of mean age group 24 years in males and clinically presented as smooth poyoidal mass 1.5 cm in diameter and histologically submucosal vascular proliferation arranged in lobules. 2 hamartomas in 25–28 years male, nasal chondromyxoid hamartoma is a tumefactive process of sinonasal tract with admixture of chondroid and stromal elements and histologically consist of lobules of cartilage and spindly stroma.

About 2 menigiomas of the meningothehtial type in 54 and 65 years male and female, respectively. Meningiomas are benign neoplasms of meningothehtial cells and outside central nervous system considered to be ectopic. They appear as polypoidal masses and the meningothehtial type is more common in sinonasal cavity. Meningioma is a common intracranial neoplasm with a variety of histomorphologic growth patterns which are usually easily recognized. However, primary extracranial (ectopic, extra calvarial) meningiomas of the nasal cavity, paranosal sinuses, and nasopharynx (here in after referred to collectively as the sinonasal tract) are rare. The largest study to date is of 12 cases reported by Perzin et al. While a degree of controversy continues to exist around the exact origin of sinonasal tract meningiomas, it seems generally accepted that primary extracranial meningiomas do occur. Histologically, meningiomas of the sinonasal tract are identical to their intracranial counterparts, although diagnostic difficulties are frequently encountered in the differential diagnosis with carcinoma, melanoma, and olfactory neuroblastoma resulting from the rarity of meningiomas in this location. With these difficulties in mind, we thought it would be legitimate to undertake this study of 30 cases of sinonasal tract meningiomas to describe the clinical findings associated with these tumors, illustrate their pathologic features, document their immunophenotype, apply meningioma grading parameters, and analyze this data as it relates to patient outcome in a single comprehensive study. 5 cases of juvenile angiofibroma in age group 11–17 years in males, nasopharyngeal angiofibroma are <1% of all head and neck tumors, restricted to young-aged male patients, arising from sphenopalatine region, can also grow into nasal cavity and has got definite endocrinal influence.

Of the total 25 cases of malignant masses, 2 chordomas in 68 years female and 65 years males with characteristic
histology of epithelioid cells with vesicular nuclei and vacuolated cytoplasm giving appearance of characteristic physaliphorous cells [Figure 1]. Chordomas are low to intermediate grade tumors that recapitulate notochord, more common in males. ICH with brachyury is confirmatory. Chordomas are rare malignant tumors of notochordal origin and may occur at any site along the course of the embryonic notochord. These tumors typically occur in the axial skeleton and have a proclivity for the sphenoid-occipital region of the skull base and sacral regions with bony changes. Imaging features of chordomas elsewhere in the body have been reported in previously published literature. The clinical findings of chordomas in the nasopharyngeal region only have been mentioned as an extension from an intracranial tumor in some studies.[4-6] The literature on CT and MR imaging of primary chordomas in the nasal cavity and nasopharynx is rather sparse. The tumor usually presents in this region as a soft tissue mass with no change in the skull base bone (clivus) and is misdiagnosed as another tumor type. This study reviews CT and MR findings of 5 cases of chordomas with no clivus destruction in the nasal cavity or nasopharynx seen from 2004 to 2008 in our hospital, in an effort to improve the value of the differential imaging features of these unusual lesions.[20,21] One case of squamous cell carcinoma, two cases of olfactory neuroblastoma in mean age group of 51 years and these are uncommon malignant neoplasms, 2–3% of sinonasal tract tumors. Histologically, they are lobular in appearance with uniform round cells and neurofibrillar material and are graded 1–4 as per Hyam criteria. Olfactory neuroblastoma is a neoplasm that can histologically mimic many tumors within the sinonasal tract, making recognition of this tumor important, as the management frequently requires a bicranial-facial surgical approach, a trephination procedure which can be quite technically difficult and challenging to achieve a good result. The management is therefore quite unique in comparison to other sinonasal tract malignancies, setting it apart diagnostically and managerially from other lesions. Our cases were hyam Grade II. Tumors are separated into four grades, although sometimes a definitive separation between grades is arbitrary. There is a continuum from Grade I to Grade IV, with grade based on the degree of differentiation, presence of neural stroma, mitotic figures, and necrosis. Lobularity is present in all tumors, although better developed in Grade I tumors, but still present in Grade IV lesions. Grade I includes the majority of tumors and is the most differentiated. The cells are syncytial, have cytoplasmic neurofibrillary extensions, and are uniform, with small round nuclei and evenly disubuced nuclear chromatin. Surrounding fibrous stroma is quite vascular. Mitotic activity and necrosis are absent. Grade II tumors show less neurofibrillary stroma and slightly more pleomorphism, with isolated mitoses. Grade III tumors show more pleomorphism, coarse chromatin distribution, hyperchromasia, with increased mitotic activity and necrosis. Flexner-Wintersteiner rosettes may be seen and calcifications are absent. Grade IV neoplasms are the most anaplastic, showing pleomorphic nuclei with prominent eosinophilic nucleoli. Necrosis, increased mitotic figures, including atypical mitotic forms is common. Neurofibrillary material is absent, as are calcifications. The grade correlates with prognosis, although not as sensitively as tumor stage. As the grade of the tumor increases so does the difficulty in diagnosis, often requiring ancillary studies to confirm the diagnosis.[21,22] Two cases each of sinonasal adenocarcinoma and two case of NHL which were of diffuse large B-cell type, Primary NHL of the nasal cavity is an extranodal form of NHL characterized by association with EBV infection, predominance of T-cell phenotype and a worse prognosis compared to nodal lymphoma. In the west, paranasal sinus NHL is more common. In contrast, in the east, nasal NHL is more common than the NHL of the paranasal sinus. Xiong et al. reported the largest series of primary NHL of the nasal cavity.[21] Median age of presentation was 44 years (Range: 11–79 years), and males were affected more often than females. Maxillary sinus was the most frequent site of involvement followed by the ethmoid sinus and the nasopharynx. The most common presenting symptoms include nasal obstruction, epistaxis, and headache. Diplopia and blurred vision are rare infrequent symptoms associated with nasal NHL. The present patients are middle-aged male who presented with nasal obstruction and extension of the tumor into the maxillary sinus. Macroscopically, these tumors are submucosal in contrast to squamous cell carcinomas which are ulcerative. Angioinvasion and necrosis are the two characteristic histological features of sino-nasal NHL. NHL of the nasal cavity is predominantly T-cell lymphomas, whereas NHL of the paranasal sinuses is B-cell lymphomas. Our patients were having sinonasal diffuse large B-cell lymphoma that is an unusual presentation. Staging of the patients is according to Ann Arbor system. In addition to CECT of the paranasal sinuses, CECT of the abdomen and thorax are required for adequate staging. Management is according to the stage of the disease. Stage IE is treated with chemotherapy or radiotherapy alone whereas stage IIE/III.[24]

We had 15 cases of nasopharyngeal carcinoma. Nasopharyngeal carcinoma is an uncommon neoplasm and is a squamous cell carcinoma arising from surface epithelium and classified into keratinizing, nonkeratinizing and further differentiated and undifferentiated types Nasopharyngeal cancer is unique among head and neck cancers. Despite definitive treatment, there is a high rate of recurrence, most commonly in the bone, lung or liver. Brain metastases and particularly, leptomeningeal carcinomatosis are extremely rare. We present a case of recurrent nasopharyngeal carcinoma with brain metastases and leptomeningeal carcinomatosis in the absence of local recurrence and systemic metastases.[24]

In the present study, we had 52 cases of neoplasm of the sinonasal and nasopharyngeal region out of which 32 were epithelial neoplasm and it stands in agreement with Panchal et al. were 69 out of 120 sinonasal cases were epithelial tumors (59.2%).[3]
Conclusion

Sinonasal and nasopharyngeal masses may arise in distinct locations and are non-neoplastic and neoplastic with benign and malignant varied histopathology and also the unusual varieties such as meningiomas, adenoid cystic carcinomas, nasopharyngeal carcinomas, and lymphomas also occur which are rare to these locations. The evaluation is based on complete clinical examination, imaging to look for extent and characteristic of the lesion and pathological examination with ICH to confirm the diagnosis to institute the definite management.

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