

A Study of Histopathological Spectrum of Masses Arising From Upper Respiratory Tract in A Rural Tertiary Care Centre

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Abstract: Introduction: Lesions of upper respiratory tract are commonly encountered in clinical practice and important from clinical and pathological point of view as they have variety of histological perspectives. Aims & Objectives: The present study was undertaken with the aim to evaluate the histopathological pattern of lesions of upper respiratory tract along with age wise and sex wise distribution of lesions. Methods: This was a four year study started from September 2012 to October 2016 and included 277 biopsy specimens of upper respiratory tract. All tissues were routinely processed and stained with Hematoxylin and Eosin. Special stains and Immunohistochemistry were used wherever required. Results: Among 277 cases, the age ranged from 18 months to 80 years with male: female ratio of 3.2:1. Thirty six cases were non-diagnostic and excluded from the study. Non-neoplastic lesions constituted 47.3% cases whereas benign and malignant cases accounted for 10.8 % and 41.9% cases, respectively. Most common non-neoplastic lesion was inflammatory polyp of nasal cavity. While in malignant lesions, Squamous cell carcinoma was most common. Conclusion: Categorising the upper respiratory tract lesions according to histopathological pattern helps us to know clinical presentation, treatment, clinical outcome and prognosis of disease. [Ivreet K NJIRM 2017; 8(3):1-6]

Key words: upper respiratory tract lesions, round cell tumor, polypi

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Introduction: The upper respiratory tract comprises of nasal cavity, paranasal sinuses, pharynx and larynx and act as conductive unit of respiratory tract. Lesions of nasal cavity and paranasal sinuses are often grouped under term sinonasal masses. In upper respiratory tract lesions, the sinonasal masses are the most common lesions encountered in clinical practice. The presentation of upper respiratory tract lesions depend on the primary site, the direction and extent of spread¹⁻³. The lesions of upper respiratory tract may be congenital, inflammatory and neoplastic (benign or malignant)^{4,5}.

Malignant tumors of upper airways account for less than 1% of all carcinomas and for about 3 % of neoplasms of head and neck region⁶⁻⁸. Despite of the fact that upper respiratory tract is rare site of malignancies, it can present broad spectrum of both epithelial and non-epithelial malignancies⁹. Thus, the presenting complaints along with clinical examination and radiological imaging can suggest a diagnosis^{5,7}. However, the histopathological examination is mandatory for correct diagnosis.

Lesions of upper respiratory tract encountered in clinical practise are important from clinical and pathological perspectives as they give rise to variety of histological patterns and grades of malignancies⁷. The present study was undertaken with the aim to categorise lesions of upper respiratory tract into non

neoplastic and neoplastic and to study the histopathological pattern and incidence of various lesions. Further, to determine the distribution of these lesions among different age and sex groups.

Methods: In the present study, the patients coming to the E.N.T department and diagnosed with upper respiratory tract lesions during the period of four years starting from September 2012 to October 2016 (retrospectively from September 2012 to August 2015 and prospectively from September 2015 to October 2016) were considered. The ethical clearance for study was obtained from institute ethical committee. Clinical data like age, sex, presenting complaints, findings on clinical and radiological examination were collected from histology forms and medical records. A total of 277 cases were received in Department of Pathology during the period of four years.

Inclusion criteria: The specimen representative of lesions were considered for the study.

Exclusion criteria: Small biopsies likely to be lost during processing, superficial biopsies not representative of the lesions were excluded from the study.

All the received specimens were processed routinely and the slides were stained with hematoxylin and

eosin. Special stains and immunohistochemistry were performed wherever required.

Observations and results: In present study, 277 specimens from upper respiratory tract were received in the period of four years. Out of these 277 specimens, 36 biopsy specimens were excluded from the study as they were inadequate for diagnosis. Thus, 241 specimens were taken for the study. The affected individuals age ranged from 18 months to 80 years with male:female ratio of 3.2:1. Majority of the affected patients were in fifth to sixth decade of life. According to site wise distribution of cases, the most common affected site was sinonasal (46.1% cases), followed by pharynx (23.2%) and larynx (30.7%).

Among 241 cases of upper respiratory tract lesions, 111 belonged to sinonasal group of lesions. There were 76 non-neoplastic lesions followed by 22 benign lesions and 13 malignant lesions (Table 1,2,3). Nasal polypi were the most common non-neoplastic lesions. The nasal polypi were further divided into allergic nasal polypi exhibiting abundant eosinophils in edematous stroma whereas diagnosis of inflammatory polypi was given when there was paucity of eosinophils. Sinonasal papilloma was the most common benign tumor. In malignant category, adenocarcinoma and round cell tumor were the most common malignant lesions. The immunohistochemical stains were employed to categorise malignant round cell tumors. Out of these five cases of round cell tumors, there were two cases each of rhabdomyosarcoma and neuroblastoma, respectively. There was single case of sinonasal undifferentiated carcinoma.

Larynx was the next frequent site of upper respiratory tract lesion. Among these 74 cases, there were 29 non-neoplastic lesions, 2 benign lesions and 43 malignant lesions (Table 4,5,6). Vocal polypi were the commonest lesion among non-neoplastic laryngeal lesions. There were only two cases in benign category; one case each of papilloma and granular cell tumor. Squamous cell carcinoma was the most frequent lesion in the malignant category.

Out of 241 lesions of upper respiratory tract, fifty six lesions were found in pharynx. The most common encountered non-neoplastic lesions were non-specific inflammation followed by actinomycosis and chronic tonsillitis. In benign category of neoplasms, there

were one case each of squamous papilloma and schwannoma. The malignant category was mainly constituted by squamous cell carcinoma.(Table 7,8,9)

Table 1: Distribution of non-neoplastic lesions in sinonasal region

Non neoplastic Lesions in sinonasal area	Number of cases
Polypi	65(85.5%)
Fungal Infections	06(8%)
Granulomatous	02(2.6%)
Wegner’s Granulomatosis	01(1.3%)
Nasolabial Cyst	01(1.3%)
Rhinoscleroma	01(1.3%)
Total	76(100%)

Table 2: Histological diagnosis of benign lesion of sinonasal area

Benign neoplasms of sinonasal area	Number of Cases
Papilloma	08(36.4%)
Haemangioma	06(27.3%)
Angiofibroma	07(31.8%)
Schwannoma	01(4.5%)
Total	22(100%)

Table 3: Categorisation of malignant neoplasm of sinonasal area

Malignant neoplasm of sinonasal area	Number of cases
Squamous cell carcinoma	02(15.4%)
Round cell tumor	05(38.5%)
Adenoid cystic carcinoma	01(7.6%)
Adenocarcinoma	05(38.5%)
Total	13(100%)

Table 4: Histologic types of non-neoplastic lesions of larynx

Non-neoplastic lesions of larynx	Number of cases
Vocal Polypi	16(55.2%)
Vocal nodules	07(24.2%)
Granulomatous pathology	03(10.3%)
Non specific Laryngitis	03(10.3%)
Total	29(100%)

Table 5: Histological subtyping of benign lesions of larynx

Benign neoplasm of larynx	Number of cases
Papilloma	01(50%)
Granular cell tumor	01(50%)
Total	02(100%)

Table 6: Pathological diagnosis of malignant lesions of larynx.

Malignant Neoplasms Of Larynx	Number Of Cases
Squamous cell carcinoma	42(97.7%)
Basaloid Squamous cell carcinoma	01(2.3%)
Total	43(100%)

Table 7: Categorisation of non-neoplastic lesions of pharynx

Non-neoplastic lesions of pharynx	Number of cases
Chronic Tonsillitis	02(22.2%)
Actinomycosis Tonsil	02(22.2%)
Non specific Inflammation	05(55.6%)
Total	09(100%)

Table 8: Distribution of benign neoplasm of pharynx

Benign neoplasm of pharynx	Number of cases
Papilloma	01(50%)
Schwannoma	01(50%)
Total	02(100%)

Table 9: Histological diagnosis of malignant lesions of pharynx

Malignant neoplasms of pharynx	Number of case
Squamous cell carcinoma	44(97.8%)
Anaplastic large cell lymphoma	01(2.2%)
Total	45(100%)

Figure 1: Photomicrograph shows non-septate broad fungal hyphae with right angle branching conforming to morphology of mucormycosis.(H & E 400x)

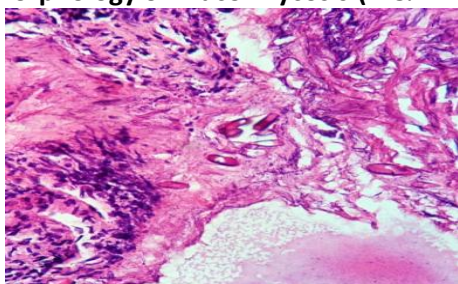


Figure 2. Photomicrograph showing downward proliferation of squamous cells in sinonasal papilloma .(H & E 100 x)

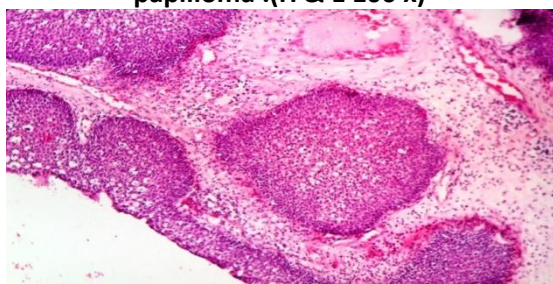


Figure 3: Photomicrograph from schwannoma revealing spindle cell tumor exhibiting hyper and hypocellular areas with formation of verocay bodies. (H & E 100 x)

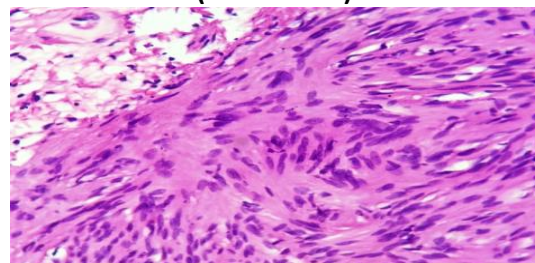


Figure 4: Photomicrograph from rhabdomyosarcoma revealing sheets of undifferentiated small blue round cells.(H & E 400x)

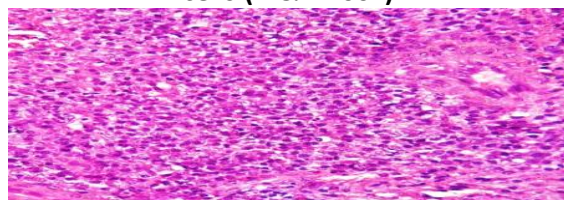


Figure 5: Immunohistochemistry staining showed some of the tumor cells with positive nuclear staining for myogenin.(IHC 400X)

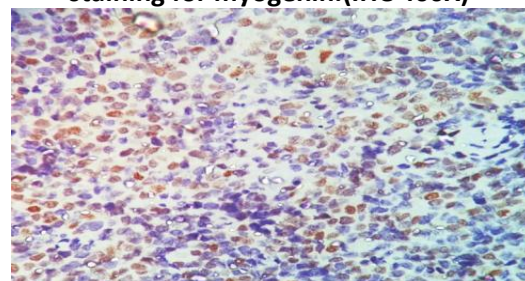


Figure 6: Photomicrograph from tonsil show presence of colonies of actinomyces (H & E 400x)

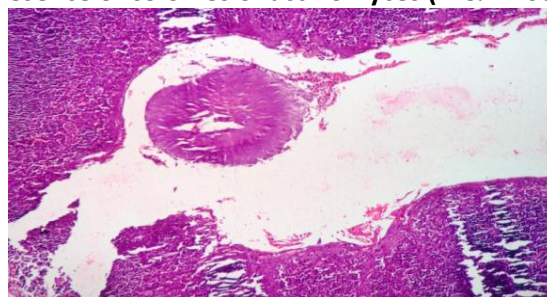


Figure 7: Photomicrograph showing sheets of anaplastic tumor cells in undifferentiated carcinoma (H & E 400x)

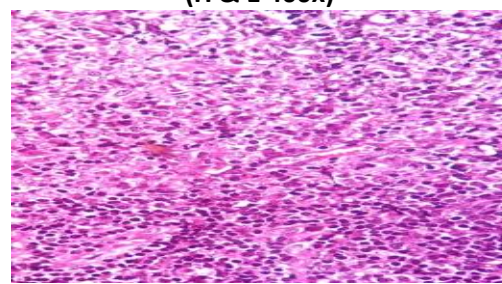
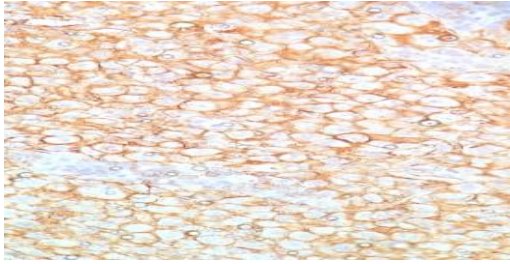


Figure 8. Immunohistochemistry staining showed membranous CD20 positivity in anaplastic tumor cells confirming the diagnosis of anaplastic large cell lymphoma. (IHC400x)



Discussion: Lesions of the upper respiratory tract form a heterogeneous group of lesions with broad spectrum of histopathological features. Most of the studies in the literature have focussed on nose and paranasal sinuses¹⁰. However, the present study has included upper respiratory tract lesions from nose, paranasal sinuses, pharynx and larynx. The present study revealed that the upper respiratory tract lesions had a predilection for males, demonstrating male: female ratio of 3.2:1 which is concordant with the other studies in the literature. The current study had shown that 5th decade of life was the most vulnerable period whereas malignant lesions have been generally reported in 6th – 7th decade, which is in concordance with study conducted by Patel¹¹ et al.

Sinonasal lesions: Among upper respiratory tract lesion, sinonasal area is the most common affected site. The non-neoplastic lesions were the most common lesions encountered in sinonasal region. The mean age of presentation among non-neoplastic group was 32.8 years with male: female ratio 2.6:1. Nasal polyp was the most common lesion which resulted from chronic inflammation of the mucosa from the nasal cavity and paranasal sinuses. The inflammatory polypi followed by allergic polypi were the most frequent diagnosis which is similar to other studies of the literature^{4,12,13}. The next frequent lesion encountered was fungal infections which included mucormycosis (Figure 1) and aspergillosis. The fungal organisms were highlighted with special stains. There were two cases of granulomatous pathology exhibiting formation of epithelioid cell granuloma with areas of caseous necrosis. However, acid fast stain was negative. The histologic spectrum of non-neoplastic lesions and demographic data with male preponderance of present study is comparable with studies done by Lathi⁴ et al, Zafar¹² et al and Thomas¹³ et al.

Among benign category, sinonasal papilloma (36.5% cases, Figure 2) was the most common lesion followed by haemangioma (31.8%) and angiofibroma (27.3%). The mean age of affected individuals is 36.5 years with male: female = 4.5: 1. The results were similar to the study done by Thomas¹³ et al and Bhattacharya¹⁰ et al. There was single case of schwannoma (Figure 3). Schwannoma of nasal cavity is a rare tumor¹. Histologic examination revealed spindle cell tumor with lack of encapsulation exhibiting Antoni A and Antoni B areas with formation of Verocay body.

Despite of the fact that sinonasal region is an uncommon site of malignant neoplasm, a variety of epithelial and non-epithelial neoplasms can be encountered at this site due to the presence of specialized tissue.¹⁰ On the contrary to other studies in the literature, adenocarcinoma was the most frequent malignant lesion of sinonasal area with mean age of presentation 38.3 years and male: female = 1:1.2 in present study. Among malignant lesions, there were five cases of round cell tumor which were found in 2nd and 3rd decade of life. Among these five cases, immunohistochemistry played important role in final diagnosis as no areas of differentiation were noted. There were two cases of rhabdomyosarcoma (Figures 4 & 5), two cases of neuroblastoma and one case of sinonasal carcinoma undifferentiated (SN-UDC). SN-UDC is a separate entity exhibiting clinically aggressive course and has to be differentiated from olfactory neuroblastoma which has less aggressive course. In study of salivary type neoplasm of nasal cavity and paranasal sinuses, done by Manning¹⁴ et al, adenoid cystic carcinoma and pleomorphic adenoma were most frequent. However, there was single case of adenoid cystic carcinoma in present study.

Laryngeal lesions: In this group in non-neoplastic category, the most frequent lesion was vocal polypi followed by vocal nodules with mean age 41.3 years with male: female of 1.9:1. These results are comparable to the studies done by Varalakshmi¹⁵ et al and Prakash¹⁶ et al. Male preponderance of non-neoplastic lesions can be attributed to their occupation involving excessive use of voice, misuse of voice and prolonged use of improper voice habits during talking. The next common lesion was non-specific laryngitis and granulomatous pathology. Three cases showed the presence of epithelioid cell granuloma with lymphoid cells. One of case showed

caseous necrosis. However, no acid fast bacilli could be demonstrated in any of these cases.

There were only two cases in the benign category; one case each of squamous papilloma and granular cell tumor. The other studies has also found the occurrence of benign tumors in the larynx is less frequent and papilloma being the commonest lesion^{15,16}. Granular cell tumor has been described in skin and mucous membranes. There was single case of granular cell tumor which was characterised by presence of large cells arranged in nests exhibiting eosinophilic granular cytoplasm.

Among 74 laryngeal biopsies, 43 cases were diagnosed malignant. In malignant category, the most common lesion was squamous cell carcinoma. These findings are supported by most of the studies on laryngeal lesions^{15,17}. In present study, there were 25 cases of moderately differentiated carcinoma, 13 cases were well differentiated and 4 cases were poorly differentiated. Most of the poorly differentiated carcinoma presented with the wide spread disease.

Pharynx: Pharynx was the least common affected site among respiratory tract lesions. In non-neoplastic category, the inflammatory lesions were common with mean age of 34.1 years and male: female of 1.6:1. There were two cases each of chronic tonsillitis and actinomycosis (Figure 6), respectively. Chronic tonsillitis is characterised by repeated attacks of acute tonsillitis or inadequately treated infection or resistant infection. Chronic tonsillitis usually affects children but in present study, it was seen in early adulthood which can be attributed to local dysfunction of the epithelium¹⁸. Actinomyces are long filamentous gram positive bacilli which is normal commensal of oral cavity. In a study by Van Lierop¹⁹ et al it was found that there is no correlation between tonsillar actinomycosis and recurrent tonsillitis. In present study similar findings were noted in two cases of actinomycosis, there was no tissue reaction.

Among benign neoplasm, there was one case each of squamous papilloma and schwannoma. As evidenced by most of the studies in the literature pharynx is rare site of benign neoplasm¹⁸.

Carcinoma arising at this site is usually squamous type and has close association with smoking and HPV infection. They usually affects in later life i.e. fifth to

seventh decade of life with male preponderance¹⁸. Squamous cell carcinoma was the most frequent malignancy in malignant subgroup of larynx with mean age of 54.3 years and male:female ratio of 4.6:1. In a study by Sulhyan¹⁸ et al and Bhattacharya¹⁰ et al similar results were found. There was single case of anaplastic large B cell lymphoma (Figures-7&8). This case was initially diagnosed as undifferentiated carcinoma. Further, immunohistochemical panel was employed for final diagnosis. Thus, it was concluded that large cell lymphoma is the main differential diagnosis of undifferentiated carcinoma which can be differentiated with the help of immunohistochemistry.

Thus, present study provides the detailed data of age and sex distribution and histologic pattern of lesions of upper respiratory tract over the period of four years in a rural based tertiary care centre of north region.

Conclusion: Histopathological examination is simple, reliable and cost effective diagnostic procedure for detection of various lesions of upper respiratory tract. Polypi are the most common non-neoplastic lesions while squamous cell carcinoma is most common malignant tumor. Immunohistochemistry plays an important role in subcategorisation of the tumor which helps in deciding the treatment protocol. As upper respiratory tract region is the site of inflammatory to rare neoplastic conditions with considerable overlap in their presentations, the histopathological evaluation is challenging and is mandatory for proper and early treatment of patient.

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