Original Article

Diagnostic challenges in malignant tumors of nasal cavity and paranasal sinuses

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Abstract

Introduction: Malignant tumors of sinonasal tract are extremely rare and comprise 3% of all head and neck malignant tumors. They constitute 0.2% of all invasive carcinomas. Sinonasal space is a small anatomical place, but is the site of origin for tumors with diverse histological features. Many of the tumors are similar to those that occur in various parts of the body and have overlapping histological features. A panel of immunohistochemical (IHC) markers is essential to diagnose these tumors. Most of the tumors arise in the maxillary sinus followed by ethmoid sinus. History and complete head and neck examination along with biopsy are mandatory for evaluating the disease.

Aim and Objectives: To study the age-, sex- and site-wise incidence of different malignant lesions of the nasal cavity and paranasal sinuses. To subtype and classify the malignant tumors as per the WHO guidelines.

Materials and Methods: Forty-seven cases of sinonasal tumors reported over a period of 3 years were retrieved from the archives of the department of pathology. The tissues were subjected to paraffin processing and stained with hematoxylin and eosin. IHC was done with a panel of markers, wherever necessary.

Results: The present study included a total of 47 malignant lesions. Of which, 24 cases (51.06%) were squamous cell carcinomas (five cases each of well-differentiated SCC and moderately differentiated SCC and 14 cases of nonkeratinizing SCC). Five (10.63%) cases each were of neuroendocrine carcinoma and non-Hodgkin's lymphoma.

Conclusion: Malignant neoplasms of sinonasal tract have overlapping clinical and pathological findings; establishing the correct diagnosis is difficult without using a panel of IHC markers.

Keywords: Immunohistochemical, malignant sinonasal tumors, neuroendocrine carcinoma, non-Hodgkin's lymphoma, squamous cell carcinomas

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INTRODUCTION

Nasal cavity and paranasal sinuses are grouped as sinonasal region.[1] Sinonasal cavities occupy small anatomical space and histologically diverse group of tumors arise in the complex area of sinonasal cavity.[2] Epithelial and nonepithelial neoplasms arise from nose and paranasal sinuses. Epithelial malignancies arise from the mucosa, minor salivary glands or olfactory mucosa. Mesenchymal tissue of sinonasal tract gives rise to malignant tumors.

Sinonasal tumors are common occurrence in all age groups, and common presenting symptoms include nasal blockade, nasal discharge and epistaxis, followed by facial swelling.[3]

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Malignant tumors of sinonasal tract are extremely rare and comprise 3% of all head and neck malignant tumors. Among the epithelial tumors, squamous cell carcinoma is the most common, followed by intestinal type of adenocarcinoma.[2]

A group of aggressive nonsquamous cell malignancies and nonepithelial malignant neoplasms of varying histogenesis occur in this region, and they can be differentiated using a panel of IHC markers. They are associated with aggressive clinical behavior and pose problem for diagnosis.

This study was undertaken to classify sinonasal malignant tumors basing on morphological and immunohistochemical (IHC) features.

MATERIALS AND METHODS

Forty-seven cases of sinonasal tumors were studied in a 3-year period from the archives of the department of pathology. The tissue is processed by paraffin processing and stained with hematoxylin and eosin, and IHC is done with a panel of markers, wherever necessary.

RESULTS

Forty-seven cases of malignant tumors of sinonasal cavity were studied in a 3-year period from our institution.

Table 1 shows histological classification of tumors. Among the malignant epithelial tumors, squamous cell carcinoma constituted the largest group, followed by neuroendocrine carcinoma.

Table 2 shows age, sex and site distribution. A maximum number of cases were seen in the age group of 51–60 years (27.65%), followed by 61–70 years (23.40%). A maximum number of cases were seen in the nasal cavity (61.70%), followed by sinuses. Among the sinuses, most of them occurred in the maxillary sinus.

Table 3 shows IHC features of various tumors.

Table 1: Histological classification of tumors

Serial number	Histological grade	Number of cases (%)
1	Malignant epithelial tumors	
	Squamous cell carcinoma	24 (51.06)
	Sinonasal undifferentiated carcinoma	2 (4.25)
	Papillary adenocarcinoma	2 (4.25)
	Salivary gland type of carcinoma-adenoid cystic carcinoma	3 (6.38)
2	Neuroendocrine tumors	
	Neuroendocrine carcinoma	5 (10.63)
3	Malignant soft-tissue tumors	
	Spindle cell rhabdomyosarcoma	1 (2.12)
4	Hematolymphoid tumors	
	Non-Hodgkin's lymphoma	5 (10.63)
5	Neuroectodermal tumors	
	PNET/Ewing's sarcoma	1 (2.12)
	ONB	4 (8.51)
Total number of cases		47 (100)

Among the malignant epithelial tumors squamous cell carcinoma constituted the largest group followed by neuroendocrine carcinoma.
ONB: Olfactory neuroblastoma

Table 2: Age, sex and site distribution

Age (years)	Sex		Nasal	Paranasal
	Males	Females		
0-10	1	0	1	0
11-20	2	0	1	1
21-30	2	2	3	1
31-40	5	2	4	3
41-50	3	5	5	3
51-60	4	9	8	5
61-70	8	3	6	5
71-80	0	0	0	0
81-90	1	0	1	0
Total (%)	26 (55.31)	21 (44.68)	29 (61.70)	18 (38.29)

Table 3: Immunohistochemical features of various tumors

Histological type	IHC
Squamous cell carcinoma	PanCk - positive
Sinonasal undifferentiated carcinoma	PanCk - positive Chromogranin - negative
Neuroendocrine carcinoma	Chromogranin - positive Synaptophysin - positive PanCk - positive
Spindle cell rhabdomyosarcoma	Desmin and vimentin - positive. PanCk - negative
Adenoid cystic carcinoma	
Non-Hodgkin's lymphoma	CD45 and CD20 - positive PanCk - negative
PNET/Ewing's sarcoma	CD99 - positive

IHC: Immunohistochemical, PanCk: Pancytokeratin

DISCUSSION

Forty-seven malignant tumors of sinonasal tract were studied in a 3-year period in our institution. They were classified into malignant epithelial tumors, malignant tumors of soft tissues, bone and cartilage, hematolymphoid tumors, neuroectodermal tumors and germ cell tumors. Among the tumors studied in our institute, we had not come across malignant bone tumors and also germ cell tumors.

Out of 47 malignant sinonasal tumors, 31 cases were malignant epithelial tumors, constituting 65.94% of cases. Squamous cell carcinoma is the most common malignant epithelial tumor, constituting 51.06% of total malignancies. Most of them occurred in the maxillary sinus. Morphologically, they were showing squamous differentiation in the form of keratin pearls, dyskeratotic cells and intercellular bridges. Nonkeratinizing squamous cell carcinoma constituted 29.78% of cases, and the most

common age group is 6th decade and the most common location is nasal cavity. Microscopically, they showed ribbon-like growth pattern with cytological atypia in tumor cells. There is no evidence of keratinization [Figure 1]. All cases of squamous cell carcinoma showed strong positivity with pancytokeratin (panCK).

Two cases of sinonasal undifferentiated carcinoma (SNUC) occurred in the 4th and 5th decades of life, constituting 4.25% of cases and occurred in the nasal cavity. Both patients were male. Both cases presented with nasal obstruction and epistaxis, which was consistent with the study of Ejaz and Wenig.[4] In one case, there was proptosis. This was consistent with the study of Goel *et al*.[5] According to the literature, the age range was 3rd to 9th decade of life, with a mean age of presentation in the 6th decade.[4] Microscopy showed pleomorphic cells arranged in nests, lobules and sheets. Nuclei were medium to large with prominent nucleoli. Mitotic activity was high with extensive areas of necrosis. IHC for epithelial membrane antigen and panCK was positive, confirming the diagnosis.[4] IHC for chromogranin, neuron-specific enolase (NSE) and CD45 was negative, excluding the possibility of neuroendocrine carcinoma and lymphoma.[4,5]

Given the undifferentiated nature of this malignancy, however, IHC analysis is extremely helpful. Given the undifferentiated nature of this malignancy, IHC analysis was extremely helpful. SNUC showed positive staining to CK7, CK8, CK19, chromogranin and synaptophysin. S-100 and vimentin were negative confirming the diagnosis. These findings suggest that the tumor is of epithelial origin and lacks any evidence of neuroendocrine, muscle, melanocyte or leukocyte differentiation. This allows proper classification of the tumor as an SNUC, a malignant tumor of the sinus (sinonasal) that is of epithelial origin (carcinoma), but lacks evidence of keratin production (undifferentiated).

A 17-year-old male presented with a nasal polyp. The polyp was arising from the nasal cavity. Microscopy revealed sinonasal papillary adenocarcinoma with papillary architecture, occasional tubular glands and little intervening stroma. Mild-to-moderate pleomorphism was observed. Diagnosis of intestinal type of adenocarcinoma, papillary type, was made [Figure 2]. According to Leivo, sinonasal adenocarcinomas arise from seromucinous glands and surface epithelium of nasal cavity and paranasal sinuses.[6] Sinonasal adenocarcinoma is the third most common mucosal malignancy and represents 15% of all sinonasal cancers. These malignancies are divided into salivary-type adenocarcinomas and nonsalivary-type adenocarcinoma, which was further subdivided into intestinal-type and nonintestinal-type adenocarcinoma (ITAC). ITAC is the second most common type of sinonasal adenocarcinoma, arising mostly in males with an age range of 50–60 years.[7] In our study, it is seen in a male aged 17 years. ITAC is further subdivided into papillary–tubular, cylindrical, alveolar goblet cell type, signet ring cell type and transitional cell type. In our study, it was diagnosed as papillary–tubular variant of ITAC.

Among salivary gland type of carcinomas, three cases of adenoid cystic carcinomas were reported in individuals aged

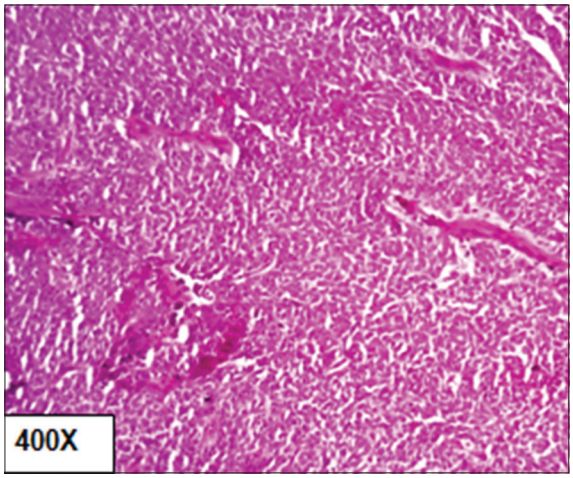

Figure 1: Nonkeratinizing squamous cell carcinoma showing round to spindle-shaped cells with marked pleomorphism, high n/c ratio eosinophilic cytoplasm, large nucleus, coarsely granular chromatin and nucleolus. There is no significant keratinization

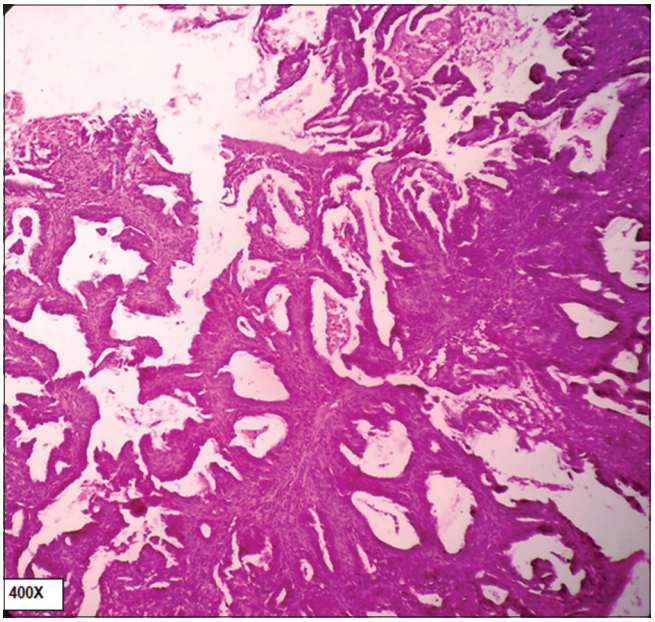

Figure 2: Complex papillary structures are with arborization and fibrovascular core lined by cuboidal or columnar cells with pink cytoplasm and round/oval nuclei that are variably clear or hyperchromatic

20–40 years in the present study. These patients presented with nasal obstruction, epistaxis and pain. Microscopic examination showed neoplastic cells arranged in cribriform pattern and cysts filled with mucoid material [Figure 3]. The cysts were lined by ductal epithelial cells and modified myoepithelial cells. Focal areas showed hyaline globules. Areas of perineural invasion was noted. Shah *et al*.[7] encountered a single case.

Neuroendocrine tumors of nose and paranasal sinuses are divided into typical carcinoid, atypical carcinoid and small-cell carcinoma–neuroendocrine type (WHO). We did not come across of typical carcinoid and atypical carcinoid [Figure 4]. Five cases of small-cell carcinoma–neuroendocrine type were reported in the present study, constituting 10.63% of cases. This is in concordance with the studyof Wenig *et al* majority of them occurred in 4th–5th decade. Majority of these cases occurred in posterior nasal cavity extending into the maxillary sinus. The common presenting symptoms were epistaxis and nasal obstruction. Neurofibrillary background is not observed. IHC was positive for chromogranin, synaptophysin, panCK and NSE.

Among malignant soft-tissue tumors, single case of rhabdomyosarcoma was reported in our study, constituting 2.12% of cases. A 70-year-old female presented with a nasal polyp. Microscopy shows fibrous septa separating clusters of round to spindle cells with hyperchromatic nuclei. Large cells with abundant eosinophilic cytoplasm resembling rhabdomyoblasts were also seen [Figure 5]. The stroma is myxoid. IHC was positive for desmin. The diagnosis of spindle cell rhabdomyosarcoma was offered.

Five cases of non-Hodgkin's lymphoma were reported in our study, constituting 10.63% of cases. The most common location in all these cases was maxillary sinus. Most of the patients presented with masses in the nasal cavity nasal obstruction. Majority of cases occurred in the 6th–7th decades. Microscopic examination showed diffuse infiltrate of blue, round cells [Figure 6]. The cells are small to medium in size with moderate amount of pale cytoplasm. This tumor needs to be differentiated from nonhematopoietic malignancies, especially poorly differentiated squamous cell carcinoma, olfactory neuroblastoma (ONB) and SNUC. IHC was positive for CD45 and negative for other panel of markers confirming the diagnosis of non-Hodgkin's lymphoma. All the five cases showed positivity for CD20 [Figure 6]. Hence, the diagnosis of B-cell lymphoma was made. Other investigators reported that T/NK cell lymphomas were more common in nose and paranasal sinuses.[8]

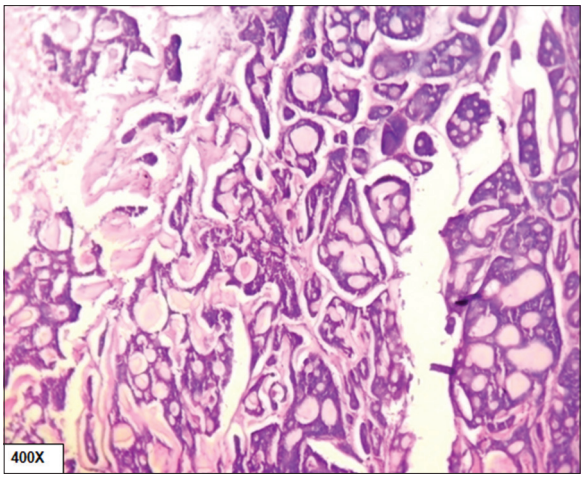

Figure 3: Adenoid cystic carcinoma showing both cribriform and tubular pattern consists of basaloid epithelial cells forming sharply demarcated nests containing multiple extracellular spaces filled with eosinophilic material

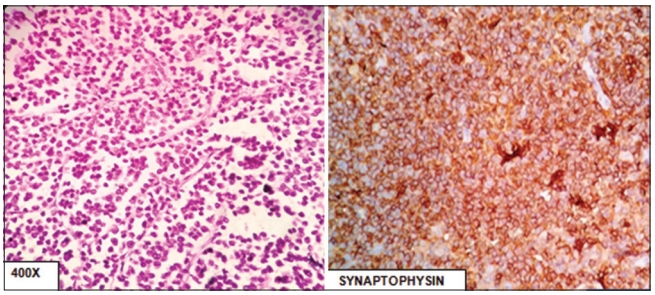

Figure 4: Small cells with nuclear molding, inconspicuous nucleoli and increased mitotic activity are characteristic for a small cell carcinoma. These cells showing positivity for synaptophysin

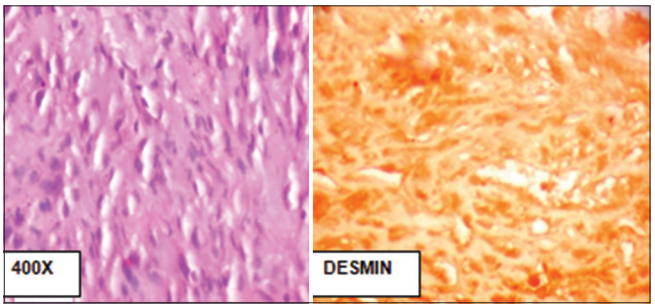

Figure 5: Rhabdomyosarcoma showing malignant spindle cells, with scant cytoplasm and hyperchromatic nuclei. Scattered rhabdomyoblasts with brightly eosinophilic eccentric cytoplasm are seen. These cells are showing positivity for desmin

The present study revealed four cases of ONB occurring in the 2nd–6th decades with male preponderance. According to Wenig *et al*,[9] these cases occurred with bimodal peak in 2nd and 6th decades of life.[10] The main presenting symptoms were epistaxis and nasal obstruction. Tumor cells arranged in nests separated by fibrovascular stroma. They have small, round hyperchromatic nucleus with background neuropil. The differential diagnosis considered were ONB,

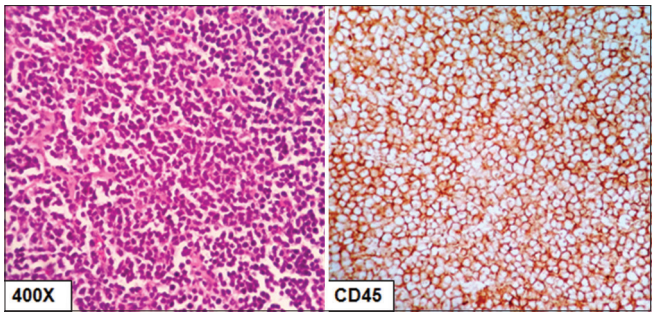

Figure 6: Diffuse infiltrate of discohesive lymphoid cells with large nuclei and clumped chromatin showing positivity for CD20

rhabdomyosarcoma and Ewing's sarcoma/PNET and lymphoma. Cells of ONB are diffusely positive for NSE with absence of positivity for epithelial, mesenchymal and leucocyte markers. Poorly differentiated sinonasal carcinoma shows NSE positivity, but only focally.

In our case, NSE is diffusely positive and PanCK, CD45 and CD99 were negative. Primary sinonasal tumors with neuroendocrine differentiation are subcategorized into SNUC, sinonasal neuroendocrine carcinoma and esthesioneuroblastoma.[11]

The histological grading of ONB was done by the criteria defined by Hyams.[12] According to Hyams, olfactory neuroblastoma is divided into four grades basing on architecture, pleomorphism neurofibrillary matrix, rosettes, mitosis, necrosis, glands and calcification. Grade 3 tumors Showed lobular architecture with interstial vascular stroma.The tumor cells were hyperchromatic with increased mitotic activity. Necrosis was seen. Necrosis is seen. Our case was concluded as Grade 3 ONB basing on histomorphological features.

CONCLUSION

In the present study, the incidence of squamous cell carcinomas is highest (51.06%). It was followed by neuroendocrine carcinomas and non-Hodgkin's lymphomas, comprising 10.63% each. Male preponderance was noted (55.31%). The most common site was nasal cavity and sinus was maxillary sinus. The most common age group is 5th–6th decades of life. Undifferentiated malignant neoplasms of sinonasal cavities have overlapping clinical and pathological findings. A panel of IHC markers is a must to establish the correct diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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