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Histopathological Study of Non-Epithelial Malignant Sinonasal Malignancies

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ABSTRACT

Background: Nasal and paranasal sinus lesions encompass a diverse range of conditions originating from various tissue types. Among these, non-epithelial malignant tumours, including soft tissue, bone, cartilage, neuroectodermal, germ cell, and hematolymphoid malignancies, are less common but clinically significant. Due to overlapping clinical and radiological presentations, histopathological evaluation is crucial for accurate diagnosis and timely intervention. This study classifies non-epithelial malignant neoplastic lesions and examines their incidence and clinicopathological characteristics.

Methods: A hospital record-based cross-sectional study was conducted over eight years in a teaching institute in Mumbai. Among 47,621 surgical pathology samples, 654 sinonasal mass lesions were analysed, including 159 biopsies and 495 resection specimens. Clinical data such as patient age, sex, and presenting symptoms were collected. Histopathological examination was performed using hematoxylin and eosin staining, and lesions were classified as per WHO guidelines. Inadequate samples were excluded from the study.

Results: Among 654 cases, 443 (67.74%) were non-neoplastic, while 211 (32.26%) were neoplastic. Of the neoplastic cases, 132 (20.18%) were benign, and 79 (12.08%) were malignant. Non-epithelial malignancies accounted for 28 cases, including soft tissue tumours (10), neuroectodermal tumours (8), germ cell tumours (2), hematolymphoid malignancies (3), and unclassified round cell tumours (4). Immunohistochemical analysis confirmed diagnoses in select cases.

Conclusion: Non-epithelial malignant sinonasal tumours, though rare, exhibit diverse histopathological features and clinical presentations. Accurate classification through histopathological and immunohistochemical evaluation is essential for appropriate management and improved patient outcomes.

Key-words: Non-epithelial, Fibrosarcoma, Melanoma, Rhabdomyosarcoma, Lymphoma

INTRODUCTION

Nose and paranasal sinuses, though occupy a small anatomical space, are involved by a variety of lesions [1]. These conditions are derived from mucosal epithelium, seromucinous glands, soft tissues, bone, cartilage, neural/ neuroectodermal tissue and haematolymphoid cells [2]. The majority of these lesions resemble their counterparts elsewhere in the body but few of them are unique to this site. They may mimic each other clinically as well as radiologically. The clinical presentation of sinonasal tract tumors is often nonspecific, with patients frequently experiencing mass-related symptoms due to obstruction or locoregional extension and invasion [3]. Common manifestations include facial pain and swelling, headache, nasal congestion, epistaxis, rhinorrhea, and anosmia.

Due to their anatomical locations, the sinonasal tumors can infiltrate adjacent structures such as the brain, orbit, optic nerve, and carotid artery, often leading to severe

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clinical consequences [4]. Additionally, their involvement in these critical regions poses significant surgical challenges, frequently limiting biopsy samples and, in some cases, precluding complete or near-complete resection [5]. Hence, a detailed history, clinical examination and most importantly, thorough histopathological evaluation are essential parts of the workup, so that a correct and timely intervention is done. Non-epithelial malignant tumours of the sinonasal tract include soft tissue tumours, tumours of the bone and cartilage along with germ cell and haematolymphoid tumours.[6] In the sinonasal tract, epithelial neoplasms significantly outnumber mesenchymal tumors. Consequently, most sarcomas in this region must be carefully distinguished from the more common differentials, including spindle cell or sarcomatoid squamous cell carcinoma and spindle cell or desmoplastic melanoma. [3] Primary soft tissue tumors arising from the sinonasal tract are uncommon. Sarcomas constitute approximately 1–3% of all head and neck malignancies, with up to 15% of adult sarcomas and 35% of pediatric sarcomas originating in this region. [3] Soft tissue tumors encompass a wide array of histologically diverse entities. Due to their rarity and considerable morphologic overlap, they frequently pose significant diagnostic challenges. Surgery remains the cornerstone of treatment for sinonasal tumors, regardless of histologic subtype. Every patient diagnosed with a sinonasal tumor should undergo evaluation by a surgeon within the framework of a multidisciplinary team to ensure optimal management. [7] This study aims to classify the non-epithelial malignant neoplastic lesions and to find out the relative incidence along with analyzing the clinicopathological features of these cases presenting as masses in the sinonasal tract.

MATERIALS AND METHODS

Study Setting- A tertiary care hospital served as the location for the study.

Study Design- The overall design of the investigation was a hospital record-based observational cross-sectional study.

Study Period- The specimens that were recorded in the Histopathology department between the years 2015 and 2022 are the subject of this study.

Methodology- During this period, out of a total of 47,621 samples received in the surgical pathology section, 654 samples were from sinonasal mass lesions. The 654 cases included in this study are comprised of both biopsies (159) as well as resection specimens (495). For clinical details, the age and sex of the patient were taken from the records. The clinical presentation of the patient were noted. Any investigations carried out including clinical, radiological, and microbiological examinations were also noted. The tissue specimens were processed routinely after fixing in 10% formalin and stained with haematoxylin and eosin stains. The neoplastic lesions were classified as per the WHO classification. The inadequate samples were not included in this study.

Inclusion Criteria- Patients of all age groups with sinonasal mass lesions and having adequate diagnostic material are included in the study.

Exclusion Criteria- Samples with inadequate diagnostic material were excluded from the study.

Statistical Analysis- Patient characteristics were compared. All data was compiled in Microsoft Excel and represented as frequency and percentage.

Ethical Approval- The study was approved by the Institutional Ethical Committee.

RESULTS

This study categorizes 654 cases of sinonasal lesions as follows: Non-neoplastic lesions were the most prevalent, comprising 443 cases (67.74% of the total). Among the 211 neoplastic lesions (32.26%), benign neoplasms were identified in 132 cases (20.18%), while 79 cases (12.08%) were malignant. Of these malignant cases, 28 were non-epithelial malignancies rest being epithelial malignancies (Fig. 1, Table 1). Out of the ten malignant soft tissue tumours encountered, four cases of low-grade myofibroblastic sarcoma were seen which involved the nasal cavity and maxillary sinus. Symptoms included nasal obstruction, epistaxis, facial swelling, and eye-related complaints. Immunohistochemical studies confirmed the diagnosis in one case with SMA positivity and a Ki-67 index of 8-10%. Two cases of embryonal rhabdomyosarcoma were observed in young males. Histological examination revealed rhabdomyoblasts with varying morphology, including large strap cells.

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Table 1: Categorization of malignant sinonasal non-epithelial tumours (n=28)

S.No	Type of Lesion	No. of cases
1.	Soft tissue tumours (10)	
	a. Low grade myofibroblastic tumour	4
	b. Fibrosarcoma	2
	c. Rhabdomyosarcoma	2
	d. Glomangiopericytoma	2
2.	Tumours of bone and cartilage (1)	
	a. Chondrosarcoma	1
3.	Neuroectodermal tumour (8)	
	a. PNET	2
	b. Malignant melanoma	6
4.	Germ cell tumours (2)	
	a. Sinonasal teratocarcinoma	2
5.	Haematolymphoid malignancy (3)	
	a. Non-Hodgkin lymphoma	3
6.	Unclassified Round cell tumours (4)	4
	TOTAL	28

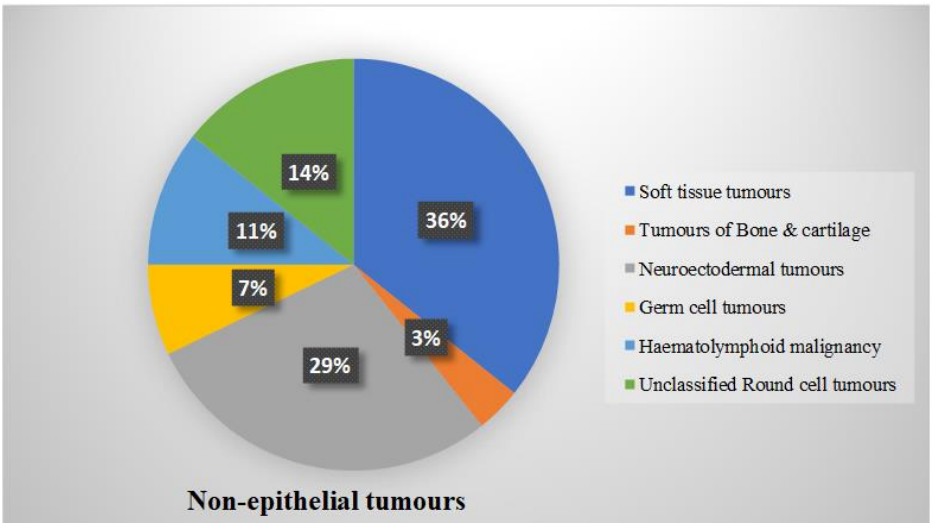

Fig. 1: Distribution of non-epithelial tumours

Two cases of fibrosarcoma were identified in the nasal cavity. Histology revealed tumour cells arranged in fascicles with elongated nuclei, prominent nucleoli, and low mitotic activity. Two cases of glomangiopericytoma were observed in the nasal cavity, presenting with nasal obstruction and a nasal mass. Histopathology showed tumour cells arranged in short fascicles with characteristic peritheliomatous hyalinization.

A single case of chondrosarcoma was documented in a 28-year-old male with nasal obstruction. Radiological findings indicated bony destruction and aggressive sinus extension. Microscopy revealed lobules of cartilaginous stroma with round-to-oval cells in lacunae. Amongst the germ cell tumours, two cases of sinonasal teratocarcinosarcoma were observed in young adult males presenting with nasal obstruction and nasal masses. Histopathology revealed epithelial, sarcomatous, and neuroblastoma-like components.

Two cases of primitive neuroectodermal tumour (PNET) were identified, with immunohistochemistry confirming Mic-2 positivity. Six cases of malignant melanoma were noted, all involving the nasal cavity with symptoms of nasal obstruction and epistaxis. Three cases of non-Hodgkin lymphoma were documented, involving the nasal cavity and maxillary sinus. Symptoms included nasal discharge, facial swelling, and orbital involvement.

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Four cases of unclassified malignant round-cell tumours were observed (Table 2). Differential diagnoses included sinonasal undifferentiated carcinoma (SNUC), rhabdomyosarcoma (RMS), PNET, and olfactory neuroblastoma (ONB).

Table 2: Unclassified malignant round cell tumours

Age	Sex	Site	Presenting symptoms	HP diagnosis
25 years	F	Nasal cavity	Nasal obstruction, proptosis	D/D: PNET vs ONB
42 years	M	Nasal cavity	Nasal obstruction, rhinitis	D/D: ONB vs SNUC
6 months	M	Maxillary sinus	Cheek swelling	Malignant round cell tumour favouring RMS
40 years	M	Nasal cavity	Epistaxis	Malignant round cell tumour

PNET: Primitive neuroectodermal tumour, ONB: Olfactory neuroblastoma, SNUC: Sinonasal undifferentiated carcinoma, RMS: Rhabdomyosarcoma

DISCUSSION

Non-epithelial malignancies of the sinonasal tract form a heterogeneous group of tumors requiring histopathology for definitive diagnosis and proper management. Biopsies may not always be representative, leading to differential diagnoses, especially in round or spindle cell lesions. Ancillary techniques like immunohistochemistry and cytogenetics aid in confirmation.

Low-grade fibroblastic/Myofibroblastic Sarcoma, often mimicking fibromatosis, predominantly affects the head and neck [8]. In our study, it constituted 14.28% (4/28) of cases, occurring in males aged 26–54 years, mainly in the nasal cavity. Nasal obstruction was the primary symptom. WHO reports a slight male predominance in adults. Histopathology revealed spindle cells in fascicles with moderate pleomorphism, eosinophilic cytoplasm, and no abnormal mitoses (Fig. 2). IHC in one case showed SMA positivity, focal CD68, and a KI-67 index of 8–10%, while CD34, CD31, EMA, HMB45, and ALK1 were negative, confirming the diagnosis [9]. Differentials include fibromatosis (low cellularity, mild atypia), myofibroma (biphasic pattern), and inflammatory myofibroblastic tumors (marked inflammation, loose stroma) [10]. Recurrence occurs in 40% of cases, but metastasis is rare [11].

Fibrosarcoma was identified in 2 of 28 cases (7.14%). Sinonasal fibrosarcomas constitute 7–10% of head and neck sarcomas [12]. Both cases, one male and one female in their fifth decade, presented with nasal obstruction. WHO notes most originate in the paranasal sinuses, with an average diagnosis age of 55.4 years. Histology showed spindle cells in fascicles with slight pleomorphism, tapering nuclei, and focal hemorrhage/necrosis (Fig. 3), with low mitotic activity. Sinonasal fibrosarcomas require differentiation from spindle cell neoplasms [13], such as monophasic synovial sarcoma and sarcomatoid carcinoma. Low-grade fibrosarcomas resemble fibromatosis and have a better prognosis. IHC markers like cyclin D1 and p53 assist in diagnosis [14].

Glomangiopericytoma, also called sinonasal hemangio-pericytoma, accounted for 2 of 28 cases (7.14%). A 52-year-old female and a 21-year-old male, both with nasal obstruction, were affected. These tumors make up less than 0.5% of sinonasal neoplasms, primarily involving the nasal cavity [15]. Histology revealed cellular tumors in short fascicles with peritheliomatous hyalinization, spindle-shaped nuclei, and mild pleomorphism. IHC confirmed SMA, MSA, and factor XIIIa positivity, distinguishing them from solitary fibrous tumors [16].

Chondrosarcoma, a malignant hyaline cartilage tumor, represented 1 of 28 cases (3.57%). A 28-year-old male presented with a midline sinonasal mass with aggressive extension. Sinonasal chondrosarcomas, comprising about 8% of head and neck sarcomas, typically affects men in their 40s–50s [17]. Common sites include the nasal septum, maxilla, ethmoid, and sphenoid bones. Microscopically, lobules of cartilaginous stroma showed round-to-oval cells in lacunae within a chondroid matrix

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and focal fibrocartilage. IHC demonstrated CD99 positivity. These tumors are locally aggressive with high recurrence rates.

Teratocarcinosarcoma, a rare malignant sinonasal neoplasm combining teratoma and carcinosarcoma features, was found in 2 of 28 cases (7.14%). Both cases involved young males (22 and 35 years) with nasal obstruction. Literature reports a broad age range (18–79 years), with frequent nasal cavity involvement and sinus extension [18]. Histology revealed epithelial components with high nuclear-to-cytoplasmic ratios, hyperchromatic nuclei, and scant eosinophilic cytoplasm, along with spindle-shaped stromal cells with neuroblastoma-like features (Fig. 4). Differential diagnoses include olfactory neuroblastoma, sarcomatoid carcinoma, and other sarcomas [19]. Proper sampling is essential to prevent misdiagnosis [19].

Rhabdomyosarcoma (RMS) is a malignant mesenchymal tumor of skeletal muscle origin. Our study identified two embryonal RMS cases (7.14%) among 28 malignancies. Sinonasal RMS accounts for 10–15% of adult head and neck RMS [20]. Both cases involved males (6 and 8 years) with ethmoid sinus and nasal cavity involvement. One case showed radiological evidence of an ethmoid sinus mass extending into the nasal cavity and nasopharynx with bony erosion. Histology revealed hypo- and hypercellular areas with fibrous, myxoid stroma. Tumor cells ranged from small round to spindle-shaped, with rhabdomyoblasts varying from strap cells to small round cells. Immunohistochemistry for desmin and muscle-specific actin aids diagnosis, with myogenin and MyoD1 serving as specific markers [21].

Primitive Neuroectodermal Tumor (PNET) and Ewing's sarcoma (EWS) are small round cell neoplasms, with PNET showing neuroectodermal differentiation. The study identified two PNET cases (7.14%).

These tumors are rare in the head and neck [22], affecting males in their second decade, and involving the maxillary sinus and nasal cavity. WHO notes maxillary sinuses and nasal fossa as primary sites. Histology showed sheets and nests of small cells with high nuclear-to-cytoplasmic ratio, hyperchromatic nuclei, and frequent mitotic figures, with Homer-Wright rosettes present.

Malignant melanoma from mucosal melanocytes accounted for 21.42% (6/28) of cases. Sinonasal melanomas are <4% of sinonasal neoplasms [23]. Patients (42–68 years) showed female predominance, universal nasal cavity involvement, and obstruction. WHO cites the nasal cavity as the most common site. Histology revealed epithelioid cells with pleomorphic nuclei, nucleoli, and melanin pigment (Fig. 5). Differential diagnoses include SNUC and lymphoma, but melanin pigment aids identification. Strong S-100, HMB-45, and vimentin immunoreactivity confirm the diagnosis [24].

Sinonasal Non-Hodgkin Lymphoma (NHL) comprises various hematolymphoid malignancies, representing 10.71% of our cases (3 out of 28). Primary sinonasal lymphomas are rare, with NHL comprising 1% of all head and neck cancers [25]. Our cases involved males (6, 38, and 45 years), with pediatric involvement in the maxillary sinus and adult cases in the nasal cavity. Histology showed diffuse lymphocytic infiltration with gland destruction, extensive necrosis, and apoptotic bodies (Fig. 6). Sinonasal lymphomas include NK/T-cell, B-cell, and peripheral T-cell types [26]. Immunohistochemistry for CD56 aids in diagnosing NK/T-cell lymphoma, though CD56 positivity also occurs in tumors like olfactory neuroblastoma, PNET, and RMS [27].

In our study, four cases exhibited round cell morphology where a definitive diagnosis was not possible with light microscopy alone. Differential diagnoses were based on clinical presentation, anatomical site, and disease extent, as immunohistochemistry was unavailable. One case had a differential diagnosis of PNET versus ONB. Homer Wright rosettes aid differentiation, though they also appear in PNET. ONBs lack MIC2 (CD99) positivity, while over 90% of PNETs express it. Additionally, PNETs show the EWS/FLI-1 transcript, with 71% immunopositive for FLI-1, unlike ONBs [28].

A 42-year-old male with a sinonasal mass extending to the anterior cranial fossa had tumor cells arranged in sheets and nests, with scant cytoplasm, large nuclei, granular chromatin, and small nucleoli. Differential diagnoses included ONB and SNUC, with ONB distinguished by Homer Wright rosettes and S100 protein positivity, absent in SNUC [29].

A 6-month-old male with cheek swelling and a maxillary sinus mass exhibiting bony destruction had round-to-spindled tumor cells with scant cytoplasm and hyperchromatic nuclei. Rhabdomyosarcoma was suspected, but confirmation required MyoD1 and myogenin IHC due to the absence of rhabdomyoblasts (strap cells) with cross-striations [21].

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A 40-year-old male with a nasal mass and epistaxis showed tumor lobules of round cells with hyperchromatic nuclei and minimal pleomorphism. ONB, small cell neuroendocrine carcinoma (NEC), and SNUC were considered. ONB can be differentiated by fibrillary cell processes, Homer Wright rosettes, and S100 protein-positive sustentacular cells, absent in NEC and SNUC [29].

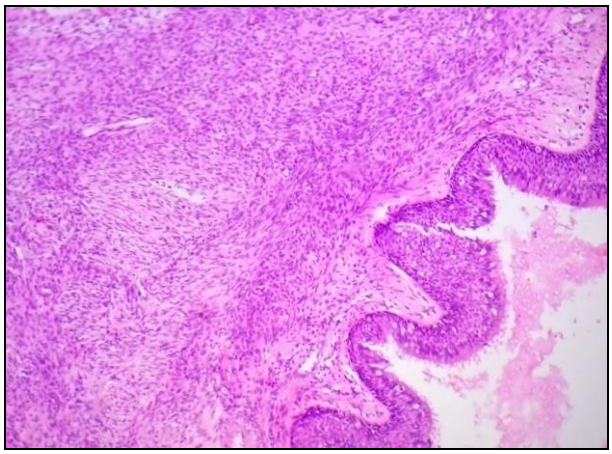

Fig. 2: Section showing Low-grade myofibroblastic sarcoma (H&E 40X)

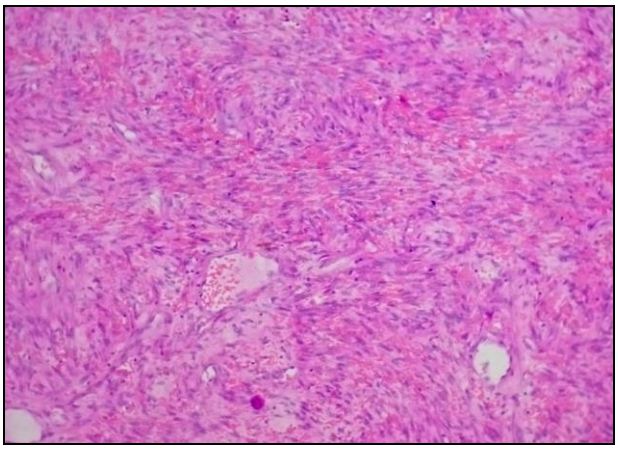

Fig. 3: Section showing Fibrosarcoma (H&E 40X)

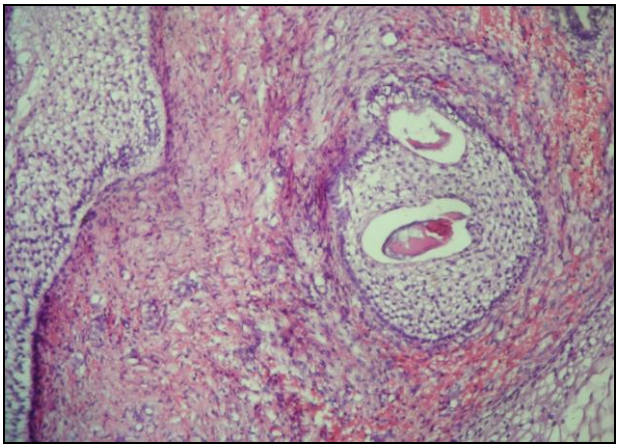

Fig. 4: Section showing teratocarcinosarcoma (H&E 40X)

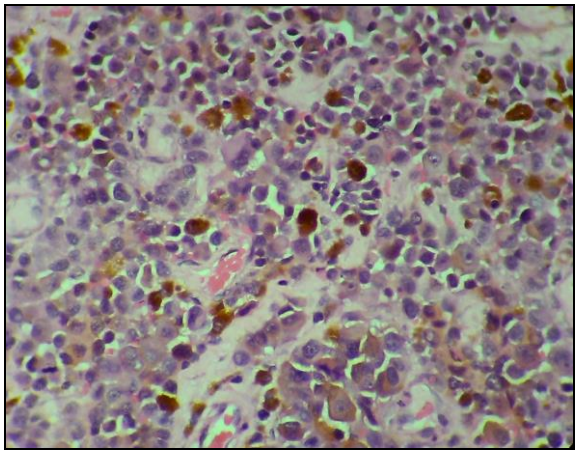

Fig. 5: Section showing Malignant Melanoma (H&E 40X)

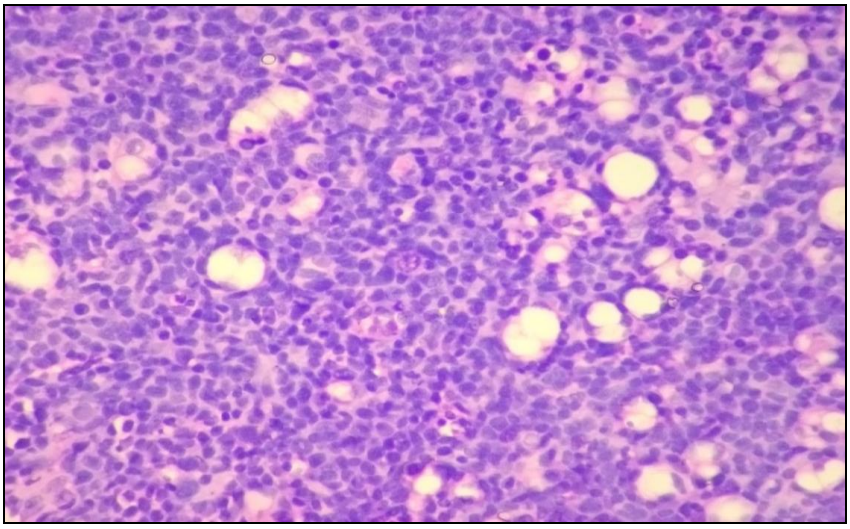

Fig. 6: Section showing Non-hodgkin lymphoma (H&E 40X)

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CONCLUSIONS

Non-epithelial sinonasal tumours encompass a diverse group of neoplasms that span multiple categories such as lymphomas, sarcomas, germ cell and neuroectodermal tumours. Accurate diagnosis based solely on light microscopy remains a challenge even for experienced pathologists and the use of ancillary techniques like immunohistochemistry helps in clinching an accurate diagnosis.

CONTRIBUTION OF AUTHORS

Research concept: Varsha Dhume, Aniket Meshram
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Final approval: Varsha Dhume, Aniket Meshram, Pratik Chide, Avinash Borkar

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