

# Sinonasal Polyps : A Diagnostic Challenge

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## ABSTRACT

### Introduction

Sinonasal polyps, presenting as mass lesion of nose and paranasal sinuses ranges pathologic entity including infective diseases to malignant lesions. 80% are non-neoplastic lesions and less than 1% are malignant. They all present with symptoms of nasal stuffiness or obstruction and mass lesion, producing significant diagnostic challenges as they possess extremely varied clinical behaviour; etiopathogenesis, treatment protocol as well as prognosis.

### Case Series

During period of one year (March 2017 to February 2018), we had six patients presenting with nasal polyp having special features that need attention. After proper investigation each case was operated and gross examination followed by histopathology was done. They revealed six different diagnoses e.g., Olfactory neuroblastoma, Adenoid Cystic Carcinoma, Basal Cell Adenocarcinoma, Sinonasal Mucosal Melanoma, Primitive Neuroectodermal Tumour (PNET) and Aspergilloma.

### Discussion

Clinicians' attention is drawn to the fact that, similar presentation may have varied differential diagnoses, some of which may be very rare and histopathology is essential for coming to definitive diagnosis.

### Keywords

Sinonasal polyp, Etiopathogenesis, Histopathology

Sinonasal polyps can occur in any age group. Polypoidal nasal mass is a very common lesion encountered in day to day clinical practice. It ranges from the simple nasal polyp or polypoidal lesions which maybe infective to granulomatous diseases and malignant ones. They produce significant diagnostic challenges with different cells types and present unique anatomic features.<sup>1</sup>

Allergic and inflammatory polyps are the common nonneoplastic lesions (80%) and the rest are neoplastic whereas sinonasal cancer accounts for less than 1% of all malignancies.

The patients usually present with symptoms of nasal stuffiness or obstruction and mass protruding from the nostril. Other symptoms are total and partial loss of smell, headache, sneezing, and mucoid or watery discharge.<sup>2</sup> Sino nasal neoplasms manifest nonspecific symptoms which can mimic numerous inflammatory pathologies. Nasosinusal malignant tumors are rare, representing less than 3% of head and neck cancers and 0.8% of all human cancers.<sup>3</sup>

## Case Series

### Case Report 1 - Olfactory neuroblastoma

A 42 year male patient presented with a soft mass protruding from left nasal cavity with a long standing history of unilateral nasal obstruction and occasional bleeding.

CECT revealed an enhancing mass lesion in left maxillary, ethmoid and sphenoid sinus. The mass was excised and sent for histopathological examination.

On gross examination, multiple tissue pieces were found, largest one measuring 3x2x1 cm and smallest one was 0.5 cm in maximum dimension.

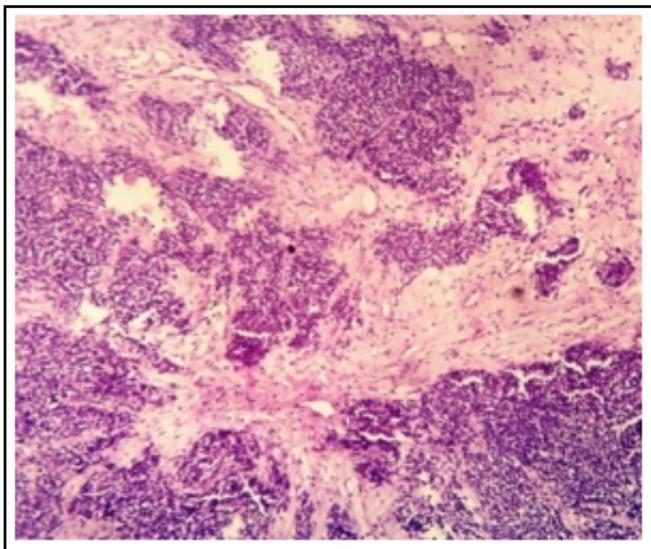
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**Fig.1. Microphotograph of olfactory neuroblastoma (H&E, 100x)**

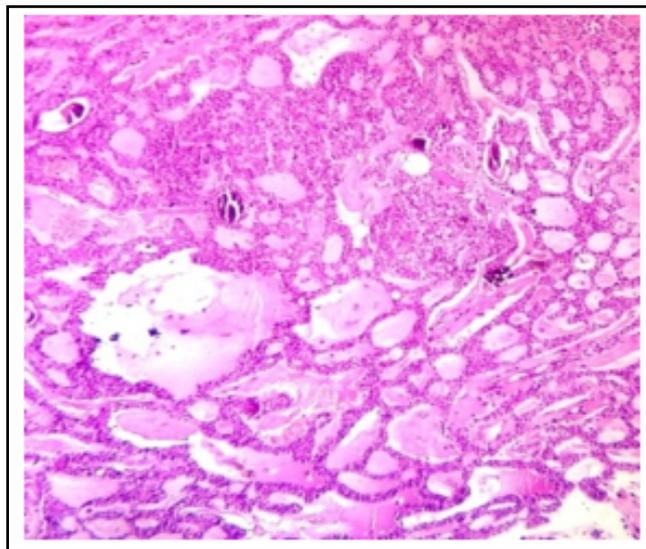
Microscopic examination shows a neoplastic lesion below an intact mucosa with lobular architecture comprised of small, round, blue cells in circumscribed lobules which were separated by a highly vascularized fibrous stroma. The cells had small and uniform nuclei with hyperchromatic, delicate, uniform 'salt-and-pepper' nuclear chromatin distribution. Nucleoli were inconspicuous. There was syncytial arrangement of tumour cells with a tangle of neuronal processes forming the background. Homer Wright pseudo rosette areas of necrosis and calcification were also present. (Fig. 1) The tumour was diagnosed as olfactory neuroblastoma grade II (Hyams' grading system).

Immunohistochemical study revealed that the tumour was positive for Synaptophysin, Chromogranin A, NSE, Calretinin and negative for CD99.

#### *Case Report 2- Adenoid Cystic Carcinoma*

A 52 year-old male presented with bilateral sinus symptoms beginning 4 months prior. The patient complained of left sided facial pain and tenderness, nasal congestion and obstruction.

Nasal endoscopy revealed unilateral polypoid mass in the left nasal cavity, septal deviation, mucosal oedema.



**Fig.2. Histopathological examination suggestive of Adenoid Cystic Carcinoma**

Neck and orbital examinations were negative. CECT scan of the sinuses revealed irregular soft tissue mass in the posterior part of left nasal cavity, extending to the left maxillary antrum, adjacent nasopharynx, left side of sphenoid sinus, left ethmoidal air cells and involving the soft tissue of the lateral nasal fold with associated bone destruction.

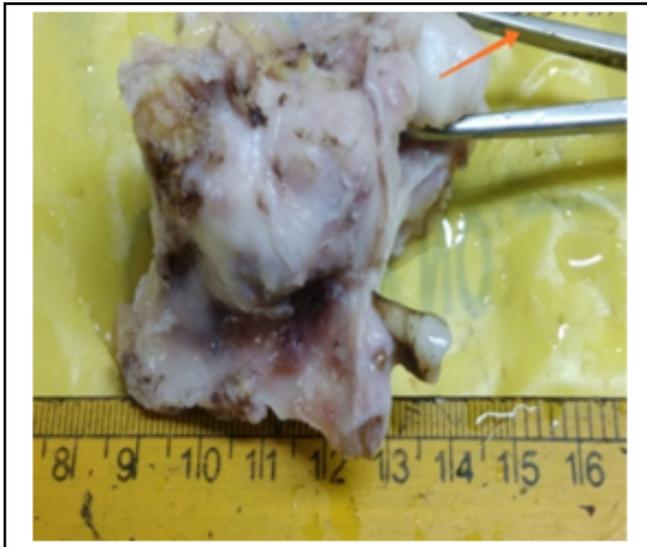
MRI was done and intracranial extension was excluded.

Surgical excision was done. Gross examination showed multiple greyish white tissue pieces with largest fragment measuring 3x2x0.5 cm.

Microscopic examination revealed a circumscribed mass under the olfactory epithelium consisting of glandular structures with cribriform architecture lined by bland looking cuboidal cells, lumens are filled with pink eosinophilic material.(Fig. 2) Overall histopathological features were in keeping with adenoid cystic carcinoma. There were some areas of solid appearance.

#### *Case Report 3-Basal Cell Adenocarcinoma*

A 73yrs old lady presented with a swelling over left cheek for 3 years. The growth was painless and gradually progressive. The patient had several episodes

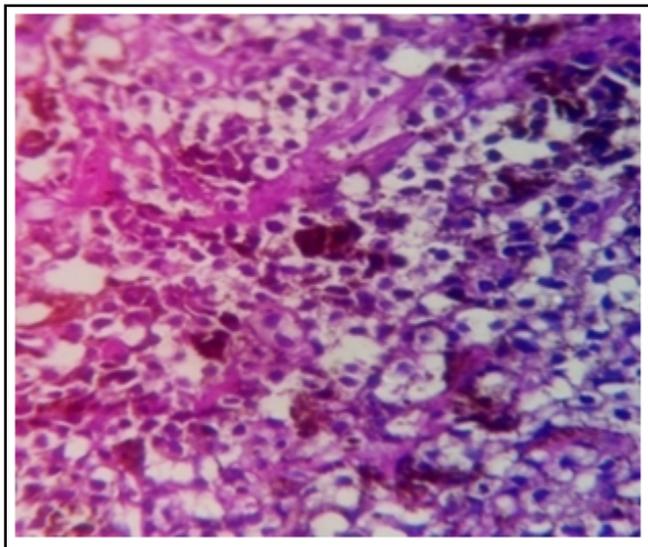


**Fig. 3. Specimen of Basal cell ADC**

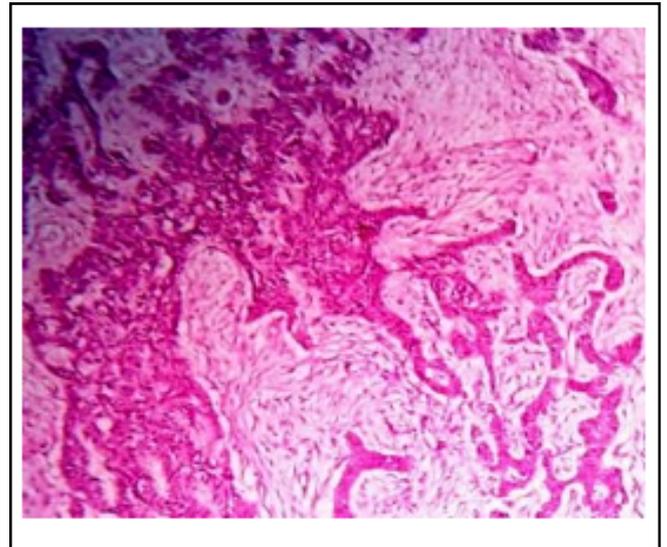
of epistaxis for last one year.

CECT scan showed a mass on left maxillary sinus having extension into adjacent anatomical spaces.

Gross examination of excised specimen revealed 5cm x 6cm lobulated mass with surface irregularities arising from maxilla (Fig.3).

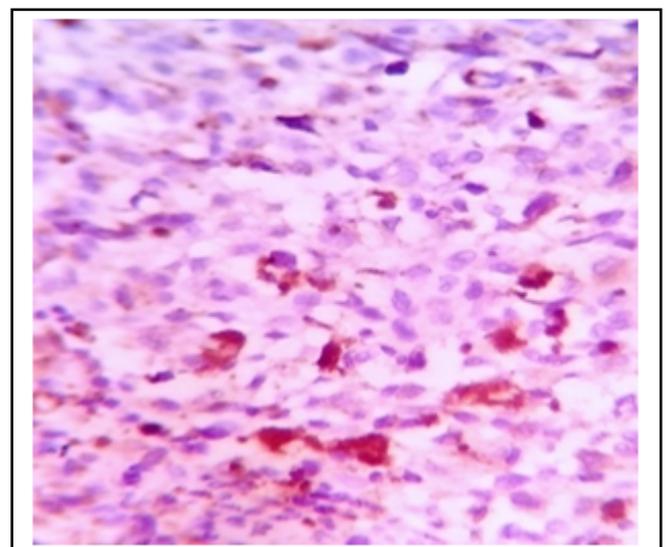


**Fig. 5. Microphotograph of Sinonasal melanoma (H&E, 100x)**

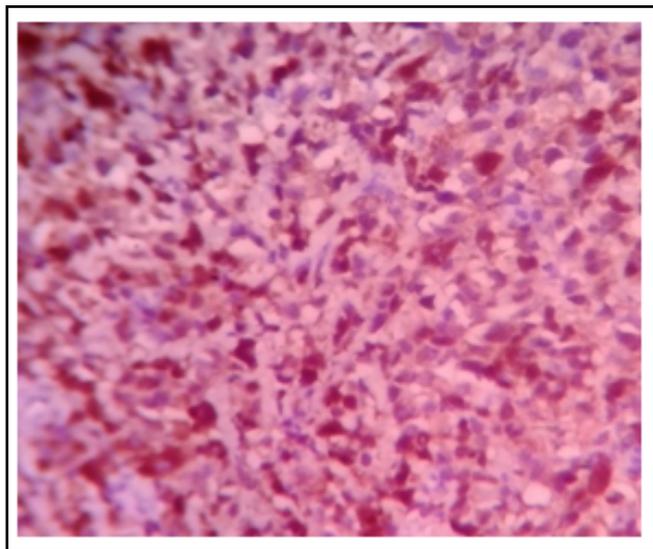


**Fig. 4. Microphotograph of basaloid adenocarcinoma (H&E, 100x)**

On microscopical examination the tumour was composed of cuboidal to columnar cells arranged in trabecular and tubular fashion with peripheral palisading. (Fig. 4) The tumour was p53 positive whereas calretinin negative.



**Fig. 6. Immunohistochemical study showing positivity for WT1 (400x)**



**Fig. 7. Immunohistochemical study showing S-100 positivity (400x)**

*Case Report 4-Sinonasal Mucosal Melanoma*

79 year old woman presented with nasal mass. She had a history of unilateral nasal blockage with epistaxis. Clinically a polypoid mass was noted. Surgery was done. Grossly, it showed multiple black tissue pieces.

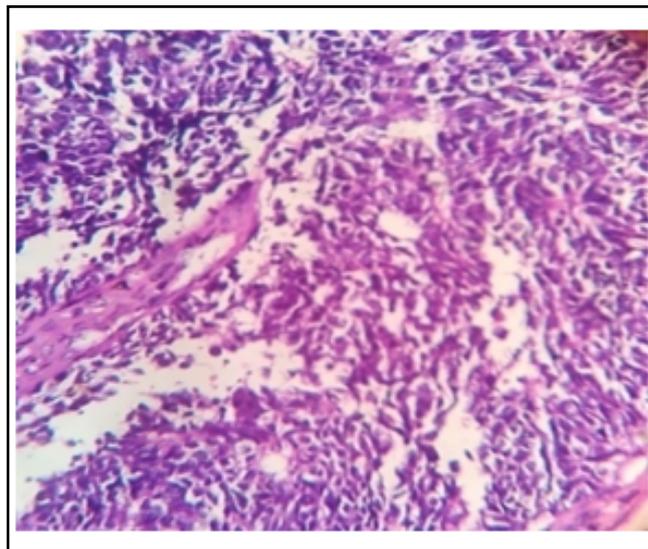
On histopathological examination, there were sheets of round to oval pigmented cells arranged in diffuse fashion having hyperchromatic nucleus. (Fig.5)

Immunohistochemical study showed the tumour was positive for WT1 (Fig.6) and S-100 (Fig.7).

*Case Report 5- Primitive Neuroectodermal Tumour (PNET)*

A 53yrs female came with history of epistaxis, unilateral nasal obstruction for 6 months. CT scan showed opacity in left maxillary sinus. Excised specimen was multiple whitish spongy tissue pieces with areas of haemorrhage on gross examination.

Microscopy showed cells arranged in lobules with prominent rosette like structure. (Fig. 8) The tumour showed positivity with Cytokeratin, p53, CD 99 but synaptophysin and chromogranin negative.



**Fig. 8. Microphotograph of PNET (H&E, 100x)**

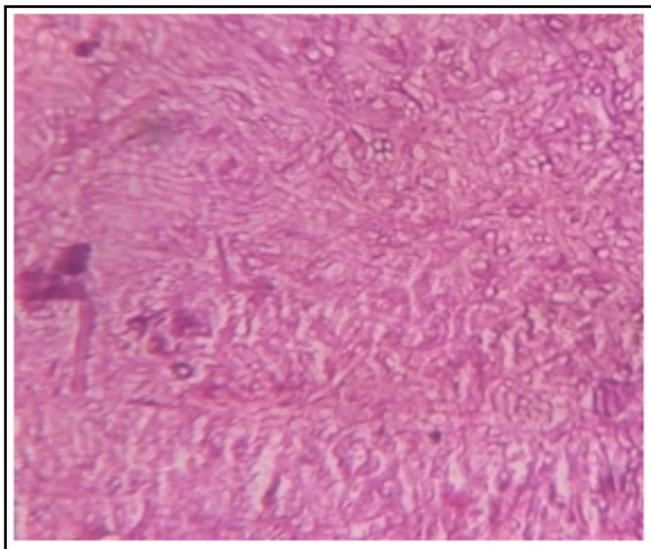
*Case Report 6-Aspergilloma*

62 year old diabetic female presented with bilateral sinus symptoms for 1year. Patient complained of left sided facial pain, nasal congestion and obstruction. CT scan revealed non-specific opacity of paranasal sinuses. Excision biopsy was followed by histopathological examination which revealed fungal colony of broad septate hyphae branching at acute angle. (Fig. 9)

**Discussion**

*1- Olfactory neuroblastoma*

Olfactory neuroblastoma (ONB), also known as Esthesioneuroblastoma, is a rare neuroectodermal tumor arising from the olfactory epithelium in the roof of nasal cavity and occasionally other parts of nasal cavity, paranasal sinuses and frontal lobe of brain. Incidence is only 2 to 3% of intranasal tumors. Patients usually present with symptoms of nasal obstruction, epistaxis, headache etc.<sup>4</sup> Metastasis to distant as well as cervical lymph nodes occurs in 10 to 30% of the cases.<sup>5</sup> Grossly, a soft glistening polypoidal mass covered by mucosa or friable mass with overlying ulceration and granulation tissue are found on microscopy. ONB has a lobular



**Fig.9. Histopathological examination suggestive of Aspergilloma (H&E, 400x)**

(organoid) pattern with intervening fibrous stroma, in a highly vascularised and occasionally hyalinised background. Individual tumor cells are uniform with background neurofibrillary matrix. Nuclei contain salt and pepper chromatin. ONB can demonstrate nuclear atypia, mitosis, calcification, necrosis, Homer-Wright and Flexner-Wintersteiner rosettes.<sup>3</sup>

ONB possess a characteristic immunohistochemical profile which includes diffuse positivity for Neuron Specific Enolase, Synaptophysin, Chromogranin, CD56, GFAP.

The sustentacular cells surrounding the tumors nests shows positivity for S100.5 Approximately one third of the ONB demonstrate focal positivity for cytokeratin. (CK AE1/AE3 and CAM 5.2).<sup>6</sup>

A widely accepted, non-quantitative, 4-tiered grading system, introduced by Hyams and co-workers is based on a constellation of features including growth pattern, presence or absence of neurofibrillary matrix, nuclear atypia, mitotic activity, presence of rosettes and necrosis. This system was modified by Even Hyams et al in order to achieve simplicity and correlate tumour grade with the outcome, classifying ONB into low grade and high grade. Even Hyams et al. grouped grade I and II as low grade tumors and grade III and IV as high grade tumours with prognostic significance.<sup>7</sup>

Common differential diagnoses of ONB include sinonasal undifferentiated carcinoma(SNUC), nasopharyngeal carcinoma (NPC),sinonasal neuroendocrine carcinomas (SNEC) and small round blue cell tumors,<sup>8</sup> sinonasal melanoma,<sup>9</sup> sinonasal paraganglioma.<sup>10</sup> Our case was of grade II.

### 2- Adenoid Cystic Carcinoma (ACC)

ACC is a relatively rare tumor in nose and nasal cavity, arising from major or minor salivary glands.<sup>3</sup> Incidence is 3 to 5% of all head and neck malignancies.<sup>11</sup> The peak incidence is from the fourth to the sixth decade and slightly more common in women.<sup>12</sup> Patients usually present with slowly growing, firm mass, producing a constant, low-grade dull ache. Pain increases in severity likely due to the tumor's predilection for perineural invasion specially the facial nerve. Perineural invasion also has poor prognostic significance.ACCs do not usually spread via regional lymph nodes. Distant metastasis can occur; with the lung being the most common site besides extensive bony invasion.<sup>13</sup> ACC is graded as cribriform or tubular (grade 1), less than 30% solid (grade 2), or greater than 30% solid (grade 3), with grade 3 representing the worst prognosis. The tumour is c-kit positive. p63 positivity in ACC is an independent predictor of survival and also helpful in distinction from basaloid squamous cell carcinoma and high-grade neuroendocrine carcinoma.<sup>14</sup> Our case was a 52 year male and was of grade 1.

### 3-Basal Cell Adenocarcinoma(BCAC)

BCAC is a low grade tumour accounting for only 1.6% of all salivary gland neoplasms. They mainly arise from submucosal seromucinous glands of parotid and rarely minor salivary glands. Our case is unusual in its occurrence in the nasal cavity. Two main differential diagnoses include basal cell adenoma and adenoid cystic carcinoma. The infiltrating growth and tendency of of vascular and perineural involvement distinguishes basal cell adenocarcinoma from basal cell adenoma along with , higher Ki-67 proliferation index, loss of bcl-2 ,greater expression of p53 and EGFR. Adenoid

cystic carcinoma can be differentiated by absence of cytokeratin 17 staining.<sup>15</sup>

Pluripotent ductal reserve cells are considered as possible origin of the tumour in this unusual location.<sup>16</sup>

On microscopy, the tumor cells form solid (most common), tubular, trabecular, and membranous patterns. There are two types of tumor cells: central larger cells with pale nuclei and peripheral smaller cells with dark nuclei with a tendency to form nuclear palisading.<sup>15</sup> Squamous metaplasia, nuclear atypia, necrosis and mitotic activity may be encountered.<sup>17</sup>

In our case, the tumor was solid and p53 immunostain positive.

#### 4-Sino nasal Mucosal Melanoma

A highly aggressive tumour representing between 0.7 and 1% of all melanomas in Caucasian populations and between 4 and 8% of malignant sinonasal tumours.<sup>18</sup> The tumour has extremely poor prognosis, mostly occurring in elderly males, extremely rare in young people. The risk of local recurrence and distant metastasis is 31-85% and 25-50% respectively. Common sites affected are the nasal cavity, septum, inferior and middle nasal conchae, the lateral wall of the nasal cavity, and the facial sinuses.<sup>19</sup>

Higher density of melanocytes in the mucosa of the nasal cavity and paranasal sinuses is responsible for higher incidence of mucosal melanoma in these sites.<sup>20</sup>

Intracytoplasmic melanin pigment can be detected by Fontana stain. Histopathological examination should identify ulceration, necrosis, number of mitoses, inflammation and bone, perineural, lymphatic and vascular invasion.<sup>19</sup>

Histologically, they are either epithelioid or large fusiform cells having abundant eosinophilic cytoplasm. Around one-third of tumours are composed of undifferentiated cells and should be differentiated from close differentials like sinonasal undifferentiated carcinoma, lymphoma, rhabdomyosarcoma, angiosarcoma, neuroendocrine carcinoma, neuroblastoma, and plasmacytoma. IHC markers are S100 and melanocytic markers (HMB45, Melan-A,

tyrosinase, MITF).<sup>21</sup>

We had 70-year-old female, with a melan A, S-100 & WT1 positive pigmented nasal polyp.

#### 5- Primitive Neuroectodermal Tumour (PNET)

The incidence of PNETs in the head and neck region is 2-7% and occurrence in sinonasal region is rare.<sup>22</sup>

It is highly aggressive in behaviour with worse outcome compared to other small round cell tumours.

It can occur at any age with peak incidence during adolescence in second decade of life with male preponderance.

Grossly, PNET in nasal cavity is a multilobulated, polypoidal tumour with cut surface being gray-yellow in colour, soft and friable associated with necrosis.<sup>23</sup> Microscopically, it has small round cells arranged in lobules with occasional rosette like structure specially Homer-Wright rosette.<sup>24</sup>

Ultra-structurally, tumour cells contain neurosecretory granules, microtubules and microfilament.

Immunohistochemically, PNET shows positivity for vimentin and neurofilaments, neuron-specific enolase (NSE), Leu-7 (CD57), and S-100. Necrosis is a poor prognostic factor.<sup>23</sup>

PNET in nasal cavity is prognostically very poor and the most significant prognostic factor is the presence of metastasis.<sup>23</sup>

Our case shows CD 99 positivity and was negative for synaptophysin and chromogranin.

#### 6-Aspergilloma

Aspergillosis of the nasal and paranasal sinuses is a very common opportunistic fungal infection in immunocompromised patients. However, invasive variant in healthy and mildly immunocompromised hosts can also be seen.<sup>25</sup>

Veress et al. reported that two factors are important in pathogenesis of paranasal sinus aspergillosis: secretion of a toxic substance by fungi and tissue necrosis caused by an immune mediated mechanism.<sup>26</sup> Rowe-Jones et al classified aspergillosis in 1994.<sup>27</sup> There are three

main types: Noninvasive, Invasive and Destructive noninvasive types. The third variety is further classified into: Aspergilloma, Fungus ball and Mycetoma (affecting one sinus) or Aspergillus sinusitis (affecting more than one sinus).

Grossly, Aspergillosis developing in tissues as fungus ball or necrotic material is green-black in colour with a cheesy consistency. On hematoxylin and eosin stained sections the branching hyphae are usually 2–5 µm in diameter, splitting dichotomously at 45° angle. Methanamine silver stain is ideal for demonstration of hyphae. Conidiospores can also be seen. This fungus should be differentiated from mucormycosis which have broader non-septate hyphae with dichotomous branching at 90° angles.<sup>28</sup>

## Conclusion

Sino nasal polyps of the nasal cavity and paranasal sinuses are common, with extremely varied clinical behaviour, etiopathogenesis, treatment protocol as well as prognosis. We hope that our case reports can draw attention of clinicians to the diverse nature and lack of symptom specificity. Overall, histopathology is extremely useful for proper diagnosis and to avoid unnecessary delay in management.

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