Sinonasal Ameloblastic Carcinoma in a 48-year-old Filipino Male: A Rare Fortuity*

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Abstract

Objective: To report a case of sinonasal ameloblastic carcinoma in a 48-year-old Filipino male & discuss its clinical manifestations, diagnosis, histopathology and possible treatment options.

Methods: Design: Case Report, Setting: Tertiary Government Hospital, Patient: One

Results: A 48-year-old Filipino male consulted at our OPD due to progressive right- sided nasal obstruction, rhinorrhea, hyposmia & intermittent controlled episodes of epistaxis for one year. On anterior & posterior rhinoscopy, a fleshy, soft tissue mass is seen in the nasal floor. On further examination with rigid nasal endoscopy, the same pink, fleshy, soft tissue mass was seen occupying entirely the right nasal floor with nasopharynx hardly to be visualized, and friable upon insinuation. A preoperative punch biopsy of the mass was done at our OPD revealing histologic features consistent with ameloblastoma. Contrast-enchanced computed tomography (CT) scan of the paranasal sinuses revealed a prominent soft tissue density mass lesion filling right sinonasal cavity. It is further noted the heterogenous characteristic of an isodense mass in the right nasal cavity enhancing from the nasopharyngeal area, with complete obstruction of the osteomeatal unit (OMU) and some lytic changes on the medial maxillary sinus wall however no bony changes noted on bilateral orbital floor and skull base. The mass was completely excised by medial maxillectomy via midfacial degloving. Final histopathologic studies showed islands of lace-like areas and nests of atypical odontogenic cells with central stellate reticulum, palisading columnar cells exhibiting reverse polarity and moderate mitotic activity with atypical mitotic figures present on two specimens labelled as "posterior nasal septal mass" & "nasopharyngeal mass".

Conclusion: Ameloblastic carcinoma is an uncommon entity of malignant odontogenic tumors that may originate *de novo* or from a benign ameloblastoma which exhibits malignant histologic features in the primary lesion and/or distant metastasis. On the other hand, malignant ameloblastoma exhibit benign histologic features both for the primary and distant metastasis. This report depicted an uncommon case of ameloblastic carcinoma found extragnathically, that is in the sinonasal region. This is the second case of ameloblastic carcinoma of the sinonasal region documented in the Philippines. This case report might be a step on the ladder to generate more information regarding the biologic behavior of this entity and might ignite the enthusiasm in performing more evidence-based studies needed for its treatment as well as for its surveillance. Wide surgical resection, which is the treatment of choice, can pose challenge to otolaryngologist in the case of sinonasal ameloblastic carcinoma due to the surrounding vital structures present. Role of chemotherapy and radiotherapy is as yet conclusive due to very limited evidence- based studies available.

Keywords: sinonasal ameloblastoma, ameloblastic carcinoma, sinonasal ameloblastomic carcinoma

**2nd Place, 2019 Philippine Medical Association Case Report Presentation Contest, May 15, 2019*

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INTRODUCTION

Ameloblastoma is a common benign locally aggressive odontogenic epithelial tumor with slow growth, usually arising in the mandible or maxilla. An entity with high propensity for recurrence that are believed to be a remnants of odontogenic epithelium, lining of odontogenic cysts, and the basal layer overlying oral mucosa.[1] Suggested sources for odontogenic epithelium are cell rests of the dental lamina, a developing enamel organ, the lining of odontogenic cyst, basal cells of oral mucosa, or heterotopic embryonic organ epithelium. [1]

Although it is the most common true odontogenic neoplasm with an incidence of 11%, only 1% comprises all head and neck tumors.[2] The estimated incidence of ameloblastomz is approximately 0.5 per million populations per year.[3] Approximately 80% of ameloblastoma occur in the mandible and roughly 15-20% as growing masses in the maxilla.[2] Majority of the case reports documented regarding ameloblastoma arising within the sinonasal cavity are found to have originated from the maxilla. However rare case reports document true primary sinonasal ameloblastomas without connections to gnathic sites.

With the rarity of ameloblastoma arising primarily from the sinonasal cavity, malignant variants are exceptionally rare. It accounts for 1.5% to 2% of all odontogenic tumors. The largest population-based series of malignant ameloblastoma & ameloblastic carcinoma conducted by Rizzitelli et al. revealed an overall incidence of 1.79 per 10 million person/year. The study also showed a male predilection with a ratio of 1.59:1 and apparently significantly higher incidence among blacks.[5] In the past, terms malignant ameloblastoma and ameloblastic carcinoma have been used interchangeably for this variants, however a distinction has been made wherein malignant ameloblastoma tends to metastasize in spite of the benign histology while ameloblastic carcinoma exhibit features of both ameloblastoma and carcinoma with or without metastasis. It may arise *de novo* or from transformation of a long-standing primarily benign lesion which has undergone several excisions.[4] Ameloblastic carcinoma can be further divided into two subtypes: primary or secondary. Primary ameloblastic carcinoma arises *de novo*, while secondary ameloblastic carcinomas are a result of sdf

malignant transformation of a previously diagnosed benign ameloblastoma.[5] Swelling of the involved site is the commonest manifestation of patient with maxillary involvement of ameloblastic carcinoma.[7]

To date, only one study has been published regarding sinonasal ameloblastic carcinoma in the country, wherein the author described a 50-year-old Filipino woman with a previous reported diagnosis of sinonasal ameloblastoma underwent Endoscopic Sinus Surgery last July 2010 and was lost to follow up thereafter. She experienced recurrence of unilateral, right-sided epistaxis with associated right -sided nasal obstruction last December 2012 and finally consulted on March 2013 wherein a fleshy mass was seen in the right nasal cavity. Total maxillectomy with right orbital exenteration and prosthetic reconstruction was done last July 2013 consistent with the diagnosis of ameloblastic carcinoma on histopathologic examination. Further surgery was done to address positive margins at the superior & inferior margins of the resection area as well as the ethmoids and inferior orbital wall. Intraoperatively, tumor in the superior ethmoid area was positive for ameloblastic carcinoma on frozen section. Bare bone excision was attempted with tumor noted in the area of the cribriform plate. Further work up revealed hepatic and pulmonary metastases hence several cycles of chemotherapy was delivered. The patient died after two years of treatment.[6] This represent a secondary type of ameloblastic carcinoma in relation with the previously cited literature. In contrast with the patient in this study, the histopathologic diagnosis after the definitive surgery (i.e. right medial maxillectomy via midfacial degloving) was an outright ameloblastic carcinoma. This can be a case of ameloblastic carcinoma arising *de novo*.

Aside from the extreme rarity of ameloblastic carcinoma's occurrence in the gnathic site, this report made it more uncommon since the patient's ameloblastic carcinoma in this case report was found extragnathically, that is in the sinonasal area. Thus, this deserves high academic interest.

CASE REPORT

A 48-year-old Filipino male presented in our hospital with seven months history of progressive right-sided nasal obstruction with associated rhinorrhea, and frontonasal headache. He had a history of intermittent controlled epistaxis and hyposmia then subsequently proceeding to anosmia three months prior to admission. Past medical history of previous self-dental extractions from various years ago was also noted from the patient. There is no history of visual defect (i.e. diplopia, ptosis), atopy or previous trauma to the nose. His weight was stable and his general health was satisfactory.

Upon inspection of the oral cavity, missing teeth were noted (numbers 15, 16, 17, 30 & 32) as these were the teeth he extracted by himself from various years ago. The hard & soft palates are without lesions, bleeding and/or bulge/mass. Upon anterior rhinoscopy, a pink, fleshy, soft tissue mass was seen in the nasal floor with associated foul-smelling, mucoid rhinorrhea with the same mass noted on posterior rhinoscopy. Otoscopy of both ears showed intact tympanic membrane with no noted retractions or opacifications. Tuning fork tests (i.e. Weber and Rinne Tests) were unremarkable. Diagnostic rigid nasal endoscopy of the right nasal cavity (Fig. 1) revealed a pink, soft, fleshy, ill-defined mass occupying entirely the nasal floor that easily bleeds upon manipulation. The nasopharynx was not appreciated due to mass obliteration even with insinuation. Also in the same nasal cavity, a pale, glistening, grape-like grade 2 polypoid mass (Fig. 2) was seen attached to the lateral nasal wall. Nasal endoscopy of the contralateral nasal cavity revealed unremarkable result except for the presence of the same mass as previously described in the right nasal floor, seen in the nasopharyngeal area but not completely obliterating it.

A preoperative contrast-enhanced computed tomography (CECT) of the paranasal sinuses (PNS) was done. A representative CECT axial cut of PNS (Fig. 3a) demonstrated a prominent large, ill-defined heterogeneously enhancing isodense mass occupying the right nasal cavity extending to the nasopharyngeal area measuring 3.8 x 3.5 x 3.6 cm with associated multiple hyperdense materials thought to be part of the tumoral calcifications. The mass is noted obstructing the right ostiomeatal unit (OMU) with associated air-fluid level and some lytic changes seen in the medial maxillary sinus wall (Fig. 3b). Lateral pterygoids are without lytic changes. Contralateral nasal cavity and maxillary sinus is unremarkable. Representative coronal cut of the PNS CECT (Fig. 4) depicted extension of the isodense mass on bilateral ethmoids and sphenoid sinuses. No lytic change was observed on the cribriform plate and bilateral orbital floors. On sagittal cut (Fig. 5), the mass is seen enhancing from the nasopharyngeal area with extension to anterior & posterior ethmoid sinuses and sphenoid sinus. Frontal sinus is well aerated with no noted lytic changes in skull base or intracranial extension.

A preoperative punch biopsy was done showing minute pieces of tan to dark brown irregular soft tissues measuring 1.5 x 1.5 x 0.5 cm in aggregate. On light microscopic examination (Fig. 6), low power view showed a micrograph shedding two distinct histologic findings, that is the presence of inflammatory nasal polyp (Fig. 7a) lined by a respiratory epithelium (i.e. pseudostratified columnar ciliated epithelium) with neutrophils & lymphocytes scattered in a background of myxoid stroma while the second histologic finding labeled as a "suspicious fragment" (Fig.7b) demonstrated an odotogenic epithelium with conspicuous calcifications (consistent with the hyperdense material noted in the CECT of the PNS). On further investigation of the "suspicious fragment" in high power view (Fig. 8 & 9), it revealed islands of cells presented predominantly follicular histologic pattern resembling enamel organ epithelium with stellate reticulum at the center. Peripheral palisading columnar cells are seen exhibiting *Reverse Polarization*. This was signed out as a case of ameloblastoma. Patient underwent excision of the mass with medial maxillectomy, right via midfacial degloving. Intraoperatively, a pink, fleshy, soft tissue, irregularly-shaped mass was noted along the nasal floor up to the nasopharynx and posterior nasal septum with no noted extension into the right maxillary sinus. Only mucous secretions are noted and suctioned in the maxillary, ethmoids and sphenoid sinuses. Three separate tissue samples (Fig. 10a, 10b, 10c) were sent to Anatomic Laboratory for histopathological diagnosis. Section of the specimen labeled "right lateral nasal mass" (Fig. 10a) show fragments consistent with polyp and fragments of benign nasal mucosal epithelium admixed with unremarkable bony fragments.

Sections of the specimen labeled "posterior septal nasal mass" and "nasopharyngeal mass" (Fig. 10b & c respectively) revealed fragments of a malignant mesenchymal neoplasm. The tumor cells are arranged as nodules to elongated structures of atypical odontogenic epithelium with central stellate reticulum (Fig. 11). On HPO, odontogenic epithelium is seen lined by peripheral palisading columnar cells exhibiting *reverse polarization* with polyhedral cells at the center (Fig 12). Microscopic characteristics of carcinoma were also present as demonstrated on HPO, depicting island of focal lace-like areas and nests of moderately atypical odontogenic cells with large ovoid nuclei, coarse chromatin, and prominent nucleoli with associated moderate mitotic activity and atypical mitotic figures (Fig. 13). This was signed out as Ameloblastic Carcinoma with specimens labeled as "posterior nasal septal mass" and "nasopharyngeal mass" while Inflammatory Polyp for specimen labeled as "right lateral nasal mass".

After learning the result of the histopathology, series of metastatic work-up were done both for the laboratory and radiologic exams. Liver profile test result is within the normal range. Neck CT Scan with contrast showed no nodal metastasis. Other radiologic studies include cranial, chest and abdominal CT scan which revealed unremarkable results.

The postoperative course was uncomplicated and the patient was eventually discharged improved after two hospital days. Nasal packing was kept in place and was removed after five days.

DISCUSSION

Ameloblastoma is a locally aggressive epithelial-derived odontogenic tumor with benign histologic components that exhibit a high recurrence rate if surgical resection is not adequate. The malignant forms of ameloblastoma have been controversial for many years. Before, malignant ameloblastoma and ameloblastic carcinoma have been used interchangeably. However, a delineation have been made between the two wherein the former has the ability to metastasize despite its benign histology in either/both the primary and/or the metastatic lesion while the latter demonstrates histologic features of both ameloblastoma and carcinoma regardless of the presence of metastasis.[8] As in the representative slides of the patient (Fig. 10), lace-like areas and nests of moderately atypical odontogenic epithelium with central stellate reticulum are noted. Features of carcinoma like the presence of odontogenic cells with large ovoid nuclei, coarse chromatin and prominent nucleoli were also seen. Other features suggestive of malignancy are the presence of moderate mitotic activities with atypical mitotic figures in the micrograph.

They are extremely rare malignant odontogenic epithelial neoplasm that may arise *de novo* or from a pre-existing benign odontogenic lesion accounting for 1.5% to 2% of all odontogenic tumors. The overall incidence rate of these ameloblastic carcinomas was 1.79 per 10 million person/year.5 The commonest involved area is the mandible (i.e. the posterior portion of the mandible).[7] It occurs in a wide range of age groups. Male population is more affected than that of the female in a 1.59:1 ratio and showed a higher incidence among black population.[5] Usual presenting manifestation is swelling of the involve area and others have associated pain, rapid growth, trismus and dyshonia.[7]

Aside from the rarity of the malignant variants of ameloblastoma, extragnathic ameloblastic carcinoma arising primarily from the sinonasal region is extremely uncommon. To the best of my knowledge, there are no statistical figures yet regarding the incidence rate of ameloblastic carcinoma arising primarily from the sinonasal region. Review of literatures reveals reports and incidence of primary benign sinonasal ameloblastoma but not for their malignant counterpart. Only one case report has been published in the country regarding this rare malignant entity. del Mundo6 described a 50-year-old patient with an initial diagnosis of extragnathic soft tissue ameloblastoma who subsequently lost to follow up and came back for consult after three years after experiencing the same symptoms (right-sided epistaxis and nasal obstruction) prior to the first surgery (i.e. endoscopic sinus surgery). Total maxillectomy with right orbital exenteration & prosthesis reconstruction was done revealing histopathologic features consistent for ameloblastic carcinoma. This is believed to be a malignant transformation arising from a benign lesion, contrary to the finding of the largest comprehensive literature published by Schafer et al., wherein no malignant transformation was accounted among the 24 cases of ameloblastoma arising exclusively in the sinonasal tract from the

20,000 sinonasal tumors for over 40 years.[11] However, the patient in this case revealed a histopathologic diagnosis of an outright ameloblastic carcinoma that is thought to be a product of a *de novo* process. This is in contrary to the published report of del Mundo.[6]

The embryologic development of the sinonasal tract and odontogenic apparatus is closely related. The sinonasal tract arises from the ectodermally derived nasal pits that invaginate to cover the oronasal membrane, conchae, primary and secondary palatine processes, and diverticula of the lateral nasal wall. The odontogenic apparatus is a combination of an endophytic proliferation of the basal layer of the ectodermally derived mesenchyme. Although hypothetical, it appears quite likely that this embryologic approximation allows the sinonasal tract mucosa either to incorporate odontogenic epithelium or to acquire cells capable of odontogenesis during development.[9,10]

Schafer *et al*. stated that extragnathic ameloblastomas may have arisen ectopically or a misplaced odontogenic rests.[11] Moreover, Bakay[12] proposed the basal cell layer of the surfaced epithelium as the origin of these extragnathic ameloblastoma. Other author like Woo *et al.* suggested that the possible origins of extragnathic ameloblastomas are from the pluripotential cells in the basal layer of the buccal mucosa. Of interesting account is that sinonasal ameloblastomas can occur after some inductive process on the sinonasal epithelium that results in the neoplastic transformation of retained or acquired odontogenic cells towards ameloblastomatous differentiation. The presence of chronic sinusitis and squamous metaplasia in the areas adjacent to the ameloblastoma could be that initiating event.11 In relation to our patient, he presented with chronic sinusitis and nasal endoscopy findings revealed chronic inflammation, that is the presence of nasal polyposis, could be the initiating event.

No pathognomonic radiographic findings yet were documented for ameloblastic carcinoma due to its rarity although, they appear with aggressive presentation. Conventional multilocular and radioluscent ("soap bubble") appearance was not seen in the patient in this report in contrast with their gnathic counterpart but showed an enhancing heteregenous isodense lesion with aggressive presentation of conspicuous calcifications and lytic changes (i.e. medial maxillary sinus wall). A definitive tissue biopsy is hence required in the diagnosis of ameloblastic carcinoma.

Microscopically, the histomorphologic features of extragnathic sinonasal ameloblastomas mirror their gnathic counterparts which include sheets of odontogenic epithelium.[12] The epithelium is composed of a peripheral palisading and hyperchromatic nuclei oriented away from the basement membrane (known as *reverse polarization*) and centrally placed stellate reticulum with loosely arranged cells surrounded by a supporting stroma compatible with the diagnosis of ameloblastoma, both for gnathic and extragnathic variants. Furthermore, ameloblastic carcinomas have these characteristics with histologic evidence of carcinoma. Patient's histopathology in the report revealed histopathologic findings consistent with ameloblastoma with features of carcinoma (i.e. odontogenic cells with large ovoid nuclei, coarse chromatin, prominent nucleoli and atypical mitotic figures).

Controversy still exists regarding its treatment due to the lack of evidence- based study particularly studies dealing with the ameloblastic carcinoma arising exclusively in the sinonasal region. Surgery is the treatment of choice for its gnathic counterpart with an en bloc removal of 1-2 cm of normal bone. Surgical resection is the mainstay treatment for sinonasal ameloblastic carcinoma however the extent of the resection may be limited related to adjacent pivotal anatomical structures. Neck dissections should only be performed for clinically positive lymph nodes.[13]

Authors have doubt on the effectiveness of radiotherapy since it is considered a radioresistant tumor. But Atkinson et al,14 retrospectively reviewed 10 patients with ameloblastomas treated with megavoltage irradiation and concluded that ameloblastoma is not an inherently radioresistant tumor. Recommended treatment dosages are between 3,000 cGy and 5,000 cGy.

Chemotherapy does not appear to have a role in ameloblastoma. Results of such treatment for non-metastatic disease have been poor however in the setting of metastatic disease, Ramadas et al. found the use of cisplatin, adriamycin and cyclophosphamide to be beneficial.[15] Due to the limited evidence-based studies, the role of radiotherapy and chemotherapy is as yet conclusive.

The median survival was 17.6 years from the time of diagnosis and increasing age was associated with a statistically significant poorer survival.5 Recurrence of ameloblastic carcinomas locally vary from 0.5 – 11 years after definitive therapy.16 Dissemination may result from multiple recurrences or repeated surgical procedures for the treatment of these recurrences causes implantation of tumor cells into the blood or lymphatic vessels. The most common site of metastasis is the lung followed by the bone, liver and brain. Distant metastasis can occur in the absence of a local or regional recurrence.[17] However once metastases occurred, the median survival was 2 years.[18]

CONCLUSION

This report depicted an uncommon case of ameloblastic carcinoma found extragnathically, that is in the sinonasal region. Clinical manifestations are non-specific such as rhinorrhea, nasal obstruction, hyposmia and epistaxis. Diagnosis is mainly by histopathology. Unlike with their gnathic counterparts, radiologic findings for sinonasal ameloblastic carcinoma are not pathognomonic, wherein local invasion such as lytic changes and calcifications can be observed. This only shows that ameloblastoma can show a variety of histologic & biologic behavior ranging from benignity to frank malignancy. This is the second case of ameloblastic carcinoma of the sinonasal region documented in the Philippines. This case report might be a step on the ladder to generate more information regarding the biologic behavior of this entity and might ignite the enthusiasm in performing more evidence-based studies needed for its treatment as well as for its surveillance. Surgical resection is still the treatment modality for ameloblastic carcinoma, with neck dissection if with evidence of nodal metastasis. Patients with ameloblastic carcinomas should undergo active surveillance or a life-long judicious follow-up including regular CT or MRI scan for early detection of recurrence.

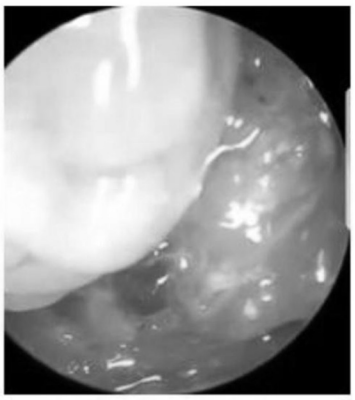

Fig 1: Nasal endoscopy of right nasal cavity showing a pink, soft, fleshy, ill-defined, friable mass completely obliterating the nasal floor

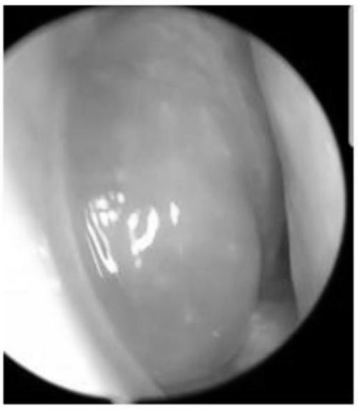

Fig 2: Nasal endoscopy of right nasal cavity showing a pale, glistening, grape-like , grade 2 polypoid mass attached to the lateral nasal wall

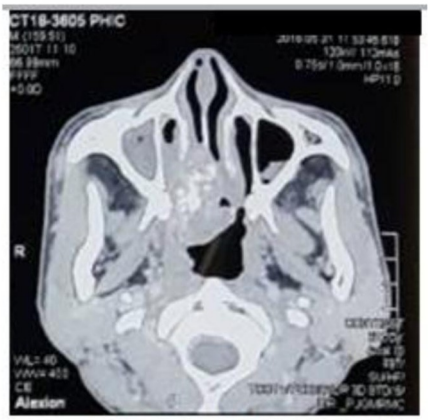

Fig 3a: Axial CECT scan of PNS showing a large, ill-defined heterogenous isodense mass occupying the right nasal cavity with multiple hyperdense material

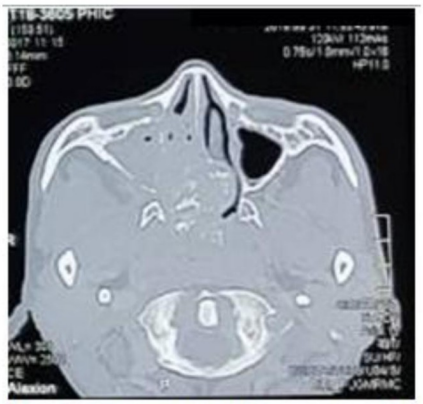

Fig 3b: Bone window of Axial CECT scan of PNS with evident lytic changes on right medial maxillary sinus wall

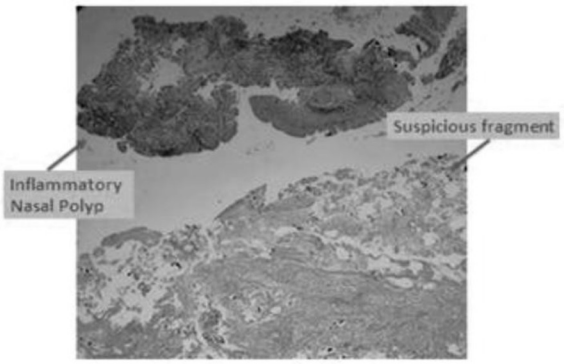

Fig 6: Light Microscopy (LPO) depicting two different histologic findings in one specimen showing an "Inflammatory Nasal Polyp" & "Suspicious Fragment"

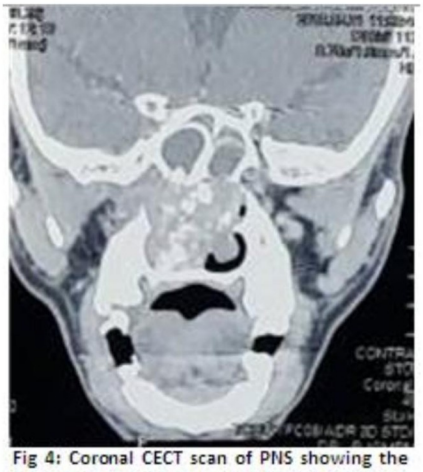

Fig 4: Coronal CECT scan of PNS showing the extent of the mass to bilateral ethmoid & spenoid sinuses

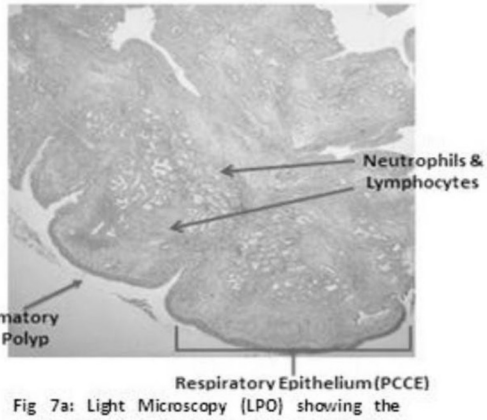

Fig 7a: Light Microscopy (LPO) showing the epithelial lining of a nasal polyp with admixed neutrophils & lymphocytes

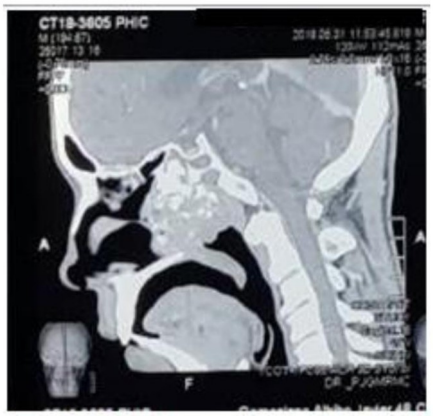

Fig 5: Sagittal CECT scan of PNS showing the extent of the mass enahancing from the nasopharynx to the nasal cavity, ethmoids & sphenoid sinuses

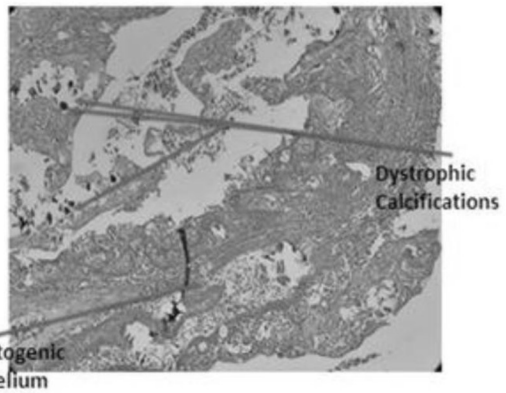

Fig 7b: Microphotograph (LPO) of "suspicious fragment" demonstrating an odontogenic epithelium with conspicuous calcifications

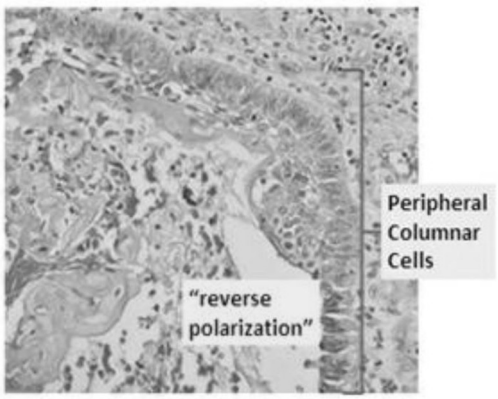

Fig 8: High power view of the "suspicious fragment' showing peripheral palisading columnar cells exhibiting *"reverse polarization"*

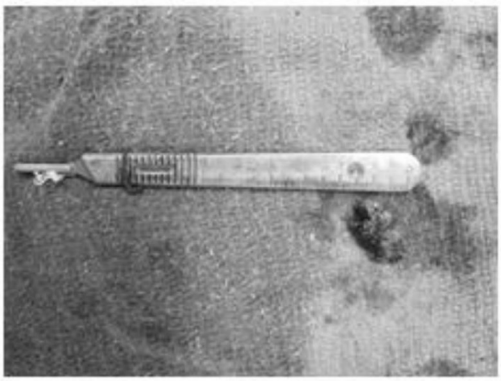

Fig 10b: Posterior nasal septal mass consisting of few fragmented pieces of dark brown, rubbery tissues measuring 2.0 x 1.5 x 0.5 cm

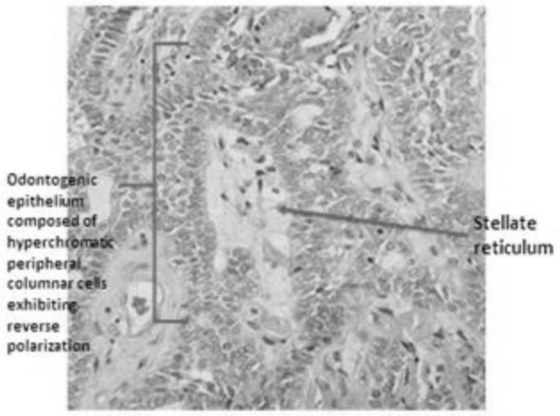

Fig 9: High power view of the "suspicious fragment' showing hyperchromatic peripheral palisading columnar cells in *"reverse polarity"* with centrally located stellate reticulum

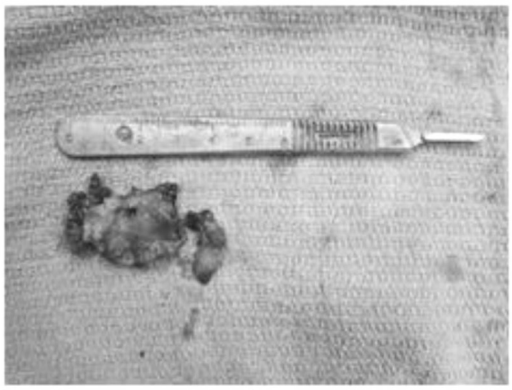

Fig 10c: Nasopharyngel mass consisting of few fragmented pieces of brown, soft tissues measuring 3.0 x 2.0 x 1.0 cm in aggregate

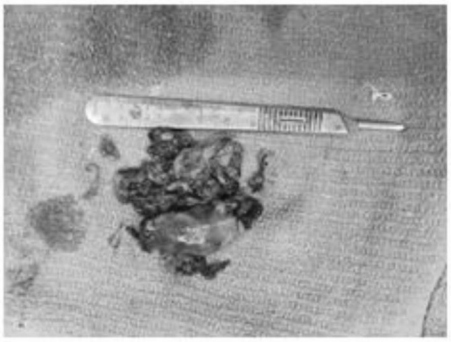

Fig 10a: Right lateral nasal mass consisting of few fragmented pieces of dark brown, rubbery tissues admixed with bone fragments measuring 6.0 x 6.0 x 1.0 cm in aggregate

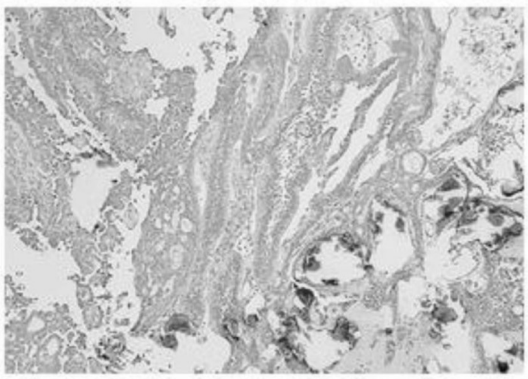

Fig. 11: LPO. The tumor cells are arranged as nodules to elongated structures of atypical odontogenic epithelium with central stellate reticulum (center). A small area of bony trabecular involvement is present (bottom right).

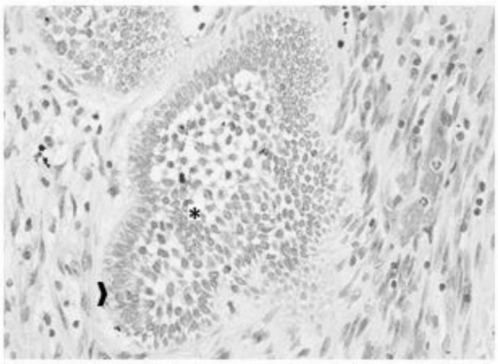

Fig. 12: HPO. Island of odontogenic epithelium with peripheral palisading columnar cells (arrowhead) exhibiting *reverse polarization* and polyhedral cells at the center (asterisk).

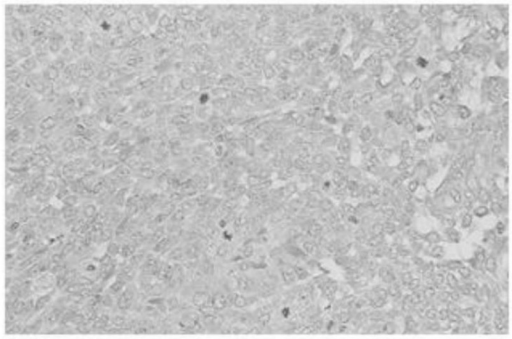

Fig. 13: HPO. Sheet of atypical odontogenic cells with moderate mitosis

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