

## CASE REPORT

# Papillary Variant of Nasopharyngeal Carcinoma: An Unusual Variant Previously Unreported in Malaysia

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### ABSTRACT

Nasopharyngeal carcinoma is a commonly encountered malignancy in endemic regions of the world namely South East Asia, China and Hong Kong. In Malaysia, the ethnic Chinese population is particularly at risk due to genetic susceptibilities and environmental exposure to carcinogenic agents. We herein report a case of nasopharyngeal carcinoma in a middle-aged man of Malay ethnicity who presented with nasal blockage and neck nodes. The biopsy of the nasopharyngeal mass came back as papillary variant of nasopharyngeal carcinoma. The commonly reported histopathological types are the keratinizing and non-keratinizing types, and rarely the basaloid type. In this case report, we aim to highlight one of the rare variants of the non-keratinizing nasopharyngeal carcinoma. When diagnosing the non-keratinizing type, appreciation of the different morphological variants is crucial not only to help aid in procuring an accurate histopathologic diagnosis, but also to help in subsequent treatment plan.

**Keywords:** Papillary NPC, Nasopharyngeal carcinoma, Malaysia, Non-keratinizing NPC

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### INTRODUCTION

Nasopharyngeal carcinoma (NPC) presents commonly in certain parts of the world, especially in the south east Asian region. This is due to the high numbers of ethnic Chinese population. Various classifications and histopathological types have been reported over the years. The latest World Health Organization classification classifies NPC into keratinizing, non-keratinizing and basaloid squamous cell carcinoma(1). The non-keratinizing type is further subdivided into differentiated and undifferentiated type. Non-keratinizing type of NPC may present with variants of histomorphology which are not commonly seen. We would like to highlight such a variant in our case report which was diagnosed in a patient not of Chinese ethnicity.

### CASE REPORT

A 53-year-old male of Malay ethnicity presented with swelling over the right side of neck of 3 months duration. The swelling was painless, measuring 8x9 cm, and gradually increasing in size. He also complained of minimal intermittent blood-stained discharge from the nose and numbness over his right lower jaw and

cheek. Rigid nasoendoscopy revealed an ulcerative and friable mass protruding into bilateral nasal cavities, completely occluding the posterior choanas. The origin of the mass was not able to be visualized, however bilateral spheno-ethmoidal recesses, bilateral olfactory clefts and bilateral osteo-meatal complexes were well visualized and normal. The clinical diagnosis and staging at this point was nasopharyngeal carcinoma T4N3Mx. Biopsy of the mass was taken and computed tomography (CT) images showed a heterogenous mass obliterating the entire nasopharynx and eroding into the right lateral pterygoid plate with metastasis to liver. He successfully underwent concurrent chemoradiotherapy and is now free of locoregional disease 1 year after his initial presentation as evidenced by post treatment nasoendoscopy and repeat CT scan.

### DISCUSSION

Nasopharyngeal carcinoma has a varying incidence rate based on geographical location, ranging from 1 per 100,000 person years in the United States to more than 15 per 100,000 person years in south eastern Asian populations (1). In such areas of endemicity, Epstein Barr virus (EBV) is highly associated with majority of the cases, and EBV appears necessary for the development of non-keratinizing squamous cell carcinoma of nasopharynx. In most cases, (>90%) the non-keratinizing type of NPC (NK-NPC) will show nuclear representation of the EBV with a wide range of histological morphology

(2). Rare morphologies can occur in up to 10 % of NPC cases in these endemic areas (3). The classical types of morphology seen in NK-NPC are the Regaud-pattern (tumour cells arranged as syncytial sheets) or the Schmincke-pattern (small nests and isolated malignant cells mixed with lymphocytes and plasma cells) (4). The rare variants of NK-NPC morphology are tumours consisting of spindle cells, clear cells, papillary, presence of bizarre tumor cells (Reed-Sternberg like), non-caseating granuloma, desmoplastic stromal reaction, amyloid globules, reticular cord like arrangement and also adenomatous differentiation (2-4). A retrospective study by F. Cheung *et al.*, identified only 3 cases of confirmed NPC with papillary configuration (5). We would like to present our case of a nasopharyngeal non-keratinizing carcinoma with unusual histologic pattern. The biopsy taken was a fragment of tissue measuring 13mm in aggregate diameter. Histologically the tumour tissue mainly appeared to be arranged in papillary architecture, sheets and nests. The papillary structure was composed of hyalinized fibrovascular core and was lined by dysplastic epithelium. The tumour cells were polygonal to spindle in shape with indistinct cytoplasmic border. On high power magnification, the neoplastic cells show loss of polarity with overt malignant features. The nuclei were moderately pleomorphic with vesicular appearances and prominent nucleoli and moderate amount of cytoplasm. Mitoses were readily identified. There was no gland formation or keratinization observed. (Fig. 1, Fig. 2). Based on the morphology, papillary variant had to be ruled out. The immunohistochemical studies showed that the neoplastic cells are strong and diffusely positive for p63 and CK5/6 (Fig. 3, Fig. 4). The p53 stain showed diffuse positivity while the epithelial membrane antigen (EMA) showed focal immunopositivity. CK7, CK20, and TTF-1 stains were not expressed. The initial histopathology examination gave us an impression of sinonasal non-keratinizing squamous cell carcinoma (NKSCC) due to the papillary

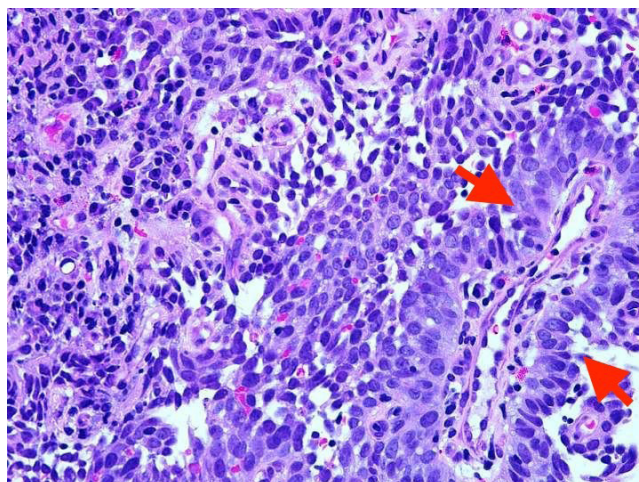


Figure 2: The neoplastic tumour exhibit papillary configuration with hyalinizing fibrovascular core lined by columnar epithelium (red arrows). The neoplastic cells are moderately pleomorphic, display round to oval vesicular to hyperchromatic nuclei, prominent nucleoli, and indistinct eosinophilic cytoplasm (H&E 400X).

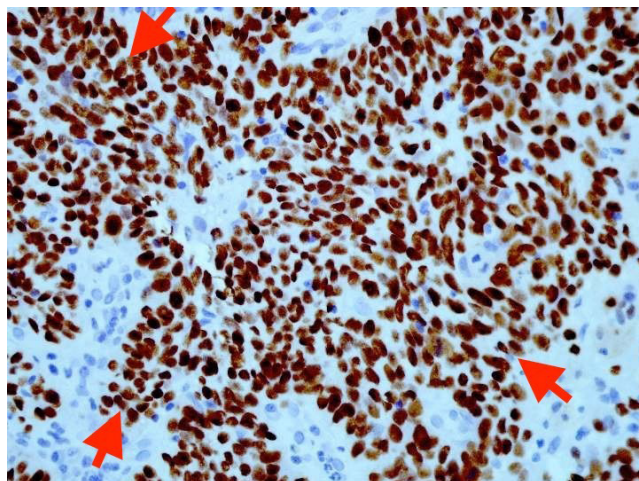


Figure 3: The tumour cells (red arrows) show strong nuclear expression (brown color)towards p63 (400X)

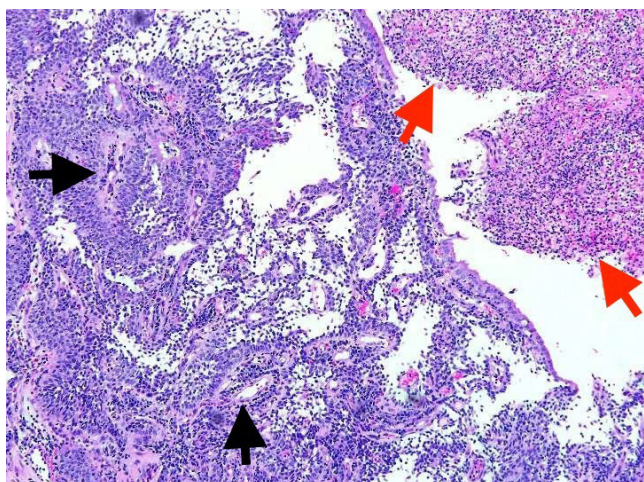


Figure 1: The tumour cells arranged in papillary architecture (black arrows) with adjacent necrotic tissue (red arrows) (H&E 200X).

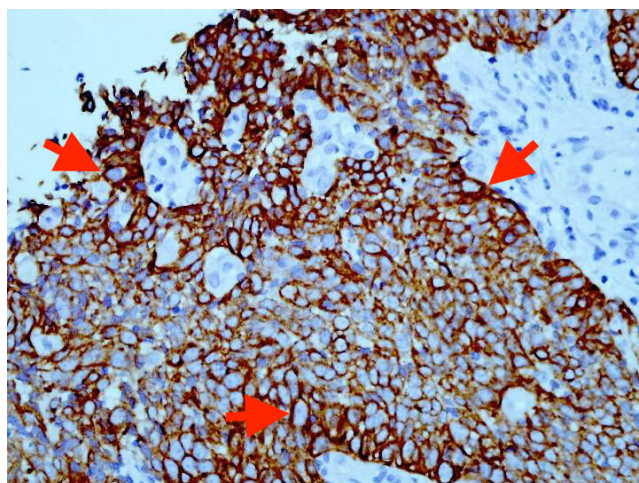


Figure 4: The tumour cells (red arrows) show membranous expression (brown color) towards CK5/6 (400X)

architecture. However, the radiological findings showing an ill-defined heterogenous mass from the nasopharynx encroaching into posterior nasal cavities was highly suggestive of nasopharyngeal carcinoma. The presence of multiple cervical lymphadenopathy also favoured nasopharyngeal carcinoma instead of sinonasal NKSCC. Given the papillarity with hyalinized fibrovascular core and loss of polarity, we also considered nasopharyngeal papillary adenocarcinoma (NPAC). However, due to the absence of glandular formation and no obvious nuclear features of papillary thyroid cancer (PTC) and negativity for CK7 and TTF-1, the likelihood of NPAC was low. In addition, diffuse positivity of p53 suggested that the tumour was of a high-grade nature as compared to NPAC which is a low grade tumour.

The histologic morphology and immunohistochemistry aided in procuring the diagnosis and excluding other sinister causes such as NPAC or sinonasal carcinoma. It is crucial for the pathologist reporting the biopsy sample and the treating physician reading the histopathology report to be aware of such variation or uncommon patterns. As a result, appropriate treatment regime was started, and patient responded well.

Despite this, it must be borne in mind that, the overall prognosis and outcome is dismal for this type of NPC (5) with high chances of locoregional failure. Treatment options that can be offered are either radiation therapy, or a combination of radiation therapy with cisplatin chemotherapy. The 5-year overall survival rate was reported as 75.6% in patients receiving both radiation therapy and chemotherapy. The rate dropped to 64.8% in patients receiving only radiation therapy alone (5).

## CONCLUSION

We wish to highlight a hitherto undescribed variant of non-keratinizing nasopharyngeal carcinoma morphology. The treating physician and the reporting

pathologist should always bear in mind such entities especially when dealing with limited tissue samples. Ancillary studies like immunohistochemistry are indispensable to diagnose such cases and differentiate it from other possible malignancies.

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