



## Case Report

## Nasopharyngeal papillary adenocarcinoma: A case report and clinicopathologic review

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## ABSTRACT

Nasopharyngeal papillary adenocarcinoma (NPAC) is an extremely rare malignant tumor derived from the nasopharyngeal surface epithelium, with only a limited number of cases reported in the literature. NPAC presents as a slow-growing exophytic mass, with an excellent prognosis and rare recurrence following appropriate surgical management. In contrast, ordinary nasopharyngeal carcinoma is typically accompanied by metastatic neck masses, and radiotherapy is the mainstay of treatment. The immunohistochemical profile supports the derivation of NPAC from the surface epithelium rather than from the subjacent minor salivary glands. This tumor most commonly involves the roof, lateral wall, and posterior wall of the nasopharynx. Nasal obstruction is the main presenting symptom. The diagnosis can be confirmed readily by endoscopic biopsy. This report describes NPAC in a 50-year-old man with symptoms of blood-tinged rhinorrhea and morning headache. The patient is currently well without tumor recurrence after surgical treatment.

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## 1. Introduction

Nasopharyngeal papillary adenocarcinoma (NPAC) is an uncommon primary tumor of the nasopharynx with no gender predilection. NPAC occurs over a wide age range from the 2<sup>nd</sup> to 7<sup>th</sup> decades of life (median age, 37 years). It may occur anywhere in the nasopharynx, but is most common in the posterior and lateral nasopharyngeal walls, and on the nasopharyngeal roof [1]. The most common symptom is nasal obstruction. Other symptoms may include otitis media with or without associated hearing deficits, and postnasal drip. There is no known association with carcinogens or Epstein-Barr virus. A single case has been reported in association with Turner syndrome [2].

## 2. Case report

A 50-year-old man was brought to Taipei Tzu-Chi General Hospital with complaints of blood-tinged rhinorrhea and morning

headache for 10 days. On clinical examination of the nasal cavity, a 7-mm nodular mass was noted in the left nasopharynx, and was biopsied. Physical examination of the neck revealed no abnormal mass.

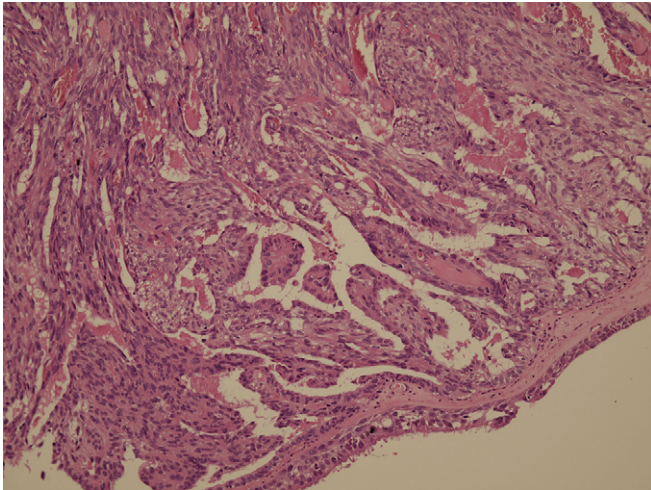
Histopathologic examination of the exophytic nasopharyngeal mass revealed a low-grade NPAC (Fig. 1). The tumor consisted of delicate arborizing papillary fronds and crowded glands lined by cuboidal or pseudostratified epithelium. The lining cuboidal cells had bland, round to oval nuclei, and tiny nucleoli. Mitotic figures were rare, and necrosis was not identified. The tumor was unencapsulated, and infiltrated into the surrounding stroma. Intraluminal and intracytoplasmic mucicarmine-positive material was identified. Immunohistochemical staining was reactive for cytokeratin (CK) and thyroid transcription factor-1 (TTF-1; Fig. 2) and negative for S100 protein and thyroglobulin.

A Tc-99 m MDP bone scan at 4 hours after injection revealed several faint spots in the right frontal sinus, maxilla, skull base, and T11, T12, L4, and L5 vertebrae, and both knee joints in the whole-body survey. There was mildly-increased activity of a radio-tracer, and the nature was hard to be determined by only the bone scan. Post-operative magnetic resonance imaging revealed no evidence of mucosal thickening in the nasopharynx and lymphadenopathy of the neck region. One month later, a nasopharyngectomy using a Diode laser was done, and there was no evidence of a tumor. Some nasal polyps were removed from the left maxillary sinus and the frontal

Conflict of interest: none.

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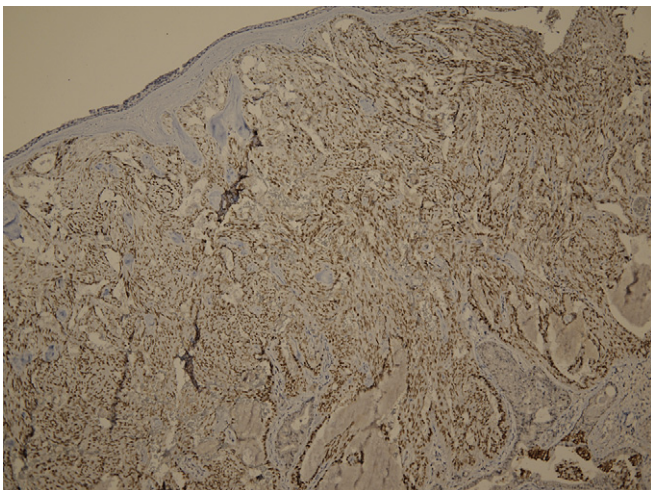
**Fig. 1.** Nasopharyngeal papillary adenocarcinoma shows arborizing delicate papillae and crowded glands lined by columnar or pseudostratified epithelial cells with bland, round to oval nuclei.

sinus. The operation was finished smoothly. The patient was regularly followed-up for 3 months, and no tumor recurrence was noted.

### 3. Discussion

The most common type of nasopharyngeal tumor is nasopharyngeal carcinoma. A broad range of additional neoplasms can arise in the nasopharynx, including epithelial, lymphoid, mesenchymal, and neurogenic tumors [3]. NPAC is rare, and only a limited number of cases have been reported in the English-language literature. The tumors range from 0.3 to 4.0 cm, and most often involve the roof, or the lateral or posterior walls of the nasopharynx. Patients range in age from 11 to 64 years (median age, 37), and the male-to-female ratio is 5:4 [4].

Macroscopically, the tumors are soft or gritty, and exophytic with a papillary, nodular, or polypoid appearance. These tumors are unencapsulated and infiltrative, and composed of papillary and glandular growth patterns on histopathologic examination. Papillary structures are complex, with arborization and hyalinized fibrovascular cores, and complex glandular patterns characterized



**Fig. 2.** Immunohistochemical staining shows reactivity for thyroid transcription factor-1.

by back-to-back and cribriform growth. Transition areas from normal nasopharyngeal surface epithelium to neoplastic proliferation are suggestive of derivation from surface epithelium [1].

The tumor cells vary in appearance from pseudostratified columnar to cuboidal. Nuclei are round to oval with a vesicular to optically-clear chromatin pattern; the cytoplasm is eosinophilic. Mild to moderate nuclear pleomorphism and loss of basal polarity are seen, but nucleoli, mitoses, and necrosis are uncommon. Vascular, lymphatic, and neural invasion are not seen. Petersson et al, reported a case of thyroid-like, low-grade NPAC with a significant spindle cell component [5].

The tumor cells were positive for intracytoplasmic diastase-resistant, periodic acid-Schiff-positive material. Intracytoplasmic and intraluminal mucicarmine provides evidence for epithelial mucin. Immunohistochemical stains are diffusely reactive for CK and epithelial membrane antigen, and focally reactive for carcinoembryonic antigen. TTF-1 is positive in nasopharyngeal adenocarcinoma, and is generally used in histopathologic examination as a marker to determine if a tumor has arisen from the lung or thyroid. TTF-1 positive cells are found in the lung as type II pneumocytes and Clara cells. In the thyroid, follicular and parathyroid cells are also positive for TTF-1. Among cancers of the lung, adenocarcinomas are usually TTF-1 positive, while squamous cell carcinomas and large cell carcinomas are rarely positive. Small cell carcinomas are usually positive. TTF-1 is also positive in thyroid cancer, and is used to monitor for metastasis and recurrence.

The tumor had no immunoreactivity with thyroglobulin, S100 protein, or glial fibrillary acidic protein. The differential diagnoses included papillary thyroid carcinoma, low-grade papillary adenocarcinoma of salivary gland origin, and a papillary variant of intestinal-type adenocarcinoma. Because of the papillae, the occasional psammoma bodies, and optically-clear nuclei, NPAC can easily be mistaken for metastatic papillary thyroid carcinoma. NPAC, however, is negative for thyroglobulin, and will typically show dysplasia or *in situ* changes of the surface epithelium.

Distinguishing a papillary variant of intestinal-type adenocarcinoma from NPAC may be more problematic. The former in contrast to NPAC, occurs primarily in the nasal cavity and paranasal sinuses, and is often associated with occupational exposure to wood dust. This variant also tends to be less glandular and more papillary. Rather than cuboidal cells, the papillae are covered by tall columnar and goblet cells, the latter of which are sparse to absent in NPAC. The papillary variant of intestinal-type adenocarcinoma may also contain Paneth cells and scattered endocrine cells that may express somatostatin, gastrin, serotonin, and/or other secretory substances that can be revealed on appropriate staining. Such cells are not seen in NPAC. NPAC is CK7 positive, but CK20, CDX-2, and villin negative. All intestinal-type adenocarcinomas are positive for CK20, CDX-2, and villin, and some are CK7-positive [6]. The expression pattern of CK7, CK20, CDX-2, and villin positivity may be useful in separating these tumors from other nonintestinal-type adenocarcinomas of the sinonasal tract and nasopharynx.

Low-grade papillary adenocarcinoma of salivary gland origin occurs almost exclusively in the oral cavity, especially in the palate. Furthermore, it arises submucosally from minor salivary glands rather than from the surface epithelium, as does NPAC. Staining for S-100 protein may also be helpful. Thus far, NPAC has been reported negative for S-100 protein, whereas low-grade papillary adenocarcinomas of the salivary gland origin are usually positive. The latter are also more aggressive, with frequent local recurrence (27%), and at times, lymph-node metastasis (17%) [7].

NPAC is a slow-growing, indolent neoplasm that rarely recurs, and thus far there are no reports of metastasis to either the cervical lymph nodes or more distant sites [1,3,8]. The treatment of choice is simple and complete surgical excision. Patients with low-grade

adenocarcinoma have a good prognosis. Most patients have localized disease at presentation, and do not require radical surgical procedures for complete resection [8]. The value of radiotherapy is unknown. Recurrences developed in as many as 30% of the cases of low-grade adenocarcinoma of the sinonasal tract reported by Heffner et al [9]. Postoperative adjuvant photodynamic therapy for an incompletely resected primary NPAC can cure an otherwise difficult-to-treat disease with preservation of a good quality of life for the patient. Potential complications of photodynamic therapy (e.g., photosensitivity) can be prevented by a special formulation of topical 5-aminolevulinic acid [10].

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