Case Report
Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma originating from the nasal septum

Bo-Nien Chen¹,³, Shiuan-Li Wey²

Departments of ¹Otolaryngology-Head and Neck Surgery, ²Pathology, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan; ³Mackay Junior College of Medicine, Nursing and Management, New Taipei, Taiwan

Received December 8, 2017; Accepted July 12, 2018; Epub October 15, 2018; Published October 30, 2018

Abstract: Objectives: Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma (TL-LGNPPA) was first described in 2005. TL-LGNPPA is an extremely rare neoplasm that predominantly occurs in the nasopharynx and at the posterior edge of the nasal septum. Only a few cases of TL-LGNPPA have been reported in English-language literature to date. Methods: We report the case of a 34-year-old woman with TL-LGNPPA originating at the left posterior end of the nasal septum. A brief review of the clinical, morphological, and immunohistochemical characteristics of TL-LGNPPA was conducted. Results: The patient had neither local recurrence nor distant metastasis 3.5 years after surgical resection of the tumor. Conclusion: We present a novel case of TL-LGNPPA originating from the nasal septum. Physicians should be aware of this entity; it is rare but amenable to surgical resection and carries an excellent prognosis.

Keywords: Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma, nasal septum, thyroid transcription factor-1

Introduction

Primary nasopharyngeal adenocarcinoma is rare, comprising < 0.5% of malignant nasopharyngeal neoplasms, and can be classified into two subtypes: the surface origin type and the salivary gland type. The surface origin type is usually a low-grade malignancy with papillary and glandular features, such as low-grade nasopharyngeal papillary adenocarcinoma (LGNPPA), which likely originates from the nasopharyngeal surface mucosa, whereas the salivary gland type includes tumors such as mucopidermoid adenocarcinomas, adenoid cystic carcinomas, and polymorphous low-grade adenocarcinomas [1].

LGNPPA was first described by Wenig et al. in 1988 and included in the World Health Organization classification system of malignant epithelial tumors of the nasopharynx in 2005 [2, 3]. However, thyroid-like LGNPPA (TL-LGNPPA) with nuclear positivity for thyroid transcription factor-1 (TTF-1) was first described by Carrizo et al. in 2005 [4]. TL-LGNPPAs represent a small minority of LGNPPAs and are characterized by abnormal expression of TTF-1, mimicking papillary thyroid carcinoma (PTC) [1]. Only seventeen cases of TL-LGNPPA have been reported in English-language literature to date [1, 5-7]. In this study, we report an extremely rare case of TL-LGNPPA originating in the nasal septum and provide a brief review of its clinical, morphological, and immunohistochemical characteristics.

Case report

A 34-year-old woman was referred to our hospital for a nasal septum tumor that had been incidentally discovered by a local medical doctor. She denied any nasal symptoms, and there were no remarkable physical or laboratory test findings.

On endoscopic nasal examination, a tumor was observed at the left posterior end of the nasal septum. Computed tomography (CT) with contrast revealed a 0.5 × 0.3-cm polypoid tumor at the posterior end of the left nasal septum with no evidence of bone destruction (Figure 1A).
No cervical lymph node abnormalities were determined through CT.

The patient subsequently underwent tumor biopsy. Histopathological examination demonstrated that the tumor comprised arborizing delicate papillary fronds and crowded glands. The lining columnar or pseudostratified cells had bland, round-to-oval nuclei and small nucleoli. Mitotic figures were rare, and the tumor was focally connected with the epithelium. All histologic features were compatible with those of low-grade papillary adenocarcinoma (Figure 2A and 2B). Immunohistochemistry results showed that tumor cells were positive for TTF-1 (Figure 2C) but negative for thyroglobulin (TG; Figure 2D). Histopathological examination and immunohistochemical studies together confirmed the diagnosis of TL-LGNPPA.

A bone scan subsequently confirmed no metastatic lesions; ultrasonography was used to evaluate the thyroid gland and no abnormality was detected, and thyroid function tests confirmed that the patient was euthyroid.

The patient then underwent complete excision of the tumor through resection of the posterior part of the nasal septum under endotracheal general anesthesia. No postoperative adjuvant treatment was administered, and the patient’s postoperative course was uneventful (Figure 1B and 1C). There was neither local recurrence nor distant metastasis 3.5 years after surgical resection of the tumor.

Discussion

TL-LGNPPA is an extremely rare neoplasm characterized by a morphological analogy to PTC and an aberrant TTF-1 expression. The age of presenting patients ranges from 9 to 68 years (median, 35 years) with a male: female ratio of 1:1 [7]. TL-LGNPPA predominantly occurs in the roof of the nasopharynx and at the posterior edge of the nasal septum and commonly presents as nasal obstruction and less often with epistaxis [1, 5-7]. Horino et al. also reported a case of TL-LGNPPA presenting with fever of unknown origin and hypothesized that overexpression of TTF-1 in the tumor may have induced the local expression of IL-6. This may subsequently have stimulated the hypothalamus, which was in close proximity to the tumor, ultimately leading to fever [1].

Histologically, TL-LGNPPA frequently exhibits papillary architecture lined by moderately pleomorphic columnar epithelial cells with fibrovascular cores, overlapping nuclei with clear optically chromatin, and psammoma bodies. These features are also generally ascribed to PTC. However, four case reports have described a biphasic pattern of TL-LGNPPA with a spindle cell component [1, 8-10], although no obvious spindle cell component was observed in the current case.

Immunohistochemically, TL-LGNPPA is positive for TTF-1, pancytokeratin (AE1/AE3), cytokeratin (CK)7, CK19, vimentin, and HBME1, but negative for TG, Pax8 and CK5/6 [10]. The most common characteristic of TL-LGNPPA is TTF-1 positivity, and this has been noted in every reported case [1, 5-7]. TTF-1 is a 38-kD tissue-
specific transcription factor that is important in the development of epithelial cells of the lung and thyroid [6]. Although the etiology of TTF-1 positive staining in TL-LGNPPA is unclear, three mechanisms have been proposed to explain this phenomenon. First, TL-LGNPPA may develop from the ectopic thyroid tissue; second, a gene rearrangement that affects TTF-1/NKX2-1 may result in an abnormal expression of TTF-1; and finally, genetic instability and reprogramming of cancer cells can cause disdifferentiation and lead to the deregulation of TTF-1/NKX2-1 [7].

TL-LGNPPA shows a striking resemblance to PTC, and it is therefore important to exclude nasopharyngeal metastasis from PTC to enable accurate diagnosis and treatment of the patient and associated prognosis [7]. TL-LGNPPA is usually negative for TG, whereas PTC is diffusely positive for TG, and this finding strongly emphasizes the importance of immunostaining for TG to make a differential diagnosis [1]. However, a case of TL-LGNPPA with a focal expression of TG has previously been reported [11]. Despite the morphological and immunohistochemical similarity to PTC, no mutations at position 1799 (exon 15) in the BRAF-gene (BRAFV600E) or in exons 9 and 11 of the KIT gene have been detected in the molecular genetic studies of TL-LGNPPA [9, 10].

With the exception of PTC, there are limited options available to make a differential diagnosis of a papillary lesion in the nasopharynx. Polymorphous low-grade papillary adenocarcinoma is more aggressive and positive for vimentin and S100-protein. To date, positivity for TTF-1 has not been reported in polymorphous low-grade papillary adenocarcinoma. Papillary variants of the intestinal type of adenocarcinoma are more nuclear atypical and commonly display mucinous differentiation. Moreover, these are often positive for CK20 and CDX2. Acinic cell carcinomas with a papillary component are frequently cystic and variably positive for S100-protein and vimentin according to the range of differentiation. However, extraventricular choroid plexus papillomas at unusual localities should be taken into consideration because most of them are positive for S100 and negative for EMA and some are positive for GFAP [7].

The prognosis for TL-LGNPPA is excellent because all cases reported to date have been cured by complete surgical excision, and local recurrence or metastasis have not been reported in any of these cases [1, 5-7].

Conclusion

In conclusion, we present a novel case of TL-LGNPPA and provide a review of the associated main clinicopathological features. This
Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma

neoplasm presents rarely; therefore, physicians should be aware of this entity. In addition, it is amenable to surgical resection and carries an excellent prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Bo-Nien Chen, Department of Otolaryngology-Head and Neck Surgery, Hsinchu MacKay Memorial Hospital, No. 690, Sec. 2, Guangfu Road, East Dist, Hsinchu 30071, Taiwan. Tel: +886 36119595; Fax: +886 36110900; E-mail: chenbonien@yahoo.com.tw

References