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Thyroid-Like Low-Grade Nasopharyngeal Papillary Adenocarcinoma

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Abstract
Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma (TL-LGNPPA) is a rare entity. Patients often present with complaints of nasal fullness, obstruction, and epistaxis. It may be confused with metastatic papillary thyroid carcinoma due to its histologic similarity and overlapping immunohistochemical studies, but it is important to distinguish between the two because of differing treatment modalities and prognosis. A significant difference between the two is that despite both entities demonstrating TTF-1 positivity, TL-LGNPPA usually does not stain for thyroglobulin. TL-LGNPPA exhibits indolent growth, with no incidence of metastasis or recurrence after surgical excision.

Keywords Thyroid-like low-grade nasopharyngeal papillary carcinoma · Nasopharynx · TTF-1 · Papillary adenocarcinoma

History

A 26 year old male presented with a complaint of headaches; characterized as global and pounding in nature with nausea, light-sensitivity, dizziness, and sound-sensitivity. He reported some nasal congestion of fluctuating severity as well as epistaxis. The episodes of epistaxis occurred up to twice a day, each lasting a maximum of 15 minutes in duration.

Radiographic Features

A multiplanar MRI without contrast demonstrated an 8 mm soft tissue density polypoid lesion at the junction of the posterior nasal cavity and nasopharynx (Fig. 1). A background of moderate inflammatory paranasal sinus disease was noted. Sinonasal polyposis was considered likely and ENT evaluation recommended.

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Diagnosis and Treatment

An excisional biopsy was performed and entirely submitted for histopathologic evaluation. Microscopic examination revealed a polypoid mass with a distinctly papillary proliferation underlying the normal mucosa (Fig. 2). The cells showed pale eosinophilic cytoplasm and round to oval, vesicular nuclei. In some cells, clear inclusion bodies or a "ground glass" appearance of the chromatin lended an "orphan Annie eye" presentation. Nuclear grooves and overlapping nuclei were also appreciated. Glandular areas with intraluminal secretory material were identified (Fig. 2). The stroma contained areas of dense hyalinization. Psammoma bodies were noted in the specimen (Fig. 2). Immunohistochemical studies revealed positivity to TTF-1, CK 7 and EMA. The tumor cells were negative for CK5/6 and thyroglobulin.

Discussion

Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma is a rare entity; to date, only 27 cases have been reported [1]. This tumor is most frequently found in patients in the 4th decade of life and does not appear to have a sex predilection [2]. TL-LGNPPA most frequently occurs in the nasopharynx and posterior edge of the nasal septum [3]. It presents as a polypoid or nodular growth and most frequently presents with nasal obstruction, fullness, epistaxis

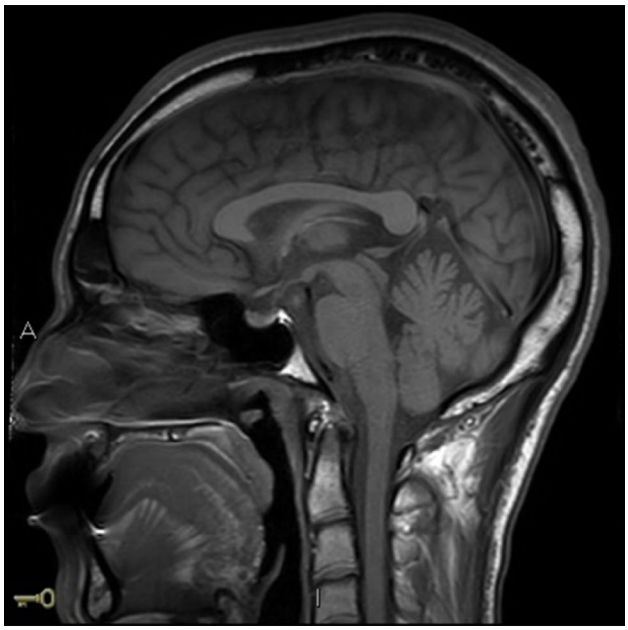

Fig. 1 Multiplanner MRI without contrast showing polypoid lesion at junction of the posterior nasal cavity and nasopharynx

or non-descript sinus complaints [4]. There is one reported case with the only presenting symptom being a fever of unknown origin. In this instance it was hypothesized that TTF-1 increased the expression of IL-6, which, due to its close proximity stimulated the hypothalamus, resulting in a fever [3]. Fever has not been reported in other patients.

Histologically, TL-LGNPPA has a papillary configuration with fibrovascular cores and can include intra-nuclear cytoplasmic inclusions, nuclear grooving, ground glass nuclei, psammoma bodies and colloid. Mitotic figures are rare. A distinguishing feature of this entity is its diffuse positivity of staining with thyroid transcription factor-1. Thyroid transcription factor-1 is a protein composed of 371 amino acids and is encoded by the NKX2-1 gene on chromosome 14q13 [5]. TTF-1 is most commonly expressed in thyroid and lung and can be used to distinguish cancers occurring metastatically from primaries in these locations [6]. Recently, however, evidence has come to light that TTF-1 positivity can be found in association with carcinomas arising from non-lung or thyroid organs, such as ovaries, endometrium, breast, colon and central nervous system [5]. There has been no reported evidence of Epstein–Barr virus (EBV) or human

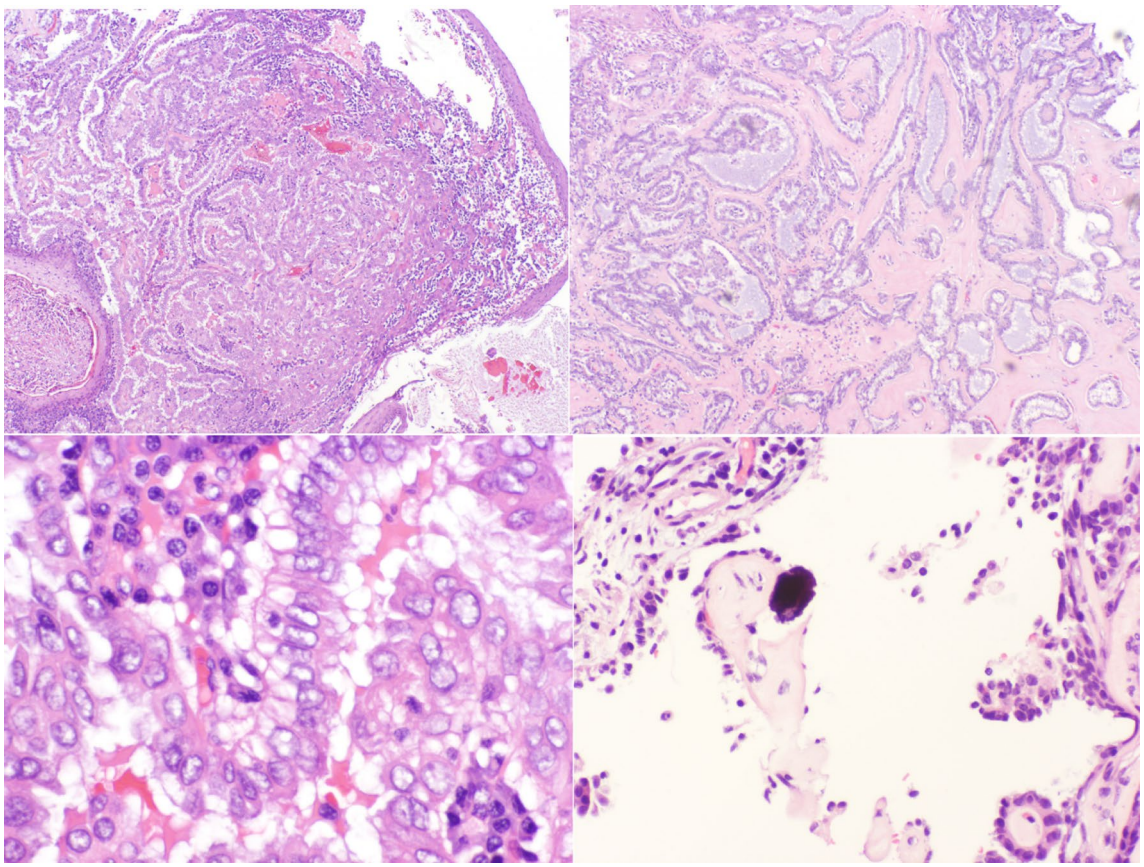

Fig. 2 Top left: ×40 view of TL-LGNPPA showing the papillary proliferation underlying normal mucosa. Top right: ×40 view of glandular areas of the lesion showing the intraluminal secretory material. Bottom left: ×400 view of "orphan Annie eye" and overlapping nuclei. Bottom right: ×200: psammoma body

papilloma virus (HPV) causative relationship [7]. This could help with diagnosis as most nasopharyngeal carcinomas are associated with EBV [8].

Due to its histologic appearance and the possibility of a more significant diagnoses, it is imperative that the practitioner rule out a metastatic papillary thyroid carcinoma. Since both entities stain with TTF-1, thyroglobulin negativity in TL-LGNPPA is helpful as a distinguishing feature [9]. However, Ozer et al. presented a case in 2013 of TL-LGNPPA that expressed focal thyroglobulin positivity. In instances such as this, care should be taken to rule out a metastatic papillary thyroid carcinoma.

Local excision is the treatment of choice for this entity and there have been no reported cases of recurrences or metastasizes. Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma is a rare entity but should be included in a microscopic differential of lesions in the nasopharynx that present with a papillary architecture. Given the benign pathologic course and lack of evidence for metastasis and recurrence, adenocarcinoma may be the incorrect terminology for this entity. Future consideration of reclassifying TL-LGNPPA as an adenoma may be considered.

The views expressed in this article reflect the results of research conducted by the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the United States Government.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of retrospective case report, formal consent is not required. The tumor tissue included in the manuscript was obtained as part of the standard of care for the patient and retrospectively collected for the case report.

Informed Consent No identifier information is included in the case report.

References

1. Li L, Zhou F, Lin F, Han C. Clinicopathologic characteristics of thyroid-like low-grade nasopharyngeal papillary adenocarcinoma: a case report. Appl Immunohistochem Mol Morphol. 2018;60(00):1–4.
2. Thomspon LDR. Nasopharyngeal papillary adenocarcinoma. Ear Nose Throat J. 2017;96(12):456–7.
3. Horino T, Osamu I, Kazu H-O, Tatsuki M, Shimamura Y, Inoue K, Terada Y. Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma: a case report. Mol Clin Oncol. 2016;5:693–6.
4. Dina NH, Gendeh BS. The rare primary low grade papillary adenocarcinoma of nasopharynx: a diagnostic challenge and management. Med Health. 2015;10(2):137–40.
5. Ordóñez N. Value of thyroid transcription factor-1 immunostaining in tumor diagnosis: a review and update. Appl Immunohistochem Mol Morphol. 2012;20(5):429–44.
6. Rajeswari B, Nair RKS, Parukuttyamma K, Mathews A. Low-grade papillary adenocarcinoma of nasopharynx with expression of thyroid transcription factor-1: case report and review of literature. Indian J Pathol Microbiol. 2016;59(4):518–20.
7. Zhang W-L, Ma S, Havrilla L, Cai L, Yu C-Q, Shen S, Xu H-T, Liang W, Yu J-H, Lin X-Y, Wang E, Yang L-H. Primary thyroid-like low-grade nasopharyngeal papillary adenocarcinoma: a case report and literature review. Medicine. 2017;96(47):1–4.
8. Ohe C, Sakaida N, Tadokoro C, Fukui H, Asako M, Tomoda K, Uemura Y. Thyroid-like low-grade nasopharyngeal papillary adenocarcinoma: report of two cases. Pathol Int. 2010;60:107–11.
9. Huang C-H, Chang Y-L, Wang C-P, Wu H-P. Positive immunostaining of thyroid transcription factor-1 in primary nasopharyngeal papillary adenocarcinoma. J Formos Med Assoc. 2015. https://doi.org/10.1016/j.jfma.2013.04.012.