Low-grade papillary adenocarcinoma of nasopharynx with expression of thyroid transcription factor-1: Case report and review of literature

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ABSTRACT

Low-grade papillary adenocarcinomas with expression of thyroid transcription factor-1 (TTF-1) are rare tumors of the nasopharynx, with only a few cases reported in the literature. These tumors have an excellent prognosis following complete surgical excision. We report a 13-year-old boy with this rare tumor in the nasopharynx. The patient underwent complete surgical excision of the tumor and was on follow-up without evidence of recurrence.

KEY WORDS: Low-grade papillary adenocarcinoma, nasopharynx, thyroid transcription factor-1

INTRODUCTION

Nasopharyngeal adenocarcinomas (NPACs) are rare tumors, especially in childhood accounting for <0.5% of nasopharyngeal carcinomas. Thyroid transcription factor-1 (TTF-1) is a tissue-specific transcription factor commonly expressed in thyroid and lung cancers, rarely reported to be expressed in NPACs. Here, we report a case of low-grade NPAC with expression of TTF-1 and a brief review of the literature.

CASE REPORT

A 13-year-old boy presented with a history of nasal obstruction of 2 months duration, which was worse at night. He also had a single episode of epistaxis which was mild. On examination, he did not have any obvious swelling of the nose, proptosis, or significant lymph node enlargement. He was evaluated with a computed tomography (CT) scan of the paranasal sinuses which revealed a polypoidal lesion in the nasopharynx reaching up to the choana, with no evidence of bone destruction [Figure 1]. The possibility of adenoid hypertrophy was considered, and surgical excision of the lesion was performed.

The histopathologic examination showed an adenocarcinoma with a papillary–glandular pattern with luminal secretory material [Figure 2]. The papillae were complex with delicate fibrovascular cores. These were lined by cuboidal to low columnar epithelium with round to oval, vesicular nuclei with mild atypia, nuclear overlapping, and pale eosinophilic cytoplasm with secretory feature. Mitotic activity was inconspicuous. The overall morphology resembled papillary carcinoma of the thyroid (PTC). On immunohistochemistry, there was a diffuse and strong expression of cytokeratin 7 and patchy expression of TTF-1 [Figure 3] in the tumor cells. Cytokeratin 20 and thyroglobulin were negative. An evaluation of the thyroid did not reveal any abnormality.

Postoperative CT scan showed only minimal thickening in the nasopharynx. There was no evidence of residual disease in the tumor bed. There was an enlarged left cervical level II lymph node of size 23 mm x 12 mm. Fine-needle aspiration cytology from the lymph node showed no involvement by the disease. Nasal endoscopy was also done, and there was no definite mass in the nasopharynx. He has completed 1 year of follow-up with no evidence of recurrence.

DISCUSSION

NPACs are rare tumors. They constitute <0.5% of NPACs.[1] Primary
NPACs have been classified based on their morphology and clinical behavior as low-grade nasopharyngeal papillary adenocarcinoma (LGNPPA) of surface origin type and salivary gland-type adenocarcinomas. These tumors usually arise from the roof, lateral wall, and posterior wall of the nasopharynx and present commonly with nasal obstruction and less often with epistaxis.

TTF-1 is a 38 kD tissue-specific transcription factor important in the development of the epithelial cells of the lung and thyroid. The expression of TTF-1 is, therefore, most commonly used in the diagnosis of lung and thyroid cancers. Initially, it was thought to be very specific for these cancers. However, recently, it has also been found to be expressed in carcinomas of ovaries, endometrium, bladder, and colon – both in the primary and metastatic sites.[2] TTF-1 is also expressed in neuroendocrine tumors of both pulmonary and nonpulmonary origins. Expression of TTF-1 has been very rarely reported in LGNPPA.[3-8]

Morphologically, these tumors resemble PTC. They show strong positivity for TTF-1 but are negative for thyroglobulin. A review of literature showed that these tumors are designated by some authors as thyroid-like LGNPPA.[3-5]

In the largest series of 44 cases of NPACs reported in the literature (age range of 9–74 years) with a follow-up over 15 years, there were only 13 conventional LGNPPAs of surface origin type. The remaining were salivary gland-type adenocarcinomas (28 cases) or metastatic adenocarcinomas from a primary in the thyroid (2 cases) and lung (1 case).[9] Patients with LGNPPA had a far better outcome than those with salivary gland-type adenocarcinomas. [9] All the 13 patients were alive at 5–20 years with no evidence of disease following complete surgical excision. In contrast, in the group of salivary gland-type NPAC, 18 (64.2%) of the 28 patients had died of the disease or were alive with evidence of disease at the last follow-up.

There is a histologic similarity between PTC and LGNPPA. The presence of cervical lymph node enlargement and the TTF-1 positivity could also suggest the differential diagnosis of PTC. However, on follow-up, the lymph node regressed completely without any further treatment. There was no palpable thyroid nodule. He has now completed 1 year of follow-up with no evidence of recurrence or reappearance of the lymph node. The fact that tumor cells were negative for thyroglobulin on immunohistochemistry is also against a diagnosis of PTC.

Petersson et al. have reported a case of biphasic LGNPPA arising from the posterior nasal septum. In this report, they have done a molecular genetic study to assess the mutation status of BRAF gene as these mutations are estimated to occur in 60–70% of PTCs, especially the BRAF V600E mutation. However, in their case, no mutation was detected.[6] Oishi et al. have also reported the absence of the BRAF V600E mutation in a case of thyroid-like LGNPPA.[7] However, we do not have facilities for doing this mutation study, hence was not done.

**CONCLUSION**

Nasopharyngeal low-grade papillary adenocarcinomas including those with expression of TTF-1 are a group of tumors that can
morphologically mimic PTC but lacks thyroglobulin expression. These have an excellent prognosis and can be treated with complete surgical resection alone. Recurrences are rare following surgery. Pathologist and oncologists should be aware of the different types of NPACs because their clinical behavior, treatment, and prognosis differ considerably.

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Conflicts of interest
There are no conflicts of interest.

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