



Sinonasal Non-Intestinal Type Adenocarcinoma of the Nasopharynx: A Case Report

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Abstract

Sinonasal non-intestinal type adenocarcinoma is a rare head and neck cancer characteristically found in the nasal cavity and paranasal sinuses. A 17 year old female, with a history of infantile acute lymphoblastic leukemia and total body irradiation, presented with a mass in the nasopharynx. The patient underwent full excision of the mass with final pathology confirming non-intestinal type adenocarcinoma of the nasopharynx. This has previously been described in one adult patient. We present the first case of sinonasal non-intestinal type adenocarcinoma of the nasopharynx in a pediatric patient.

Introduction

Sinonasal Non-Intestinal Type Adenocarcinoma (Non-ITAC) is a tumor of seromucous gland origin characterized by a respiratory-type profile [1]. It is a rare head and neck cancer found in the nasal cavity and paranasal sinuses [2]. We present an extremely rare case of Non-ITAC originating in the nasopharynx of a pediatric patient. To our knowledge, this is the second case of non-ITAC of the nasopharynx to be reported, and the first in a pediatric patient.

Case Presentation

A 17-year-old female with a past medical history significant for infantile Acute Lymphoblastic Leukemia (ALL), presented with a 2-week history of tasting blood. There were no other symptoms such as headache, nasal obstruction, rhinorrhea or epistaxis. She had undergone chemotherapy and Total Body Irradiation (TBI) at 10 months of age, in remission since that time. Nasopharyngoscopy was performed revealing a large vascular mass in the nasopharynx with dried blood but no active bleeding (Figure 1).

Magnetic Resonance Imaging (MRI) was obtained and confirmed the presence of a homogenous 2.4 cm oval mass in the middle nasopharynx. There was associated moderate narrowing of the nasopharyngeal airway. The mass was isointense to adjacent tissue. A 1.6 cm mass of the right thyroid was incidentally found (Figure 2). A Magnetic Resonance Angiography (MRA) scan revealed mild arterial enhancement of the mass, but no evidence that it was a high flow vascular lesion.

A transoral biopsy was obtained and a friable mass was noted coming from the posterior pharyngeal wall, adjacent to the tori and choana (Figure 3). Histological examination resulted in a differential diagnosis of sinonasal low-grade Non-ITAC, mucoepidermoid carcinoma, Acinic Cell Carcinoma (ACC), myoepithelial tumor, and secretory carcinoma. However, due to the small size of the biopsy, it was difficult to make a definitive diagnosis.

The patient was taken back to the operative room for a repeat transoral biopsy which showed a well-circumscribed tumor underneath a squamous epithelium adjacent to minor salivary gland tissue. The tumor was largely composed of cells with abundant eosinophilic cytoplasm and bland appearing nuclei with scattered microcystic spaces filled with mucinous material (Figure 4A and 4B). Cells were arranged in ribbons, glands and solid sheets with a vague lobular pattern. Focally the tumor cells showed nuclear pleomorphism (Figure 4C). Mitoses were rare and no tumor necrosis or vascular invasion was noted.

Due to the patient's two childhood malignancies, she was evaluated by a genetic counselor. DNA testing was negative for Constitutional Mismatch Repair deficiency and Li-Fraumeni syndrome. It was concluded that her secondary cancer was most likely a result of her previous radiation therapy.

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Figure 1: Trans-nasal view of nasopharyngeal lesion with flexible nasopharyngoscope.



Figure 3: Trans-oral view of the friable mass coming from the posterior pharyngeal wall, adjacent to the tori and choana.

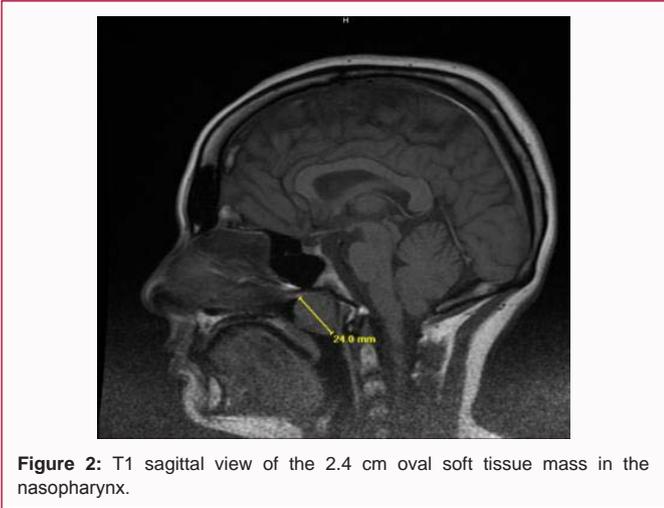


Figure 2: T1 sagittal view of the 2.4 cm oval soft tissue mass in the nasopharynx.

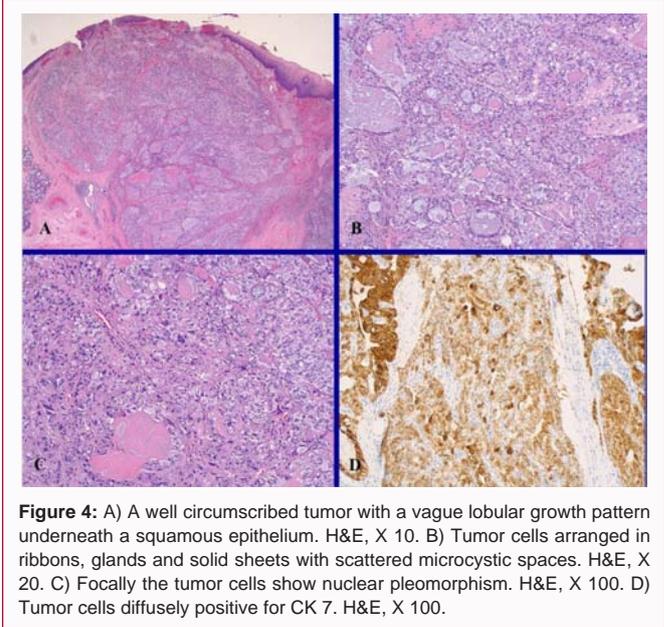


Figure 4: A) A well circumscribed tumor with a vague lobular growth pattern underneath a squamous epithelium. H&E, X 10. B) Tumor cells arranged in ribbons, glands and solid sheets with scattered microcystic spaces. H&E, X 20. C) Focally the tumor cells show nuclear pleomorphism. H&E, X 100. D) Tumor cells diffusely positive for CK 7. H&E, X 100.

Regarding her previous malignancy, the patient was diagnosed with ALL at 10 months of age. She underwent TBI and received a total of 1200 cGy. Her chemotherapy regimen consisted of Vincristine, L-asparaginase, Daunorubicin, Cyclophosphamide, Prednisone, Anthracycline, Etoposide and Methotrexate. She underwent allogeneic bone marrow transplant 1 month following TBI. She then received a 600 cGy pleural boost of radiation 1 month following the transplant. Unfortunately, the patient’s history has been further complicated with diabetes mellitus type 2, hypothyroidism, growth hormone deficiency, cataracts, osteochondromas, hypercholesteremia, café-au-lait spots, and pulmonary function testing abnormalities.

Following the second biopsy results, the decision was made to proceed with excision of the mass followed by post-operative proton therapy. An Endoscopic Expanded Endonasal (EEE) approach was used to resect the tumor, with a transoral approach for the most inferior portion. The resection was done by first performing a wide sphenoidotomy and removing the floor of the sphenoid and the underlying nasopharyngeal mucosa. A posterior septectomy was used to provide enough access to the nasopharynx. The nasopharyngeal mucosa was then removed completely down to the underlying bone of the clivus with lateral margins to the torus tubarius, and the inferior margin inferior to Passavant’s ridge.

On pathology, the tumor showed similar morphology as that seen in the previous biopsy specimen and surgical margins free of tumor. Final pathology confirmed the diagnosis of nasopharyngeal Non-ITAC. Due to the safe margins and the increased risk of additional

malignancy with further radiation, the decision was made to closely monitor the patient in clinic for recurrence rather than move forward with radiation.

Aside from post-operative pain, the patient’s only other complaint was voice change as she exhibited Velopharyngeal Insufficiency. However, at her 2-month follow up, flexible nasopharyngoscopy revealed full closure of the palate with normalization of her voice resonance. She has now been followed by our clinic 9 months post-excision with no complications and no evidence of recurrence.

A thyroid ultrasound was performed to follow up on the mass noted in the MRI at original admission. It revealed small bilateral thyroid nodules. Fine needle aspiration exhibited atypia of undetermined significance. Due to the presence of bilateral nodules and history of radiation, a total thyroidectomy was performed. Final histopathology confirmed the diagnosis of microscopic papillary thyroid carcinoma, the patient’s third childhood malignancy.

Discussion

The World Health Organization (WHO) classifies Non-ITAC as a tumor of the nasal cavity and paranasal sinuses. It is classified as a non-salivary gland-type adenocarcinoma, distinct from the salivary-type carcinomas [3]. The non-salivary gland-type adenocarcinomas are divided into intestinal-type adenocarcinoma and Non-ITACs, which is further, subdivided into high-grade and low-grade. The low-grade non-ITAC is an uncommon tumor, representing only 13% of

sinonasal adenocarcinomas [4]. These tumors are difficult to diagnose as they are markedly heterogeneous [5]. Immunohistochemistry often enables diagnosis as the tumors commonly stain positive for CK7 and negative for CK20, CDX2, and villin, demonstrating a respiratory-type profile rather than an intestinal-type [5].

This case was diagnostically challenging; therefore, specimens were sent to two outside institutions for consultation. Extensive immunohistochemical stains were performed. The tumor was strongly positive for CK 7, pancytokeratin, very focally positive for SOX-10, and negative for P63, calponin, S100, mammaglobin, CK 20, CDX2, p40, and CK5/6 (Figure 4D). Ki-67 proliferation index was approximately 2%. The immunostaining pattern was not supportive of a diagnosis of mucoepidermoid tumor, which is typically CK5/6 and p63 positive, and CK7 negative, also morphologically no epidermoid component was noted. Diagnoses of myoepithelial tumor, secretory carcinoma and adenoid cystic carcinoma were also unlikely based on the tumor morphology and negative immunostains of S100, calponin, and mammaglobin. ACC's are typically positive for SOX-10 and DOG1, which is a marker of salivary acinar cells. In this case, DOG1 was reported positive at one of the institutions. However, the other institution had a negative DOG1 stain in the initial and second biopsy specimen. The tumor also showed only a very focally positive stain for SOX-10 making a diagnosis of ACC less favored. The aggregate of tumor morphological features and immunostaining profile overall fit best with the diagnosis of sinonasal low-grade non-ITAC.

The WHO categorizes malignancy of the nasopharynx into nasopharyngeal carcinomas, nasopharyngeal papillary adenocarcinomas, and salivary gland-type carcinomas [3]. To date, Non-ITACs have only been classified as originating from the sinonasal tract, not the nasopharynx, thus making our case difficult to diagnose. Due to the rarity of this case, it was also challenging to determine an accurate treatment plan and prognosis. The 2018 National Comprehensive Cancer Network (NCCN) guidelines recommend definitive radiation to nasopharynx and elective radiation to the neck for a T1, N0, M0 malignancy of the nasopharynx [6]. However, the recommended treatment of sinonasal Non-ITAC is surgical resection with radiation or observation, or definitive radiation [6]. A literature search provided us with one reported case of low-grade non-ITAC of the nasopharynx in a 67-year-old woman. The patient was initially treated with radiation alone, however, the tumor did not respond well and transformed into a high-grade Non-ITAC 3 months following treatment [5]. The tumor was then excised; however, there was recurrence 1 year later. After trials of chemotherapy, the tumor finally responded to FOLFIRI (irinotecan-fluorouracil-leucovorin) with regression of the disease [5].

Our tumor board initially met following the second biopsy to determine course of treatment. Due to the variation in pathology reports and location of the tumor, it was difficult to determine treatment. We considered definitive radiation vs. surgical excision with the option of post-operative radiation, ultimately deciding to proceed with surgery based on available access to the tumor and past medical history of the patient. Once the resection was complete and the final pathology report came back with negative margins, the final decision was made to proceed with observation rather than post-

operative radiation therapy. Because of the patient's history of two childhood malignancies, and the presence of café-au-lait spots on her abdomen and breast, she was sent to genetic counseling. Fortunately, DNA testing was negative for Constitutional Mismatch Repair deficiency and Li-Fraumeni syndrome. It was determined that the second childhood malignancy was likely due to the TBI she received in the first year of life. This news aided in our decision to proceed with observation after excision rather than further radiation that could potentially put her at increased risk of another malignancy.

Following surgery, the patient recovered well with no significant complications and no recurrence of disease to date. There was initial concern for persistent Velopharyngeal Insufficiency (VPI) which occurs when the soft palate fails to close against the pharyngeal wall during speech and swallowing. This results in hypernasal speech, nasal air emission, and nasal turbulence [7]. VPI is a known complication of adenoidectomy thought to be due to increasing the size of the nasopharyngeal airway [8]. It is often temporary, resolving in a few weeks, however, in some patients it may persist requiring speech therapy or surgery. Our patient did initially present with a voice change following excision. However, her VPI was temporary and resolved after two months.

Conclusion

Sinonasal Non-ITAC is a rare disease that has yet to be categorized by the WHO as originating from the nasopharynx. To our knowledge, this is the first case of Non-ITAC of the nasopharynx reported in a pediatric patient. The patient was successfully treated with full excision of the malignancy. There were no significant complications and the patient remains disease-free 9 months post-surgery.

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