AACE Clinical Case Rep. 7 (2021) 207–210

Contents lists available at ScienceDirect

AACE Clinical Case Reports

journal homepage: www.aaceclinicalcasereports.com

Case Report

Well-Differentiated Thyroid Cancer Invading the Trachea in a Pediatric Patient

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ARTICLE INFO

Article history:
Available online 23 March 2021

Key words:
pediatric airway
pediatric thyroid cancer
tracheal invasion

ABSTRACT

Objectives: Pediatric thyroid cancer is rare. Most cases are well-differentiated thyroid cancers (WDTCs). However, gross laryngotracheal invasion of WDTCs is unusual. This report details the first case in English medical literature of a pediatric WDTC invading the trachea.

Methods: Thyroid stimulating hormone, free triiodothyronine, free thyroxine, thyroglobulin, parathyroid hormone, calcitonin, thyroglobulin antibody, chest magnetic resonance imaging, neck ultrasound, neck computed tomography, and fine needle aspiration were performed.

Results: A 9-year-old boy with moderate persistent asthma presented with increasing upper respiratory symptoms. Spirometry suggested a fixed upper airway obstruction. Chest x-ray revealed a left tracheal shift, and chest magnetic resonance imaging identified a right thyroid mass. Thyroglobulin level was 809 ng/mL (normal, ≤33 ng/mL). Results of thyroid stimulating hormone, free triiodothyronine, free thyroxine, parathyroid hormone, calcitonin, and thyroglobulin antibody were normal. Neck ultrasound revealed 2 right thyroid lobe nodules. Neck computed tomography revealed tracheal compression. Fine needle aspiration of the largest nodule yielded atypia of undetermined significance. Bronchoscopy findings at his local hospital were concerning for tracheal invasion. He underwent total thyroidectomy, cricotracheal resection, reconstruction, and radioactive iodine therapy (220 mCi). Pathology demonstrated a well-differentiated papillary thyroid carcinoma without solid or diffuse sclerosing subtype components. Tumor cytogenetic and single nucleotide polymorphism microarray studies showed normal findings. One year postoperatively, neck ultrasound demonstrated no recurrence, and thyroglobulin levels were undetectable while on levothyroxine therapy.

Conclusion: Pediatric WDTC invading the trachea has not been reported.

Introduction

Thyroid cancer is a decidedly rare malignancy among pediatric patients, accounting for only 0.5% to 3.0% of all malignancies in this age group in the United States and Europe.[1] The incidence increases with age, making early childhood and prepubertal cases even more infrequent.[1] Nearly all pediatric thyroid cancers are well-differentiated thyroid cancers (WDTCs), of which papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma account for a majority (90% to 95%) and minority (5%) of cases, respectively.[1] Medullary thyroid cancer is a small fraction of pediatric WDTC (<5%) and is typically due to genetic causes.[2] Compared with adult cases, pediatric WDTCs tend to present at a higher stage. However, these cancers retain an excellent prognosis in children, with a 5- and 10-year overall survival rate of 99.3% and 98.5%, respectively.[1]

Extrathyroidal extension has been reported to occur in pediatric WDTC; however, no detailed case of laryngotracheal invasion has been described in the English medical literature. In adults, extrathyroidal extension into the upper respiratory tract in WDTC ranges

Abbreviations: PTC, papillary thyroid carcinoma; WDTC, well-differentiated thyroid cancer.

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https://doi.org/10.1016/j.aace.2021.01.005

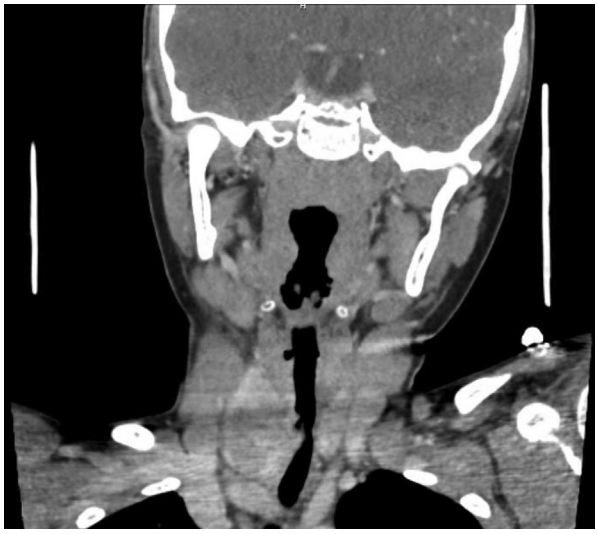

Fig. 1. Neck computed tomography, coronal view, demonstrating a large, irregular, heterogeneous, patchily enhancing soft tissue mass arising from the right lobe of the thyroid gland and extending into the tracheoesophageal groove with a resultant mass effect and tracheal compression of 7 × 4 mm.

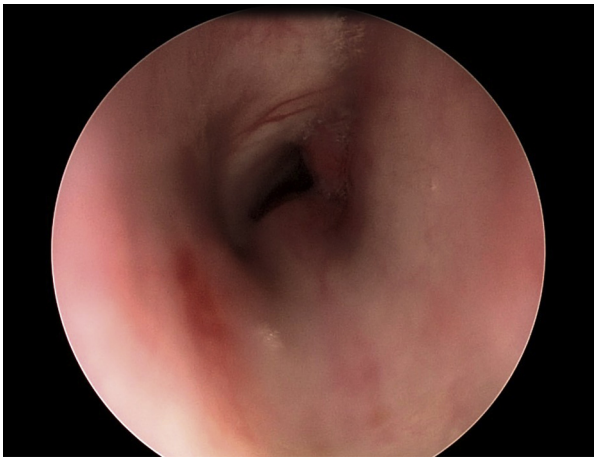

Fig. 2. Bronchoscopy demonstrating tracheal submucosal spread of the tumor and resultant airway narrowing.

from 1.0% to 13.0%.[3] Much of this variability can be attributed to the historical lack of a uniform classification system.[3] Significant questions remain surrounding the best treatment of these patients, including the optimal approach to airway management and reconstruction. This case study aims to detail one case of WDTC invading the trachea in a pediatric patient successfully managed with thyroidectomy, cricotracheal resection, reconstruction, and radioactive iodine therapy.

Case Report

A 9-year-old boy with a history of moderate persistent asthma presented with several months of increasing respiratory symptoms, including loud snoring, noisy breathing, and shortness of breath, impacting sports participation. Family history was notable for thyroid surgery performed on his biological mother and maternal aunt, although details were limited given the patient's adoption at the age of 4 years. No history of radiation exposure was reported. Spirometry results suggested a fixed upper airway obstruction. Chest x-ray demonstrated a left tracheal shift, and chest magnetic resonance imaging identified a right thyroid mass. Neck ultrasound revealed 2 right thyroid lobe nodules, one measuring 3.8 × 2.3 × 2.3 cm with lobulated margins and the other measuring 1.0 × 0.8 × 0.5 cm with smooth margins. Thyroglobulin level was elevated at 809 ng/mL (normal, ≤33 ng/mL). The levels of thyroid stimulating hormone, free triiodothyronine, free thyroxine, parathyroid hormone, calcitonin, and thyroglobulin antibody were all within normal limits.

Fine needle aspiration of the largest right thyroid nodule yielded atypia of undetermined significance. Neck computed tomography with intravenous contrast revealed an enlarged right hemi-thyroid and tracheal compression, with a diameter reduced to 7 × 4 mm in the smallest dimension (Fig. 1). The patient was scheduled for bronchoscopy and thyroidectomy at his local hospital; however, the procedure was cancelled based on bronchoscopy findings indicating tracheal invasion (Fig. 2).

The patient was then transferred to this tertiary children's hospital for further evaluation and management. Total thyroidectomy with central neck dissection and cricotracheal resection with reconstruction was performed in a coordinated procedure with pediatric surgery and otolaryngology teams. After freeing the thyroid gland and completing the central neck dissection, an inferior tracheal incision was made below the third tracheal ring. The superior incision included the right half of the cricoid cartilage, and the specimen was resected en bloc (Fig. 3). Anterior tracheal dissection and suprahyoid release were used to reduce tension on the closure. The tracheal defect was closed, and the institution's open airway reconstruction postoperative protocol was used for postoperative management.

Pathologic examination showed a 3.5-cm tumor in the largest dimension involving the right lobe with extrathyroidal extension through the trachea and into the mucosa (Fig. 4 *A*). Microscopic examination revealed a multifocal invasive well-differentiated PTC with conventional and follicular variants (Fig. 4 *B*, *C*). Angiolymphatic invasion and tumor deposits were also observed. Occasional solid sheets and nests of carcinoma that expressed both thyroglobulin and thyroid transcription factor-1 immunostains were noted, confirming the above diagnosis. Furthermore, no poorly differentiated components or areas of necrosis were identified. The KI-67 proliferation index was 5.0%. Four of the 7 central lymph nodes examined showed a positive result for metastasis (Fig. 4 *D*). Final surgical margins were narrowly free, and the tumor was classified as pT4. Cytogenetic analysis identified normal male karyotype with a nonclonal abnormality (46,XY[19]/46,XY,del(9)(q22q34)). However, it was noted that the normal result from long-term in situ cultures may have represented an outgrowth of normal stromal tissues. The result of single nucleotide polymorphism tumor microarray analysis performed using the CytoScan TM HD platform (Thermo Fisher Scientific, Waltham, MA) was normal.

Following surgery, 131-iodine scan revealed radiotracer activity in a 0.6-cm right paratracheal lymph node and 3 pulmonary metastases (with the largest measuring 0.5 cm). Given the size and location of the foci, the morbidity of resection outweighed the risk of radioactive iodine therapy failure. Radioactive iodine at a dose of 220 mCi was administered. Excellent clinical response was noted by the regression of pulmonary nodules on chest computed tomography scan and undetectable thyroglobulin level. Routine surveillance with serial imaging and laboratory work 1 year postoperatively demonstrated no concerning findings on neck ultrasound and undetectable thyroglobulin levels while on levothyroxine therapy.

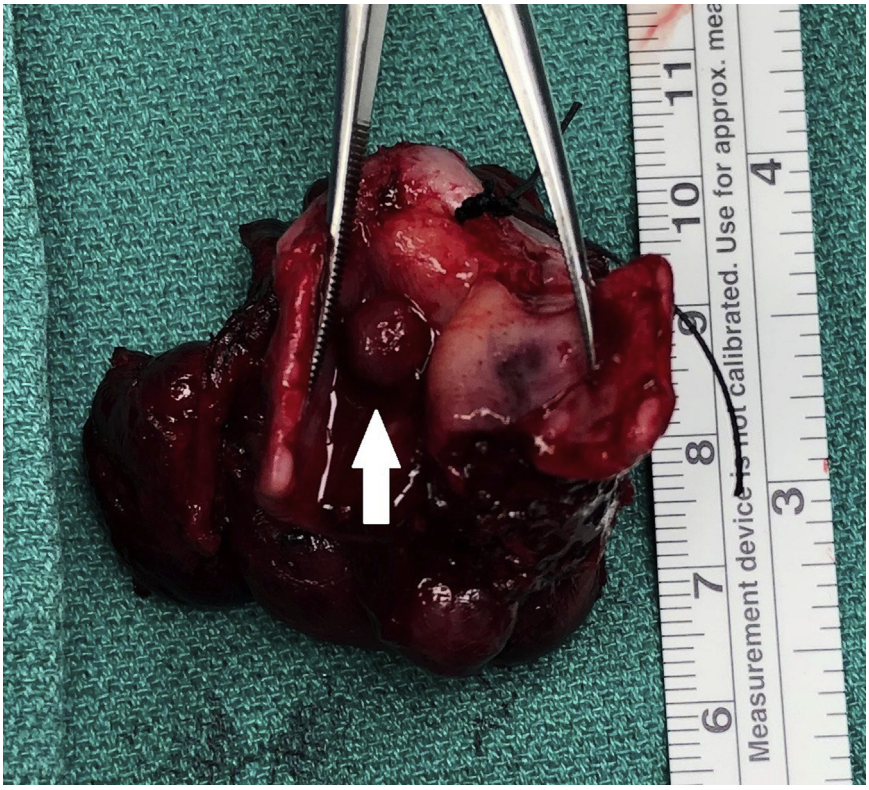

Fig. 3. Thyroidectomy and tracheal specimen, posterior surface, with the trachea resected en bloc. The arrow marks gross tracheal invasive disease. The black stitch marks the right cricoid cartilage.

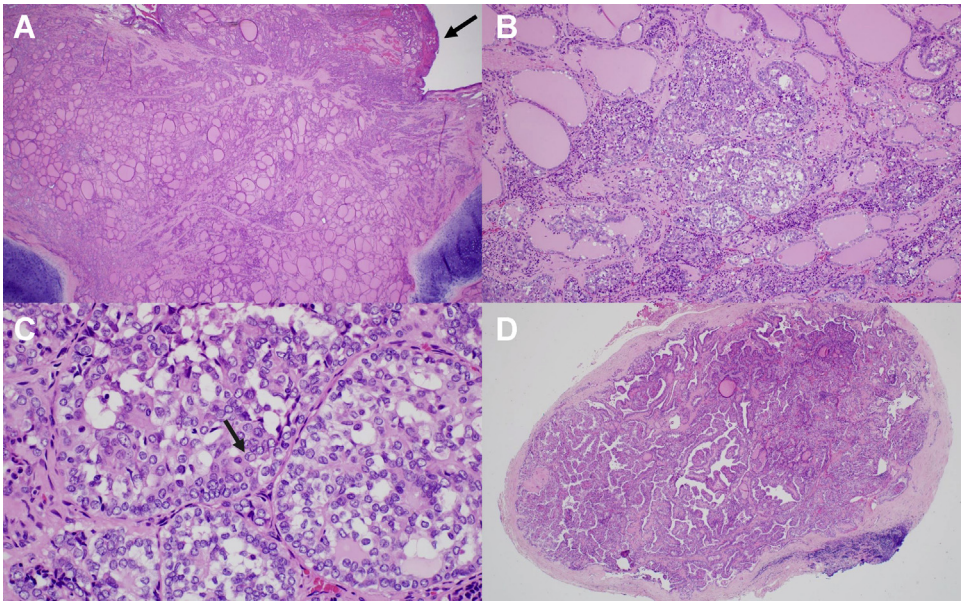

Fig. 4. *A*, Tumor infiltrating through the cartilage (lower corners) with polypoid extension into the airway lumen (arrow). Hematoxylin and eosin (H&E) stain, (magnification: x2). *B*, Tumor with complex papillary and follicular growth patterns. H&E stain, (magnification: x10). *C*, Classic nuclear features of papillary thyroid carcinoma with chromatin clearing, irregular nuclear outlines, nuclear grooves, and intranuclear inclusion (arrow). H&E stain, (magnification x40). *D*, Almost complete replacement of the lymph node by metastatic papillary thyroid carcinoma. H&E stain, (magnification: x4).

Discussion

Given its rarity, extrathyroidal spread in pediatric WDTC remains poorly described in the literature, and to our knowledge, this work represents the first case report detailing tracheal invasion in this population. Management decisions are frequently inferred from adult data. A contemporary review approximates tracheal invasive disease in 5.8% of adult patients with thyroid cancer.[4] A future understanding of the true incidence of invasive WDTC rests in part on the development of a universal classification system. Shin

et al have proposed 4 stages of airway invasion.[5,6] Stage I includes extrathyroidal extension that borders, but does not invade the perichondrium; stage II includes cartilage erosion with no transmural extension; stage III includes extension through the cartilage within the trachea, but no mucosal extension; and stage IV includes extension through the mucosa into the lumen of the trachea.[5,6] Dralle et al have also proposed a staging system primarily defined on the laryngotracheal resections required based on the extent and location of invasion.[5,7]

The challenge for determining an appropriate surgical approach lies in deciding how much of the airway is to be resected to achieve clear margins without excessive destabilization, anastomotic breakdown, or subsequent stenosis. Proposed techniques include shave resection (macroscopic disease removal), window resection (full-thickness resection less than one third of the airway circumference), and sleeve resection (circumferential resection).[4] Shave and window resections are associated with higher rates of local recurrence, and window resection in particular creates a reconstructive challenge, often requiring the use of a regional muscle flap.[4] Sleeve resection allows for the removal of a full-thickness specimen of the trachea to determine the depth of invasion and margin status, and it permits stable reconstruction using established techniques.[4] In this case, ultrasound revealed Shin stage III disease with extension through the tracheal cartilage and submucosal spread within the trachea; therefore, sleeve resection was deemed most appropriate. Regardless, the complexity of the tracheal resection and reconstruction, including postoperative care, indicates the involvement of an otolaryngology-trained specialist with expertise in airway surgery at a center with experience in managing issues unique to postoperative airway reconstruction recovery.

Conclusion

This pediatric patient, without a history of radiation exposure, presented with well-differentiated PTC exhibiting marked laryngotracheal invasion. The factors responsible for such aggressive behavior in patients with pediatric PTC remain obscure. While there is no consensus as to the optimal treatment of these patients, this case was successfully managed with thyroidectomy, cricotracheal resection, and reconstruction followed by radioactive iodine therapy.

Disclosure

The authors have no multiplicity of interest to disclose.

Acknowledgment

We thank Taubman Health Sciences Library informationist, Kathryn Vanderboll, MLS, for her assistance in conducting the literature searches required for this case report. This case report was determined not regulated by the University of Michigan Institutional Review Board, and all patient data has been de-identified.

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