Papillary Thyroid Carcinoma in Children: A Case Report and Review of the Literature

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Case

A 12 year-old female with an unremarkable past medical history was found with an enlarged neck mass of unknown time span, and subsequently referred to Langely Otolaryngology for further evaluation and work up. Labs were drawn showing a negative calcitonin, normal thyroid labs, normal calcium, negative thyroglobulin antibodies, but positive for thyroperoxidase antibodies. An ultrasound of her thyroid was ordered showing enlarged right thyroid lobe with associated lymphadenopathy. Fine needle aspiration was subsequently performed given the suspicion for possible thyroid malignancy, which showed atypia of undetermined significance. Given the patient's age and increased risk of thyroid carcinoma, it was decided the patient would undergo a total thyroidectomy for further evaluation.

Background

Thyroid cancer is rare in childhood, accounting for about 3% of all pediatric malignancies (3, 7). However, while it is still considered a rare disease, the overall incidence of thyroid cancers in children are increasing (2, 7). In adults, most thyroid nodules found are benign there is a 2-5 fold increase in the risk of cancer for thyroid nodules in children, with the most common thyroid malignancy being papillary thyroid cancer (PTC) (1, 7). Prognostic factors include age of the child, with younger children carrying a worse prognosis, and metastatic disease to include lymph node invasion and distance metastasis (1, 3, 5, 7, 8, 10). There are also thought to be prognostic indicators between the various subtypes of PTC, including increased aggressiveness in classic PTC and solid/trabecular subtypes, and classic PTC carrying a higher association with extensive vascular invasion in 25% of cases and metastasis in p to 38% of cases (1, 4). Because of this increased incidence of multifocal disease and lymph node invasion, PTC in children is typically treated with a total thyroidectomy (1, 7, 8). This total removal of the thyroid tissue allows for post-operative treatment with Radioactive Iodine (RAI). It has been shown that with total thyroidectomy and RAI results in 97% of disease free survival after 10 years, with total thyroidectomy alone resulting in 40% and 61% relapse after 5 and 10 years respectively (5, 7).

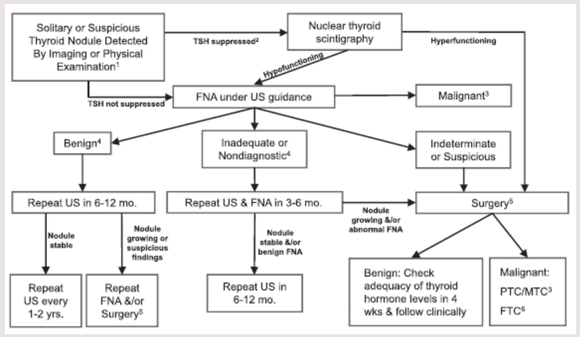

Figure 1: Algorithm recommended by Frances et al (1)

Research

Newer developments in tumor genetics have shown that most thyroid carcinomas rely on mutations in the RAS-RAF-MEK-ERK pathway (1). Within this pathway, BRAF mutations have been shown to correlate with aggressive tumor characteristics, such as extra-thyroidal extension, advanced tumor stage at presentation, tumor recurrence, and lymph node or distant metastases (6, 7, 9). BRAF mutations have also been associated with a decreased ability of tumors to trap radioiodine during RAI (6).

Tumor type	Prevalence (%)
Papillary carcinoma	
BRAF	45
RET/PTC	20
RAS	10
TRK	<5
Follicular carcinoma	
RAS	45
PAX8-PPAR	35
PIK3CA	<10
PTEN	10
Medullary carcinoma	
Familial forms *RET*	>95
Sporadic *RET*	40

Complications

Complication rates to include hypocalcemia (both temporary and permanent), vocal cord weakness, and postoperative respiratory distress are significantly more common in children in comparison to adults (10,11,12). Temporary hypocalcemia is the most common complication, defined as lasting less then 6 months, can occur in as much as 32.7% of pediatric patients (11,12). Additionally, up to 7% of pediatric patients require prolong hospitalization and IV calcium infusion (12). The only recommendation to prevent this potentially life altering complication is to ensure the operation is performed by a surgeon with significant experience in thyroidectomies (10,11,12).

Treatment

Pathologic diagnosis	Multifocal disease on ultrasound, n (%)	Unilateral disease on ultrasound, n (%)
Bilateral disease	26 (40)	40 (60.6)
Unilateral disease	20 (19)	85 (80.1)
Occult bilateral disease	11 (27.5)	40 (100)
p Value *	*0.26/0.009 +*	*0.002/0.005 +*

Figure 3: Multifocal disease correlation with ultrasound (8)

Given the increased aggressive nature of thyroid cancer in children, all children diagnosed with thyroid cancer should undergo surgical excision. If diagnosed with PTC, it is generally recommended to undergo total thyroidectomy given the increased incidence of bilateral disease. If nodal disease is detected, modified neck dissection to include at least the level VI neck and potentially level IV and V should also be performed. If residual disease or genetic testing showing increased aggressive disease, patients should also undergo RAI to decrease recurrence rates.

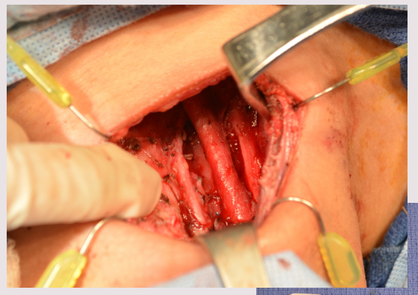

Figure 4: (top left) intraoperative photo after level VI neck dissection. (right) specimen photo of right thyroid lobe (R), left thyroid lobe (L), level IV neck lymphnodes (4), and level VI neck nodes (6).

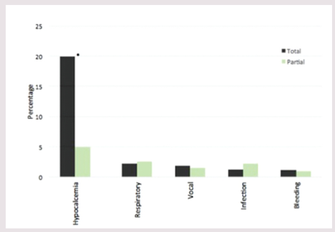

Figure 5: Complication rate in total thyroidectomy vs lobectomy (11)

Conclusion

With our patient, it was found that she had PTC. Therefore, she underwent total thyroidectomy with central neck dissection and right level IV neck dissection to remove gross tumor burden. Her pathology revealed the classic subtype of PTC with 19/26 positive lymph nodes and extensive vascular invasion. There was no extra-thyroidal extension identified. Subsequent plain chest film was obtained showing no distant metastatic disease. Given her pathology, she was diagnosed with stage 1 PTC (T2N1bM0). However, with the suggested childhood classification, she would be diagnosed with high risk of recurrence (1,3). In order to further classify her disease, BRAF mutations could be obtained which may prompt multiple rounds of RAI given possible associated with decreased radioiodine update and continued follow up for possible relapse.

It is important to understand the molecular advances in tumor classification and how this could affect future treatment for childhood thyroid malignancies. It is also important to understand that classic treatment of adult thyroid nodules do not correlate with the treatment recommendations of pediatric thyroid nodules because of their higher rate of malignancy, metastatic disease, and local aggressive nature.

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