Advances in Pediatrics 64 (2017) 171–190
ADVANCES IN PEDIATRICS

Pediatric Thyroid Cancer

Christine M. Chan, MD[a], Jonathan Young, MD[b], Jeremy Prager, MD[b], Sharon Travers, MD[a,*]

[a]Section of Endocrinology, Department of Pediatrics, Children's Hospital Colorado, University of Colorado Denver, 13123 East 16th Avenue, Aurora, CO 80045, USA; [b]Department of Pediatric Otolaryngology, Children's Hospital Colorado, University of Colorado Denver, 13123 East 16th Avenue, Aurora, CO 80045, USA

Keywords

• Medullary thyroid cancer • Differentiated thyroid cancer • Pediatric thyroid cancer

Key points

- Evidence supports that the incidence of differentiated thyroid cancers (DTCs) is increasing in the pediatric population.
- Despite the more aggressive tendency of DTCs in children, prognosis is excellent but early diagnosis could decrease the extent of intervention required and overall recurrence rates.
- Medullary thyroid cancer (MTC) is rare in children and usually hereditary.
- Treatment centers around removal of the thyroid gland prior to development of MTC.
- Care of children with thyroid cancer should include a team of experienced pediatric surgeons and subspecialists.

INTRODUCTION

Thyroid cancer remains a rare malignancy in the pediatric population, comprising 0.7% of all childhood cancers [1], and the overall incidence of thyroid cancer is increasing. The increasing incidence of thyroid cancer is largely driven by the increase in papillary thyroid cancer (PTC) and has been in part attributed to increased detection of small tumors. Studies have shown, however, an increased incidence across all tumor sizes, suggesting that surveillance, more sensitive diagnostic procedures, and earlier detection are not the sole explanations [2,3]. Historically, evaluation and management of thyroid nodules and thyroid cancer in the pediatric population has largely been based on adult

*Corresponding author. *E-mail address:* Sharon.travers@childrenscolorado.org

http://dx.doi.org/10.1016/j.yapd.2017.03.007

guidelines. Given the differences in presentation, pathophysiology, and long-term outcomes, however, the American Thyroid Association (ATA) has recently published guidelines specifically for management of thyroid nodules and DTC in the pediatric population [4].

BACKGROUND AND EPIDEMIOLOGY

Per the Surveillance, Epidemiology, and End Results program (a National Cancer Institute registry of cancer incidence and survival in the United States), 1.8% of thyroid malignancies diagnosed in the United States are in patients under 20 years of age [5]. There is a female preponderance, with a peak incidence in adolescents ages 15 years to 19 years [5]. In this age group, thyroid cancer is the second most common cancer among girls. Nearly all pediatric thyroid cancers are DTCs, with a majority (>90%) PTC. DTC cells resemble normal thyroid cells in behavior and appearance, and differentiated tumors tend to grow more slowly and be less aggressive than undifferentiated or poorly differentiated tumors. Follicular thyroid cancer (FTC), also a DTC, is less common (<10%) and medullary and undifferentiated thyroid cancers are rare in the pediatric population. The histologic criteria for DTCs are the same for children and adults.

PTCs are well-differentiated thyroid cancers arising from thyroid follicular cells. They are characteristically unencapsulated tumors with often ill-defined margins. In children, PTC is frequently multifocal and locoregional metastases are present in the majority of patients at the time of diagnosis. Children with PTC are also more likely than adults to have pulmonary metastases (up to 25%) compared with adults [6]. The diagnosis of PTC is based on a constellation of cytologic and nuclear features, including presence of psammoma bodies (calcified structures thought to arise from tumor cell necrosis), enlarged nuclei, nuclear overlapping, nuclear clearing, and nuclear grooves. Within the category of PTC, there are histologic variants, including classic, follicular, and diffuse sclerosing, the lattermost of which is more aggressive. There has been more recent discussion in the literature regarding the noninvasive encapsulated follicular variant of PTC and its reclassification as a neoplasm rather than a malignancy [7].

FTC is also a DTC, although it occurs much less often in the pediatric population than PTC and has a different clinical behavior. Histologic variants of FTC include oncocytic (Hürthle cell) and clear cell variants. In general, pediatric FTC is less aggressive than PTC, presenting with less advanced disease, fewer distant metastases, and a lower rate of recurrence. FTC in children is generally a unifocal tumor that does not have the tendency to spread to regional lymph nodes like PTC. Although FTC can be prone to hematogenous metastases, more often than not, FTC in children is minimally invasive and has a low risk for recurrence and metastases.

Genetic alterations are known to play a role in the pathogenesis of thyroid cancer. The MAPK and PI3K/AKT signaling pathways play an important role in the regulation of cell proliferation, differentiation and survival (Fig. 1). Alterations in the *BRAF* and *RAS* genes as well as *RET/PTC* and