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Guest Editorial

DIFFERENTIATED PEDIATRIC THYROID CANCER: CLINICAL PRESENTATION AND TREATMENT CHALLENGES

Pediatric Thyroid Cancer (TC) is rare, with incidence of 0.5-3%. However, its incidence is rising. In comparision to adult population, pediatric TC shows significant clinical, pathological and molecular differences. They clinically present aggressively with extra thyroidal disease, bulky neck nodes, mainly to level Ib with perinodal extension. Almost 25% of the patients have pulmonary metastasis at the time of diagnosis. Aggressiveness of disease is more common in younger children. Younger the age, more aggressive is the disease at presentation, having an inverse relation to patient age. The treatment outcome is comparatively less favorable in children less than 10 years old compared to older children and adolescents. However, with improvement of diagnostic procedure, incidence of cervical lymph node metastasis and distant metastasis is decreasing in pediatric population giving rise to better prognosis even for children below 10 years old.

Solitary Thyroid Nodule (STN) is the commonest clinical presentation like in adults. However, many patients have only cervical lymph nodes without palpable thyroid lesion at clinical presentation. Few pediatric TC are detected due to distant metastasis almost exclusively to lungs, rarely bone and CNS. A study in India on pediatric TC showed cervical lymph node to be the commonest clinical presentation (57.8%) with 19.2% having pulmonary metastasis, out of which, 31.2% patients had a negative chest X-ray and were detected only on the radioiodine scan.

Interestingly, this aggressive disease is not associated with a higher mortality rate with pediatric TC causing to less than 2% disease specific mortality. This is due to the excellent response to Iodine 131 and favorable progression free survival in children with persistent disease. The Iodine 131 may continue to respond after therapy giving rise to stable disease, evidenced with decreasing thyroglobulin (Tg) level.

Incidence of TC increases with age, even in pediatric group. Younger the age, higher the tumor volume. A study showed newly diagnosed case of pediatric TC tumor size was greater than 4 cm in 36% patients compared to 15% in adult. Due to smaller thyroid gland in pediatric population, tumor tends to invade thyroid capsule early presenting as extra thyroidal extension. Therefore, tumor less than 1 cm (microcarcinoma) is not used in pediatric TC.

Neck node metastasis is common, more at level Ib, with both extranodal and perinodal extensions. Various studies showed cervical lymph node metastasis in pediatric TC to be 61-90% as compared to 35% in adults. Similarly, distant metastasis was 7-29% in pediatric TC compared to about 2% in adults. Another study from India presented extrathyroidal extension in more than 50% of the patients. In the same study, nodal positivity was about 70% with vast majority harboring N1b disease; about 72.91% had perinodal extension in the nodes with more than 10 positive nodes in almost 50% cases.

An important difference is high prevalence of expression of Sodium Iodide Transporter (NIS) in metastatic focus of pediatric TC leading to better response to radio iodine ablation (RAI) and giving

rise to excellent prognosis compared to adults. Therefore, despite having a greater recurrence rate and persistent disease, survival is better. Post RAI Tg level continues to decrease and the persistent disease remains stable.

Hence, it is critical for the clinician to understand the variation of clinical presentation of pediatric TC vis-s-vis adults and its aggressive initial presentation. Many patients present with cervical lymph node without palpable thyroid lesion and few are diagnosed due to the distant metastasis. This knowledge helps clinician to diagnose and plan appropriate management considering the surgical challenges and possibilities of complications.

To confirm the diagnosis and plan proper management, apart from routine TFT, USG neck, FNAC of thyroid lesion and cervical lymph nodes, pediatric TC unlike in adults generally warrants CECT of neck and chest.

Management is challenging due to the small size of thyroid, extrathyroidal extension with bulky lymph nodes at presentation, possible involvement of recurrent laryngeal nerve (RLN), aerodigestive track and the rarity of the disease. However, an experienced surgeon can avert likely complications of unilateral to bilateral RLN involvement (hoarseness to persistent tracheostomy) and permanent hypoparathyroidism favoring a good outcome.

Usually, treatment consists of surgery followed by RAI and levothyroxine in suppressive doses. Total thyroidectomy with central, and lateral neck dissection (level II-V) is generally performed in view of extensive, multifocal and bilateral disease in pediatric TC. Histologically, 90-95% pediatric TC are papillary and 5% are follicular.

Post-operative RAI is needed by most of the pediatric TC patients, mainly with high and intermediate risk. High risk patients have bulky level Ib lymph node metastasis and or distant metastasis, whereas intermediate risk group has significant level Ia lymph node metastasis. Many require more than 1 dose of RAI and only high cumulative doses gives rise to complications. Many a times distant metastasis is detected during Iodine whole body scan. High expression of NIS in pediatric metastatic disease gives good response to RAI with excellent prognosis and the continued response is observed.

Levothyroxine though is controversial in pediatric age group, in view of its impact on growth of children, many studies proved its use safe. Suppressive doses of levothyroxine are given safely in a controlled way to avoid TSH stimulating tumor growth. Follow up is as in adults but life-long follow-up is needed with Tg and appropriate imaging in view of persistent disease and high recurrence rate though the prognosis is excellent with 5 and 10 years' survival of 99% and 98% respectively.

In Nepal, studies on the prevalence of pediatric TC are yet to be conducted. However, the awareness on common presentation of cervical lymph node without palpable thyroid lesion in pediatric TC is steadily increasing. Duly noting its aggressive clinicopathological presentation and management challenges, requiring life-long follow-up, pediatric TC has excellent prognosis even in our country in the hands of experienced surgeons.

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