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Case Report

Pediatric papillary thyroid carcinoma successfully managed with a multimodal approach

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ABSTRACT

Malignant tumours of the thyroid gland are rare in children. The tumours tend to be advanced at the time of presentation, but the overall survival is still better as compared to adults. The use of radioiodine ablation or treatment for the post-thyroidectomy gland remnants or recurrences improves patient survival. The reports of a multimodal approach that involves surgery as the primary treatment along with radioiodine ablation (RIA) are rare in the pediatric age group. We describe here a child with metastatic papillary thyroid carcinoma treated with a multimodal approach.

Keywords: Children, Multimodal approach, Papillary thyroid carcinoma, Radioiodine (^{131}I) ablation

INTRODUCTION

Thyroid malignancies are rare in children constituting 1.5-3% of all pediatric tumors.[1] Differentiated thyroid carcinomas (DTC) represent the most common endocrine tumor in childhood affecting 0.1-2.2 children per million persons.[1] Of all the DTCs, papillary thyroid carcinoma (PTC) constitute 70-80% of cases followed by follicular carcinoma.[1] The clinical presentation and outcome of pediatric DTCs is different from that of adults. In children, DTCs tend to be more advanced at the time of presentation as compared to adults. Regional lymph node metastasis is detected in 90% of children at the time of initial diagnosis as compared to only 35% in adults.[1] Pediatric DTCs present with multifocal lesions, extra-thyroidal invasion and distant metastasis, indicating that childhood thyroid carcinomas have an aggressive clinical course.[1] However, the overall survival rates exceed 95% in children as compared to an average of 80-90% in adults.[2] Treatment modalities include surgery and radioiodine (^{131}I) ablation (RIA) or treatment aimed at eliminating normal-thyroid remnants or any neoplastic focus. Most pediatric DTCs being PTCs, they show avid radioiodine uptake and hence are susceptible to ablation therapy. However, there exists limited evidence in literature regarding the activities of ^{131}I needed for radioablation in children.[3] Herein, we report a case of an 11-year-old-boy with PTC treated successfully with a multimodal approach consisting of total thyroidectomy and RIA.

CASE REPORT

A 11-year-old-boy presented with a history of an anterior neck swelling for the last 4 months. The swelling had been gradually increasing in size. There was no pain, change in quality of voice and difficulty in deglutition or breathing. There were no constitutional symptoms such as fever, loss of appetite or weight. There was no past history of radiation exposure or family history of thyroid disorders. Examination revealed a 2.0 x 2.0 cm nodule in the middle and part of the right half of the anterior neck (Figure 1A). The swelling was globular, firm and was moving upwards with deglutition, suggestive of a solitary

thyroid nodule. Rest of the thyroid gland was not palpable. Bilateral subcentimetric submandibular, posterior cervical and axillary lymph nodes were palpable. His pulse rate was 92 beats/min and blood pressure 108/60 mm Hg (50th to 75th percentile for age). His body weight (31 kg, -0.42 z-score) and height (139.6 cm, -0.55 z-score) were normal for age. Testicular volume was 6.0 ml each (Tanner stage 2). Deep tendon reflexes were normal and there were no ocular signs suggestive of thyrotoxicosis. Indirect laryngoscopy revealed bilateral mobile vocal cords. The systemic examination was unremarkable.

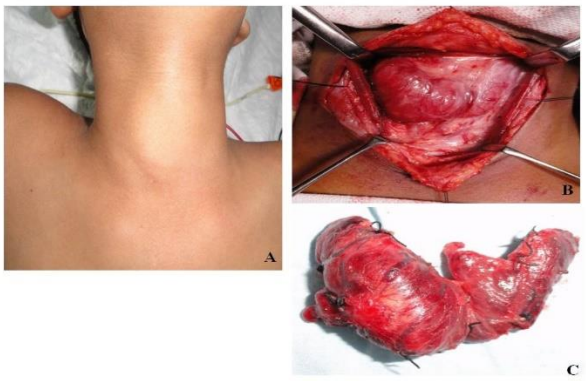

Figure 1: Clinical photograph of the patient showing right thyroid lobe enlargement (A), per-operative photograph (B) and resected thyroid gland showing enlarged right lobe and normal left lobe (C).

Investigation revealed normal routine hematological and biochemical parameters. Serum total triiodothyronine (T3), total thyroxine (T4) and thyroid stimulating hormone (TSH) levels were 1.28 ng/mL (normal, 0.8 - 2.0 ng/mL), 7.64 µg/dL (normal, 4.5 - 12.5 µg/dL) and 2.44 mIU/mL (normal, 0.4-4.0 mIU/L) respectively. Anti-thyroid peroxidase (TPO) antibody titer was <5.0 IU/mL (normal, <32 IU/mL). Serum thyroglobulin (Tg) level was elevated (2068 ng/mL, normal range 1.6-60 ng/mL). Ultrasonography of the neck showed an approximately 2.2 x 1.7 x 2.4 cm heterogeneous isoechoic to hyperechoic lesion in the right lobe of the thyroid gland along with multiple tiny echogenic foci in its periphery. Rest of the thyroid gland appeared normal on ultrasonography. There were multiple sub-centimetric level Ib and level IV lymph nodes. Fine-needle aspiration (FNA) of the thyroid nodule was suggestive of PTC. A contrast-enhanced computed tomography (CECT) of the chest excluded pulmonary metastasis. The boy underwent total thyroidectomy with central compartment neck lymph nodes dissection (Figure 1B). The removed thyroid gland weighed 102 gm (mean normal weight 15.0 gm). The right lobe was enlarged and firm (Figure 1C). A soft fleshy lesion was identified on serial slicing in the right lobe while the left lobe appeared normal. The histopathological features were that of an invasive multifocal PTC. The tumor cells were arranged predominantly in papillary pattern with the individual cells showing oval nuclei, overcrowding, clearing and grooving of nuclei. There were foci of calcification. The tumor seemed to infiltrate the adjacent thyroid parenchyma but sparing the isthmus. The lymph nodes also showed features of metastatic carcinoma. The serum Tg levels done two and six weeks after surgery were 559 ng/mL and 216 ng/mL respectively. Levothyroxine replacement was initiated at 1.6 µg/kg/day.

Two months after surgery, a diagnostic whole-body radioiodine scan showed tracer uptake in the thyroid remnant, level VI and right sided level III group of lymph nodes indicating radioactive avidity. Subsequently he underwent therapeutic RIA with a dose of 86 mCi of ^{131}I. Post-therapy diagnostic radioiodine scan performed one week later showed findings similar to the pre-therapy scan. Levothyroxine was gradually hiked to 2.5 µg/kg/day to achieve TSH suppression (serum TSH 0.91 mIU/mL at 3 months post-surgery). At the second follow up visit six months after surgery, serum Tg was 2.43 ng/mL. Ultrasonography of the neck revealed bilateral sub-centimetric submandibular lymph nodes (level Ib). A repeat diagnostic whole-body ^{131}I scan did not show any tracer uptake. His thyroid function tests at subsequent 6 monthly follow up visits showed normal values and serum Tg levels ranged between 2.0-4.5 ng/mL. At the last evaluation three years after surgery, he was completely asymptomatic. Serum total T3, total T4 and TSH levels were 1.19 ng/mL, 9.6 µg/dL and 0.1 mIU/mL respectively. Serum Tg was 0.186 ng/mL. He is currently receiving levothyroxine at a dose of 3.0 µg/kg/day.

DISCUSSION

This report presents a case of pediatric PTC managed successfully with multimodality approach, notably, surgery and curative RIA therapy. Our patient had the most commonly observed presentation as a solitary palpable thyroid nodule although presentation with only palpable neck lymph nodes without a palpable thyroid nodule is also well described in the pediatric age group.[2] Lymph node involvement at presentation have been reported in about 40-90% of patients, while distant metastasis, predominantly pulmonary, is seen in 20-30% of cases.[2] The uptake of radioiodine by cervical lymph nodes suggested local spread of PTC in our patient. However, there was no clinical or radiological evidence of distant metastasis. This could partly be explained by the fact that as the age at disease presentation increases, the tumor tends to be less aggressive.[4] The tumor tends to be less invasive in terms of extrathyroidal extension, lymph node spread and distant metastasis in pubertal as compared to pre-pubertal children.[4,5] Our patient was 11 years old and had already entered puberty at the time of initial presentation.

The ultrasonographic finding of an isoechoic to hyperechoic nodule was not typical of a neoplastic lesion which is usually hypoechoic.[6,7] However, thyroid nodules are 5 times more likely to be malignant in children than

in adults requiring a low threshold for suspicion of malignancy.[8] Accordingly, the FNA was performed which confirmed the presence of PTC in our patient. Total thyroidectomy was done as advocated in most studies.[2,4,9] It is preferred over subtotal thyroidectomy or lobectomy as PTCs tend to be multifocal and the remnant thyroid tissue may interfere with post-operative radioiodine scans.[9]

Post-operative ^{131}I scan in pediatric DTC patients has been a matter of controversy. Although routinely performed in clinical practice, radioiodine administration in children is theoretically fraught with the risk of second primary malignancies, effects on salivary glands, pulmonary fibrosis and reproductive issues.[2] In addition, there is no evidence in literature regarding the ideal dose of ^{131}I required for adjuvant RIA therapy in pediatric PTC. Usually an empirically derived fixed dose is used which is repeated if necessary. The dose may be adjusted to the patients' disease stage as well as for body weight. Alternatively, a dosimetric strategy can be employed wherein the patient's individual iodine bio-kinetics is determined to calculate the ^{131}I activity which needs to be administered for therapy.[3] Some clinicians advocate 'fractionated' RIA therapy similar to fractionated radiotherapy. Such form of therapy alters PTC biokinetics and leads to selection of relatively radioresistant malignant cells, thereby, leading to decreased therapeutic efficacy of ^{131}I.[10]

In our patient, a post-operative diagnostic ^{131}I scan showed tracer uptake in the thyroid remnant and cervical lymph nodes suggestive of metastasis. Hence, he underwent therapeutic ablation; the dose of ^{131}I was calculated based on dosimetric strategy. Successful ablation was confirmed at the follow up scan 6 months later. The low Tg levels in follow up suggest that there is no biochemical recurrence either. Similar responses to RIA have been reported previously. In a cohort of pediatric DTCs, complete ablation was achieved in 100% patients with only residual thyroid tissue and in 83% patients with associated nodal metastases.[11] Distant metastasis were more resistant to ablation.[11] Absence of distant metastasis probably contributed to good response in our patient. Moreover, response to treatment is better and recurrence rates seem to be low in pubertal children than in the pre-pubertal group.[12] However, long-term follow-up is needed as DTCs have a recurrence rate of 31% in the age group of 10-14 years.[1-4]

CONCLUSION

In conclusion, we present a child with multifocal PTC treated successfully with a combination of total thyroidectomy and postoperative radioiodine therapy.

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