

Case Report

Short Interval Occurance of Papillary Thyroid Carcinoma Following Radiotherapy for Hodgkin's Disease: A Case Report

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Abstract

Introduction: Hodgkin's disease (HD) is a common pediatric malignancy that is treated with a combination of chemotherapy and radiation. Although cure rates are very high (~90%), secondary malignancies are not uncommon and radiation has been shown to be a risk factor for their development. Secondary malignant neoplasms (SMNs) of the thyroid gland are common solid tumors found in patients treated for HD. Current literature shows that these SMNs generally appear an average of 5-15 years later, even in patients under surveillance.

Presentation of Case: We present 16 year old patient with secondary thyroid papillary carcinoma four years after completion of radiotherapy.

Conclusion: This case may have implications for the future management and post radiation care of these patients.

Keywords: Secondary Malignant Neoplasms; Papillary Carcinoma; Hodgkin's Disease

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Consent: We the authors confirm that our patient and his family have given informed assent/consent for the publication of this case report.

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Introduction

Hodgkin's disease (HD) is the most common malignant lymphoma found in children aged 15-19 [1]. HD is usually treated with a combination of chemotherapy and low-dose radiation. Radiation treatment is a well known risk factor in the development of secondary malignant neoplasms [2, 3]. These neoplasms generally appear 5-15 years after completion of radiation treatment. We present a case of a 16 year old male with secondary thyroid papillary carcinoma, four years after completion of radiotherapy for HD manifested by a change in thyroid signal intensity and unilateral enlargement on CT without a thyroid nodule. We will also discuss how the unique features of this case may have implications for the future detection of SMNs and the post radiation care of these patients.

Case Presentation

A 16 year old African American male with no family history of cancer was diagnosed with stage Ib, nodular sclerosing Hodgkin's disease at the age of 12 years. At the time, he was found to have disease limited to the mediastinum. He underwent 4 cycles of chemotherapy with doxorubicin, bleomycin, vincristine, etoposide, cyclophosphamide, and prednisone according to COG protocol AHOD0031 and was also given 2100 Grey of localized radiation therapy to the neck and mediastinum. The patient did well and continues to remain in remission from his Hodgkins Disease. A routine follow-up CT

scan 4 years later showed no evidence of disease. However, the right thyroid gland was noted to be heterogeneous and enlarged twice the size of the left lobe (Figure 1). Ultrasound of the thyroid showed a diffusely heterogeneous, enlarged right thyroid lobe with no discrete mass. Thyroid function tests were within normal limits and physical exam revealed an easily palpable thyroid lobe without cervical lymphadenopathy. Fine needle aspiration was attempted but was unsuccessful due to the firm nature of the gland and lack of distinct mass. Preoperative chest x-ray revealed no evidence of adenopathy, lung parenchymal lesions or other evidence of metastatic disease.

The patient was taken to the operating room for a thyroid lobectomy for diagnosis. Pathologic examination of the thyroid revealed a two cm papillary carcinoma with multiple separate microscopic nodules of carcinoma without evidence of lymphovascular or extrathyroidal extension. A completion thyroidectomy was then performed which showed no further evidence of papillary carcinoma giving him a stage 1 T1N0M0 multifocal papillary carcinoma of the thyroid. Post-operatively, the patient received 46.3 mCi of radioactive iodine (I^{131}). Currently, following thyroidectomy and radioactive I^{131} treatment (2.5 and 1.5 years respectively), the patient is doing well with no evidence of disease. His thyrogen stimulated thyroglobulin level two years post resection is 9.2 ng/ml (within normal range), and his I^{123} uptake scan shows no uptake.

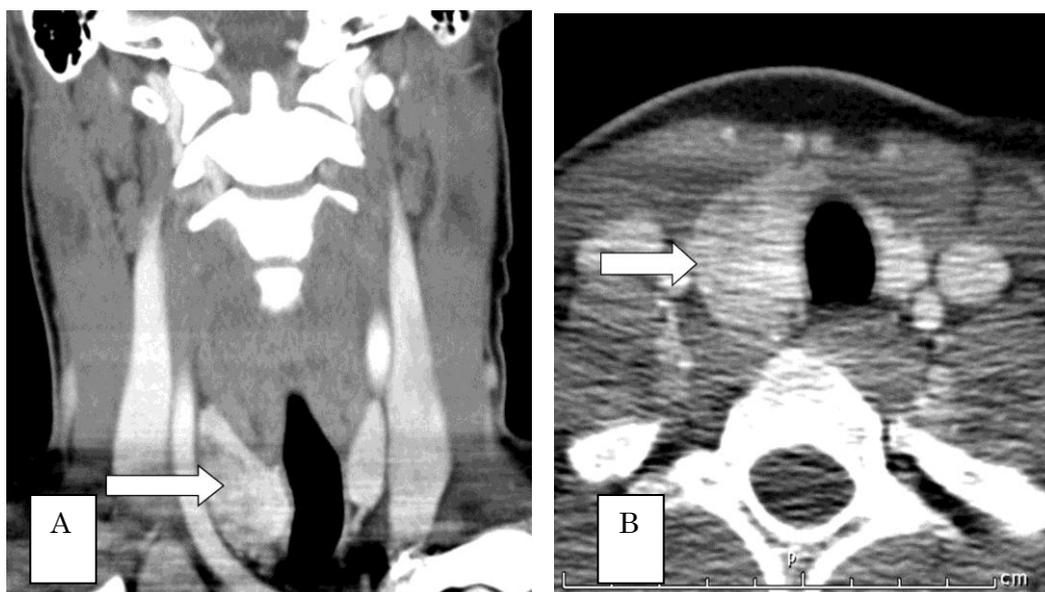


Figure 1 CT scan of neck. Coronal (A, left) and axial (B, right) views of neck demonstrating an enlarged right thyroid lobe, prompting workup for secondary thyroid malignancy. Arrow on both figures identifies enlarged right thyroid lobe.

Discussion

Malignant lymphomas in the pediatric and adolescent population are not a rare occurrence. In fact, the latest US Surveillance, Epidemiology, and End Results (SEER) data indicate that malignant lymphomas make up 26% of all cancers in the 15-19 age group [1]. Hodgkin's Disease (HD), the most common subtype of the malignant lymphomas in this age group, is treated with a variable chemotherapy regimen (dependent upon the clinical trial of choice) and low dose radiotherapy to the affected region [2, 4, 5]. These pediatric clinical trials are pushing chemotherapy to the thresholds of toxicity while minimizing the doses of radiotherapy [5]. Although cure rates for HD are rising above 90% in the young population, secondary malignancies are not uncommon [6].

The incidence of secondary malignant

neoplasms (SMNs) following radiotherapy, including thyroid cancer, has been well documented in literature [2, 3]. In three separate studies, the cumulative 20 year incidence of any SMNs was 9-17 percent [2, 3, 7].

Secondary malignant neoplasms of the thyroid gland are common solid tumors found in patients treated for HD at a young age [2]. Thyroid carcinoma risk is highest among younger patients, even when using radiotherapy below 20 Grey (Gy) and the risk of secondary thyroid cancer increases linearly with the dose of radiotherapy received [2, 8-10]. There may also be a genetic link between HD radiotherapy and thyroid carcinoma. Mertens *et al.* report a nonsignificant increased risk of thyroid carcinoma in individuals lacking genes Glutathione-s-transferase M1 (GSTM1) or glutathione-s-transferase T1 (GSTT1) [11]. Though the results in this study were nonsignificant, further studies with a larger

percentage of patients with thyroid carcinoma may yield a significant increased risk of development of thyroid cancer following HD radiotherapy.

Development of a papillary carcinoma following treatment of HD was reported only 28 months after diagnosis of HD and 22 months after receiving 1980 cGy of radiotherapy in a 13.5 year old boy. This patient had the quickest development of a SMN of the thyroid reported in the literature.

He presented with cervical lymphadenopathy, a globally enlarged thyroid gland, markedly elevated serum thyroglobulin and an ultrasound that revealed a large nodule. The diagnosis was made by fine-needle-aspiration [12]. According to current literature, development of thyroid cancer secondary to radiotherapy of HD is not detected until an average 5-15 years later, even in those patients under SMN surveillance (see Table 1).

Table 1 average time to development of Secondary Malignant Neoplasms of the thyroid following radiotherapy for Hodgkin’s disease

References	No. of patients in study	Average age at radiation	Latent period between irradiation and thyroid cancer diagnosis in years (age range)
[9]	2	4	4
[2]	5	11.3	15.5 (8.2-24.4)
[12]	1	12	1.8
Current Case	1	12	4
[8]	20	14	15.5 (5-26)
[3]	6	15.3	7.79-23.5
[15]	11	17.7	20.7 (6-38)
[20]	1	25	35
[21]	1	30	25

Thyroid abnormalities can also present sub-clinically, as in the current case. If thyroid cancer is diagnosed, the standard of care is to remove the thyroid with a thyroidectomy, and to give postoperative radioactive iodine ablation [13]. Prophylactic central neck dissections to remove cervical lymph nodes performed at the same time as the thyroidectomy show no significant increased risk of permanent damage, although the benefits of central neck dissections are not clear [14].

Treatment for thyroid cancer is highly

effective. The largest series involving childhood thyroid cancer patients is a retrospective study from Belarus that reported the long term follow-up on children with thyroid cancer in the post Chernobyl era following surgical resection. Seven hundred and forty pediatric patients were followed for a mean length of 10 years and overall survival was 99.5% at 5 years and 98.8% at 10 years [15-17]. Current mortality risk assessments show that survivors of HD treatment have an 18.5 year reduction in life expectancy, largely in part due to adulthood

SMNs [18]. Although the prognosis of papillary thyroid cancer is good, lymphatic seeding to the lungs is a definite risk. Physicians in charge for providing care to those with prior radiotherapy should remain vigilant and educate these patients on how to monitor changes in their thyroid structure and function.

Conclusion

The development of papillary thyroid cancer in our patient as well as the patient mentioned earlier in the discussion less than five years following cervical radiotherapy for HD is a rare occurrence that suggests that cancer following HD radiotherapy may be an earlier phenomenon than previously believed. This highlights that our knowledge of the incidence of all secondary cancers, specifically thyroid, prior to five years post HD treatment may be limited. If it is indeed an earlier phenomenon, it is unlikely to be appreciated by examination of the current cohort databases available given that most only include five year or greater patient survivors. In addition to the short time interval in the presentation of our patient's carcinoma, another unique aspect is the atypical presentation of the SMN. Our patient had no identified thyroid nodule on physical exam or imaging, only changes in signal intensity and unilateral enlargement on routine CT. This differs from the other short interval case mentioned earlier in our discussion as that patient did in fact have a nodule on imaging. Our case reemphasizes the need to monitor the recurrence of the HD and also the development of possible SMNs at an even shorter interval after irradiation. It also highlights that unilateral or bilateral gland enlargement and signal intensity changes on imaging are physical exam and

imaging characteristics that should be assessed for and monitored in the follow up post radiation care for these patients.

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