Chronic Myeloid Leukemia After Treatment with ^{131}I for Thyroid Carcinoma

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A 27-year-old male developed Philadelphia chromosome-positive chronic myeloid leukemia (CML) 13 years after a first dose of radioiodine (^{131}I) therapy for papillary thyroid carcinoma. He had received a cumulative ^{131}I dose of 670 mCi, in 8 divided doses over 8 years, up to April 1998, for ablation of ^{131}I avid tissues over the anterior neck region. The leukemogenic potential of radioactive iodine has been pointed out by many authors, but most reported cases have been acute leukemias. A literature review disclosed only 9 cases similar to ours. At present, there is no evidence to prove whether the development of CML after thyroid carcinoma represents a treatment-induced complication, a coincidence, or an increased susceptibility to secondary malignancies due to the malignant process itself. [*J Chin Med Assoc* 2005;68(5):230–233]

Key Words: chronic myeloid leukemia, radioiodine therapy, thyroid cancer

Introduction

Radioiodine (^{131}I) has been the treatment of choice for toxic nodular goiter, Graves' disease and metastatic thyroid cancer for over half a century. We have used ^{131}I whole body scans and serum thyroglobulin measurements to follow patients with differentiated thyroid cancer to detect local recurrences or distant metastases. If ^{131}I ablation therapy for thyroid remnants is performed after total thyroidectomy, the sensitivity and specificity of ^{131}I whole body scans and serum thyroglobulin measurements will increase. Further, ^{131}I treatment for differentiated thyroid carcinoma with lung and bone metastases prolongs survival and improves quality of life. However, ionizing radiation is believed to be leukemogenic, and although uncommon, leukemia after exposure to ^{131}I therapy for thyroid cancer has been reported.[1–5] Many cases were of acute myeloid leukemia, usually occurring after cumulative dosages of more than 800 mCi, in patients older than 50 years, and with intervals of less than 12 months between ^{131}I therapy.[2,5] Only 9 cases of chronic myeloid leukemia (CML) after ^{131}I therapy for thyroid cancer have been reported in the English medical literature. Here, we describe an additional case of CML, which was noted 13 years after the first dose of ^{131}I treatment for papillary thyroid cancer.

Case Report

In November 1987, a 12-year-old male underwent total thyroidectomy and cervical lymph node resection for papillary carcinoma of the right thyroid lobe with lymph node metastasis. In July 1990, October 1991, and August 1992, he received ^{131}I radiotherapy (doses of 30, 30, and 60 mCi, respectively) for avid uptake of ^{131}I over the anterior neck region on ^{131}I whole body scan. Lung metastasis was suspected on the post-^{131}I therapy scan in August 1992, but a repeat scan in March 1993 found complete resolution of the pulmonary lesions. Later, because of persistent

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accumulation of ^{131}I in the thyroid bed on subsequent scans, he took ^{131}I in doses of 100, 100, 100, and 150 mCi, respectively, in July 1993, September 1994, November 1995, and April 1998. After the last 150 mCi of ablation therapy, a follow-up scan still showed increased ^{131}I uptake in the thyroid bed and right pulmonary hilum (Figure 1). However, no more ^{131}I was given. The patient was maintained on suppressive, exogenous thyroid hormone therapy, with the level of thyroid stimulating hormone maintained at 0.1–0.4 μIU/mL. The total dosage of ^{131}I was 670 mCi, administered in 8 doses from July 1990 to April 1998. The time intervals between ^{131}I doses ranged from 10–13 months.

In January 2003, when he was 27 years old, the patient presented to our oncology ward with a 2-month history of general weakness, skin eruption, and night sweats. Priapism had occurred weeks earlier. The patient was first treated at Da-Lin Tzu-Chi Hospital, where laboratory examination revealed a white blood cell count of 56,920/mm^3, with 32% neutrophils, 13% bands, 11% monocytes, 10% lymphocytes, 9% basophils, 8% metamyelocytes, 5% promyelocytes, 3% blast cells, 2% myelocytes, and 2% eosinophils. Hemoglobin was 10 g/dL and platelet count was 826,000/mm^3. Leukocyte alkaline phosphatase score was 0, and lactate dehydrogenase level was 364 U/L. Bone marrow aspiration and biopsy showed marked hypercellularity. The Philadelphia (Ph) chromosome was present, and repeated bone marrow examination and chromosome analysis in our oncology ward confirmed the diagnosis of Ph-positive CML (Figure 2).

The patient had no family history of leukemia or thyroid disease, and he had not received external radiotherapy in the past. He was treated with hydroxyurea and prepared for allogeneic stem cell transplantation from his human leukocyte antigen (HLA)-identical sibling.

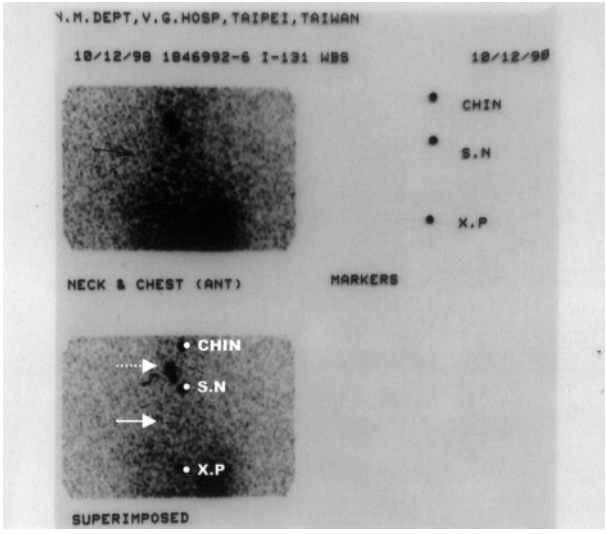

Figure 1. ^{131}I whole body scan (9 October 1988) showing persistent remnants in the thyroid bed and possible right hilar lymph node metastasis. In the lower figure, markers are superimposed on the scan. SN = sternal notch; XP = xyphoid process; ----→ = remnant thyroid tissue; → = possible right hilar lymph node metastasis.

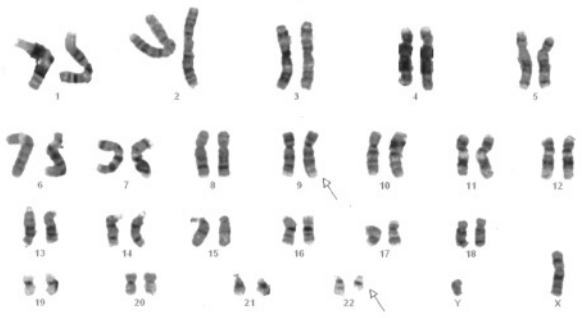

Figure 2. Karyotype of bone marrow cells showing the translocation t(9;22)(q34;q11.2).

Discussion

Leukemia as a complication of ^{131}I therapy is rare, but there is still concern about the possible carcinogenic effect of ^{131}I. For example, in 1963, Haynie and Beierwaltes[6] reported transient, dose-dependent, hematopoietic changes in patients receiving ^{131}I for thyroid cancer, and in 1986, Van Nostrand et al[7] found transient bone marrow suppression in post-^{131}I therapy patients; some of these patients still had reduced baseline blood counts 1 year after ^{131}I therapy.

The development of leukemia in patients treated for thyrotoxicosis or thyroid carcinoma has also been reported. Pochin,[1] in reviewing 60,000 cases of thyrotoxicosis treated with ^{131}I, found 17 cases of leukemia, of which 13 were acute, 1 was subacute, and 3 were chronic monocytic. The same author described 4 cases of acute leukemia in 175 patients treated with ^{131}I for thyroid cancer, thus giving a leukemia incidence of 2.3%, compared with an expected incidence of 0.4% in the general population.[2] Saenger et al[3] reported a mildly increased risk of leukemia in hyperthyroid patients treated with radioiodine (n = 22,000) versus surgery (n = 14,000) ($p < 0.05$); these authors also suggested an association between hyperthyroidism