Case Report

Acute myeloid leukemia following radioiodine therapy: Case report and brief literature review

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ABSTRACT

Radioiodine (RI) has been widely used in treatment of hyperthyroidism and thyroid cancer. The development of acute or chronic leukemia is a very rare complication of RI therapy. Here, we report two cases of acute myeloid leukemia occurring after the completion of RI therapy for follicular thyroid carcinoma along with a brief review of literature.

Key words: Acute leukemia, radioiodine, review

INTRODUCTION

Radioiodine (^{131}I) (RI) has been used in the treatment of thyroid cancer to eliminate residual thyroid tissue after thyroidectomy and to treat metastatic disease. Leukemia is an uncommon complication following exposure to ionizing radiation, and there are very few case reports documenting the occurrence of acute myeloid leukemia (AML), subsequent to RI therapy.[1-9] We hereby document two patients of follicular thyroid carcinoma (FTC) who developed AML after 3 years and 1 year completion of RI therapy.

CASE REPORTS

Case 1

A 56-year-old female presented with complaints of fatigue, loss of weight, and pallor to the hematology outpatient department (OPD) in 2011. She had undergone total thyroidectomy in 2004 for FTC. She had received 3 cycles of low-dose RI therapy (100 mCi) for 3 years. Simultaneously, she was administered high-dose RI (125 mCi) twice, during management. The cumulative dose received during the treatment period, until 2008, was 550 mCi. Her current hematological investigations in 2011 revealed pancytopenia and a bone marrow aspiration was performed. Bone marrow was found to be hypocellular [Figure 1, inset] with reduced normal hematopoiesis along with proliferation of approximately 60% blasts [Figure 1]. Immunophenotyping using flow cytometry showed these blasts to be positive for CD13, CD33, CD34, CD117, and human leukocyte antigens-DR, thus confirming a diagnosis of AML. Conventional cytogenetics showed a normal karyotype (46, XX). She was treated with standard doses of cytarabine and daunorubicin, using 3 + 7 induction protocol and was in morphological remission postinduction. Thereafter, the patient lost to follow-up.

Case 2

A 58-year-old male presented with weakness, petechial rashes to the hematology OPD in 2011. He had history of FTC with scalp metastases 8 years back. After thyroidectomy, he received low-dose RI therapy with I^{131} and remnant ablation high-dose RI (6 monthly) till December 2008, followed by low-dose therapy till October 2010. The total amount of RI received was 1050 mCi. A complete blood count presently showed bicytopenia with hemoglobin of 4.8g/dl, platelet count (16,000/cumm), total leukocyte count of 6800/cumm

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with 25% circulating blasts. Bone marrow aspiration showed hypercellular marrow with marked erythroid hyperplasia. There was reversal of myeloid to erythroid ratio, with megaloblastic erythroid maturation and features of dyserythropoiesis [Figure 2]. There were approximately 40% blasts among the nonerythroid cell population. Flow cytometry showed positivity for CD13, CD34, CD33, CD117, CD2, and CD71 in the blasts, thus confirming a diagnosis of AML, morphologically consistent with FAB AML-M6. The patient was lost to follow-up.

DISCUSSION

Leukemia as a second malignancy after treatment of thyroid cancer is rare and was first reported in 1955.[1] Majority of the cases of leukemia documented in literature are of acute leukemia, both myeloid and lymphoid,[1-16] followed by chronic myeloid leukemia[17-21] and rarely chronic lymphocytic leukemia. The overall incidence of acute leukemia following RI therapy, however, is low as documented by Menzel *et al*.[22] and Chow.[23] Chow in his cohort of 1348 patients did not observe any case of acute leukemia after a mean dose of 3.4 GBq (91.8 mCi) in papillary thyroid carcinoma and 4.14 GBq (111.89 mCi) in FTC. Similarly, de Vathaire *et al*.[24] in their study followed 1497 patients receiving an average of 7.2 GBq (194.59 mCi) of RI but found no instances of leukemia. A brief summary of the cases of acute leukemia developing in patients treated with ^{131}I for thyroid disorders has been tabulated in Table 1. In a recent study by Schroeder *et al*.,[15] they found 39 patients within a cohort of 3845 patients obtained from Dusseldorf Myelodysplastic Syndromes Registry in Germany, over approximately 30 years, who had developed myeloid neoplasm following RI therapy. These 39 patients comprised 18 patients of AML and 21 patients of myelodysplastic syndrome. The median time interval of progression to hematological abnormality was about 6.6 years (6–440 months). They also observed chromosomal aberrations in 68% of their cases. In our patients, the latency period was 3 years and 1 year, respectively, and conventional cytogenetics showed normal karyotype.

It has been observed that leukemias following RI therapy usually occur after cumulative doses higher than 800 mCi[6,8] although there have been cases of acute leukemia developing after dosage of 150 mCi[9] and as low as 22.1 mCi.[11] This suggests that other factors may be interplaying in leukemogenesis. The exact etiopathogenesis of leukemias induced by RI therapy is not well-understood although its clastogenic effects and induction of chromosomal aberration, specifically of chromosome 17, are well documented in literature.[25,26] It is believed that ^{131}I at any dose could cause sublethal damage to the bone marrow, and individual susceptibility plays an important role in patients developing leukemia after ^{131}I treatment. Thus, it is recommended that the bone marrow should not receive a total dose which exceeding 1000 mCi, and there should be an interval of at least 1 year between the doses.[7]

CONCLUSION

Though the use of ^{131}I appears to be increasing even for nonmalignant thyroid diseases and its benefits in the treatment of hyperthyroidism and thyroid cancer are proven, these patients require a regular follow-up even after completion of therapy. Although the development of the secondary malignancies can be due to aging or other causes rather than exposure to ^{131}I treatment, there is sufficient cumulative evidence suggesting the role of RI therapy in leukemogenesis. Thus, a strict hematological follow-up is warranted in such patients, for early detection of myelodysplastic syndromes, leukemias, or other hematological disorders.

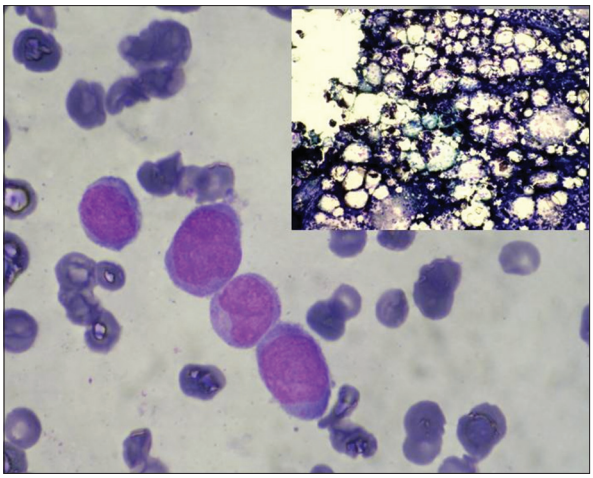

Figure 1: Leishman-stained bone marrow aspirate smears showing proliferation of large blasts with opened up chromatin and scant to moderate amount of cytoplasm. The inset shows a hypocellular marrow particle

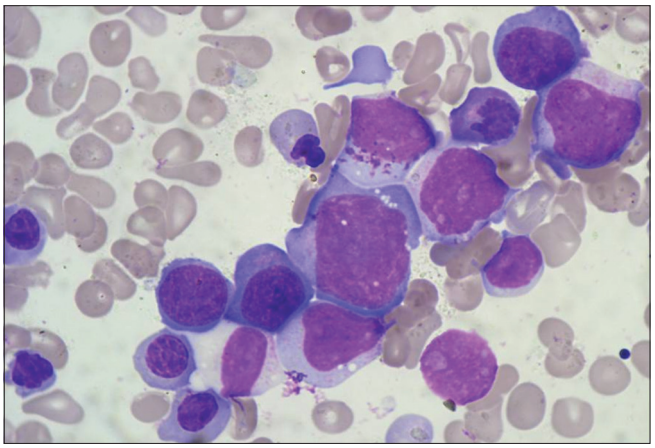

Figure 2: Leishman-stained bone marrow smears showing erythroid hyperplasia with dyserythropoiesis, and distinct population of blasts with opened up chromatin and 2–3 prominent nucleoli

Table 1: Brief review of patients with acute leukemia following radioiodine therapy

Authors, year	Number of patients	Age (years)/ sex	^{131}I dose (mCi)	Time interval from first dose	Type of leukemia (FAB, subtype)
Blom *et al.*, 1955[1]	1	67/female	63 mCi	19 months	AML, M4
McCormack and Sheline, 1963[2]	1	48/male	2.7 mCi	14 years	AML
Brincker *et al.*, 1973[3]	1	75/male	483 mCi	7 years	AML
Hall *et al.*,* 1992[4]	195		14 mGy (absorbed dose)	2 years	NA
Richards and Marcus, 1993[5]	1	28/male	6.21 Ci	NA	APML
Bitton *et al.*, 1993[7]	1	28/female	300 mCi	14 months	AML
Laurenti *et al.*, 1998[8]	2	45/female	27 mCi	14 months	AML, M2
		44/male	1 Ci	8 years	AML, M6
Roldán Schilling *et al.*, 1998[9]	2	34/female	150 mCi	2 years	AML
		43/female	150 mCi	5 years	APML
Piccirillo *et al.*, 1999[10]	1	48/female	295 mCi	12 years	ALL L1
Kolade *et al.*, 2005[11]	1	51/female	22.1 mCi	27 months	APML
Grudeva-Popova *et al.*, 2007[12]	1	47/male	NA	NA	APML
Focosi *et al.*, 2007[13]	1	55/female	90 mCi	12 years	AML
Ankit *et al.*, 2009[14]	1	45/male	80 mCi	17 months	AML, M5A
Schroeder *et al.*,** 2011[15]	18	63 years (mean age)	1216 mCi (mean dose)	79 months (average time)	AML
Gilabert and Prebet, 2012[16]	10	52 years (mean age)	<1000 mCi for each	Bimodal (1-3 years/8-10 years)	AML (12) B ALL (3)

*Hall *et al.* studied the incidence of leukemia among 46,988 Swedish patients exposed to ^{131}I for diagnostic reasons or to treat hyperthyroidism or thyroid cancer. Overall incidence being 0.4%, **They studied Dusseldorf myelodysplastic syndromes register and 5 other German myelodysplastic syndromes centers between 1982 and 2011. ^{131}I: Iodine-131, NA: Not available, AML: Acute myeloid leukemia, B ALL: B-cell acute lymphoblastic leukemia, APML: Acute promyelocytic leukemia, FAB: French-American-British

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Conflicts of interest
There are no conflicts of interest.

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