

## Case Report

# Acute Myeloid Leukemia after Low-Dose Radioiodine Therapy for Papillary Thyroid Carcinoma

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## Keywords

Leukemia · Radioiodine · Thyroid cancer

## Abstract

Papillary thyroid carcinoma is the most common primary thyroid cancer. Most frequently treated with surgical resection, some cases require radioactive iodine (RAI) therapy. Studies have suggested that there is an increase in second primary malignancy after RAI therapy amongst thyroid cancer survivors including acute myeloid leukemia (AML) as an infrequent cancer related to RAI therapy; it has a higher relative risk ratio in patients on higher doses of radiation exposure. We would like to report a 30-year-old lady who was diagnosed with papillary thyroid carcinoma. She underwent total thyroidectomy and received a low-dose RAI <sup>131</sup>I therapy at a dose of 150 mCi, after which she developed therapy-related AML. Here we would like to highlight the association of AML with low-dose RAI as an infrequent cause of a second primary tumor compared to high doses.

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## Introduction

The thyroid gland located at the base of the neck is part of the endocrine system. It is responsible for the production, storage, and release of iodine-containing hormones from its thyroid follicles called tri-iodothyronine (T3) and thyroxine (T4) hormones which are necessary to regulate various vital body functions. It also secretes calcitonin hormone from its parafollicular cells, which is responsible for the regulation of blood calcium levels. The

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**Table 1.** Case reports of RAI therapy-induced AML in thyroid cancer [10–13]

Case	First Author [Ref]	Age	Gender	Primary disease	RAI cumulative dose <sup>131</sup> I	Time to secondary tumor	AML cytogenetics	Remission
1	Schilling [10]	34	Female	Papillary thyroid carcinoma	150 mCi	5 years	Acute promyelocytic leukemia Not reported on cytogenetics	Achieved
2	Richards [11]	28	Male	Mixed papillary and follicular adenocarcinoma of thyroid	621.6 mCi	15 months	APL, AML FAB M3 T(15;17)(q22;21)	Achieved
3	Bitton [12]	28	Female	Metastatic follicular thyroid cancer	300 mCi	14 months	Acute myelogenous leukemia	NA
4	Grudeva-Popova [13]	47	Female	Thyroid cancer (type not specified)	NA	NA	t-APL t15;17(q22;q21)	Achieved

NA, not available.

thyroid gland is covered by a fibrous capsule that extends a thin collagenous septum to divide the follicles into lobules [1].

Thyroid cancer can be subclassified into differentiated or undifferentiated thyroid cancer depending on the epithelial cell the tumor cells are derived from. Papillary thyroid cancer is the most common type of differentiated thyroid cancer, which comprises the vast majority (>85%) of all thyroid cancers. This is followed by follicular thyroid cancer and anaplastic (undifferentiated) thyroid cancer [2].

The basic goals of initial therapy for patients with papillary thyroid cancer would be to improve survival and reduce disease recurrence. Initial therapy following risk stratification of the disease burden is by surgical resection of the primary tumor and adjacent metastatic lymph nodes as it is an important factor in determining disease outcome, while residual metastatic lymph nodes represent the most common site of disease persistence/recurrence. Other therapies such as radioactive iodine (RAI) treatment, TSH suppression or other adjuvant therapies might be necessary in certain cases [3].

Leukemia is a type of blood cancer that affects the bone marrow and there are two forms: acute and chronic leukemia. Acute myeloid leukemia (AML) is characterized by a rapid increase in the number of immature white blood cells. In most cases with RAI therapy-induced leukemia reported in the literature it developed after higher cumulative doses of RAI therapy [4] (Table 1).

Here we present a rare case of acute leukemia secondary to radioiodine-induced therapy after a low dose of <sup>131</sup>I of 150 mCi.

### Case Presentation

Our patient was a 30-year-old female diagnosed with hyperthyroidism in 2013. Later on her US thyroid showed thyroid enlargement with focal lesions in the right lobe containing tiny areas of punctate calcification giving rise to a suspicion of papillary thyroid carcinoma. A <sup>99</sup>Tc thyroid scan revealed multinodular goiter with two cold nodules in the right lobe. In June 2015 the patient underwent total thyroidectomy with level VI lymph node dissection. Histopathology revealed multifocal well-differentiated papillary thyroid cancer with deposits in

the local lymph nodes. In July 2015, she received RAI  $^{131}\text{I}$  therapy at a dose of 150 mCi orally. A thyroid scan done at this time revealed significant residual thyroid tissue in the neck. A follow-up  $^{131}\text{I}$  scan at a 3-mCi dose revealed complete ablation. She was doing well on her follow-up post-treatment.

Sixteen months later the patient was admitted with acute menorrhagia and symptomatic anemia. Her peripheral smear revealed severe anemia, thrombocytopenia, and leukocytosis with many circulating blasts suggestive of acute leukemia. Flow cytometry of bone marrow aspirate was consistent with AML with 29% blasts and 44% monocytes. Chromosome analysis revealed 46,XX,inv(16)(p13.1q22)CBFB-MYH11 cytogenetic abnormality.

After her diagnosis she received two cycles of induction with a (3 + 7) protocol, to which she responded well and achieved complete remission.

## Discussion

Thyroid cancer is classified into differentiated or undifferentiated depending on the epithelial cell the tumor cells are derived from. Differentiated thyroid cancers account for >95% of thyroid cancer with papillary thyroid cancer as the most common type of differentiated thyroid cancer (85%) followed by follicular thyroid cancer [2].

Papillary thyroid carcinoma is the most common primary thyroid cancer with an incidence of 15.8 per 100,000 individuals every year. It has an excellent prognosis with a survival rate of more than 90% [5].

The primary treatment for papillary thyroid cancer is surgery. For patients undergoing RAI remnant ablation, or RAI treatment of presumed (adjuvant therapy) or known (therapy) residual or metastatic disease, removal of all normal thyroid tissue is an important element of initial surgery [3].

RAI therapy is a type of nuclear medicine treatment, the principle of which involves systemic ingestion of  $^{131}\text{I}$  with, thereafter, the selective absorption of the drug carrying the radioactive element in it, resulting in a zone of localized high-radiation dosage in the selective absorption tissues to destroy any remnant of normal thyroid tissue after total thyroidectomy [6]. RAI therapy is reported to increase the risk of a second primary malignancy. In a systematic review it was observed, although rarely, that patients had a higher risk of subsequent leukemia after thyroid cancer treated with iodine therapy [7].

Therapy-related acute myeloid neoplasms (t-AML) is a type of AML that is caused by previous treatment with chemotherapy or radiation therapy such as alkylating agents, ionizing radiation therapy, topoisomerase II inhibitors, and others [8].

In a 2016 review of 37 patient with t-AML the most common subtype noted was trans t(15;17), less commonly inv(16) type reported after RAI therapy [4, 9].

In this report we would like to highlight (1) the association of AML with low-dose RAI as an infrequent cause of a second primary tumor compared to high doses, (2) how chromosome abnormality associated with 46,XX,inv(16)(p13.1q22)CBFB-MYH11 was a an uncommon mutation in our case compared to RAI therapy-induced leukemia that has shown a favorable response, and (3) how it compares to other RAI therapy-related AML reported in the literature.

## Conclusion

Very high doses of RAI (exceeding 600 mCi) have been known to increase the risk of acute leukemia. However, leukemia following a lower dose of RAI can also occur.

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## Statement of Ethics

Consent was obtained from the patient.

## Disclosure Statement

The authors have nothing to disclose.

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## Author Contributions

Arwa Alsaud, Mohamed A. Yassin: manuscript writing and editing.  
Amr Ashour, Khaldun Obeidat, Bahjat Azrieh, and Shehab Mohamed: clinical management.

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