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Case Report

POOR SURVIVAL AND INCREASED RELAPSED RATE OF ACUTE MYELOID LEUKEMIA FOLLOWING RADIOACTIVE IODINE THERAPY FOR PAPILLARY CARCINOMA OF THYROID

Ishwor Man Singh[1], Bajarang Prasad Sah[2]

[1]Department of Haemato Oncology, [2]Department of ENT and Head and Neck Surgery, Purbanchal Cancer Hospital, Birtamode, Jhapa, Nepal

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ABSTRACT

Radioactive iodine (RAI) therapy is widely used and has an important role in the management of hyperthyroidism and thyroid malignancies. The development of therapy related acute or chronic leukemia is a very rare complication of RAI therap**.** Therapy-related acute myeloid leukemia (t-AML) comprises 10–20% of all newly diagnosed cases of AML and is related to previous use of chemotherapy or ionizing radiotherapy for an unrelated malignant non-myeloid disorder or autoimmune disease. We report a case of Papillary Carcinoma of Thyroid who underwent total thyroidectomy followed by treatment with a cumulative dose of 300mCi of RAI later on, developed acute myeloid leukemia after 18 months post therapy. Then after completion of induction and consolidation for AML relapsed after 8 months. Thus suggesting that prognosis for patients with t-AML to be considered worse than that for patients with primary de novo AML which could be due to presence of adverse karyotypic abnormalities and molecular lesions.

Keywords: *Radioactive iodine (RAI), Therapy-related acute myeloid leukemia (t-AML), Allogeneic Stem Cell Transplantation (All0-SCT), Papillary Carcinoma of thyroid, Chemotherapy*

INTRODUCTION

According to the 2017 World Health Organization (WHO) classification system for tumors of hematopoietic and lymphoid tissues, therapy-related myeloid neoplasms include cases of acute myeloid leukemia (t-AML), myelodysplastic syndromes (t-MDS), and myelodysplastic/myeloproliferative neoplasms (t-MDS/MPN), which arise as a complication of cytotoxic chemotherapy and/or radiation therapy administered for a prior neoplastic or non-neoplastic disorder [1]. Epidemiologic evidence shows that the incidence of t-AML has greatly increased during the past three decades as a result of better (but also mutagenic) cancer treatments and the increased survival of cancer patients [2]. Therapy-related AML accounts for 10–20% of all cases of newly diagnosed AML. Most cases of t-AML associated with a prior neoplastic disorder. (~70%) occur after the treatment of solid tumors (e.g., after treatment for breast cancer) and ~30% after treatment of hematological neoplasms, e.g., non-Hodgkin's lymphoma (NHL).[3,4]

CASE REPORT

A 50−year−old female a diagnosed case of Papillary Carcinoma of right lobe of Thyroid gland, Classical variant in june,2022. She underwent Total

***Corresponding author:**
Ishwor Man Singh
Email:ishwor6153@gmail.com
ORCID: https://orcid.org/0000-0001-6831-3300

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Thyroidectomy with Right CNC followed by RAI therapy (150 mci each, total of 2 cycles). Postoperatively she was well and was hypothyroid under thyroxine 125mcg(TSH: 28mIU/L) until Jan, 2024 when she presented with a complain of Weakness on exertion, tingling and numbness, fatigue, and pallor and purpura. Then on routine investigations, she was found to have severe anemia, thrombocytopenia and leukocytosis with increased blasts cells of 10% with hemoglobin level of 55 g/L, mean corpuscular volume of 101fL, , leukocyte count of 35.6 × 10^9 /L, and platelet count of 72 × 10^9/L and hypocalcaemia (5.5 mg/dl) . In view of her low blood counts, she received multiple transfusions and evaluated as a suspected case of leukemia. Bone marrow aspiration and trephine biopsy showed acute leukemia with presence of increased blasts (> 20%). Flowcytometry for acute leukemia panel proved to be Acute Myeloid Leukemia with monocytic differentiation (AML- M5)with Positive markers CD 13, CD117, CD33, CD34 (heterogeneous), CD38, CD64(dim), CD123, CD73,HLA-DR (heterogeneous), Atypical cells/Blast >20% and Cytogenetic showed presence of Inv 16 positive. She was then given induction chemotherapy with DA 3+7 AML protocol for 7 days. End of Induction BM done on D28 showed morphological remission status with 1 % blasts and Normocellular marrow. Induction was followed by 3 cycles of monthly consolidation with HIDAC regimen. She was stable hematological and clinically for 10 months post chemotherapy, until March,2025 when she presented with gum swelling,bleeding and purpura over different parts of body. On Peripheral blood film showed anemia, thrombocytopenia and leukocytosis with blasts (12%) suggesting for relapsed AML. Then after discussion about poor prognosis and need for intensive regimen with FLAG-Ida and consolidation with Allo-SCT but opted due for palliative azacyditine and venetoclax due to poor financial condition and increased risk due to advanced age.

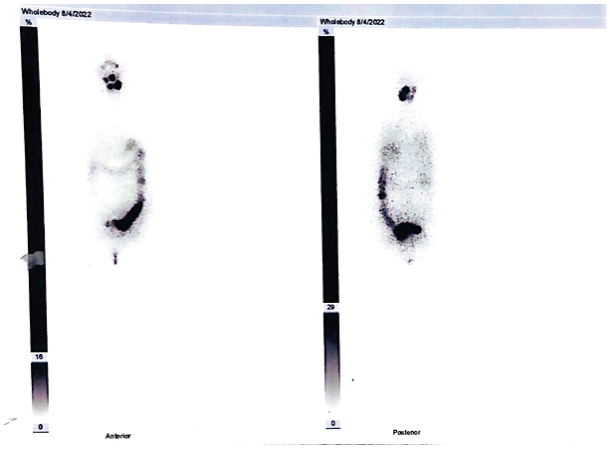

Figure 1: Pre therapy Iodine whole body scan showing increase uptake

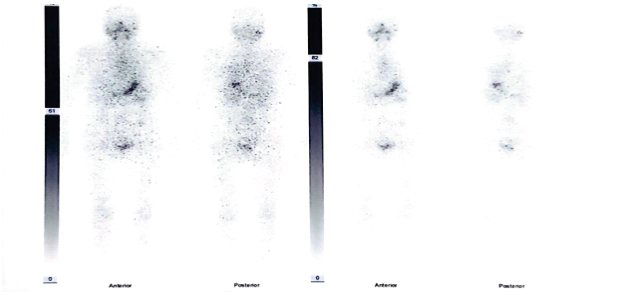

Figure 2: Post therapy Iodine whole body scan showing decrease in uptake

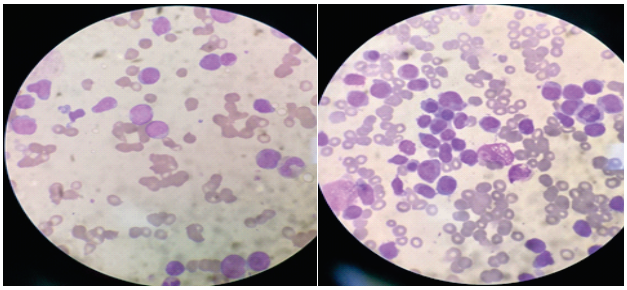

Figure 3: (a) Peripheral blood picture showing Acute leukemia with presence of blasts (b)Bone marrow aspiration showing presence of myeloblasts

DISCUSSION

Therapy-related acute myeloid leukemia (t-AML) is one of the most serious long-term complications of cancer chemotherapy. Various cytotoxic agents and exposure to ionizing radiation can lead to the development of t-AML, which is usually associated with adverse genetic changes and a poor prognosis. Over the past decade, insights into leukemogenesis have generated significant advances in the risk stratification of t-AML, and have offered us the opportunity to develop individualized options for treatment that target disease biology.

Leukemia as a second malignancy after treatment of thyroid cancer is rare and was first reported in 1955.[5] The majority of the cases of leukemia documented in the literature are of acute leukemia, both myeloid and lymphoid,[5,6] followed by chronic myeloid leukemia and rarely chronic lymphocytic leukemia.[11,12] The overall incidence of acute leukemia following RAI therapy, however, is low as documented by Menzel et al. [10] and Chow.[13] 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. A German cohort studied 107 patients with thyroid carcinoma with bone metastasis. In that study, four patients developed AML. These patients received the maximum dose of RAI (11.1 GBq) within a very short interval and showed high uptake in bone metastasis.[14] It has been observed that leukemias following RAI therapy usually occur after cumulative doses higher than 800 mCi[6,7]although there have been cases of acute leukemia developing after a dosage of 150 mCi[5] and as

low as 22.1 mCi.[9] The exact etiopathogenesis is not well−understood although its clastogenic effects and induction of chromosomal aberration, specifically of chromosome 17, are well documented in the literature.[15,16] It is believed that 131I at any dose could cause sublethal damage to the bone marrow, and individual susceptibility plays an important role in patients developing leukemia after 131I 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.[8]Overall, the prognosis for patients with t-AML is considerably worse than that for patients with primary de novo AML. It is estimated that the median overall survival (OS) is 8–10 months and the 5-year OS is 10–20% [8,9]. Therefore, allogeneic hematopoietic-cell transplantation (HCT) from a suitable donor has been established practice for all patients with non-acute-promyelocytic-leukemia (non-APL) t-AML in first complete remission (CR1) for more than 30 years. More recently, however, this generalized approach has become controversial due to the increasing recognition of the prognostic significance of the molecular tumor genetics in relation to the risk of relapse.[9]There are clearly no universal right approaches and there may well be different levels of benefit from HCT in the different risk groups of patients with t-AML. Therefore, efforts have been made to individualize treatment even for patients with t-AML

CONCLUSION

The use of 131I appears to be increasing even for nonmalignant thyroid diseases and its benefits in the treatment of hyperthyroidism and thyroid cancer are proven but these patients require a regular follow−up even after completing the therapy. Although the development of the secondary malignancies can be due to aging or other causes rather than 131I exposure, there is sufficient evidence suggesting the role of RAI therapy in leukemogenesis. Thus, strict follow-up is recommended in such patients, for early detection of MDSs, leukemias, or other hematological disorders.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed

REFERENCES

1. Mcnerney, M.E.; Godley, L.A.; Le Beau, M.M. Therapy-related myeloid neoplasms: When genetics and environment collide. Nat. Rev. Cancer 2017, 17, 513-527. [Cross Ref] [PubMed]
2. Nilsson, C.; Linde, F.; Hulegårdh, E.; Garelius, H.; Lazarevic, V.; Antunovic, P.; Cammenga, J.; Deneberg, S.; Eriksson, A.;Jädersten, M.; et al. Characterization of therapy-related acute myeloid leukemia: Increasing incidence and prognostic implications.Haematologica 2022. online ahead of print. [CrossRef] [PubMed]
3. Fianchi, L.; Pagano, L.; Piciocchi, A.; Candoni, A.; Gaidano, G.; Breccia, M.; Criscuolo, M.; Specchia, G.; Pogliani, E.M.;Maurillo, L.; et al. Characteristics and outcome of therapy related myeloid neoplasms: Report from the Italian network on secondary leukemias. Am. J. Hematol. 2015, 90, E80-E85. [CrossRef]
4. Kayser, S.; Döhner, K.; Jürgen Krauter, J.; Köhne, C.H.; Horst, H.A.; Held, G.; Lilienfeld-Toal, M.; Wilhelm, S.; Kündgen, A.;Götze, K.; et al. The impact of therapy-related acute myeloid leukemia (AML) on outcome in 2853 adult patients with newly diagnosed AML. Blood 2011, 117, 2137-2145. [CrossRef] [PubMed]
5. Blom PS, Querido A, Leeksma CH. Acute leukaemia followingx?ray and radioiodine treatment of thyroid carcinoma. Br JRadiol 1955;28:165?6.
6. Alsaud A, Mohamed S, Yassin MA, Ashour A, Obeidat K,Azrieh B. Acute myeloid leukemia after low?dose radioiodinetherapy for papillary thyroid carcinoma. Case Rep Oncol2020;13:207?11.
7. Jeong JH, Ahn JY, Park SH, Park MJ, Kim KH, Hong JS.A case of therapy?related acute myeloid leukemia with inv(16)(p13.1q22) after single low?dose iodine?131 treatment for thyroidcancer. Korean J Hematol 2012;47:225?8.
8. Grudeva?Popova J, Yaneva M, Zisov K, Ananoshtev N.Therapy?related acute promyelocytic leukemia after treatmentwith radioiodine for thyroid cancer: Case report with literaturereview. J BUON 2007;12:129?32.
9. Brincker H, Hansen HS, Andersen AP. Induction of leukemia by131?I treatment of thyroid carcinoma. Br J Cancer 1973;28:232?7.
10. Menzel C, Grünwald F, Schomburg A, Palmedo H, Bender H,Späth G, et al. "High?dose" radioiodine therapy in advanced differentiated thyroid carcinoma. J Nucl Med 1996;37:1496?503.
11. Walgraeve D, Verhoef G, Stul M, Cassiman JJ, Mecucci C,Van den Berghe H, et al. Chronic myelogenous leukemia aftertreatment with 131?I for thyroid carcinoma. Report of a case andreview of the literature. Cancer Genet Cytogenet 1991;55:217?24.
12. Shimon I, Kneller A, Olchovsky D. Chronic myeloid leukaemiafollowing 131?I treatment for thyroid carcinoma: A report oftwo cases and review of the literature. Clin Endocrinol (Oxf)1995;43:651?4.
13. Chow SM. Side effects of high-dose radioactive iodine forablation or treatment of differentiated thyroid carcinoma. J HongKong CollRadiol 2005;8:127-35.
14. Petrich T, Widjaja A, Musholt TJ, Hofmann M, Brunkhorst T,Ehrenheim C, et al. Outcome after radioiodine therapy in107 patients with differentiated thyroid carcinoma and initialbone metastases: Side?effects and influence of age. Eur J NuclMed 2001;28:203?8.
15. Lopes Rodrigues C, Corbo R, Proença Martins FP,Barbosa da Fonseca LM, Aranha IP, Gutfilen B. Low dosageof 131iodine effects on chromosomes. Yale J Biol Med2003;76:109?14.
16. Ramírez MJ, Puerto S, Galofré P, Parry EM, Parry JM, Creus A,et al. Multicolour FISH detection of radioactive iodine?induced17cen?p53 chromosomal breakage in buccal cells fromtherapeutically exposed patients. Carcinogenesis 2000;21:1581?6.