

# Therapy - Related Myeloid Neoplasms: A Case Report

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**Abstract:** ***Introduction:** Therapy - related myeloid neoplasms is a neoplasm that occur as a late complication of cytotoxic chemotherapy and/ or radiation therapy administered for a prior neoplastic or non - neoplastic disease. This neoplasm account for 10 - 20% of all cases of myeloid neoplasm. This paper reports a case of a 61 - year - old male with complaints of saddle - back fever for 1 month. The patient previously had a parotid gland malignancy in 2015 and had been treated with radiation therapy for 25 times. **Case description:** Microscopic examination shows a trephine biopsy consist of trabecular bone with a marrow spaces. Bone marrow shows a hypercellular appearance. Focus of ALIP (abnormal location of immature precursor) can be observed. The hemopoietic cells consist of myeloid, erythroid and megakaryocytic lineage. The erythroid lineage consists of normoblast. The myeloid lineage shows maturation with focus of increased blast count < 20% (monoblast, myeloblast and promonocyte). Megakaryocyte shows prominent hypolobated - micromegakaryocytic features (suggest a dysmegakariopoiesis features). **Conclusions:** Based on clinical data, laboratory and histopathological examination, the patient was diagnosed with therapy - related myeloid neoplasms.*

**Keywords:** Therapy - related myeloid neoplasms, blast count, dysmegakariopoiesis

## 1. Introduction

Therapy - related myeloid neoplasms is a neoplasm that occur as a late complication of cytotoxic chemotherapy and/ or radiation therapy administered for a prior neoplastic or non - neoplastic disorder<sup>1, 2</sup> and as a unique clinical syndrome distinguished by prior iatrogenic exposure to mutagenic agents.<sup>1</sup>

Therapy - related myeloid neoplasms account for 10 - 20% of all cases of myeloid neoplasms. Therapy - related myeloid neoplasms can occur at any age depends on previous exposure or therapy and the incidence increases with age.<sup>4, 5</sup> Patient often present with marrow failure and one or more cytopenia.<sup>1</sup> This paper reports a case of Therapy - related myeloid neoplasms that occurred in 61 - year - old male.

## 2. Materials and Methods

A 61 - year - old male with complaint of fever for 1 month. The patient previously had a parotid gland malignancy in 2015 and had been treated with radiation therapy for 25 times. On physical examination, there was anemic conjunctiva. Laboratory tests showed Hb levels of 8.0 g / dL (N 14 - 18), leukocytes 2.19 /  $\mu$ L (N 4, 800 - 10, 800), platelets 732, 000 /  $\mu$ L, MCV 88.7 fL (N 79.0 - 99.0), MCH 28.9 pg (N 27.0 - 31.0), MCHC 32.6 g / dL (N 33.0 - 37.0).

On 29<sup>th</sup> July 2020, biopsy was performed on the patient from the anterior posterior iliac spine. We received two specimens of trephine without fixation with a length of 2 and 2.5 cm and one aspirate specimen with a volume of approximately 6 cc. Microscopic examination of a bone marrow touch imprint shows increased blast cells and a prominent hypolobated - micromegakaryocytic features suggests a dysmegakaryopoiesis appearance (Figure 1). A trephine biopsy consists of a bone trabecular with a marrow spaces. The bone marrow shows a hypercellular appearance. ALIP focus (abnormal location of immature precursor) can be observed with conventional H&E staining and confirmation

with IHC is required. The tissue consists of myeloid lineage with maturation, erythroid and megakaryocytic proliferation with morphology as same as aspirate.

Aspirate in the form of cell block shows hematopoietic cells consist of myeloid lineage, erythroid and prominent megakaryocytic. Erythroid lineage consists of normoblast cells. Myeloid lineage with maturation and focus of increased number of blast cells (monoblast, myeloblast and promonocyte) < 20% in this specimen (Figure 2). Megakaryocyte shows a prominent hypolobated - micromegakaryocytic features (suggests a dysmegakariopoiesis appearance) and others morphology was within normal limits (Figure 3).

From the histopathology examination, we concluded marrow spaces with hypercellular appearance in trephine biopsy tissue and shows Abnormal Localization of Immature Precursor (ALIP) and aspirate shows myeloid lineage with increased blast cells (<20% in this specimen) and prominent dysmegakariopoiesis) which can be an entity with a differential diagnosis of Therapy - related Myelodysplastic syndrome / Myeloproliferative Neoplasm, Unclassifiable with excess blast (t - MDS / MPN, U - EB) and Therapy - related Myelodysplastic syndrome, Unclassifiable with excess blast (t - MDS, U - EB).

## 3. Discussion

Therapy - related myeloid neoplasms (t - MNs) include therapy - related cases of acute myeloid leukemia (t - AML), myelodysplastic syndrome (t - MDS) and myelodysplastic/ myeloproliferative neoplasms (t - MDS/MPN) that occur as a late complication of cytotoxic chemotherapy and/ or radiation therapy administered for a prior neoplastic or non - neoplastic disorder.<sup>1 - 4</sup> Although cases may be diagnosed morphologically according to the number of blasts in the blood and/ or bone marrow, these t - MNs are best considered together as a unique clinical syndrome distinguished by prior iatrogenic exposure to mutagenic

agents.<sup>1, 6</sup> Cytotoxic agents implicated in therapy - related myeloid neoplasms such as alkylating agents, ionizing radiation therapy, topoisomerase II inhibitors and others.<sup>1</sup>

Therapy - related myeloid neoplasms account for 10 - 20% of all cases of myeloid neoplasms. t - MNs can be affected any age group but the risk associated with alkylating agents or radiation therapy generally increases with age, whereas the risk associated with topoisomerase II inhibitors is similar across all ages.<sup>1, 7</sup> Most patients have been treated for a previous malignancy, about 70% have been treated for a solid tumor and 30% for a hematological neoplasm.<sup>1, 5</sup>

Two subsets of t - MNs are generally recognized clinically. The more common occurs 5- 10 years after exposure to alkylating agents and/ or ionizing radiation. These cases often present with an MDS with marrow failure and one or more cytopenia, although a minority present with t - MDS/MPN or t - AML.<sup>1, 5</sup> The second t - MN subset accounts for 20 - 30% cases has a shorter latent period (1 - 5 years) and follows treatment with agents that interact with topoisomerase II inhibitors. Most cases in this subset do not have a myelodysplastic phase but present with overt acute leukemia.<sup>1, 8</sup>

Microscopy examination of t - MNs present with an MDS or acute leukemia associated with multilineage dysplasia. The peripheral blood shows one or more cytopenia which anemia was found with the red blood cell morphology characterized by macrocytosis and poikilocytosis. The bone marrow may be hypercellular, normocellular or hypocellular and reticulin fibrosis is common. Dysgranulopoiesis and dysmegakariopoiesis are usually present but most cases show dysmegakariopoiesis. Cases presenting with myelodysplasia and cytopenia may be designated as t - MDS or t - AML depending on the blast percentage.<sup>1, 4</sup>

More than 90% patient with t - MNs show an abnormal karyotype. Cytogenetic abnormalities implicated in patients with a history of exposure to alkylating agents and radiation such as unbalanced chromosomal aberration 5 and 7 and complex karyotype<sup>2, 9</sup> whereas abnormalities in patients with history of topoisomerase II inhibitors show balanced translocations 11. q23.3 (KMT2A) and 21. q22.1 (RUNX1).<sup>2, 10</sup>

There are no specific immunophenotypic findings in t - MNs and varies between cases. Blasts are generally CD34

positive and express panmyeloid antigens such as CD13, CD33 and MPO.<sup>1, 2</sup>

The prognosis of t - MNs is generally poor, although it is strongly influenced by the associated karyotypic abnormality as well as the comorbidity of the underlying malignancy or illness for which the cytotoxic therapy was administered. Overall 5 - year survival rates of < 10% are commonly reported. Cases associated with abnormalities of chromosome 5 and/ or 7, TP53 mutations and a complex karyotype have a poor outcome, with a median survival time of < 1 year while cases with balanced chromosomal translocations generally have a better prognosis.<sup>1</sup>

#### 4. Conclusion

Therapy - related myeloid neoplasms is a neoplasms that occur as a late complication of cytotoxic chemotherapy and/ or radiation therapy administered for a prior neoplastic or non - neoplastic disorder. Cytotoxic agents implicated in therapy - related myeloid neoplasms such as alkylating agents, ionizing radiation therapy, topoisomerase II inhibitors and others. This case can be diagnosed morphologically and categorized as t - MDS or t - AML according to the number of blasts in the blood and/ or bone marrow.

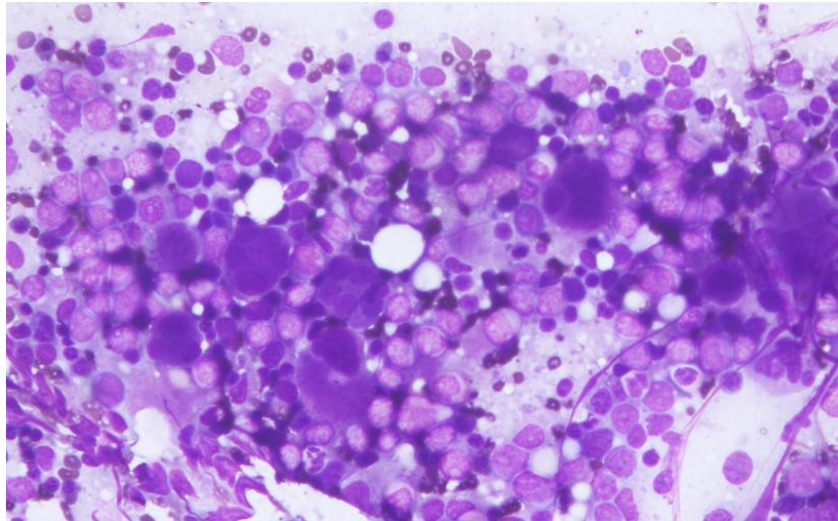
Therapy - related myeloid neoplasms account for 10 - 20% of all cases of myeloid neoplasms and any age group can be affected. In this case, it occurred in a 61 - year - old male. The patient came with complaint of fever for 1 month. Based on clinical, laboratory and histopathology examination, the patient was diagnosed with therapy - related myeloid neoplasms with differential diagnosis Therapy - related Myelodysplastic syndrome / Myeloproliferative Neoplasm, Unclassifiable with excess blast (t - MDS / MPN, U - EB) and Therapy - related Myelodysplastic syndrome, Unclassifiable with excess blast (t - MDS, U - EB).

#### 5. Acknowledgements

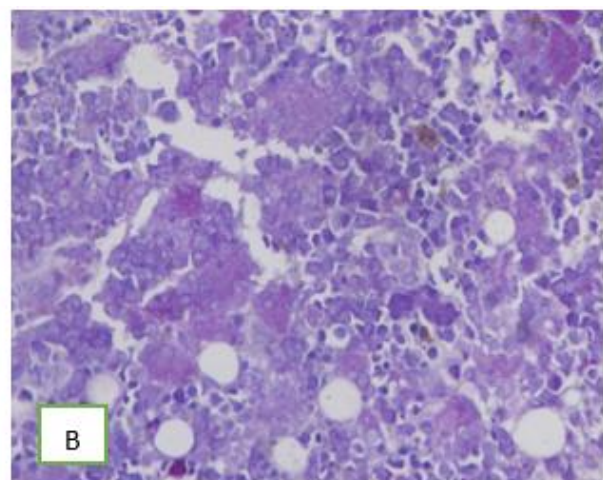
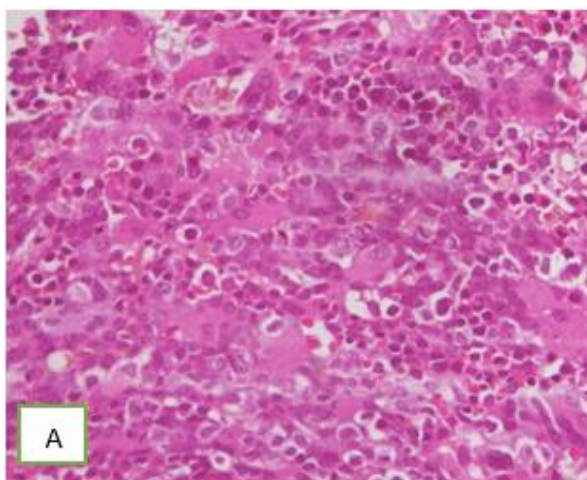
There is no conflict of interest between authors and the department of pathology during this time of writing.

#### Tables and Figures

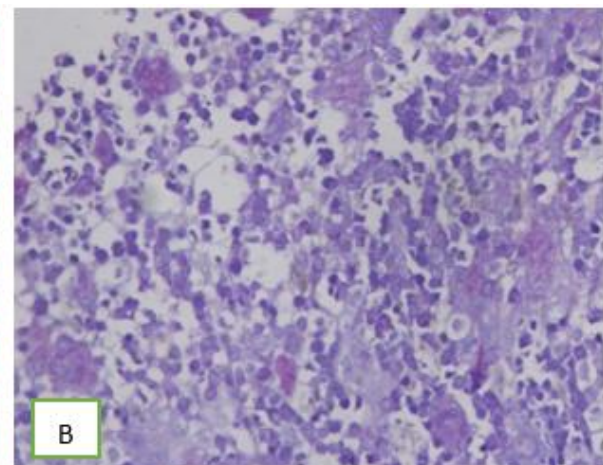
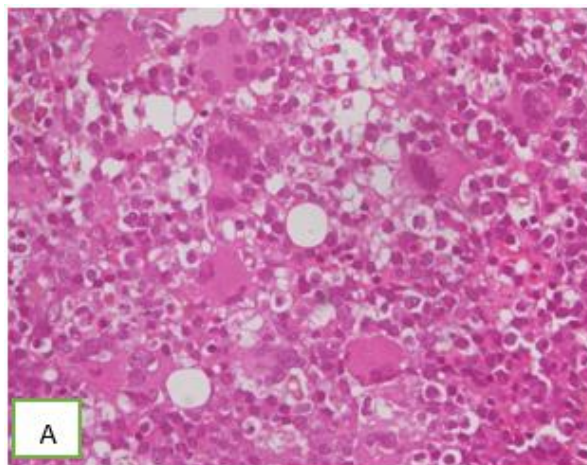




**Figure 1:** Touch imprint shows increased cell blast and dysmegakariopoesis (Wright - Giemsa, magnification 400x)



**Figure 2:** A) There was an increased number of cell blast (H&E, magnification 400x), B) (Wright - Giemsa, magnification 400x)



**Figure 3:** A) Megakaryocyte shows prominent hypolobated – micromegakaryocytic features (suggests a dysmegakariopoesis appearance) (H&E, magnification 400x), B) (Wright - Giemsa, magnification 400x)

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