



Case Report

Acute myeloid leukemia with t(8;21)(q22;q22.1); runx1-runx1t1 with tuberculosis - A case report

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ABSTRACT

Background: In patients suffering from malignancies incidence of tuberculosis is highest in cases of hematological malignancies in comparison to solid organ malignancies.¹ Despite the fact tuberculosis remains under-diagnosed condition in hematological malignancies like acute leukemia and it may be a cause of febrile neutropenia in these cases. Rescheduling and/or alterations in therapies are required in these cases.²

Case History: A 16year old male diagnosed as case of AML with t(8;21)(q22;q22.1);RUNX1-RUNX1T1 was on therapy after 6 weeks interval from initiation of therapy he presented with fever, weakness, lymphadenopathy and cough with expectoration since 15 days.

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1. Introduction

Acute myeloid leukemia with t(8;21)(q22;q22.1); RUNX1-RUNX1T1 is an AML with predominantly neutrophilic maturation and associated with a high rate of complete remission having favorable long term outcome.³ Patients of Acute myeloid leukemias are predisposed to developing infections, most commonly due to bacterias and fungi, also including tuberculosis due to, cellular and humoral immune paresis.^{4,5} The risk remains higher in Tb endemic areas. Tuberculosis often remains under-diagnosed condition in acute leukemia cases and may be a cause of febrile neutropenia. Antitubercular therapy is feasible in these patients undergoing high dose chemotherapy though rescheduling or altering therapies are required and may be associated with higher mortality if not initiated early. Diagnosing Tb earliest in Acute leukemia cases especially in the subtypes having favorable prognosis can significantly aid in achieving better prognosis.²

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2. Case History with Hematological Findings

16 years old male child presented with history of fever, weakness and hepatomegaly.

2.1. Hemogram revealed

Hemoglobin-10gm%, Total Leukocyte Count-1,56,000/mm,³ Platelet count – 66,000/mm.³ Differential Leukocyte Count – Neutrophils- 16%, Lymphocytes- 05%, Monocytes-01%, Eosinophil-01%, Band form-10%, metmyelocytes-3%, Myelocyte-1%, Blasts-63%.

2.2. Blast morphology

Large blasts with abundant basophilic cytoplasm having azurophilic granules. Auer rods were present as single long and sharp rod with tapered ends (Figure 1).

2.3. Diagnosis based on hemogram findings

Features favoring Acute Myeloid Leukemia.

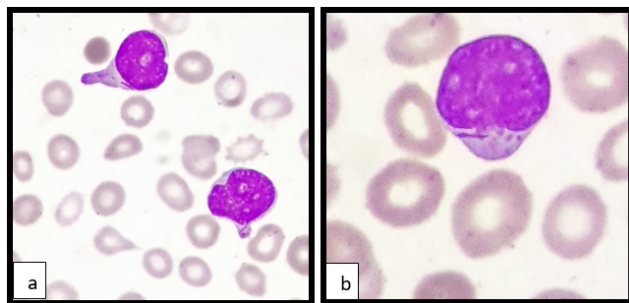


Fig. 1: Peripheral blood smear, Leishman stain, 1000X showing Large blasts with Auer rods having single long sharp rod with tapered end.

Bone marrow aspiration was carried out which revealed 60% blasts features favoring AML.

(Figure 2). The aspirate was also subjected for flowcytometry analysis.

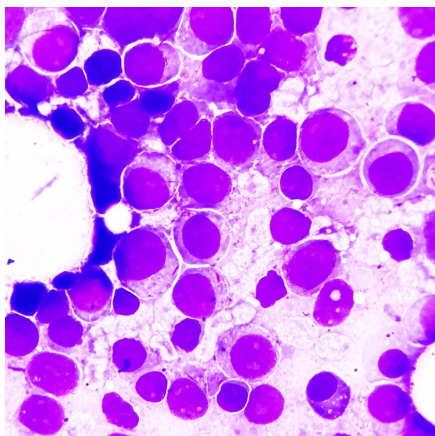


Fig. 2: Bone marrow aspirate, Giemsa stain, 1000X showing blasts with auer rods.

2.4. Immunophenotyping findings

Showed high intensity positive expression for CD34, HLADR, cMPO, CD13, CD33 and CD15.

2.5. On RT-PCR leukemia translocation panel

t(8;21)(q22;q22.1) was Detected.

RUNX1-RUNX1T1 fusion transcript was detected.

2.6. Final diagnosis

Case of AML with t(8;21)(q22;q22.1); RUNX1-RUNX1T1 positive.

After 6 weeks of therapy on regular follow-up patient presented with history of lymphadenopathy, fever, weakness and cough with expectoration since 15 days.

2.7. Peripheral blood smear examination

RBCs-Anemia, WBCs TLC- Within normal limits, DLC- Neutropenia, Platelet- Mild reduced.

2.8. On Chest X Ray

Tiny nodular deposits in bilateral upper zone with homogenous radio-opacity in right mid zone were noted. Features were suggestive of tuberculosis.

2.9. On CT thorax (plain & contrast)

Bilateral axillary lymphadenopathy was present with many few subcentimetric lymph nodes present showing necrosis.

2.10. FNAC from bilateral axillary lymph nodes

Chronic granulomatous lymphadenitis suggestive of tuberculosis.

3. Sputum culture for Acid fast bacilli

Positive for tuberculosis.

4. Discussion

Acute myeloid leukemia with t(8;21)(q22;q22.1) resulting in RUNX1-RUNX1T1 is an AML showing neutrophilic maturation. This subtype of AML corresponds to AML-M2 of FAB classification (i.e AML with maturation).^{3,6}

These are found in 1 to 5% of AML cases and usually found in younger patients. These cases have few common morphological features which include presence of large blasts with basophilic cytoplasm, perinuclear hofs, azurophilic granules and presence of auer rods which are slender single long sharp rod with tapered ends which differentiate them from auer rods of Acute promyelocytic leukemia whose auer rods are large, thick, coarse and usually found in multiple numbers with periodicity of 250nm compared to 6-20nm of auer rods in other subtypes of AML. Maturing cells like neutrophils, band forms, metamyelocytes, myelocytes are usually present.^{3,6}

Immunophenotype of these patients are classically positive for CD34, HLADR, CD13 and MPO. Weak expressions of CD33 and TdT can be present in few cases. Maturing myeloid cells are typically positive for CD15. These cases can aberrantly express lymphoid markers like CD19, Cd79a, PAX5 and CD56 can also be positive which is associated with adverse prognosis.⁷⁻⁹

This subtype of AML has RUNX1-RUNX1T1 fusion transcript positive and are usually associated with a good response to chemotherapy, a high completion rate and long-term disease free survival when treated with intensive consolidation therapy.¹⁰

The subtype is associated with a favorable prognosis if no CD56 positive and no presence of secondary mutations

like KIT mutations.^{10,11}

In our case the patient responded well with the initial induction chemotherapy but in due course of 6week interval after initiation of therapy he developed tuberculosis.

Due to high suspicion of Tuberculosis and early diagnosis of the same antitubercular therapy was initiated without any delay to the patient.

In a study conducted by Arihant jain et al in a period of 3 years 26 patients of acute leukemia developed tuberculosis and the median time to diagnosis of Tb was 8weeks following the diagnosis of Acute leukemia. Out of which 21 cases presented with febrile neutropenia at the time of Tb diagnosis in cases of Acute leukemia.²

In our case the median time to diagnosis of Tb was 6weeks following the diagnosis of acute leukemia. And at the time of diagnosis of Tb patient presented with neutropenia.

Rescheduling &/or alteration in chemotherapy is required following the diagnosis of tuberculosis in cases of acute leukemia. A delay in planned antileukemic therapy schedule by more than 2weeks due to Tb was rescheduling and change in planned chemotherapeutic drug regimen due to Tb was alteration.²

Tuberculosis as a complication during Acute leukemia treatment is rarely suspected, therefore very uncommonly diagnosed. Amongst the patients suffering from malignancies incidence of Tb is highest in hematological malignancies.

The presence of Tb often presents as PUO (pyrexia of unknown origin) in patients of Acute leukemia which leads to delay in institution of therapy and an adverse impact on survival overall even in an favorable subtype of Acute leukemia.

Suspicion of possibility of tuberculosis must always be kept in mind especially in Tb endemic areas and all possible attempts to diagnose it at its earliest should be made in these cases rather than instituting blanket treatment with empiric antibacterial and antifungal therapies.

In our case due to high suspicion of Tb and earliest definitive diagnosis and treatment of Tuberculosis in a case of Acute myeloid leukemia lead to better survival overall. The diagnosis and treatment of Tb in AML had significant impact of prognosis. The patient is in remission till date.

5. Conclusion

AML with t(8;21)(q22;q22.1) having RUNX1-RUNX1T1 fusion transcript is associated with favorable prognosis, but when complicated with aberrant markers or presence of secondary infections like Tuberculosis can worsen the prognosis and lead to high risk of mortality. Hence, in first place suspecting tuberculosis in a Tb endemic area, in a patient having hematological malignancy like acute leukemia, with associated symptoms and presenting with febrile neutropenia after initiation of therapy is of utmost importance. Diagnosing tuberculosis in acute leukemia is

of significance for selection of therapeutics and achieving a complete remission rate or a good disease free survival period.

6. Source of Funding

None.

7. Conflict of Interest

None.

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