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CASE REPORT

Importance of bone marrow biopsy in assessment of treatment response in a case of acute myeloid leukemia

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Abstract

Chemotherapy response in acute leukemias is usually assessed by bone marrow examination along with ancillary studies like flowcytometry/ polymerase chain reaction for minimal residual disease (MRD). Decisions regarding post induction chemotherapy are based on bone marrow remission status. Bone marrow aspiration alone is asked by many oncologists/ hematologists for assessing the remission status. Rarely pockets/ clusters of blasts may not be picked up in the aspiration and the same for MRD also. Hence, bone marrow biopsy is necessary for those clusters/ pockets of blasts. In this case report we are highlighting the importance of both aspiration and biopsy for assessing the treatment response.

Keywords: bone marrow biopsy; remission; treatment response; acute leukemia

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Introduction

Response to chemotherapy in acute myeloid leukemia (AML) is assessed by gauging the bone marrow remission status by morphological, cytogenetic or molecular tests out of which morphological criteria are most commonly used. Morphologically, the bone marrow could be in complete remission or partial remission [1-3].

Morphological criteria for complete remission are blast percentage - < 5% (and without Auer rod in the blasts), absolute neutrophil count (ANC) - > $1x10^9$ /L, platelet count - > $100x10^9$ /L, no evidence of extramedullary disease, transfusion independent. Partial remission is presence of 6 -19% blasts in the peripheral blood or bone marrow.

Decisions regarding post-induction therapy and allogenic haematopoietic stem cell transplant are based on the bone marrow remission status. In

acute leukemias, particularly myeloid (non acute promyelocytic leukemia) standard chemotherapy includes an induction phase and a consolidation phase. Usually the 7 + 3 regimen is used for induction comprising of 7 days of cytarabine and 3 days of anthracycline.

Consolidation phase involves high dose cytarabine (HiDAC) [4]. Post-induction bone marrow assessment is usually done once the total leucocyte count recovers. Bone marrow aspiration alone is asked for by most treating clinicians for assessing the treatment response. Biopsy is done at baseline but it is omitted during the post-induction assessment.

In this case report, we wish to highlight the importance of both aspiration and biopsy for assessing the treatment response.

Case report

A 4-year-old child with a ventricular septal defect (VSD) presented to the medical oncology department with low grade fever of one month duration. His peripheral blood showed 66% blast. A bone marrow examination showed 90% blasts with myeloid morphology (Auer rods were seen in the blasts). He was diagnosed to have AML with t(8;21) (AML - ETO1) with low allelic ratio of FLT3 - ITD mutation. Remission induction therapy was started with the (7+3 regimen) combined with midostaurin (FLT3 tyrosine kinase inhibitor).

Post-induction bone marrow was in complete morphological remission. Induction was followed by consolidation with high dose cytarabine. Three months after completion of the consolidation phase of chemotherapy, the child started having high grade fever. Evaluation revealed 70% blasts in the peripheral blood thus confirming AML relapse. He also developed chloromas of bilateral orbits causing proptosis. CSF examination did not show any blasts. He was started on re - induction with G - CLAM regimen (filgrastim, cladribine, cytarabine and mitoxantrone). Post re – induction, a bone marrow examination was repeated to assess the remission status. While his bone marrow aspirate did not reveal any blasts, the biopsy specimen showed clusters of atypical cells in two intertrabecular areas. Immunohistochemistry (IHC) with CD34 and CD117 highlighted those atypical cells as blasts thus confirming failure of re-induction (Figures 1 to 4)).

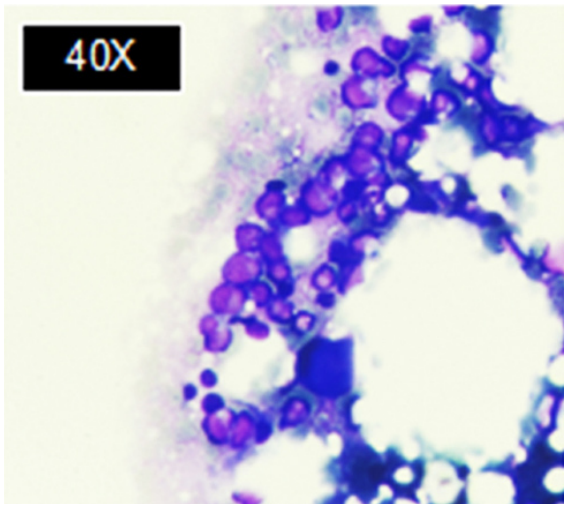

Figure 1: Cluster of blasts in the imprint smear.

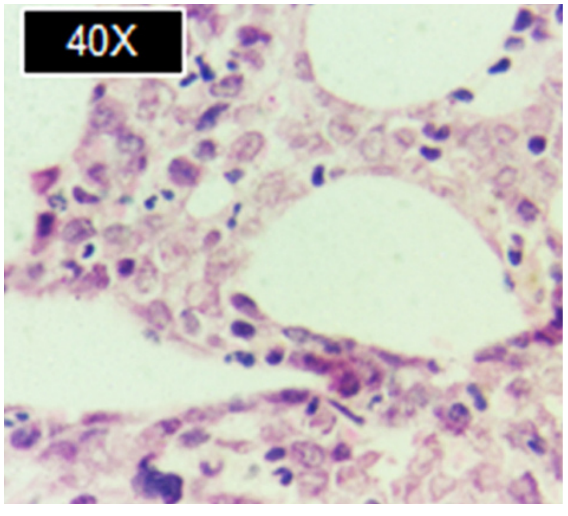

Figure 2: Cluster of blasts in the biopsy.

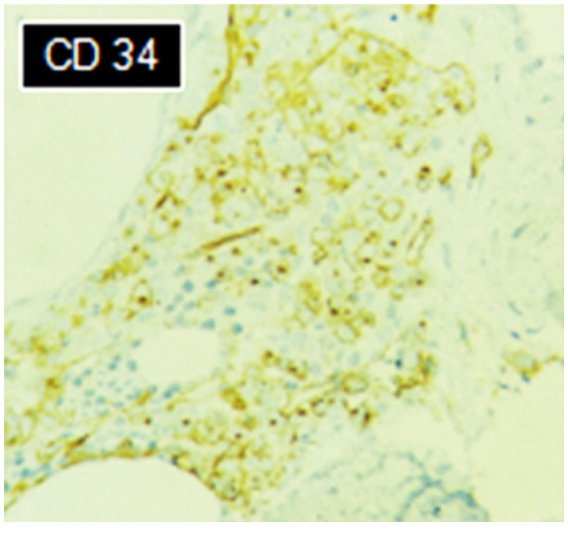

Figure 3: IHC with CD34 Showed cluster of blasts.

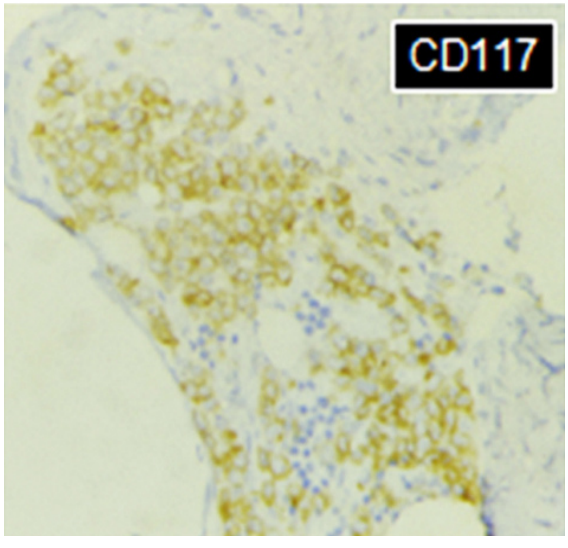

Figure 4: IHC with CD117 showed cluster of blasts.

In the next week, the child developed a frank relapse with increase in peripheral blood blasts. Due to non-availability of a HLA-matched, donor he was started on azacytidine and sorafenib (a multikinase inhibitor) but he had disease progression. Palliative radiation was given to the chloromas of the orbit followed by some symptomatic relief. He succumbed to the disease a few weeks after radiation.

Discussion

Response to therapy in acute leukemias is assessed by examination of the peripheral blood and bone marrow. With the advent of minimal residual disease (MRD), the importance of morphological examination of the marrow has reduced. Still, bone marrow morphological examination of both the aspirate and the biopsy) is essential before sending the sample for determination of MRD. Based on the percentage of blasts, remission may be complete or partial. Complete remission is the presence of less than 5% blasts in the bone marrow while a blast percentage of 6 - 19 is considered as partial remission. A minimum of 500 nucleated cells should be counted for an accurate differential count [5]. Each corner of every smear has to be examined for blasts. Rarely, pockets or cluster of blasts may be seen in the marrow, which are suggestive of an impending relapse. Those pockets of blasts (either intratrabecular or paratrabecular) may not be picked up in the aspirate (as in this particular case). Hence, a bone marrow biopsy is necessary to look for those pockets or clusters of blasts.

As further treatment decisions are taken based on the bone marrow remission status, an accurate determination of the same is of utmost importance. Consolidation will be initiated when there is complete remission and re - induction/ salvage chemotherapy for partial remission or induction failure which should be followed by allogenic haematopoietic stem cell transplantation. In resource limited settings where MRD determination may not be feasible for every patient, a thorough examination of bone marrow biopsy for pockets of blasts (in addition to examination of aspirate) may be a useful alternative to MRD.

Conclusion

A histopathological examination of bone marrow biopsy is an important adjunct to examination of aspirate and MRD determination and must be a part of assessing the remission status post-induction chemotherapy in acute leukemias for further treatment planning.

Conflicts of interest

Authors declare no conflicts of interest.

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