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Safe Targeted Therapy in Case of CD-7 Positive Acute Myelogenous Leukemia Using CD-7 CAR-T Cell, to Avoid Risk of unwanted Myeloablation

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Abstract

There are very few cases of AML-M0 with aberrant CD-7 expression, carrying poor prognosis.[5]Acute Myelogenous Leukemia with minimal differentiation and CD-7 expression is known to have bad prognosis with conventional chemotherapy. Hence, there is need for research on newer treatment modalities like CD-7 CAR T cell therapy. On 4thjune 2021 TMH, IIT Bombay team and cancer care in India did the first CAR-T cell therapy at Bone Marrow transplant unit at ACTREC, Tata Memorial Centre in Mumbai.[4]

Keywords: Chimeric Antigen Receptor-T Cell, Acute Myeogenous Leukemia, AML With Minimal Differentiation.

Introduction

Acute myelogenous leukemia with minimal differentiation (AML-M0) is a rare subtype of acute leukemia, in which blasts fail to show morphologic differentiation and conventional cytochemical stains and myeloid markers are negative.[6]Acute myeloid leukemia (AML) with normal cytogenetics represents approximately 40% to 50% of de novo AML.There are very few cases of AML-M0 with aberrant CD-7 expression, carrying poor prognosis.Incidence of CD-7 positive patients in each AML FAB subgroups is as follows : M0-35%,M1-31.8%,M2-20.5%,M3-4.3%,M4-21.4%,M5-38.2%.[5]

In the immunophenotyping and molecular genetics era, aberrant expression of lineage marker carries more importance. A T-cell lineage marker CD-7, has been detected on the leukemic cells in minority of AML cases.[1]Pan T-cell antigen CD-7 expression has been reported in 35% of AML-M0 cases and is frequently associated with immature markers such as CD-34, TdT& HLA-DR, while solitary CD-7 expression in AML

correlates with higher TCR-delta and beta rearrangement in majority of cases.[1] Solitary CD-7 expression is associated with poor prognosis in T-ALL & mediastinal non-Hodgkin's lymphoma. The poor clinical outcome of CD-7 positive AML patients may be due to CD7 expression with a minimal differentiation .[1]Normal myeloid progenitor and mature cells are spared by CD-7 CAR-T,AsCD-7 is expressed by AML Blasts but is absent on normal myeloid cells in peripheral blood.[2]CD-7 CAR-T cells are highly cytotoxic against CD-7 AML cell lines.[2]Incidence of CD-7 antigen was particularly significant in the less differentiated FAB AML-M0 group, whose prognosis is known to be poor.[5]Since CD-7 expression by malignant blasts is also linked with chemoresistance and poor outcomes, targeting this antigen may be beneficial in this subset of AML patients. Hence, CD-7 chimeric antigen receptor T-cell (CAR-T) therapy should be a safe choice to avoid risk of unwanted myeloablation.[2]In CAR-T cell therapy, T-cells are taken from the patients' blood and are altered by adding a gene for the chimeric antigen receptor, which will bind to cancer cells and kill them. These CAR-T cells are then grown and multiplied in the lab which takes several weeks to make in large number.[7]

Case Report

A 2-year-old female child brought by her parents to paediatric opd with the complaints of high-grade fever since 28 days, total WBC count of 32100/µl & blasts 61 % which was suspicious of Acute Leukemia morphologically. Hemoglobin was 5 gm/dl, RBC count 1890/µl & platelet count 10100/µl. On examination there was no lymphadenopathy, hepatosplenomegaly. On peripheral smear examination morphologically distinguishing features of the lineage remained unrevealed. Phenotyping was advised, Subject to bone marrow aspiration showing features of acute leukemia. Further Flow Cytometry showed blasts (moderate SCC/dim CD-45), expressing CD-7 (heterogenous) in 93%, CD 11b (partial/dim, CD-33(dim) 82%and CD-117(heterogenous)79%. Other markers CD-1a, CD-34, CD-41, CD-61, HLA-DR, cytoplasmic CD-3 and cytoplasmic MPO were negative in blasts. The findings were suggestive of Acute Myelogenous Leukemia with minimal differentiation and CD-7 expression.

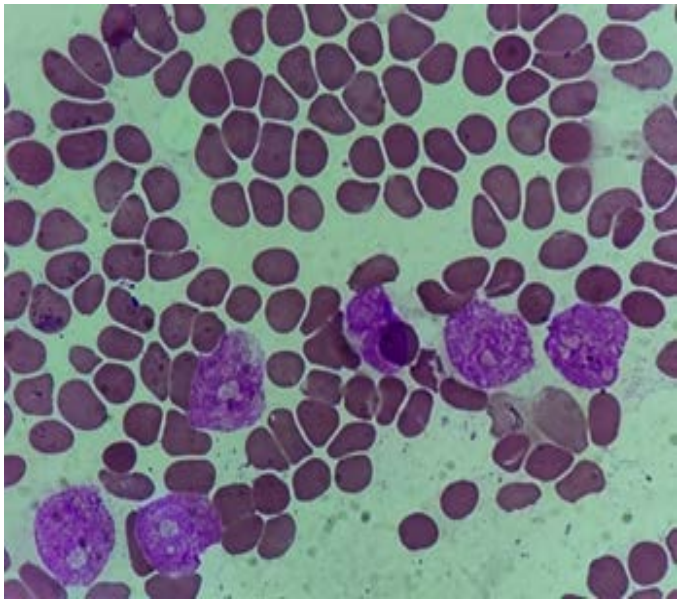

Figure 1: Blasts

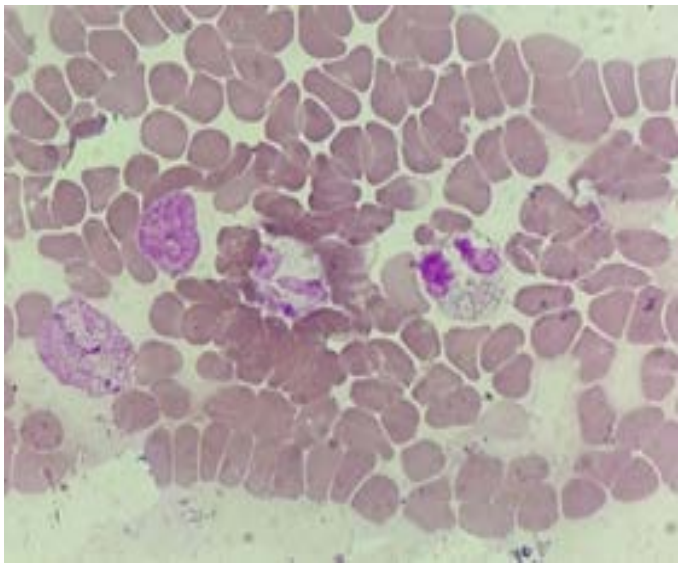

Figure 2: Blasts

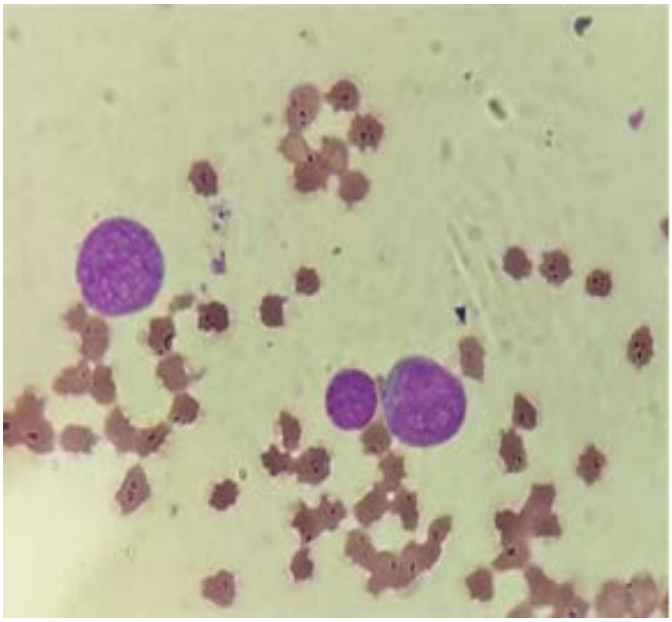

Figure 3: Blasts

Discussion

Patient was managed with chemotherapy that is BHAC-DMP (Behenoyl cytosine arabinoside, daunorubicin,6-mercaptopurine, prednisolone) but remission was not achieved, she was referred to higher centres for CAR-T cell therapy but due to financial constraints, was not possible and she succumbed. As per D.G. SilvaEtal CD-7 CAR T cell is safe targeted therapy in such cases with CD-7 Positive AML to avoid risk of unwanted myeloablation and good prognosis of disease.[2]Thechimeric Antigen Receptor (CAR-T) therapy has emerged as breakthrough in cancer treatment. Clinical trials conducted globally have shown promising results in end stage leukemia patients. On 4thjune 2021 TMH, IIT Bombay team and cancer care in India did the first CAR-T cell therapy at Bone Marrow transplant unit at ACTREC, Tata Memorial Centre in Mumbai.[4]CD-7 CAR T cell therapy will be useful in reducing mortality and morbidity. It should be applicable after further studies on its implication. As per the trail at various higher centres further work-up will be helpful for permanent application.

Conclusion

Determining CD-7 expression on leukemic cells can be a part of immunophenotyping in AML.In cases with resistance to conventional AML chemotherapy i.e.BHAC-DMP(Behenoyl cytosine arabinoside, daunorubicin,6-mercaptopurine, prednisolone) CD-7 CAR-T Cell therapy is thought to be one of the best therapy[2&3].Myeloid and erythroid progenators,mature cells are not known to express CD-7.Hence approach to the study is towards CD-7 which is known to be expressed on immature cells mostly for treatment of fetal CD7 positive AML.2Therefore in refractory and relapsed CD-7 positive AML cases CD-7 CAR-T cell therapy should be considered as the best option.3

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