ABSTRACT
The presence of cytoplasmic granules in the blasts cells is a one of the main accepted and widely used morphological criteria to diagnose acute myeloid leukemia. A case of Acute lymphoblastic leukemia to have numerous cytoplasmic granules in the blasts is rare and can easily be misdiagnosed as acute myeloid leukemia. We describe a rare case of hyper-granular precursor B-cell acute lymphoblastic leukemia (ALL) in an adult male expressing CD10, CD19, TdT, HLA-DR, CD22, CD34 while negative for CD33, CD14, CD64, CD7, CD5, cMPO, and CD117. There can be chances of erroneous typing of granular ALL as AML when the limited antibody panel is used based on the basis of morphology. Hence it is important to be aware of such rare entity and to confirm the accurate lineage of acute leukemia by using a comprehensive antibody panel for immunophenotypic analysis.

KEYWORDS: Acute lymphoblastic leukaemia (ALL), Acute Myeloid Leukaemia (AML), APML, Immunophenotyping, Cytoplasmic Granules.

TRIAL REGISTRATION- No.

INTRODUCTION
Granular ALL accounts for 2 to 8% of all ALL cases in children but is very rare in adult[1,2] The presence of azurophilic cytoplasmic granules and aur rods are important morphological clues to diagnose a case of acute myeloid leukemia (AML). Hyper granularity is also noted in abnormal promyelocytes in acute promyelocytic leukemia (APML).[3] Rare cases of granular ALL may show the quite similar cytoplasmic granules such cases granular blast cells can mimic myeloblasts leading to a misdiagnosis of AML.[4,5] The present case was reported as G-ALL in an adult female patient.

CASE HISTORY
A 45-year-old male presented with low-grade intermittent fever for 2 months along with bone pain and decreased appetite and weight loss. No significant past medical or surgical history or family history was noted. On general physical examination, his vitals were normal with a poor oral hygiene. No pallor or icterus or organomegaly was noted. His central nervous system, respiratory system examinations were normal. Kidney function test and liver function test were normal. On ultrasonography mild hepatosplenomegaly, along with periportal lymphadenopathy were noted. On hematological investigation his TLC was raised 60,000/cumm, Hb (9.4g/dl) was slightly low, platelet count was 1.4 lakh/cumm. Peripheral blood smears stained with May-Grunwald-Giemsa revealed 48% blasts which were intermediate to large in size with high N/C ratio, evident nucleoli, the moderate amount of basophilic cytoplasm, cytoplasmic granules were seen in 32% of blasts. Cytoplasmic granules were azurophilic, multiple in number and large in size (“Figure 1”). Red blood cells were normocytic normochromic. On cytochemistry MPO stain was negative and PAS was inconclusive. A provisional diagnosis of Acute myeloid leukemia was made.

On flow, blasts constitute 32% of total acquired events. These cells showed dim CD45 expression and low to intermediate forward scattering. These cells showed bright expression of CD10, CD19, TdT and HLA-DR, however, moderate expression of CD22 and CD34. These cells were negative for CD33, CD14, CD64, CD7, CD5, CD4, CD8, CD57,CD56, cMPO and CD117. An aberrant expression of CD13 was noted (“Figure 2”).
The final diagnosis of CALLA-positive B-cell Acute Lymphoblastic Leukaemia was made. The patient was referred for chemotherapy.

FIGURE LIGANDS

Figure 1: a. Peripheral blood smear showing blasts (Giemsa 100X) b and c. Blasts of intermediate to large in size with high N:C ratio, evident nucleoli, moderate amount of cytoplasm with granules (Giemsa 200X), d. Blasts with granules in cytoplasm (Giemsa 400X).

Figure 2: Flowcytometry images- a. FSC Vs SSC, b. CD45 Vs SSC showing blast population in green with low to intermediate forward scatter and dim CD45 expression, c. CD19 and CD10 positivity, d. CD34 and CD 45 positive blast cells, e. HLD-DR positivity by blasts, f. Aberrant expression of CD 13 while CD33 negativity by blasts.

DISCUSSION

The criterion used for diagnosis of granular ALL is the blast cells having more than 1% of lymphoblasts with at least three or more clearly defined azurophilic granules. However, the majority of granular ALL mostly showed more than 5% of blasts with small numbers of distinctive azurophilic granules. Large granular lymphocytes (LGL) leukemia have few azurophilic granules in a small percentage of large granular lymphocytes but these two can be easily differentiated on the basis of granule size. The granules of granular ALL are much larger than those seen in the LGL leukemia. However, these granules are very similar to those seen in the myeloid cells which may lead to misdiagnosis of acute myeloid leukemia.

Granules in lymphoblasts are relatively rare morphological finding. There is case report and few case series about granular ALL, mostly are in pediatric patients, only very few individual case reports are on adult granular ALL. Granular ALL in children have been reported by pediatric oncology group (POG), granular ALL was found in 56 out of total 1252 cases included in the study, more commonly in FAB L2 subtype of acute leukemia (4.5%). Invermizze et al found the overall frequency of granular ALL ranges from 1.7% to 7% of all the ALL cases. They found that granular ALL had worse prognosis regardless of any other risk factors, immunophenotype or FAB subtype. Another study performed by Aieop Cooperative Group for cytology of Acute Leukemias, they found granular blast cells in 4% of cases, but they did not found any prognostic significance of granular ALL. In another study at St. Jude Children Hospital they found granular ALL in 7% cases (5 out of 66 patients). A rare case of granular acute lymphoblastic leukemia (ALL) was noted in a 45-year-old woman with a history of multiple myeloma. However, its clinical importance and also the correlation with FAB subtype remains uncertain.

In our case, the blasts were positive for CD10, CD19, TdT, HLA-DR, CD22, and CD34. These cells are negative for CD33, CD14, CD6, CD7, CD4, CD8, CD5, cMPO and CD117.

CONCLUSION

To avoid diagnostic dilemma there should be the use of cytochemical stains like myeloperoxidase and PAS along with immunophenotypic analysis using a comprehensive antibody panel. It is important to diagnose this entity as it is a poor prognostic factor in adult patients, unlike pediatric granular ALL.

CONFLICTS OF INTEREST

No conflict of interest.

AUTHORS’ CONTRIBUTIONS

SY collected the data, analyzed and written the paper, VK, AS and SM diagnosed the case and helped in writing, NK helped in analysis and writing paper. All the authors approved the final manuscript.

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