CORRESPONDENCE

T-Lineage Acute Lymphoblastic Leukemia with Granular Blasts

Pulkit Rastogi¹ · Shano Naseem¹ · Deepak Bansal² · Neelam Varma¹

Received: 24 November 2016 / Accepted: 12 January 2017 / Published online: 27 January 2017
© Indian Society of Haematology & Transfusion Medicine 2017

Dear Editor

We would like to share the following rare case with the readers. An 11 year old male child presented with a history of bilateral swellings in neck—for 2 months, fever—for 1 month and bilateral pedal edema since 5 days. On examination there was bilateral cervical (3 × 3 cms), inguinal (2 × 2 cms) and epitrochlear (1 × 1 cm) lymphadenopathy, with hepatomegaly (5 cms below right costal margin) and splenomegaly (10 cms below left costal margin). Complete blood counts revealed hemoglobin of 7.9 g/dl, platelet count of $31 \times 10^9/L$ and total leucocyte count of $199.3 \times 10^9/L$ with 92% blasts. The bone marrow aspirate was hypercellular with 83% blasts. Morphologically, blasts were 1.5–3 times the size of mature lymphocytes with round to convoluted nuclear margins, opened up chromatin, inconspicuous nucleoli and scanty to moderate amount of basophilic cytoplasm. About 50% blasts showed ≥ 5 fine or coarse azurophilic cytoplasmic granules (Fig. 1a). However, no Auer rods were seen. Cytochemically, these were negative for myeloperoxidase (Fig. 1b) and showed positivity for PAS stain (Fig. 1c). Immunohistochemistry on the trephine biopsy section showed positivity for CD3 (Fig. 1d) and was negative for myeloperoxidase and CD22. Further, flow cytometry of blasts showed positivity for T-cell markers [cytoplasmic CD3, CD5 and CD7], CD34, CD45, CD38 and aberrant expression of CD19 and CD33. The blasts were negative

for TdT, HLA-DR, CD1a, CD2, sCD3, CD4, CD8, TCR $\alpha\beta$, TCR $\gamma\delta$, CD16, CD56, CD57, myeloid antigens (CD13, CD117, CD36, CD14, CD64), megakaryocytic antigens (CD41a, CD61a) and B-cell antigens (CD 10, CD20, CD22, CD79a).

Based on above, case was diagnosed as T-ALL and immunophenotypically categorized as Pre-T ALL, by the European Group for the Immunological Characterization of Leukemias (EGIL) classification [1].

According to National Cancer Institute (NCI) criteria [2], the case is stratified into T-cell high risk ALL (WBC $\geq 100 \times 10^9/L$, bulky disease, pre-T-ALL). The patient was given induction chemotherapy with dexamethasone, vincristine, asparaginase, daunorubicin and intrathecal methotrexate. Remission was achieved on day 35 bone marrow, which showed $<5\%$ blasts. Currently, the patient is on augmented Berlin–Frankfurt–Munich (BFM) consolidation therapy with intrathecal methotrexate, cyclophosphamide, cytarabine, *E. coli* asparaginase, vincristine and mercaptopurine.

As per WHO 2008 classification of hematolymphoid malignancies, morphology, cytochemistry, immunophenotyping and molecular genetic studies are a pre-requisite for a definite categorization of acute leukemia. However, initially, it is morphology only which guides for the further workup of a case. Granular blasts are usually seen in AML, though rarely, by few studies they have been described in ALL also [3, 4]. Granular blasts are defined as blasts containing three or more well defined cytoplasmic azurophilic granules, each 0.5 μm or greater in diameter and these blasts should constitute $\geq 5\%$ of all blasts [4]. Some studies have conducted ultrastructural studies of these blasts and described these granules variably as membrane bound vesicles, parallel tubular arrays, collection of virus like-vesicles, detached masses of nuclear chromatin and

✉ Shano Naseem
shanonaseem@yahoo.co.in

¹ Department of Hematology, Postgraduate Institute of Medical Research and Education, Chandigarh, India

² Department of Pediatrics, Postgraduate Institute of Medical Research and Education, Chandigarh, India

Fig. 1 **a** Bone marrow aspirate smear showing granular blasts (arrows) (May-Grunwald-Giemsa stain, $\times 1000$); **b** Blasts are myeloperoxidase negative (MPO stain, $\times 1000$); **c** Blasts showing block positivity for periodic acid Schiff's stain (arrow) ($\times 1000$); **d** IHC on trephine biopsy section showing diffuse cytoplasmic positivity for CD3 ($\times 400$)

detached nuclear clubs [5]. The reported prevalence of granular-ALL is 1.7–7% of all ALL cases with a predominant precursor B-cell immunophenotype, L2 morphology and a variable prognosis [4].

Till date, there is only a single case report of granular T-ALL confirmed by flow cytometry in a 7 year male child [6]. In this case, granular blasts constituted 23% of total blasts and were positive for T-lymphoid antigens (CD2, CD3 and CD7) and negative for B-lymphoid and myeloid antigens. This patient was treated with induction chemotherapy by vincristine, L-asparaginase and prednisone, went into remission, followed by three blocks of intensification. This case like our case also showed a good response to induction chemotherapy.

Our case describes that granular blasts although rarely, can also be seen in T-ALL and these need to be differentiated from AML with appropriate ancillary techniques. These findings represent morphological changes in the form of cytoplasmic granules which can be seen in ALL, besides their more reported occurrence in AML.

Acknowledgements All sources of support, including pharmaceutical and industry support, that require acknowledgment—none to declare.

Compliance with Ethical Standards

Conflict of interest There are no conflicts of interest to declare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Bene C, Castoldi G, Knapp W et al (1997) Proposals for the immunological classification of acute leukemias. European group for the immunological characterization of leukemias (EGIL). *Leukemia* 9:1783–1786
2. Smith M, Arthur D, Camitta B et al (1996) Uniform approach to risk classification and treatment assignment for children with acute lymphoblastic leukemia. *J Clin Oncol* 14:18–24
3. Pitman SD, Huang Q (2007) Granular acute lymphoblastic leukemia: a case report and literature review. *Am J Hematol* 82:834–837
4. Cerezo L, Shuster JJ, Pullen DJ, Brock B, Borowitz MJ, Falletta JM et al (1991) Laboratory correlates and prognostic significance of granular acute lymphoblastic leukemia in children: a Pediatric oncology group study. *Am J Clin Pathol* 95:526–531
5. Cantu-Rajnoldi A, Invernizzi R, Biondi A et al (1989) Biological and clinical features of acute lymphoblastic leukaemia with cytoplasmic granules or inclusions: description of eight cases. *Br J Haematol* 73:309–314
6. Tsoi WC, Lai HD, Feng CS (1997) T-acute lymphoblastic leukemia with cytoplasmic granules. *Am J Hematol* 56:193–194