

GRANULAR ACUTE LYMPHOBLASTIC LEUKEMIA IN A PAEDIATRIC PATIENT- A RARE CASE REPORT

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PRESENTATION OF CASE

A one-year male child presented with pyrexia, periorbital puffiness and excessive cry for 8 days. No history of melena or blood loss. The infant's birth history and medical history were unremarkable. His development was normal, and he had no unusual dietary intake.

Physical examination revealed a well-developed, irritable male infant. His temperature was 38.9°C; pulse 186/min; respirations 32/min; oxygen saturation 95% on room air; and weight, 7.5 kg (25th percentile for his age). He had pallor, distended abdomen and hepatosplenomegaly, with a liver edge palpable 5 cm below the right costal margin and a spleen tip palpable 4 cms below the left costal margin. Abdominal ultrasound revealed liver of 12 cm and spleen of 15 cm size.

CLINICAL DIAGNOSIS

Leukemia

DIFFERENTIAL DIAGNOSIS

- Acute Lymphoid Leukemia (ALL)
- Acute Myeloid Leukemia (AML)
- Leukemoid Reaction due to some infection or severe nutritional anaemia.

PATHOLOGICAL DISCUSSION

Haemogram revealed bi-cytopenia with Hb- 7.0 gm/dl and platelets $56 \times 10^3 / \mu\text{l}$. However, there was leukocytosis with total leucocyte count of $280 \times 10^3 / \mu\text{l}$. Differential revealed 85% blasts, 08% lymphocytes and 07% neutrophils.

Peripheral smear stained with Leishman stain revealed 85% blasts, morphologically lymphoblasts - little variation in size of blast population, round to oval nuclei, finely granular chromatin with dispersed foci of condensation, scanty to moderate amount of basophilic cytoplasm and inconspicuous nucleoli. 30% of blasts showed coarse intracytoplasmic granules [Figure 1]. No Auer rods were found.

Bone marrow aspirate revealed hypercellular marrow with marked depletion of all three elements, i.e., erythroid,

myeloid and megakaryocytic. 80% cells were blasts, morphologically similar to peripheral smear blasts with high nuclear to cytoplasmic ratio, scanty to moderate cytoplasm and inconspicuous nucleoli. Intracytoplasmic coarse granules were observed in 40% of blasts [Figure 2]. These granules were small to medium sized light pink to dark purple. Several granular blasts tended to form small clusters, a feature more commonly seen in ALL [Figure 2]. No Auer rods were identified.

Cytochemical analysis was in favor of ALL as blasts were PAS positive with fine and coarse granular positivity and completely negative for MPO [Figure 3]. On the basis of morphology and cytochemical studies, a definitive diagnosis of Granular ALL was made. The patient was advised immunophenotyping and cytogenetics for which he was referred to higher center; however, patient was lost to follow up.

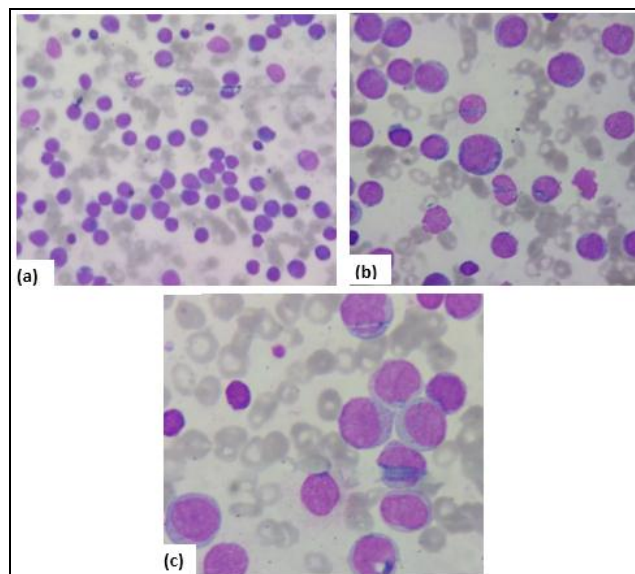


Figure 1. Peripheral Smear (a) High Power Showing Leukocytosis and Heterogenous Population of Large Mononuclear Cells. (b) & (c) Lymphoblasts Showing Coarse Azurophilic Granulations

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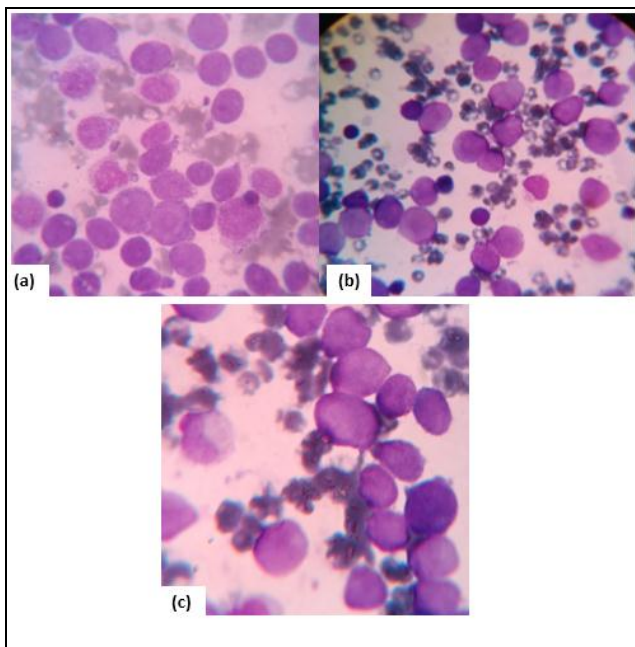


Figure 2. Bone Marrow Aspiration Smears (a) (b) (c) Hypercellular Marrow with Depletion of All Three Elements, i.e., Erythroid, Myeloid and Megakaryocyte. Majority Are Lymphoblasts of FAB L1 and L2 Morphology with Few of Them Showing Coarse Cytoplasmic Granules

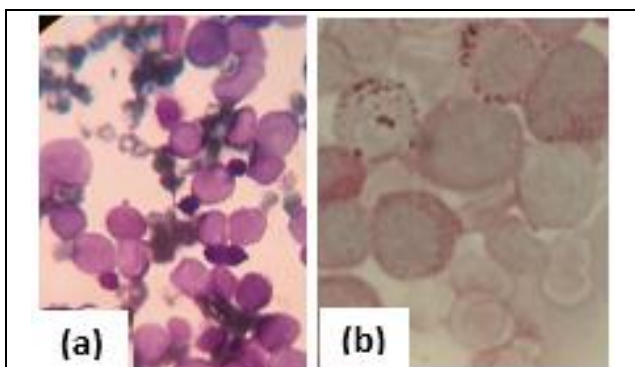


Figure 3. Cytochemistry (a) MPO Stain: MPO Negative Blasts. One Neutrophil in The Bottom Right Shows Positivity (b) PAS Stain: Blasts Show fine and Coarse Granular Positivity

DISCUSSION

WHO Classification is now regarded as gold standard for leukemia diagnosis which combines morphology, cytochemistry, immunophenotyping, clinical presentation and genetic abnormalities. But in majority of centers in developing countries including our country, all these facilities are not available. In such cases, morphology and cytochemical evaluation of peripheral blood and/or bone marrow aspirate smears can give initial clue to diagnosis. Further, these patients can be referred early to the higher centers for immunophenotyping and cytogenetics after which specific therapy can be started at the earliest, as if not treated, such cases are rapidly fatal.

G-ALL may create diagnostic confusion with AML due to the presence of cytoplasmic granules found in the lymphoblasts.^[1-5] This rare variant of ALL is commonly seen in children. In a large study by Paediatric Oncology Group (POG),^[6] Granular ALL was identified in 56 out of the 1252

cases, more commonly in FAB L2 subtype of acute leukemia (4.5%). Others have found similar occurrence in paediatric population ranging from 2-7% of childhood ALL cases.^{[7],[1],[3],[4]} Rare occurrences have been reported in adults.^{[3],[2],[8],[4],[9]}

Granular ALL has been defined largely as having more than 1% of lymphoblasts having at least three or more clearly defined azurophilic granules.^[1] However, most of studies have reported cases with more than 5% of lymphoblasts with small numbers of distinctive azurophilic granules. The pathogenesis of granules of granular ALL has been hypothesized as being the result of dysplastic organelle formation, fusion, or degeneration.^{[7],[2]} These granular lymphoblasts are positive for PAS, may occasionally also be positive for Sudan Black B, causing further confusion with myeloid blasts,^{[7],[2]} however they are completely negative for myeloperoxidase which is a more specific marker for myeloid differentiation. However in few cases, Immuno-phenotyping by flow cytometry and/or immunohistochemistry would be crucial for lineage determination if morphologic and cytochemical features are equivocal.^{[7],[2],[3],[10],[11],[12]}

FINAL DIAGNOSIS

Granular ALL

With high degree of clinical suspicion, especially in childhood population, even the presence of granules in lymphoblast like cells with absence of Auer rods should prompt evaluation by cytochemistry. Negativity for MPO and positivity for PAS will clinch the diagnosis of Granular ALL which can further be confirmed by Immunophenotyping. Diagnosing this rare variant-Granular ALL is important as it has worse prognosis than other forms of ALL and requires early intensive intervention.

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