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B lymphoblastic leukemia with granules mimicking acute myeloid leukemia in a 4 years female child

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Abstract

Granular acute lymphoblastic leukemia [ALL] is a rare morphological variant of ALL characterized by cytoplasmic azurophilic granules or inclusions positive for aspecific esterase and acid phosphatase with heterogeneous features at the ultrastructural level. Granular ALL usually occur in children [2-7%] but is extremely rare in adults. It is important to perform cytochemical staining and flow cytometry to make the distinction between acute myeloid and lymphoblastic leukemia.

We review the case history and pathological findings in a 4 years female child with initial cytomorphological diagnosis of AML which after flow cytometry turned out to be granular ALL.

Keywords: Acute lymphoblastic leukemia, cytoplasmic granules

Introduction

Diagnostic confusion can arise when acute lymphoblastic leukemia (ALL) patients present with intracytoplasmic granules which typically are found in acute myeloid leukemia (AML). Granular ALL is extremely rare in adult. We describe a case of granular ALL in 4 years female child.

The presence of azurophilic granules in the cytoplasm is one of the key distinguishing features of AML which differentiates it from ALL. However, on rare occasions, these intracytoplasmic inclusions may be found in ALL blasts, termed granular ALL that defy conventional teaching and diagnostic pathways [1]. We review the case history and pathological findings in a 4 years child with granular ALL.

Case history

A 4 years female child presented with fever, cough, cold and pain in bilateral lower limbs. She was found to have leukocytosis with white blood cell count 1,20,000/mm³, thrombocytopenia and blasts in peripheral blood. These blasts [Fig.1] were of medium sized with round to slightly irregular nuclear contours, fine chromatin, prominent nucleoli with multiple eosinophilic cytoplasmic granules. More than 25% of peripheral leukocytes were described as blasts. These blasts were accompanied with other myeloid precursor like cells. The patient's blasts contained large numbers of distinctive cytoplasmic granules closely mimicking heavily granulated myeloblasts of acute myeloid leukemia. Cytomorphological diagnosis of AML was rendered initially. However, flow cytometric immunophenotyping showed moderate positive expression for CD19, CD10, HLADR, dim to moderate expression of CD38 and dim expression of CD22 and CD45. CD13, MPO [Myeloperoxidase] and rest of the markers were negative. These findings were consistent with a precursor B-ALL [B lymphoblastic Leukemia].

Granular ALL occurs approximately 2-7% in childhood populations but is extremely rare in adults [2, 3, 4]. Such cases may cause problematic distinction from myeloid differentiation and lead to misdiagnosis of AML [2].

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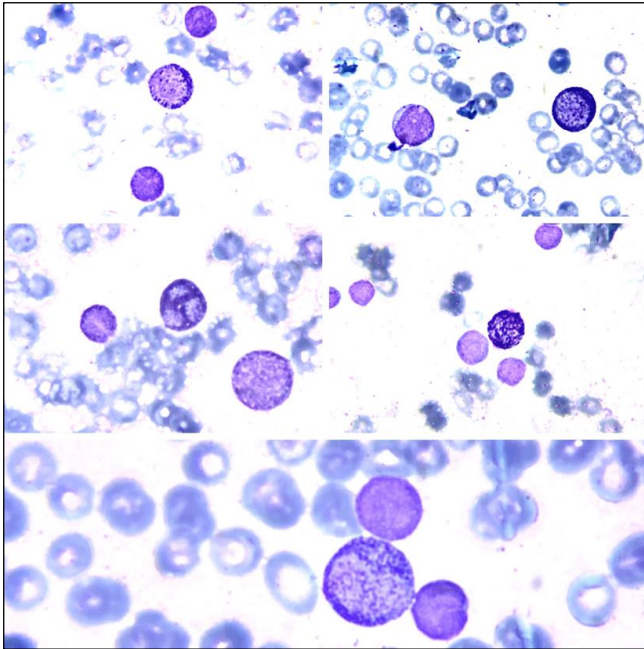


Fig 1: Peripheral smear showing blasts with cytoplasmic granules accompanied with myeloid precursor cells like basophil, myelocytes and metamyelocytes. [Leishman's stain: 100X]

Discussion

Cytoplasmic granules are one of the key morphologic features differentiating AML from ALL. These granules in AML are fused lysosomes and contain lysosomal enzymes and crystalline inclusions but are rarely present in adult ALL cells^[5]. In pediatric cases of ALL, these granules present at a higher frequency. Granular ALL is defined by more than 5% marrow blasts having at least three azurophilic cytoplasmic granules. The Pediatric Oncology Group study also found that granular ALL was more frequent amongst FAB L2 compared to FAB L1 and that those with granular lymphoblasts had a significantly lower complete remission rate and event free survival^[6].

Conclusion

An accurate diagnosis is critically important for treatment implementation and prognosis in acute leukemia. Diagnostic confusion may arise in ALL with cytoplasmic granular inclusions resembling that of AML. It is important to confirm the type of acute leukemia with flow cytometric immunophenotyping in all cases^[6].

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