

TITLE PAGE

ARTICLE TITLE: Lymphoblasts with Auer rod – like inclusions in a case of paediatric B lymphoblastic leukemia.

SHORT RUNNING TITLE: Auer rod – like inclusions in B lymphoblasts.

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1002/psc.26392](https://doi.org/10.1002/psc.26392).

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WORD COUNTS FOR TEXT: 509 words

NUMBER OF FIGURES: 1

KEY WORDS: B-lymphoblastic leukemia, Auer rod like inclusions, lymphoblasts, paediatric.

CONFLICT OF INTEREST AND FINANCIAL DISCLOSURES: Authors declare that there are no conflicts of interest nor any financial support for this work.

PREVIOUS PUBLICATIONS: There are no prior publications or submissions with any overlapping information, including studies and patients

AUTHOR CONTRIBUTIONS: Dr. Anurag Gupta and Dr. Manu Goyal both performed microscopic analysis, flowcytometric immunophenotyping studies, capturing and processing of the image. Dr. Anurag Gupta and Mr. Nagaraju Nalla performed cytogenetic analysis and interpretation of results while the clinical management is under the care of Dr. Krishna Reddy and clinical inputs are provided by him. All the authors drafted, reviewed and edited the manuscript and take full responsibility of the manuscript. No honorarium, grant, or other form of payment was given to anyone to produce the manuscript.

TABLE OF ABBREVIATIONS

ABBREVIATIONS	FULL FORM
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
ARLI	Auer rod - like intracytoplasmic inclusions
PB	Peripheral blood
TdT	Terminal deoxynucleotidyl transferase

To the Editor

A 5 year old male on treatment with steroids and methotrexate for idiopathic rheumatoid arthritis was detected to have anaemia and thrombocytopenia without organomegaly or lymphadenopathy. Peripheral blood (PB) smear revealed 43% blasts with <1% blasts showing presence of Auer-rod-like intracytoplasmic inclusions (ARLI) (Figure1).

Myeloperoxidase cytochemistry was negative. Flow cytometry was consistent with B-lymphoblastic leukemia with blasts expressing CD34, CD19, CD10, CD22, CD38, CD79a, and HLA-DR and negative for CD45, CD20, CD2, cytoplasmic CD3, CD5, CD7, CD13, CD33, CD117 and myeloperoxidase. Cytogenetics revealed hyperdiploidy with karyotype reported as

56,XY,+X,+4,+5,der(5)t(5;5)(q22;q13),+6,+8,+10,+14,+17,+18,+21[2]/57,idem,+21[13]/58,+X,+4,+5,+5,+6,+8,+10,+14,+17,+18,+21,+21[4]/46,XY[1]. The patient was treated on a good risk Berlin-Frankfurt-Münster (BFM) protocol. Day 35 bone marrow showed complete morphological remission. The patient is alive and currently under follow-up.

Auer rods, first described by John Auer, are rod-shaped peroxidase-positive intracytoplasmic structures formed by aggregation and concentration of the peroxidase granules in the leukemic blasts and are diagnostic of myeloid differentiation.[1],[2],[3] Auer rods are seen in M1 to M6 French-American-British classification of acute myeloid leukemia (AML), most commonly associated with AML-M3.[4] These have also been reported in immature myeloid cells from PB of normal human foetuses.[5]

ARLI in lymphoid cells have been described rarely in chronic lymphocytic leukemia, prolymphocytic leukemia, multiple myeloma, follicular lymphoma and peripheral marginal zone lymphoma. These inclusions on electron microscopy were found to be swollen mitochondria or immunoglobulins.[6],[7],[8],[9]

Round to oval intracytoplasmic inclusions resembling microtubules, lysosomes, ribosomal-lamellar complexes, viral particles, and mitochondria have been reported in acute lymphoblastic leukemia (ALL).[10] However, ARLI in B-lymphoblasts have been reported only in two cases of adult ALL:[11],[12] a 28 year old female with 80% blasts in bone marrow and a 27 year old male with 83% blasts in PB. Rare blasts showed ARLI in both cases, which were peroxidase and Sudan black-B positive in former and negative in the latter.[11],[12] Except for terminal deoxynucleotidyl transferase (TdT), immunophenotyping was not available for the former case;[11] hence the possibility of myeloid phenotype cannot be ruled out. TdT positivity is well known in AML with t(8;21) and t(6;9).[4] In the second case, blasts expressed CD19, CD10, CD24, CD34, HLA-DR, TdT and CD20 while CD13 and CD33 were negative, with no information available on CD117 or myeloperoxidase.

In the present case, the possibility of mixed phenotype acute leukemia was ruled out using extensive set of antibodies including myeloid lineage defining antibodies - myeloperoxidase. Electron microscopy performed in the second case revealed the inclusions to be composed of nuclear membrane material; however, this could not be ascertained in our case.[12]

This case highlights a rare scenario of the presence of ARLI in lymphoblasts, indicating that the presence of such inclusions does not preclude the diagnosis of ALL. In places where resources are limited and vital clinical decisions are taken based on morphology alone, one should be aware of such variations which may lead to an erroneous diagnosis. The significance of flow cytometric evaluation with a combination of antibodies is essential to rule out a possibility of underlying mixed phenotype acute leukemia or ALL, thus helping patients make judicious well informed decisions for the use of limited resources.

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LEGEND TO THE FIGURE: Lymphoblast showing intracytoplasmic Auer rod - like inclusion – arrow mark (Leishman stain, original magnification $\times 100$ oil immersion).

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Author