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Technical Notes & Surgical Techniques

The "Mystique" of Acute Leukemia: **MPAL-BAL-AUL-ALAL-aBLL-HAL-MLL**: Initial presentation of MPAL as extramedullary neurological compromise; A case report and review of literature

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aBLL (acute BiLineal Leukemia)
HAL (Hybrid Acute Leukemia)
MLL (Mixed Lineage Leukemia)
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ABSTRACT

Introduction: **MPAL** (Multi Phenotypic Acute Leukemia), **BAL** (Biphenotypic Acute Leukemia), **AUL** (Acute Undifferentiated Leukemia), **ALAL** (Acute Leukemia of Ambiguous Lineage), **HAL** (Hybrid Acute Leukemia), **HAL** (Hybrid Acute Leukemia), **MLL** (Mixed Lineage Leukemia) and **aBLL** (acute BiLineal Leukemia) represent different names of the same pathology or do these entities represent completely separate disease processes? These rather uncommon manifestations of acute leukemia complicate strict taxonomical sub grouping as well as their management. Rapid identification & swift management may restrict further neurological damage, while achieving hematological remission.

Case description: A 16 year female presented with gradual onset paraplegia for 7 months, a history of multiple blood transfusions in the past 2 years, pancytopenia, atypical cells in peripheral smear; the hematological and bone marrow work up revealed a diagnosis of: **MPAL, B/Myeloid**, **NOS** [Multi Phenotypic Acute Leukemia, B cell {lymphoid}/Myeloid, not otherwise specified]. An ALL type induction regimen was started. The management strategy, it's rationale and the clinical outcome are discussed.

Conclusion: For routine neurosurgical practice, these entities are extremely rare; and hence a working knowledge is very essential for appropriate & timely management notwithstanding the neurosurgical desire to rule out the compressive lesions first. Neurological status deterioration may be halted with timely institution of appropriate chemotherapy. In the extensive literature review in pubmed, this may be only the 1st case of MPAL with extramedullary neurological manifestation, at the first clinical presentation.

Abbreviations: MPAL, (Multi Phenotypic Acute Leukemia); BAL, (Biphenotypic Acute Leukemia); AUL, (Acute Undifferentiated Leukemia); ALAL, (Acute Leukemia of Ambiguous Lineage); HAL, (Hybrid Acute Leukemia); MLL, (Mixed Lineage Leukemia); aBLL, (acute BiLineal Leukemia); WHO, (World Health Organization); MRC, Medical Research Council Scale; (MRI), magnetic resonance imaging; DWI, (diffusion weighted imaging); MPO, (Myeloperoxidase); ALL-L2, [Acute Lymphocytic Leukemia-L2 type]; CD, (Cluster differentiation markers); HLA, (Human Leukocyte Antigen); MPAL, B/Myeloid, NOS, (Multi Phenotypic Acute Leukemia, B cell {lymphoid}/Myeloid, not otherwise specified); ALL, (Acute Lymphogenous Leukemia); CVD, [Cyclophosphamide, Vincristine, Daunorubicin]; TKI, Tyrosine Kinase Inhibitor; AML, [Acute Myelogenous Leukemia]; alloSCT, (allogenic Stem Cell Transplant); (rhG-CSF), recombinant human granulocyte colony stimulating factor; (EGIL), European Group for the Immunological Classification of Leukemias; Ly + AML, (AML with lymphoid markers); My + ALL, (ALL with myelogenous markers); (CR), Complete remission; Ara-C, (Cytosine arabinoside); miRNAs, (micro ribonucleotide acids); qRT-PCR, (Quantitative Reverse Transcriptase-Polymerase Chain Reaction); mRNA, (messenger RNA); "Mystique", fictional supervillain appearing in American comic books, published by Marvel Comics, most commonly in association with the X-Men.

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E-mail addresses: soubhagya.tripathy@gmail.com (S.R. Tripathy), drssmisra@gmail.com (S.S. Mishra), sdas@gmail.com (S. Das), itibrata@yahoo.in (I. Mohanta).

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1. Introduction

MPAL (Multi Phenotypic Acute Leukemia), **BAL** (Biphenotypic Acute Leukemia), **AUL** (Acute Undifferentiated Leukemia), **ALAL** (Acute Leukemia of Ambiguous Lineage), **HAL** (Hybrid Acute Leukemia), **MLL** (Mixed Lineage Leukemia) and **aBLL** (acute BiLineal Leukemia): - these are some of the descriptive terms used to describe this rather rare acute leukemias where there is either expansion of more than one clone of progenitor cells or expression of multi lineage immunophenotypic [B/ T/ Myeloid] markers. But how to define & characterize these leukemias? WHO (World Health Organization) monograph on acute leukemia in 2008 has tried to answer these queries by defining the term "MPAL (Multi Phenotypic Acute Leukemia)". Still the older jargons persist in the current literature, putting a systematic literature review into serious difficulty and thereby complicating the 'Optimal management' of such cases.

1.1. Case description

A sixteen year old female (Fig.1) presented with prostration, gradual progressive weakness of both the lower limbs for 7 months & inability to get up in the bed without support. She also had sacral bedsores d/t prolonged immobilization. Her higher mental function, motor & sensory examination of bilateral upper limb, examination of cranial nerves, and examination of cerebellar and autonomic nervous system function were within the normal limit. Motor system examination of the lower limbs revealed: power to be 0/5 bilaterally (MRC-Medical research Council scale), generalized hypertonia, exaggerated knee & ankle jerks and bilateral ankle clonus. Bilateral plantar reflexes were extensor, abdominal reflexes were normal; straight leg raising test couldn't be performed.

She had no meningeal signs; examination of skull & spine revealed no abnormality except mild tenderness in the dorsolumbar spine. She had diffuse tenderness all over her sternum throughout her illness. Lower limb weakness & spinal tenderness were treated at some peripheral hospital as a case of an acute spinal compressive pathology & referred to us; but the pain never subsided with the prescribed analgesic medications.

She had undergone magnetic resonance imaging (**MRI**) of the dorsolumbar spine, prior to coming to our centre, which depicted a D11–D12 non enhancing T1 iso & T2 mildly hyperintense space occupying lesion, present extradurally & compressing the bilateral exiting nerve roots foramina, with restriction diffusion on DWI (diffusion weighted imaging) studies.

On further enquiry, she reported a past history of having 3 units of blood transfusion in the past 2 years for her generalized weakness. The cause of the transfusions was not mentioned in the past medical records. A peripheral blood smear examination was done and hematology consultation was sought. The peripheral smear showed hypochromic poikilocytic anemia, normal thrombocyte cont and plenty of abnormal cells.

Subsequent bone **marrow study** (Fig. 2) revealed:

1) Hypercellular marrow with suppressed & normoblastic erythropoiesis
2) Suppressed megakaryocytosis
3) Accelerated lymphocytosis and suppressed leukopoiesis showing;
   -a) Myelo & metamyelocytic leukocytes with few myeloblasts
   -b) Dominated blasts (60%) of marrow nucleated cells.
4) MPO (Myeloperoxidase stains) was negative in most of the cells.

Differential diagnoses from the above clinical features, hematological & bone marrow work up were:

1. MPAL [Mixed phenotypic acute leukemia]
2. ALL-L2 [Acute Lymphocytic leukemia-L2 type].

An **immunophenotyping** was advised to confirm the diagnosis, which showed: CD45 (Cluster differentiation markers) = 68.06% of gated leucocytes. T cell [CD5 = 1.12%, CD7 = 3.06%]. B cell [CD 10 = 0.05%, CD 19 = 83.06%]. Myeloid/monocytic [CD 13 = 92.38%, CD33 = 88.40%, CD 117 = 68.36%]. Cytoplasmic [cCD3 = 0.01%, Ccd79a = 98.36%, cAnti MPO = 81.08%]. Others [CD34 = 94.04%, HLA (Human Leukocyte Antigen) DR = 68.93%].

Hence, the **final diagnosis** was MPAL, B/Myeloid, NOS (Multi Phenotypic Acute Leukemia, B cell {lymphoid}/myeloid, not otherwise specified).

In cases of BAL, cytogenetic analysis indicates that many B-myeloid cases are characterized by t(9;22) or 11q23 abnormalities, while T-myeloid cases exhibit frequent but generally non-recurring abnormalities [11]. The hybrid transcript for **BCR-ABL** translocation [t (9, 22)] was not found and no genomic breakpoints were noted, in further evaluation.

Pallor, lymphadenopathy, hepatosplenomegaly & fever were conspicuous by their absence. There were no signs of hepatic involvement either clinically or biochemically.

An ALL (Acute Lymphogenous Leukemia) regimen-CVD [Cyclophosphamide, Vincristine, Daunorubicin] was started with. No TKI-Tyrosine Kinase Inhibitor (Imatinib) was added. In light of the poor response to initial ALL regimens, the addition of AML [Acute Myelogenous Leukemia] regimen [Idarubicin, cytosine and etoposide] was done. The patient

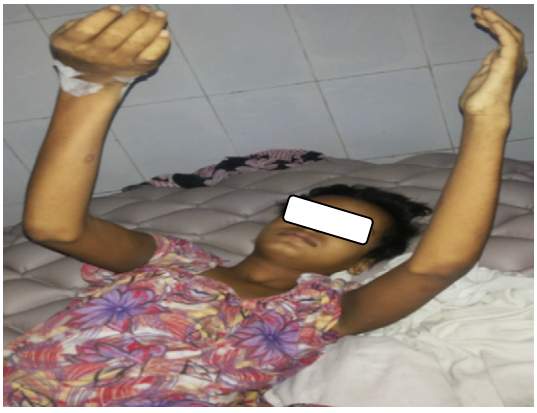

Fig. 1. The patient LS, 16/F.

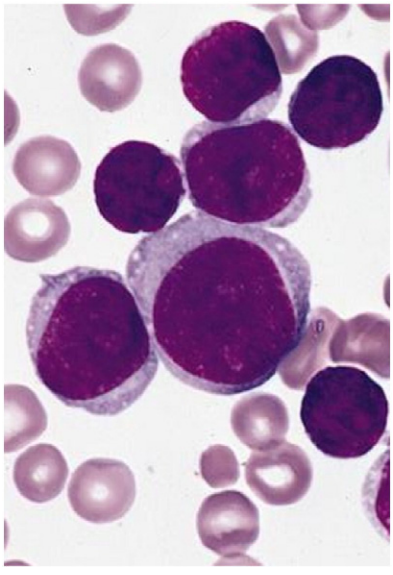

Fig. 2. ×1000 - Blasts having high nucleo-cytoplasmic ratio, scant agranular cytoplasm. Nuclei are round with regular nuclear membrane, condensed chromatin.