Acute Undifferentiated Leukemia (AUL): Rare Clinical Case

Nassima Moufid[1] MD, Chaimae El Mahdaoui[2] PhD, Siham Cherkaoui[1,2] MD, Amine Benmoussa[1] MD, Mouna Lamchahb[1] MD, Nissrine Khoubila[1] MD, Meryem Qachouh[1] MD, Rachid Mohamed[1] MD, Hanaa Bencharef[3] MD, Bouchra Oukkache[3] MD, Abdellah Madani[1] MD

[1] The Hematology And Oncology Pediatric Department of Casablanca - University Hassan II ,Casablanca, Morocco.
[2]Laboratory of Cellular and Molecular Pathology - Research team on Hematology- University Hassan II, Casablanca, Morocco.
[3] Hematology Laboratory- University Hassan II, Casablanca, Morocco.

INTRODUCTION

AUL (Acute Undifferentiated Leukemia) is an uncommon form of acute leukemia characterized by the absence of differentiation along any specific cell lineage. We present an unusual clinical case of AUL, encountering diagnostic difficulties due to molecular biology technical platforms, and facing therapeutic challenges.

Management of AUL in daily practice is still difficult and treating with chemotherapy with or without allotransplantation is a challenge.

CASE DESCRIPTION

Medical history goes back to 1 month before his admission by the progressive installation of

- Left submandibular fistulized lymphadenopathy=6cm
- An anemic syndrome.
- Infectious syndrome (Fever).

CLINICAL CONCLUSION :

A multidisciplinary staff discussed :

➔ An acute leukemia.
➔ Lymph node tuberculosis.

BIOLOGICAL FINDINGS

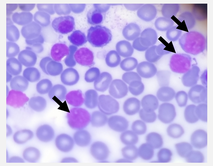
TABLE 1 : COMPLETE BLOOD COUNT

Hemoglobin	**5,4 g/dl**
MCV	**90 fL**
WBC	**830 / mm³**
Neutrophils	**144/mm³**
Lymphocytes	**648/mm³**
Platelets	**258000/mm³**

LYMPH NODE CYTOPUNCTION : No blast cells. No germs.

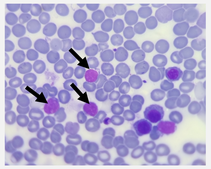
First bone marrow aspiration (BMA) :

R++ M++: 34% blast cells, heterogeneous sizes. MPO negative. Cytological appearance in favor of acute leukemia, most probably megakaryoblastic (Figure 1)



A second BMA was done :

R: ++ M: +/- 78% Blast cells, MPO negative.(Figure 2)



LUMBAR PUNCTURE :

Cytological study: absence of blast cells

Immunophenotyping 1: **(Table 1).**

Immaturity markers	CD34 HLA DR Tdt intracytoplasmic	1,30% 3,80% 2,00%
Lymphoblastic markers T	CD3c intrac. CD10 CD5	3,20% 0,10% 8,60%
Lymphoblastic markers B	CD19 CD10 CD79a	5,80% 0,10% 5,20%
Myeloiblastic markers	MPO CD33 CD117 CD13	0,20% 2,60% 0,60% 6,20%
Erythroblastic markers	CD105 CD71 Glycophorin A	2,90% 61,10% 5,40%
Megakaryocytic markers	CD61 CD41a	7,10% 7,40%
Monocytic markers	CD11c CD4	2,00% 0,60%

Immunophenotyping 2: **(Table 2)**

Immaturity markers	CD34 HLA DR Intracytoplasmic Tdt	2,00% 10,00% 1,40%
Myeloid markers	MPO CD117 CD33 CD13 CD15	2,30% 2,00% 25,00% 12,00% 0,80%
Monocyte markers	CD64 CD14 CD11c CD4	2,00% 0,10% 8,00% 0,40%
Megacaryocytic markers	CD61 CD41a CD42b	8,60% 4,00% 6,00%
Erythroblast markers	CD105 CD71 Glycophorin A CD36 intracytoplasmic	24,00% 77,00% 10,00% 37,00%
B lymphoid markers	CD19 CD22 CD79a intracytoplasmic	3,00% 6,00% 0,40%
T lymphoid markers	CD3 intrac. CD3 CD7 CD8 CD5 CD4 CD2	1,40% 0,10% 91,00% 2,00% 9,00% 0,40% 2,00%
NK lymphoid markers	CD56	0,70%

Bone marrow biopsy :

A rich bone marrow with cellular infiltration of undetermined origin and immunohistochemical aspect demonstrated a moderate blastic infiltration on the order of 20%, with positive Tdt, suggesting an acute lymphoblastic leukemia

MOLECULAR BIOLOGY

- KARYOTYPE WAS NORMAL.
- Search for recurrent fusion transcripts in acute leukemia and myeloproliferative syndromes: Results: NEGATIVE
- Analysis by high-throughput sequencing (NGS) in the context of myeloid hemopathies :
- BCOR exon 4 c.688_689insGGGG: p.A230GfsX72 (VAF 47%)
- BCORL1 exon 6 c.3733G>T: p.G1245X (VAF 1.02%)
- KDM6A exon 27 c.4028_4029insAAGCCAATAGTCC : p.M1343IfsX4 (VAF 44%).

CONCLUSION :

Mutations in the BCOR, BCORL1 and KDM6A genes., Gene copy number analysis found trisomy 22 and a subclonal deletion of the PAX5 (9p) locus. Molecular profile compatible with the diagnosis of AUL.

TREATMENT

Therapeutically, the patient received antibiotic therapy initially, corticosteroid therapy, then induction with an ALL-high-risk protocol with complete remission; currently patient still on chemotherapy.

CONCLUSION-DISCUSSION

In conclusion, we report a rare case of AUL localized to the neck lymph nodes.. This case suggests that chemotherapy for AUL should be selected based on the characteristics of the blast cells. More data are needed to understand the mechanism, pathogenesis, and best treatment, including targeted therapy for AUL.

REFERENCES

Hayashino K, Matsuda M, Fujishita K, Iwata J, Mizobuchi M, Uemura M, Yorita K, Maeshima A, Imai T. Acute undifferentiated leukemia limited to neck lymph nodes and a large mediastinal mass. J Clin Exp Hematop. 2022 Dec 28;62(4):222-225. doi: 10.3960/jslrt.22012. Epub 2022 Oct 20. PMID: 36261335; PMCID: PMC9898720.

Qasrawi A, Gomes V, Chacko CA, et al. Acute undifferentiated Leukemia: data on incidence and outcomes from a large population-based database. Leuk Res. 2020; 89: 106301.