Case Discussion

GR. BAHOUSH, MD

ALI-ASGHAR CHILDREN HOSPITAL

IRAN UNIVERSITY OF MEDICAL SCIENCES

SIOP MEMBER

HLH as initial presentation of ALL: Do you agree?

A 7-year-old girl with developmental delay for unknown cause (from three years ago),

CC: loss of appetite and persistent fever for ten days

PH. Ex.: pallor; Submandibular, cervical, and axillary lymphadenopathy; Hepato-splenomegaly

CBC Pancytopenia [WBC=2600 (ANC = 855), Plt = 46,000 and Hb = 9.5 g/dl),

Fever and cytopenia persisted for more than five days despite antibiotic therapy.

We ruled out infection diseases, rheumatologic disorders, increased intracerebral pressure, and intracerebral hemorrhage. Screening Abs were negative.

Serology of cytomegalovirus (CMV) and Epstein-Barr virus (EBV) were negative.

Other Findings

Ferritin = 5857,

Triglyceride = 365,

Fibrinogen = 0.94,

D-dimer = ↑↑↑

Perforin level was normal.

NK-Cell activity and CD25 (interleukin-2 receptors) level could not be able to do.

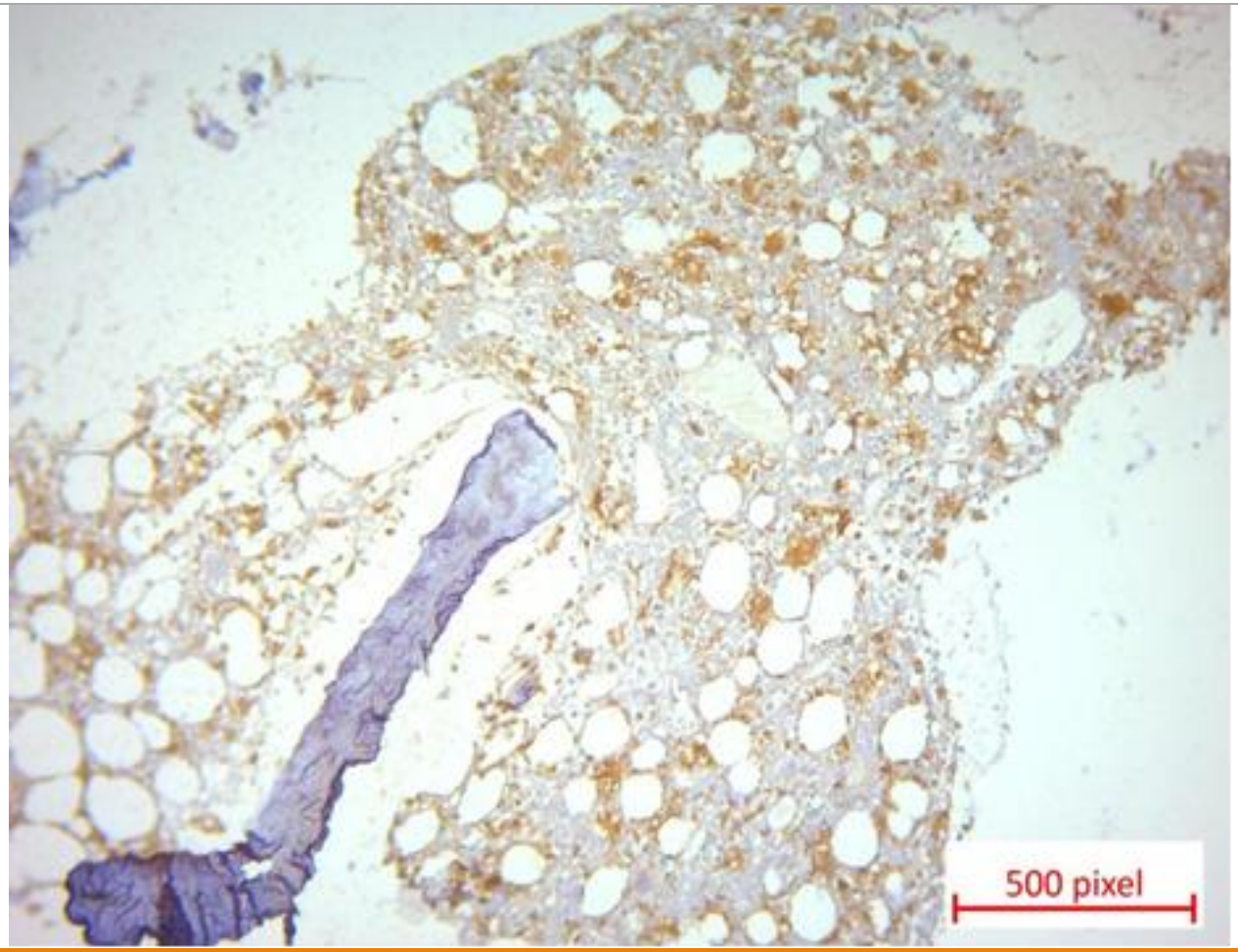
Genetic testing for the familial type of HLH other than perforin level (by flow cytometry) could not be performed.

HLH as initial presentation of ALL: Do you agree?

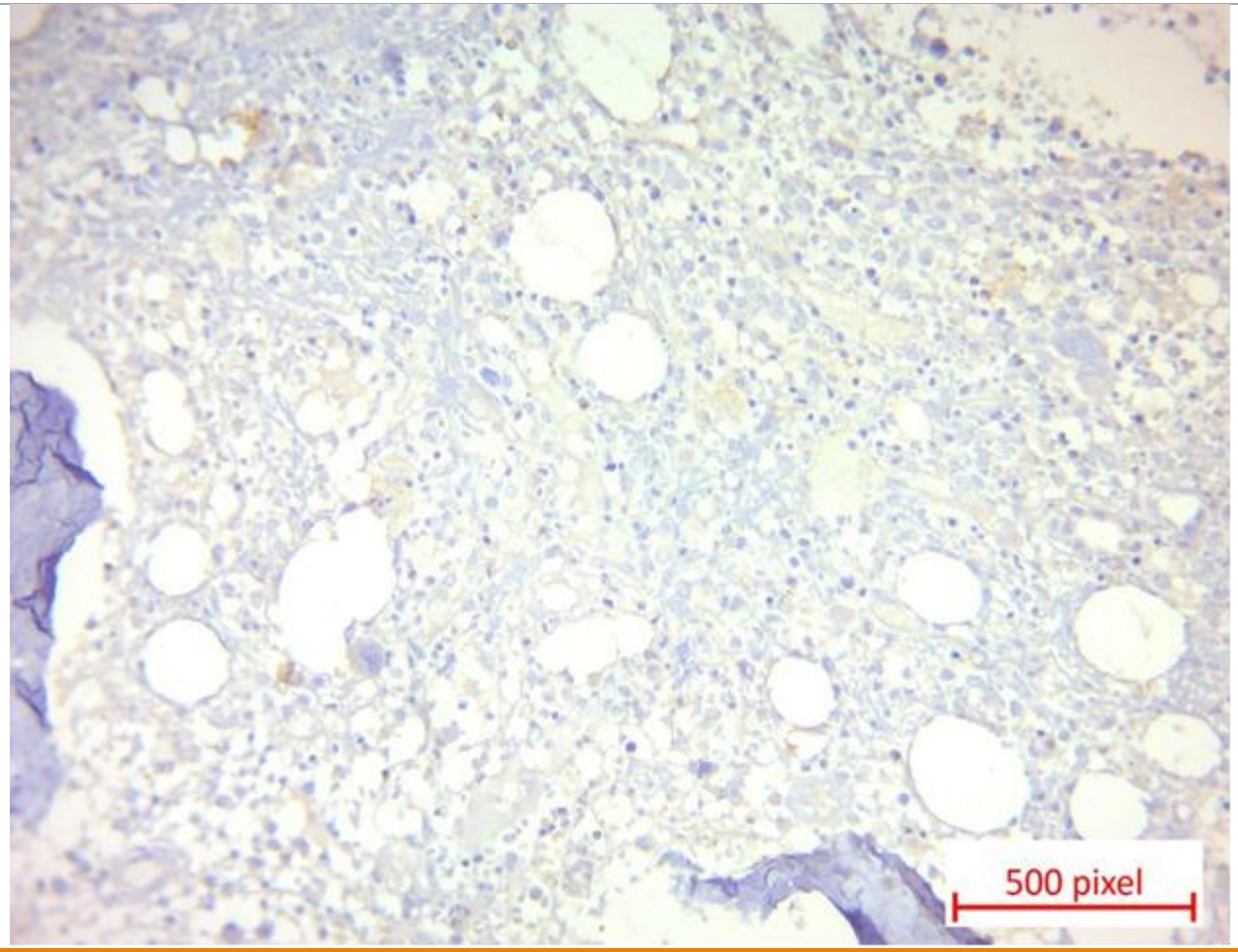
A bone marrow aspiration and biopsy:

- unremarkable bone trabeculae and cellular marrow with 80-85% cellularity.
- Megakaryocyte was adequate.
- Mild Paratrabecular fibrosis in trichrome stain
- Marked infiltration of CD68 positive and CD1a negative.
- The histological feature was in favor of Hemophagocytic lymphohistiocytosis

Immunohistochemistry of CD68 showing positive histiocytes in bone marrow biopsy.



Immunohistochemistry of CD1a is negative in bone marrow biopsy



Management and follow up

chemotherapy treatment for HLH was exactly started with the HLH-2004 treatment regimen.

The diasease was in complete remission in the end of induction.

HSCT have not been to do due to not finding a suitable donor.

Treatment was stopped after 40 weeks.

She was presented by cervical lymphadenopathy one month later with normal CBC and other lab tests (especially HLH lab thests).

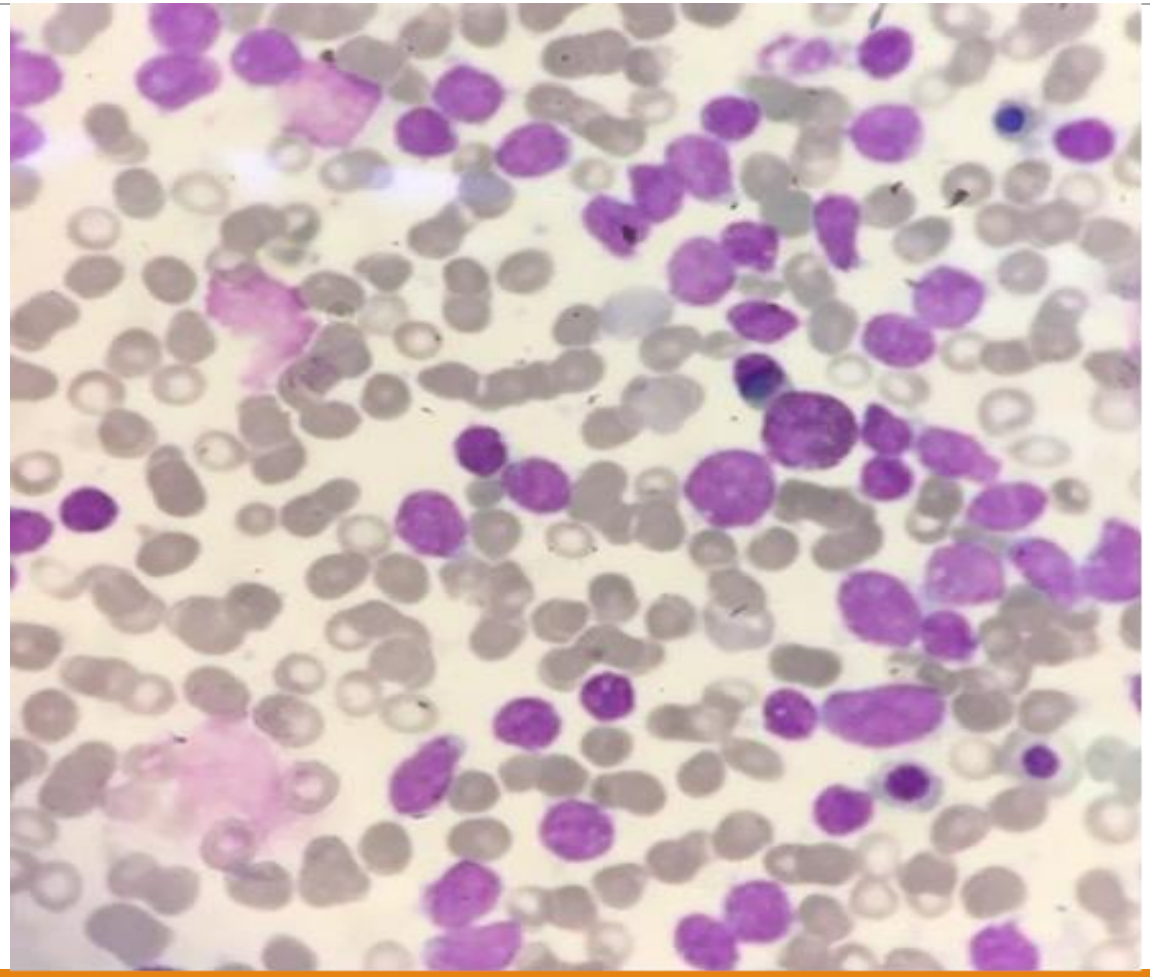
Excisional Biopsy Pre-B cell ALL !!

BMA ALL L1

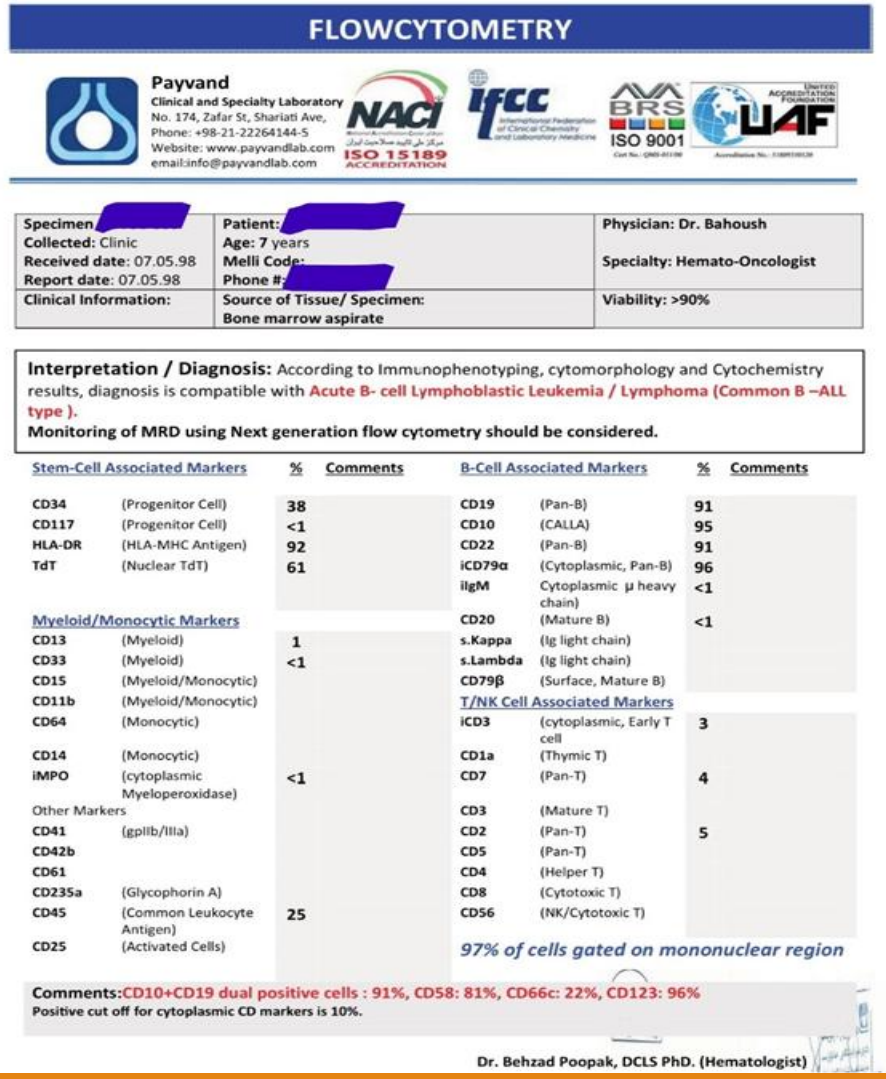
FCM Common-B cell ALL

She was treated by BFM protocol.

BMA



FCM



FLOWCYTOMETRY

Payvand
Clinical and Specialty Laboratory
No. 174, Zafar St, Shariati Ave,
Phone: +98-21-22264144-5
Website: www.payvandlab.com
email:info@payvandlab.com

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Specimen [redacted] **Collected:** Clinic **Received date**: 07.05.98 **Report date**: 07.05.98	**Patient:** [redacted] **Age:** 7 years **Melli Code:** **Phone #:** [redacted]	**Physician: Dr. Bahoush** **Specialty: Hemato-Oncologist**
Clinical Information:	**Source of Tissue/ Specimen:** **Bone marrow aspirate**	**Viability: >90%**

Interpretation / Diagnosis: According to Immunophenotyping, cytomorphology and Cytochemistry results, diagnosis is compatible with **Acute B- cell Lymphoblastic Leukemia / Lymphoma (Common B –ALL type).**
Monitoring of MRD using Next generation flow cytometry should be considered.

Stem-Cell Associated Markers		%	Comments
CD34	(Progenitor Cell)	38	
CD117	(Progenitor Cell)	<1	
HLA-DR	(HLA-MHC Antigen)	92	
TdT	(Nuclear TdT)	61	
Myeloid/Monocytic Markers			
CD13	(Myeloid)	1	
CD33	(Myeloid)	<1	
CD15	(Myeloid/Monocytic)		
CD11b	(Myeloid/Monocytic)		
CD64	(Monocytic)		
CD14	(Monocytic)		
iMPO	(cytoplasmic Myeloperoxidase)	<1	
Other Markers			
CD41	(gpIIb/IIIa)		
CD42b			
CD61			
CD235a	(Glycophorin A)		
CD45	(Common Leukocyte Antigen)	25	
CD25	(Activated Cells)		

B-Cell Associated Markers		%	Comments
CD19	(Pan-B)	91	
CD10	(CALLA)	95	
CD22	(Pan-B)	91	
iCD79α	(Cytoplasmic, Pan-B)	96	
iIgM	Cytoplasmic μ heavy chain)	<1	
CD20	(Mature B)	<1	
s.Kappa	(Ig light chain)		
s.Lambda	(Ig light chain)		
CD79β	(Surface, Mature B)		
T/NK Cell Associated Markers			
iCD3	(cytoplasmic, Early T cell	3	
CD1a	(Thymic T)		
CD7	(Pan-T)	4	
CD3	(Mature T)		
CD2	(Pan-T)	5	
CD5	(Pan-T)		
CD4	(Helper T)		
CD8	(Cytotoxic T)		
CD56	(NK/Cytotoxic T)		

97% of cells gated on mononuclear region

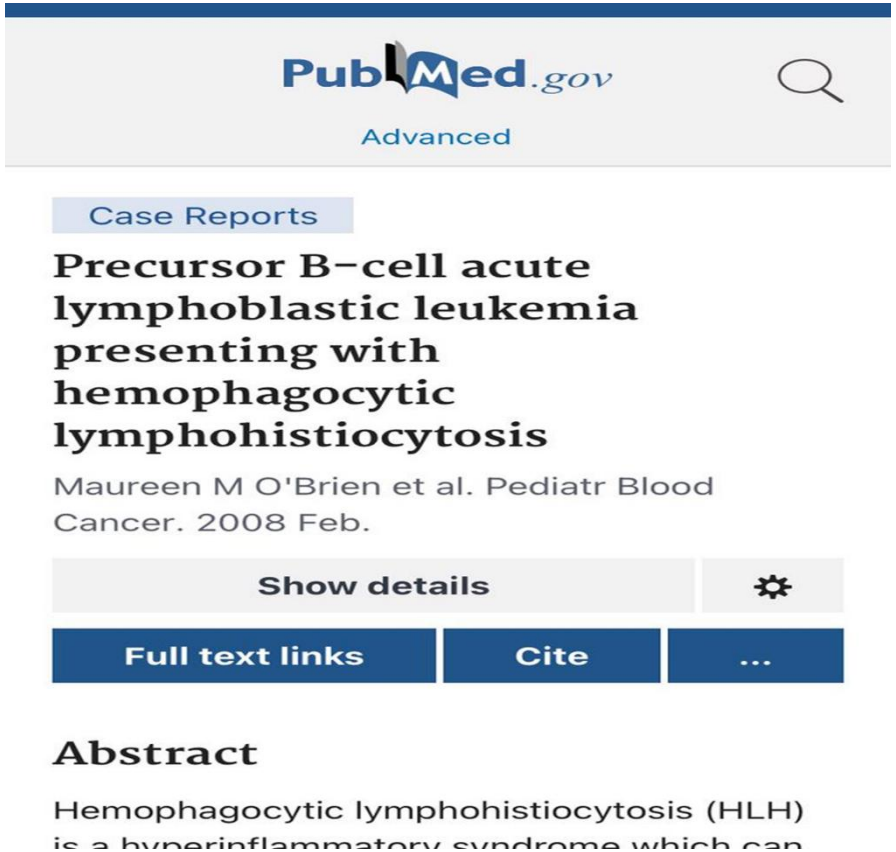
Comments:CD10+CD19 dual positive cells : 91%, CD58: 81%, CD66c: 22%, CD123: 96%
Positive cut off for cytoplasmic CD markers is 10%.

Dr. Behzad Poopak, DCLS PhD. (Hematologist)

Question

Secondary leukemia or ALL presented as HLH???

Literature review



Up to now, There were not any reports of acute lymphoblastic leukemia secondary to Etoposide-based chemotherapy.