



EUROPEAN
HEMATOLOGY
ASSOCIATION

EHA-PTHiT Hematology Mini Tutorial

Self-assessment Case: **Diffuse Large B-cell Lymphoma – Case 2**

Speaker: Jan Walewski

April 12-13, 2021



Jan Walewski, Disclosures

Roche (advisory board, research funding, lecture honoraria, travel expenses)

Abbvie (advisory board, lecture honoraria)

Takeda/Millennium (advisory board, lecture honoraria)

Gilead (advisory board, lecture honoraria)

Novartis (advisory board, lecture honoraria)

GSK/Novartis (research funding)

Servier (lecture honoraria)

Amgen (lecture honoraria)



DLBCL Case 2, learning objectives

1. Understanding risk stratification by use of the international prognostic index (IPI) and NCCN-IPI
2. Considering options of third-line therapy for relapsed/refractory DLBCL



Patient case 2

- 44 year old female,
- April 2020: fever, cough, dyspnea, weight loss
 - no improvement on oral amoxicillin
- Admitted to hospital with suspected COVID-19
 - PCR test negative x2
- ECOG PS score 2/3
- Chest X ray: bilateral pleural effusion, pneumonia?
- Chest CT: bilateral pleural effusion, pericardial effusion, lymphadenopathy
- Abdominal CT: lymphadenopathy Ø 20 mm

Patient case 2

- transferred to ICU due to respiratory distress
 - new supraclavicular lymph nodes noted (biopsy and aspiration for flow)
- History
 - Sarcoidosis (July 2019)
 - Hashimoto's struma (Hashimoto's thyroiditis)
 - Bilateral breast implants



Histopathologic examination

Lymphoma infiltration mainly with immunoblasts, partially centroblasts

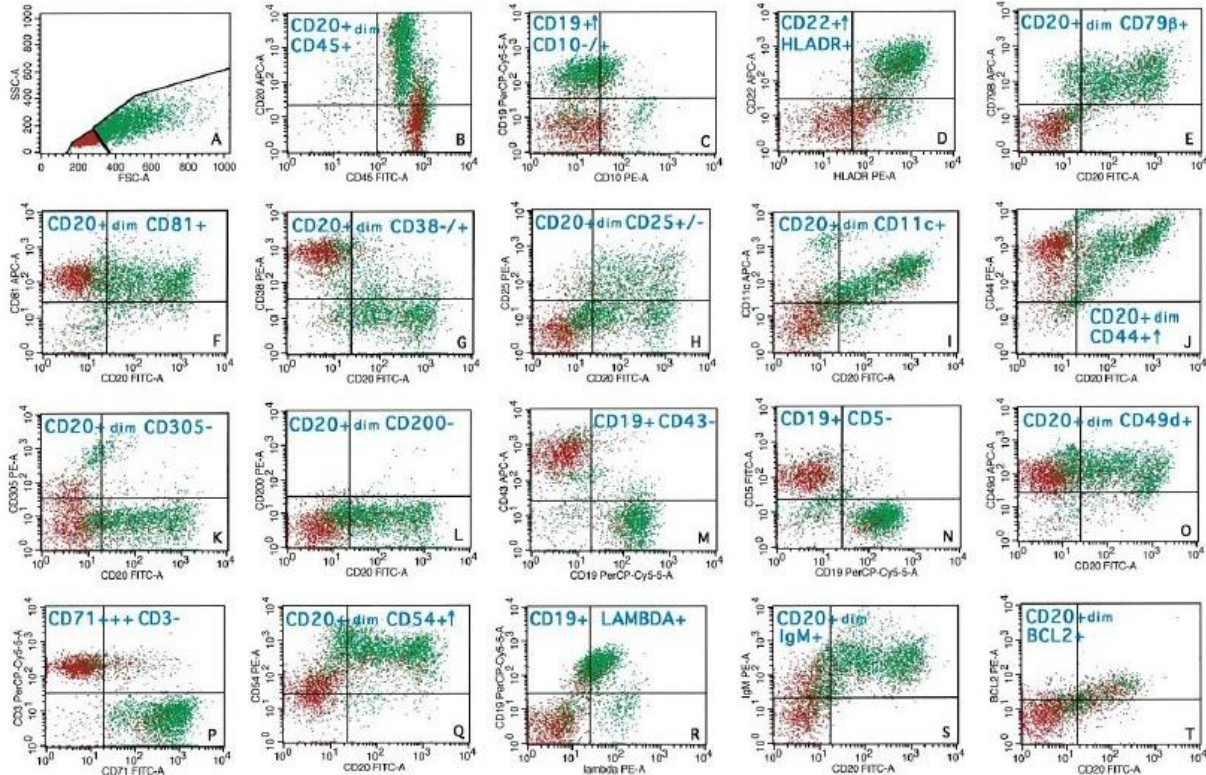
Immunohistochemistry:

- CD20(+),
- Ki67(+++) in 85% of cells
- CD30(-/+) in 10% of cells
- CD3(-), -CD15(-/+), CD 23(-), CD 5(-)
- PAX5(+)
- CD10(-), BCL6(-), -BCL2(+/-) decreased expression of BCL2 on T cells (not seen in PMBL)
- MUM1(+/-), MYC(-) nuclear staining in 20% of cells,

Cell suspension flow cytometry

Immunophenotype:

CD45+, CD20+ , CD19+ , CD22+,
CD79b+, HLADR+, CD54+, CD81+,
CD71+++ , CD52+, BCL2+/-, lambda
+/-, IgM+, CD16/56-, BCL6-, CD5-,
CD43-, CD23-, CD10-, CD305-,
CD200-, CD30-/-



Fine needle aspiration biopsy of right supraclavicular nodes under USG guidance

Q1) Is this immunophenotype consistent with:

1. Primary mediastinal large B-cell lymphoma (PMBL)
2. T-lymphoblastic lymphoma (T-LBL)
3. Diffuse Large B-cell lymphoma (DLBCL), NOS, Germinal Centre B-cell (GCB)-type
4. DLBCL, NOS, non-GCB-type
5. Marginal zone lymphoma (MZL) with mediastinal involvement

Cell suspension flow cytometry

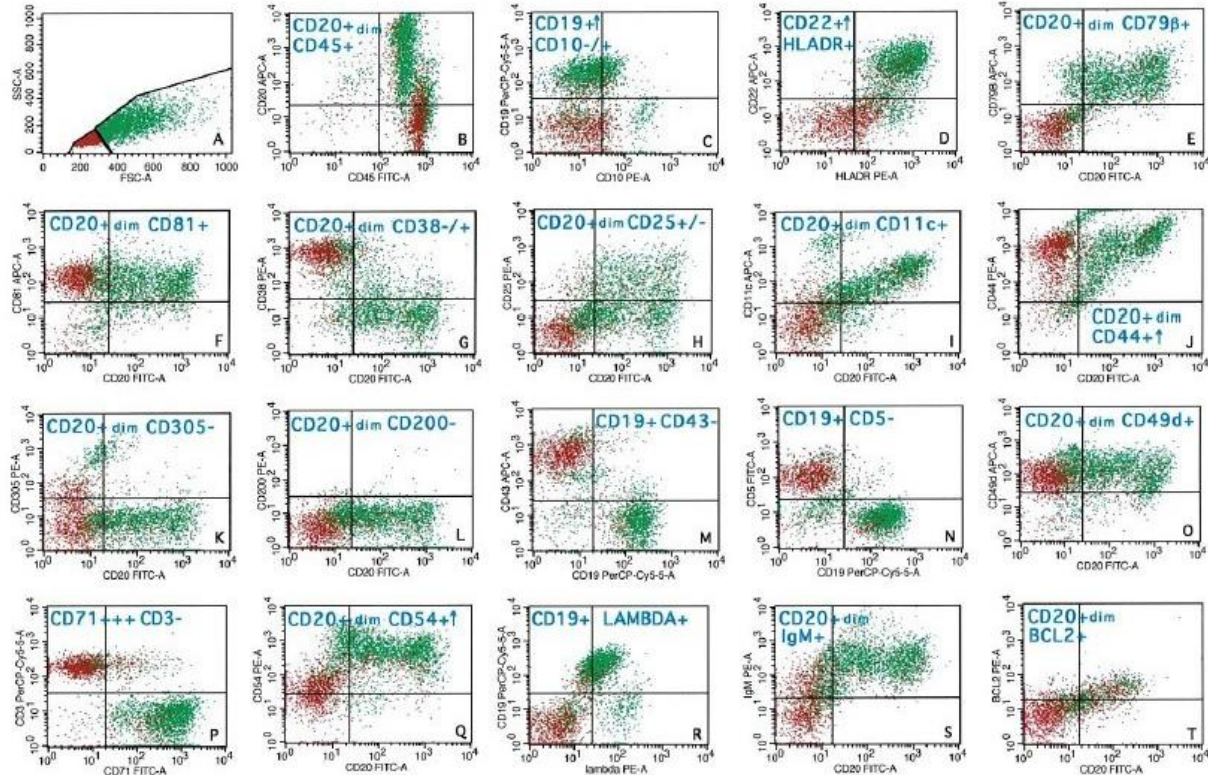
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Nodal DLBCL, NOS presenting as
mediastinal large B cell lymphoma
with peripheral lymph nodes
involvement.

DLBCL, NOS with CD20+ dim,
HLADR+, CD23-, CD200-, CD79b+
inconsistent with PMBL.

Non-GCB subtype



Fine needle aspiration biopsy of right supraclavicular nodes under USG guidance



FISH and karyotype examination

FISH:

- no *MYC*, no *BCL2*, no *BCL6* rearrangements
- duplication of *BCL6* in 85% of cells
- Duplication of *JAK2* in 92% of cells
- *PAX5* rearrangement in 90% of cells

Karyotype:

47, XX,+del(3)(p12),t(9;14)(p13;q32)[10]

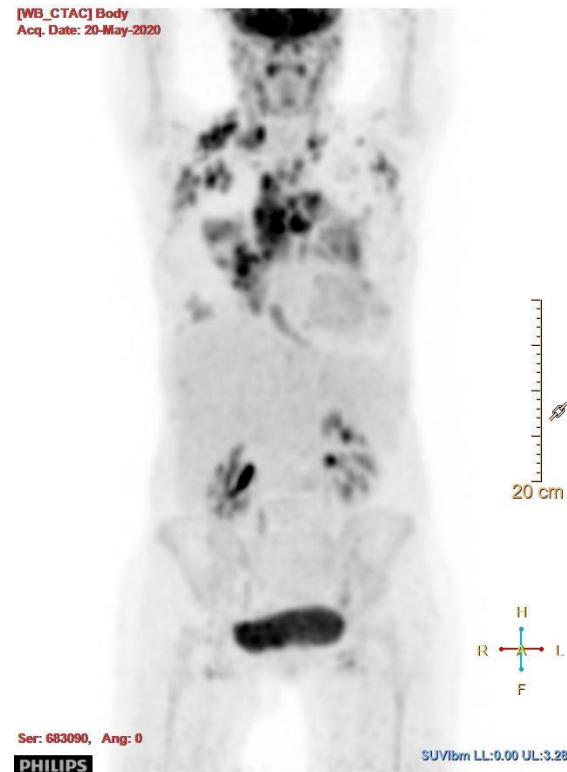
hyperdiploid karyotype with +3q (*BCL6* duplication) and t(9;14) (*PAX5* rearrangement).

Q2) Plan for further work-up

1. CT scan
2. Bone marrow examination
3. MRI
4. PET-CT
5. Ultrasound

Staging and workup

- PET-CT (April 2020) involvement of multiple lymph nodes in the chest, abdomen, lungs, bones, bone marrow, pleural and cardiac effusion
- Bone marrow involvement (15%) on trephine biopsy
- CS IVB
- LDH 504 (N<248 IU/l; 2.2xN)
- HBV, HCV, HIV serology negative
- PS 2
- IPI 4



Q3) IPI score is 4. What is the NCCN IPI score?

- 1. 1
- 2. 2
- 3. 3
- 4. 4
- 5. 5



Risk factor	score	The NCCN IPI
Age		
>40 do \leq 60	1	
>60 do \leq 75	2	
>75	3	
LDH Ratio		
>1 do \leq 3	1	
>3	2	
CS III-IV	1	
Extranodal sites:		
bone marrow, CNS, liver/G.I. tract, lung	1	
ECOG PS \geq 2	1	

Comparison of NCCN-IPI to IPI for risk stratification and outcomes

Risk category	score		5-yr OS		5-yr PFS			
	NCCN-IPI	IPI	NCCN-IPI	IPI	NCCN-IPI	IPI		
Low	0-1	19%	0-1	38%	96%	90%	91%	85%
Low-interm.	2-3	42%	2	26%	82%	77%	74%	66%
High-interm.	4-5	31%	3	22%	64%	62%	51%	52%
High	≥6	8%	4-5	14%	33%	54%	30%	39%

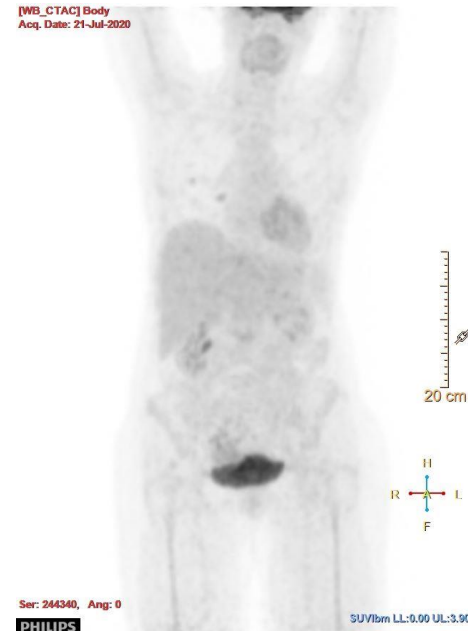
Q4) What is the optimal therapy

1. R-CHOP
2. R-CHOP + i.th. methotrexate
3. DA-EPOCH-R
4. CODOX-M/R-IVAC
5. R-CHOP + high-dose methotrexate

- May - July 2020:
 - R-CHOP x 4 + high-dose methotrexate 3.5 g/m² x 3
- August 2020 – admitted for cycle 5
 - Pleural bleeding after CVC insertion, respiratory failure,
 - admitted to ICU, recovered

Treatment

Interim PET post cycle 3:
5PS - 2



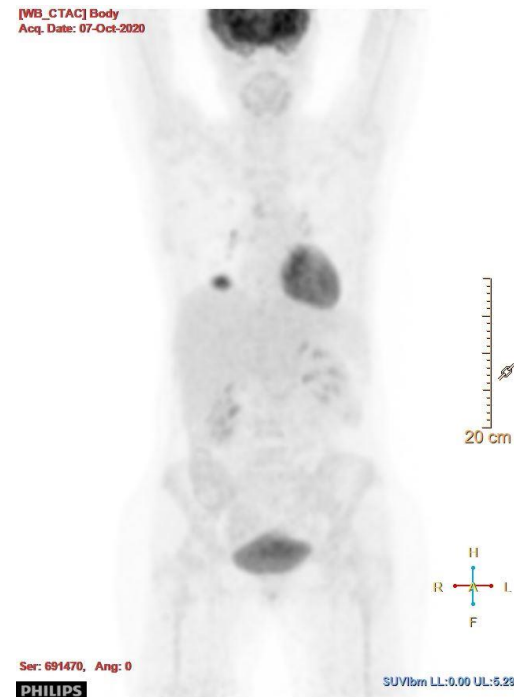
Q5) How should this serious adverse event influence further treatment?

1. Change regimen to R-DHAP
2. Continue R-CHOP with HD MTX
3. Terminate chemotherapy
4. Continue R-CHOP alone
5. Proceed to high-dose therapy and autologous HCT

Treatment

- Continued R-CHOP x 2
- End of treatment PET-CT (07.10.2020): new lesion in the right lung, 28x26mm maximum standard uptake volume (SUV max) standardised to lean body mass (lbm) 8.2
 - misinterpreted as possible sarcoidosis → observation
- Chest-CT (11.2020): tumor in the right lung 71x64mm
- Chest-CT (01.2021): tumor in right lung 83x78 mm, new mediastinal tumor 32x30 mm

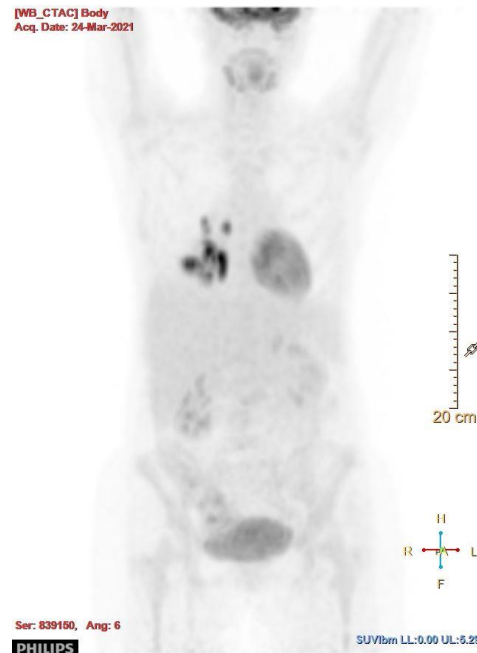
PET scan post-cycle 6 (EOT)



Treatment

- ICE x 2 (02.2021 - 03.2021)
- G-CSF
- apheresis
- PET-CT 24.03.2021: Progressive disease in the right lung

PET-CT after ICE 2



Q6) What options are available now

1. Consider clinical trial
2. Polatuzumab + bendamustine/rituximab (BR)
3. CAR-T cell therapy
4. Tafasitamab + lenalidomide
5. Pixantrone



Discussion Case 2

- Diagnostic difficulties: sarcoidosis, COVID-19 pneumonia, lymphoma
- Retrospectively, could induction therapy be better?
- Question of the third line treatment



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Case 2

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