UNIVERSITY OF PUERTO RICO SCHOOL OF MEDICINE
HEMATOLOGY AND MEDICAL ONCOLOGY SECTION

AN ATYPICAL PRESENTATION OF RICHTER'S TRANSFORMATION

LUIS R. VELAZQUEZ, MD PGY-5.

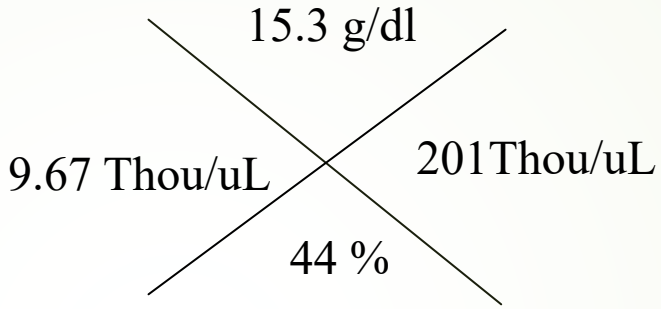
Introduction

- CLL/SLL is a mature B cell neoplasm characterized by a progressive accumulation of monoclonal B lymphocytes.
- Richter transformation is the development of an aggressive large-cell lymphoma in the setting of underlying chronic lymphocytic leukemia.
- Although diffuse large B cell lymphoma is the most common histology seen in patients with Richter transformation, Hodgkin lymphoma and T cell lymphomas have also been reported less commonly.

Clinical Case

- 60-year-old male patient with past medical history of asthma and Chronic lymphocytic leukemia diagnosed in March of 2023.
- In July of 2023, a CT performed to evaluate for nephrolithiasis discovers prominent retroperitoneal lymphadenopathy.
- Patient at the time did not present "B" symptoms.
- PET scan showed diffuse adenopathy above and below the diaphragm with a maximum SUV of 24 in the peripancreatic area.

Laboratories



- Neutrophils; 44%
- Band; 15%
- Lymphocytes; 29%
- Monocytes; 19%
- Beta2 microglobulin: 3.7 mcg/ml
- Uric Acid: 10.8 mg/dl
- LDH: 391 U/L

Clinical Case

- FNA of the peripancreatic mass, rules out Richter's transformation.
- Immunohistochemistry positive for CD5, CD20, CD23 and PAX 5.
- Molecular studies remarkable for TP53 mutation.
- Patient began treatment with Acalabrutinib and Obinutuzumab in July of 2023.
- During treatment patient suffered multiple complications including Pleural effusions; requiring multiple thoracentesis, hypercalcemia, and renal failure.

Specimen(s) Received

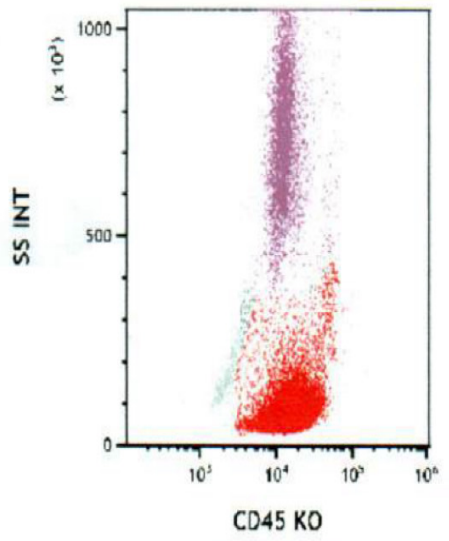
Right Pleural fluid

FLOW CYTOMETRY ANALYSIS

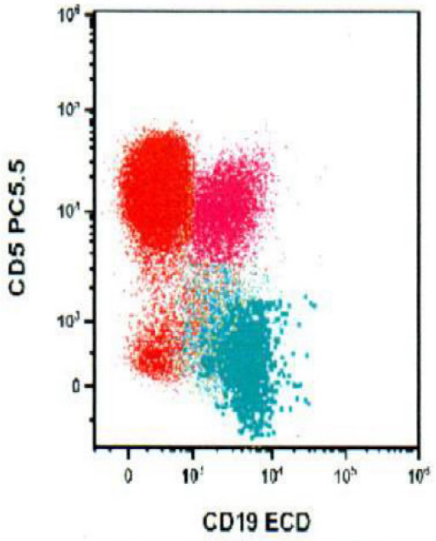
IMMUNOPHENOTYPE INTERPRETATION:

RIGHT PLEURAL FLUID FOR FLOW CYTOMETRY:

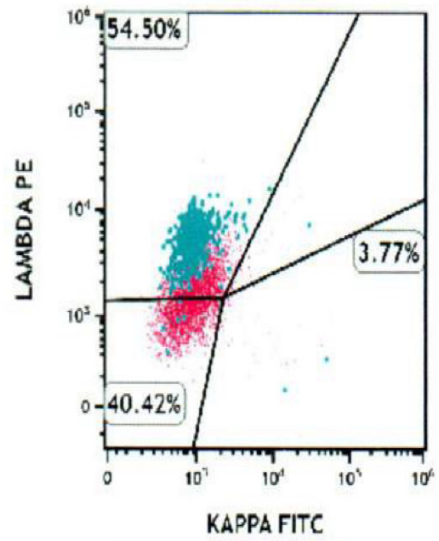
- **Two phenotypically distinct monoclonal B-cell populations.**
  - **Pink population: 6.27%, CD5+, dim-lambda-restricted with classic CLL/SLL phenotype. See comment.**
  - **Baby blue population: 1.2%, CD5-, lambda-restricted. See comment.**



CD45 vs. SS



B-cells: CD19 vs. CD5



Lambda restricted B-cells

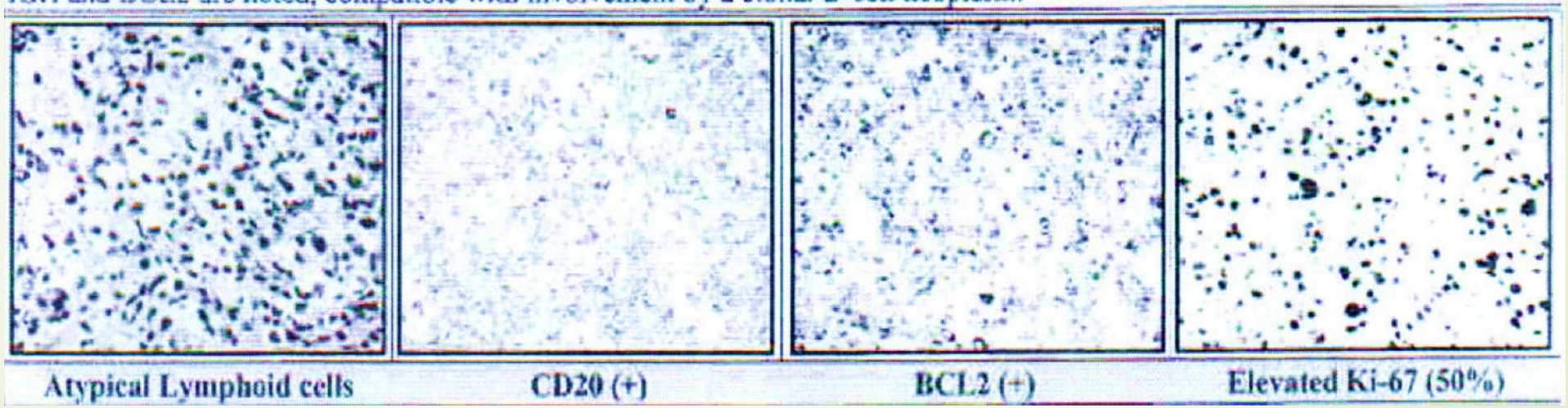
FINAL DIAGNOSIS

Mass, Right Retroperitoneal – Core Biopsy: Morphologic findings C/W Persistent Involvement by B-CLL/SLL (see comment)

Electronically Signed By: Bevan Tandon, MD Hematopathologist **Tel:** 888-599-LABS (5227) **Mobile:** 973-527-5069

COMMENT: Sections show core biopsy samples of lymph node tissue with architectural effacement by an atypical, mature lymphoid proliferation that includes probable pseudofollicules / proliferation centers. Confluent sheets of large B-cells are not identified, although focally increased, large, atypical cells are noted, probably related to proliferation centers. By immunohistochemistry, the neoplastic lymphoid proliferation is positive for CD20, PAX5, CD5 (weak), CD23 ^{partial}, and BCL2. BCL6 marks scattered positive cells. MYC, MUM1, and Ki67 appear increased in focal areas, probably related to apparent proliferation centers. CD21 highlights some intact follicular dendritic meshwork structures. The neoplastic lymphoid infiltrate is negative for CD3, CD10, CD30, CD43 and BCL1.

The overall morphologic findings are consistent with the provided history of CLL/SLL. **In the absence of confluent sheets of large B-cells, definitive morphologic evidence of DLBCL / Richter's is not identified; however, if clinical concern persists for potential involvement by a more aggressive large B-cell process, lymph node excisional biopsy is suggested, as clinically warranted and feasible.** FISH is negative for evidence of genetic "double hit" or "triple hit", and extra copies of IGH and BCL2 are noted, compatible with involvement by a clonal B-cell neoplasm.

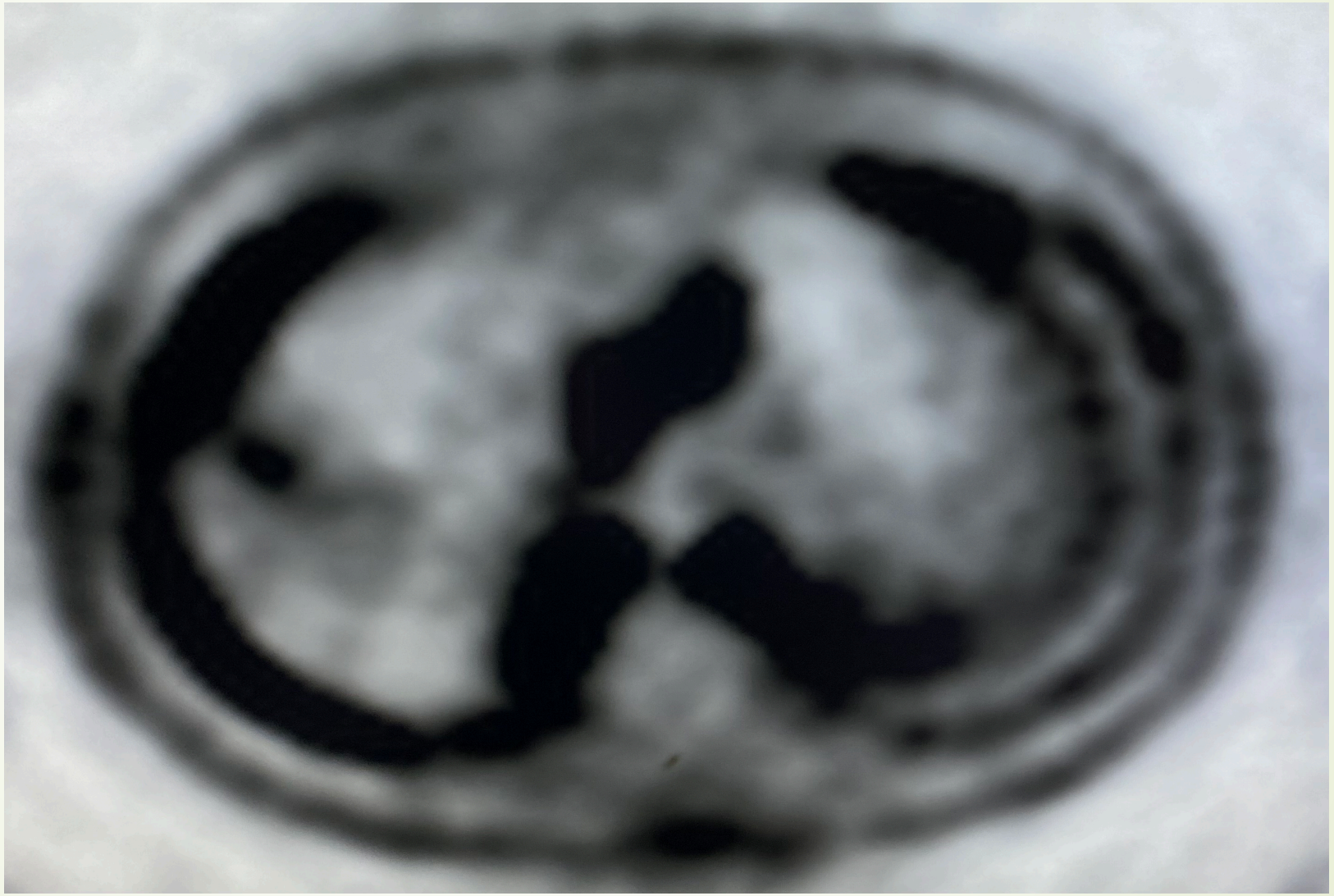


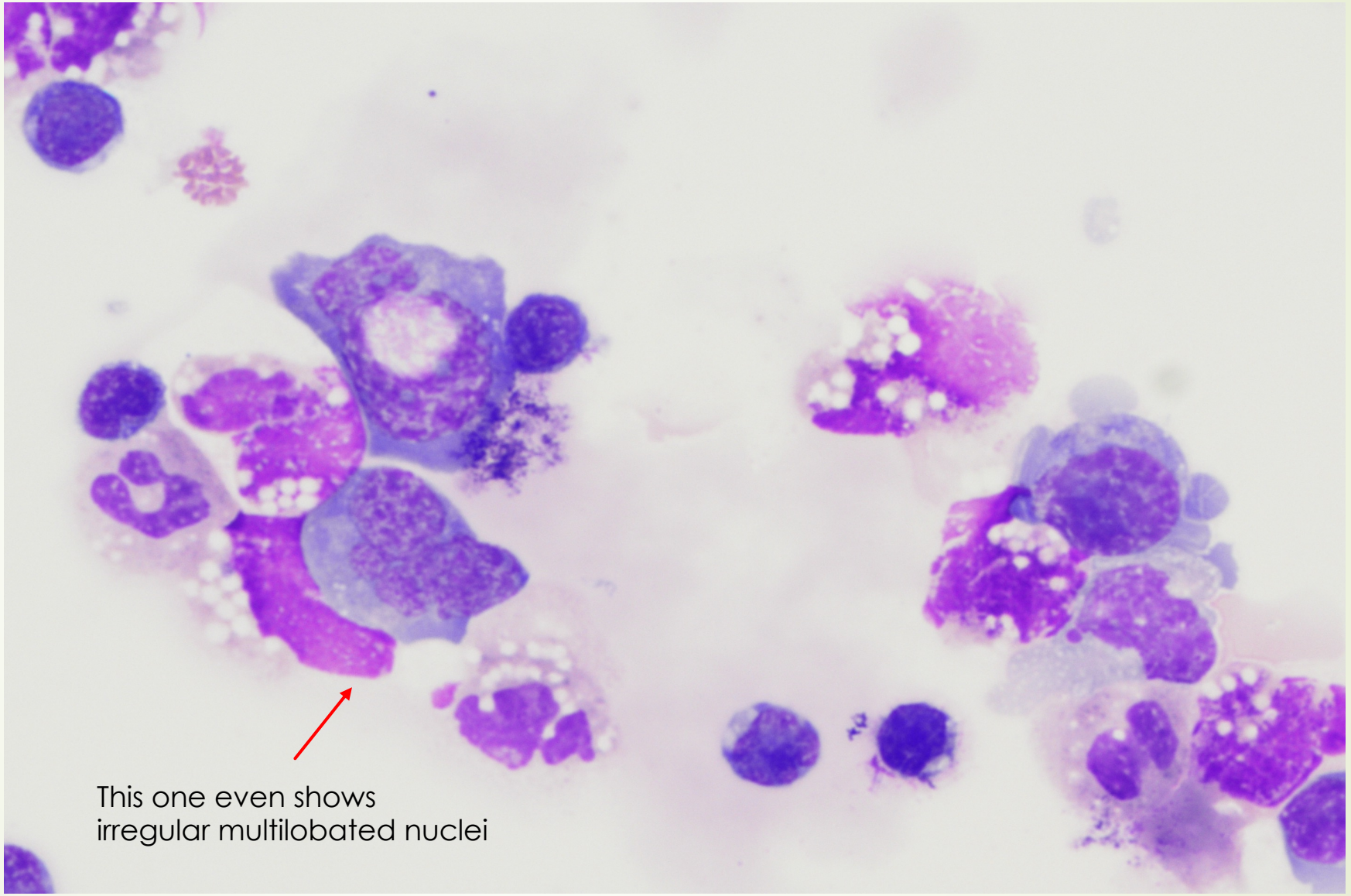
Atypical Lymphoid cells | CD20 (+) | BCL2 (+) | Elevated Ki-67 (50%)

Clinical Case

- In December of 2023 patient's disease began to progress as was evident from recurrent pleural effusions, worsening fatigue, and lymphadenopathy, as seen on chest CT.
- PET scan performed in January of 2024 demonstrates Multiple hyper-metabolic lesions involving the lung fields, gross lymphadenopathy, and gross pleural effusions.
- Cytology of pleural fluid shows forward scatter suggesting large cells and cytospin shows cells with prominent nucleoli, findings compatible with Richter's transformation.
- Treatment with R-CHOP is been planned.

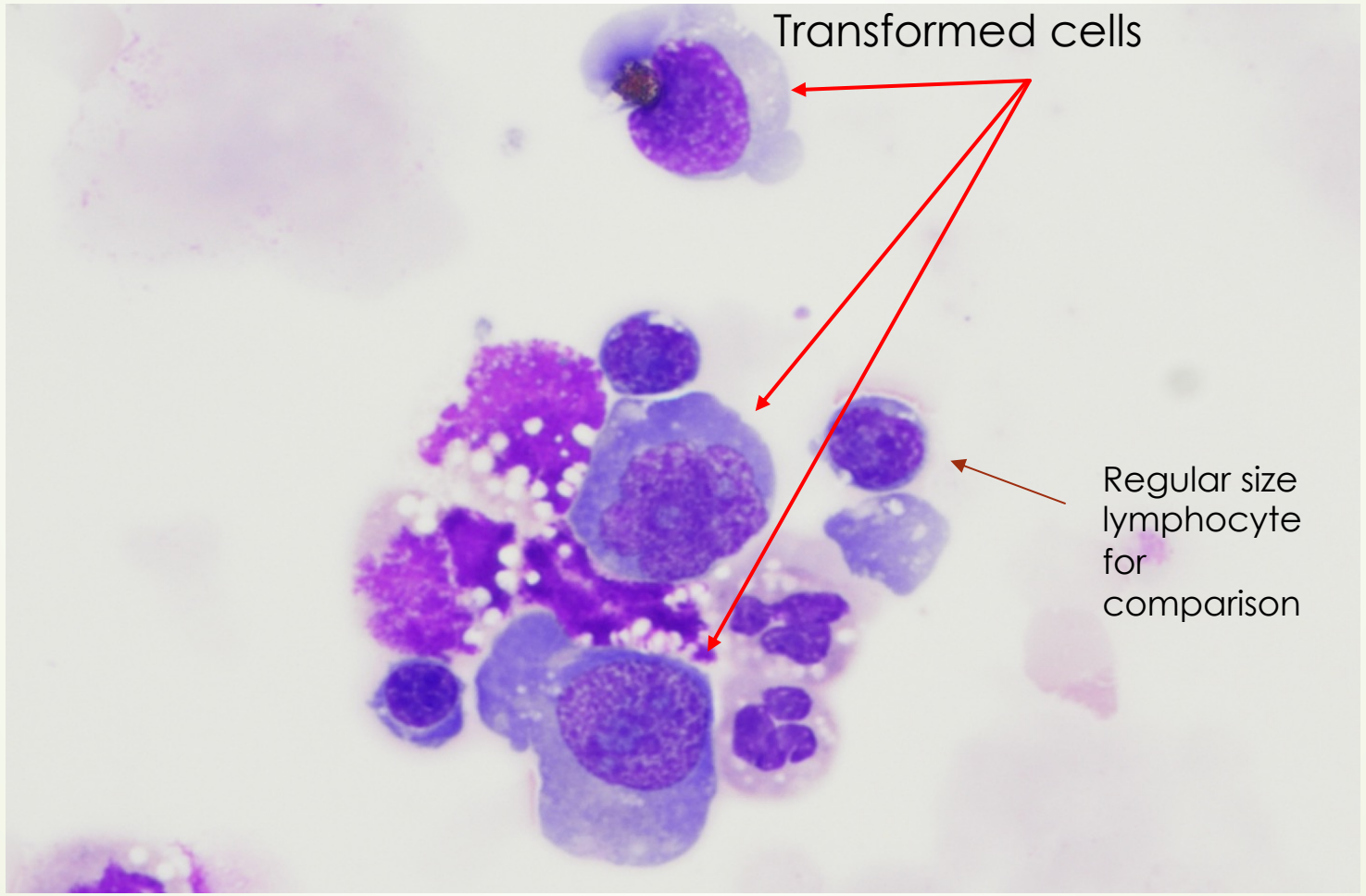
PET scan





Pictures by: Dr. José M. Rodríguez Medina

Cytospin



Pictures by: Dr. José M. Rodríguez Medina

Discussion

- The onset of Richter's transformation is announced by sudden clinical deterioration, characterized by a marked increase in lymphadenopathy at one or more sites, splenomegaly, and worsening "B" symptoms.

- The diagnosis of Richter's transformation can be challenging and a review by an experienced hematopathologist is important.

- The diagnosis of DLBCL type Richter's transformation can be difficult because progressive CLL may show an increased percentage of large cells in the absence of true Richter's transformation.

Discussion

- This was a challenging case in more ways than one.
- We witnessed an SLL with TP53 mutation undergo a Richter's transformation signal by worsening pleural effusions, without worsening lymphadenohathy, nor "B" symptoms.
- PAX 5 in uncommonly found as a marker in CLL/SLL patients, but when present, can be used as a prognostic tool to predict higher chances of suffering a transformation.

Learning Points

- Biopsy is required to confirm the diagnosis. Biopsy should aim to sample a lymph node with the highest avidity on positron emission tomography imaging.
- Histology usually shows a pattern consistent with diffuse large B cell lymphoma.
- For most patients with the DLBCL histologic pattern of Richter's transformation, the use of combination chemotherapy plus rituximab as employed for aggressive lymphoma is recommended.
- R-CHOP is usually offered in this setting, but dose-adjusted-EPOCH-R is also reasonable.
- Pleural effusion may herald a Richter's transformation, but such a condition remains a very rare event.

References

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Thank You.