Richter Transformation: Diagnostic Challenge

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Introduction

- Richter transformation (RT) is a rare complication of chronic lymphocytic leukemia (CLL) where the disease transforms into a more aggressive lymphoma
  - Most common transformation: Diffuse large B-cell lymphoma (DLBCL) - **Incidence 2-10%**
  - Less common: Hodgkin lymphoma
  - Extremely rare: Plasmacytic differentiation
- Diagnostic challenges:
  - Aberrant expression of multiple epithelial markers in the neoplastic plasma cells could lead to a diagnosis of metastatic carcinoma
  - Comprehensive analysis is crucial to avoid diagnostic pitfalls

Case Report

Age/History	75-year-old male with CLL and suspected Richter transformation with persistent pleural effusions.
Clinical Presentation	Abdominal pain; worsening abdominal lymphadenopathy on physical exam
Imaging: CT/PET	- Bilateral pleural effusions - 6 cm epicardial soft tissue density - 5.4 cm hypermetabolic mediastinal mass (SUV 16.6) - Multiple enlarged mesenteric lymph nodes
Pleural Fluid Cytology	Persistent lymphoplasmacytic infiltration; large anaplastic cells of uncertain etiology and background CLL (Figure 1)
Flow Cytometry	Clonal B cells and plasma cells with lambda light chain restriction

Results

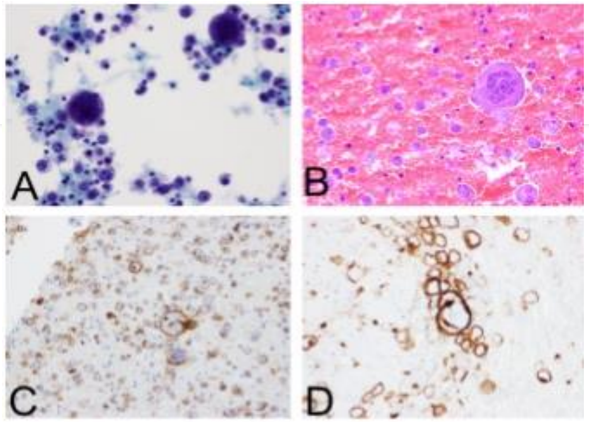

Figure 1: Cytology and Immunohistochemical Findings (400x Magnification)
ThinPrep slide showing large anaplastic cells, some with eccentrically placed nuclei (A). Cell block preparation highlighting similar atypical morphology (B). **MOC31** stain with strong membranous positivity, mimicking carcinoma (C). **CD138** stain supporting plasma cell differentiation (D).

Immunohistochemistry

Positive	Subset Positive
AE1/AE3/CAM5.2	Oscar
MOC-31	CD79a
BCMA	CD19
CD117	
MUM-1	
Vimentin	
CD-56	
CD-138	
Lambda ISH	

Negative		
Melan A	CK7/ CK20	CD-15
SOX-10	EBER ISH	SALL-4
S-100	Kappa ISH	OCT-4
Calretinin	PAX-5	CD-30
Synaptophysin	CD-20	P63
PLAP	CD-45	Glypican 3
	CD-5	

Results (Continued)

Differential Diagnosis	Morphology	IHC Profile	Molecular Features
Plasmacytic Richter Transformation (RT)	Discohesive, large anaplastic cells, eccentric nuclei, plasmacytoid features	CD138+, MUM1+, CD117+, lambda light chain restriction, variable epithelial marker (MOC31, AE1/AE3) expression	Trisomy 12, clonal B-cell receptor rearrangement
Primary Plasma Cell Neoplasm	Monotonous plasma cells, eccentric nuclei, occasional binucleation	CD138+, MUM1+, CD56+(strong; 60-80% of cases), lambda or kappa light chain restriction, negative for epithelial markers	Frequent IgH rearrangement at chromosome 14q32, Hyperploidy, 13q deletion, MYC translocations rare
Plasmablastic Lymphoma	Large plasmablastic cells, high nuclear-to-cytoplasmic ratio, eccentric vesicular nucleus with prominent nucleoli	CD138+, CD38+, MUM1+, CD45-/+, high Ki-67, EBV-associated (EBER ISH+), CD20-, CD19-, PAX5-	MYC rearrangement common, EBV positive
Primary Effusion Lymphoma	Anaplastic cells in pleural effusion, plasmacytoid features, vacuoles	CD30+, HHV-8+, CD45-, CD20-, CD138+	HHV-8 positive, frequent MYC rearrangement
Anaplastic Plasma Cell Lymphoma	Highly pleomorphic, plasmacytoid appearance, frequent mitoses	CD138+, CD56+, CD45-, high Ki-67	Variable cytogenetic abnormalities (1q21 amplification, 17p(p53) deletion, t(4:14), and/or chromosome 13 anomalies, MYC amplification
HHV-8 Positive Large B-cell Lymphoma	Large, transformed B-cells with plasmablastic, immunoblastic, or anaplastic features, angiocentric growth	CD20+, CD30+, HHV-8+, IgM+, CD138-	HHV-8 positive, MYC gene rearrangement
Poorly Differentiated Metastatic Carcinoma	Irregular, pleomorphic cells, clusters, necrosis common	Variable epithelial markers (AE1/AE3, CAM5.2), negative for CD45 and other hematologic markers	No specific hematologic clonality, variable mutations

Final Diagnosis: Richter transformation with plasmacytic differentiation

Immunohistochemistry (IHC)
- Epithelial Markers: MOC31 (+), AE1/AE3 (+)
- Plasma cell markers: CD138, MUM1, CD117, CD56, BCMA positive
- Lambda light chain restriction

Ancillary Studies
- Clonal B-cell receptor gene rearrangement
- Trisomy 12, MYC translocation, and gain of 1q21 and IGH
- Marrow myeloma FISH: negative

Conclusions

- This case presented significant diagnostic challenges due to aberrant epithelial marker expression in exceedingly pleomorphic, neoplastic plasma cells.
- Plasma cell neoplasms can express cytokeratins, especially high molecular weight cytokeratins (HMWCK), and this atypical staining pattern can complicate diagnosis, particularly in cases with anaplastic morphology.
- A comprehensive diagnostic approach, incorporating morphology, patient's history, and ancillary studies was essential in this case.
- Awareness of these potential pitfalls is crucial to avoid misdiagnosis and ensure appropriate patient management.

References & Acknowledgements

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