Chameleon Cancer: Unraveling an Extraordinary Case of a Non-Hodgkin's Lymphoma (NHL) with Multiple Transformations

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Background

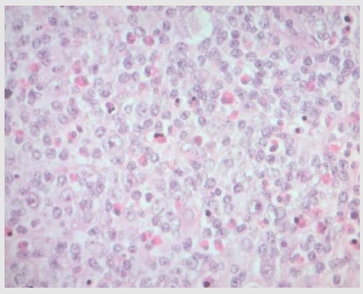
Splenic marginal zone lymphoma (SMZL) is a rare type of NHL that usually affects the spleen, bone marrow and peripheral blood. Transformation of SMZL to more aggressive forms, most commonly Diffuse Large B-cell Lymphoma (DLBCL), is well documented, though infrequent. However, transformation from DLBCL to Hodgkins lymphoma (HL) and ultimately to chronic lymphocytic lymphoma (CLL) remains exceedingly rare and undocumented.

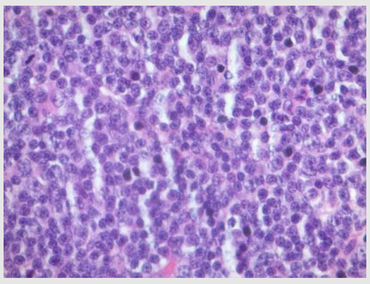
Case Presentation

A case of 69-year-old male patient initially presented in 2014 to the emergency department with abdominal pain.

Ultrasound of the abdomen revealed hepatosplenomegaly and complete blood count revealed leukocytosis with lymphocyte predominance. Peripheral blood flow cytometry was performed, suggested a monoclonal B-lymphoid population. PET showed high uptake in the spleen. Accordingly, the patient was diagnosed with **SMZL**.

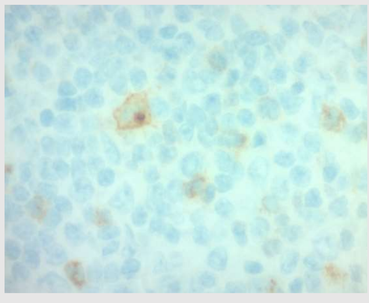
The patient responded well to R-CVP chemotherapy and rituximab maintenance and went into remission.

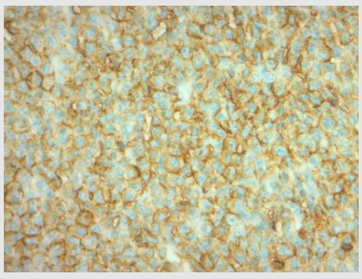




In 2016, a follow up imaging revealed abdominal lymphadenopathy and biopsy confirmed transformation to **DLBCL**, for which he received Bendamustine and Rituximab with complete response.

Four years later, in 2020, he presented with abdominal pain, CT scan revealed multiple supra and infra-diaphragmatic nodes.
Histology of the largest node showed Reed Sternberg cells confirming the diagnosis of **HL** CD30+. Patient was then treated with BV-AVD, achieving complete metabolic remission.





Surveillance imaging in 2021 revealed disease progression, prompting treatment with Nivolumab, which yielded durable disease control until late 2022. In 2024, persistent lymphocytosis led to further evaluation. Flow cytometry and FISH revealed a clonal CD5+/CD23+ B-cell population with deletions in ATM and DLEU regions, consistent with **CLL**. Patient is still on Nivolumab maintenance for HL with controlled disease stage.

Conclusion

This case represents a unique trajectory of several transformations from SMZL to DLBCL, followed by HL and finally in CLL. While transformation from indolent to aggressive lymphomas is a recognized phenomenon, this multilayered transformation, including apparent reversal to an indolent form, is rarely documented. It raises important questions about the underlying genetic mechanisms and influence of prior therapies driving such transitions.

Keywords

Lymphoma transformation, Splenic marginal zone lymphoma, Diffuse large B-cell lymphoma, Hodgkin lymphoma, Chronic lymphocytic leukemia.

References

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