Case Report

Case Report: A Composite Diffuse Large B-cell Lymphoma and Classic Mantle Cell Lymphoma in the Small Intestine

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Composite lymphomas, defined as the coexistence of two distinct lymphoma subtypes within the same tissue, are rare entities, comprising only 1–4.7% of all lymphomas. Among these, the concurrent occurrence of diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL) is exceedingly rare, with only a handful of cases reported. Accurate diagnosis and tailored treatment are critical given the distinct biological and clinical behaviors of these lymphomas. Here, we report the case of a 71-year-old male with a history of Crohn's disease, presenting with a mass involving the ileocecal valve and terminal ileum, revealed on imaging and confirmed via right hemicolectomy and small bowel resection. Histopathological analysis identified two adjacent but immunohistochemically distinct lymphomas: a classical MCL with nodular architecture and a high-grade DLBCL. Immunohistochemistry and fluorescence in situ hybridization (FISH) studies demonstrated that the MCL expressed SOX11, Cyclin D1, and CD5, with CCND1/IGH translocation present, while the DLBCL lacked these markers, confirming the two lymphomas were clonally unrelated. This case represents the first reported composite lymphoma of MCL and DLBCL arising in the small intestine. The distinction between these two lymphomas was achieved through a combination of morphological, immunohistochemical, and genetic analyses. The rarity and heterogeneity of composite lymphomas pose diagnostic and therapeutic challenges, emphasizing the need for comprehensive evaluation. Given the aggressive nature of DLBCL, treatment often prioritizes this component, although the individualized management of composite lymphomas remains essential. This case highlights the importance of thorough diagnostic workup, including advanced immunohistochemistry and genetic studies, to differentiate between lymphoma subtypes within composite lymphomas. Excisional biopsy remains critical to minimize sampling bias, and further research is needed to understand the pathogenesis and optimize treatment strategies for these rare entities. *[N A J Med Sci. 2024;18(1):001-004. DOI: 10.7156/najms.2024.1801001]*

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INTRODUCTION

Mantle cell lymphoma (MCL) is a neoplasm of mature B-cells that arises from the mantle zone of lymphoid follicles. The typical MCL is composed of small to medium-sized lymphocytes that are monomorphic in appearance and express CD5, cyclin D1, and SOX11. In over 95% of MCL cases, there is a genetic rearrangement involving CCND1 that leads to the overexpression of cyclin D1 and thus the positive staining. This characteristic translocation of t (11;14) (q13; q32) or CCND1/IGH promotes cell cycle progression and tumor cell proliferation.[1] Despite the typical staining pattern, 10% of MCLs can be negative for CD5 and rarely they can be negative for cyclin D1. In these situations, SOX11 positivity can be used to diagnose MCL in the absence of cyclin D1 positivity.[2]

MCL is an aggressive disease, but with current therapies, the overall median survival has increased to 5-10 years or more, and some patients may even be cured.[1] However, there are variants of MCL that are even more aggressive and have worse prognosis. These include pleomorphic mantle cell lymphoma (PMCL) and blastoid mantle cell lymphoma (BMCL). PMCL is characterized by larger cells that resemble the diffuse large B-cell lymphoma (DLBCL) morphology, while BMCL displays cellular morphology that resemble lymphoblasts. Both variants typically have remarkably high proliferation indices, but the distinction is made by morphology.[3] Distinguishing these variants from other entities such as DLBCL presents a diagnostic challenge.

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DLBCL is a B-cell lymphoma composed of medium to large cells in a diffuse pattern and is the most common non-Hodgkin lymphoma. The classification of DLBCL has changed overtime, becoming subdivided by morphological variants or molecular subtypes. Separate and distinct disease entities have also arisen to further describe and classify large B cell lymphomas.

With all these changes, “diffuse large B cell lymphoma, not otherwise specified” (DLBCL, NOS) remains to encompass cases which do not belong to a specific diagnostic category.[4] This entity is an important consideration when considering a diagnosis of PMCL. Proper diagnosis of these aggressive variants is important, as they require different treatment approaches.[2]

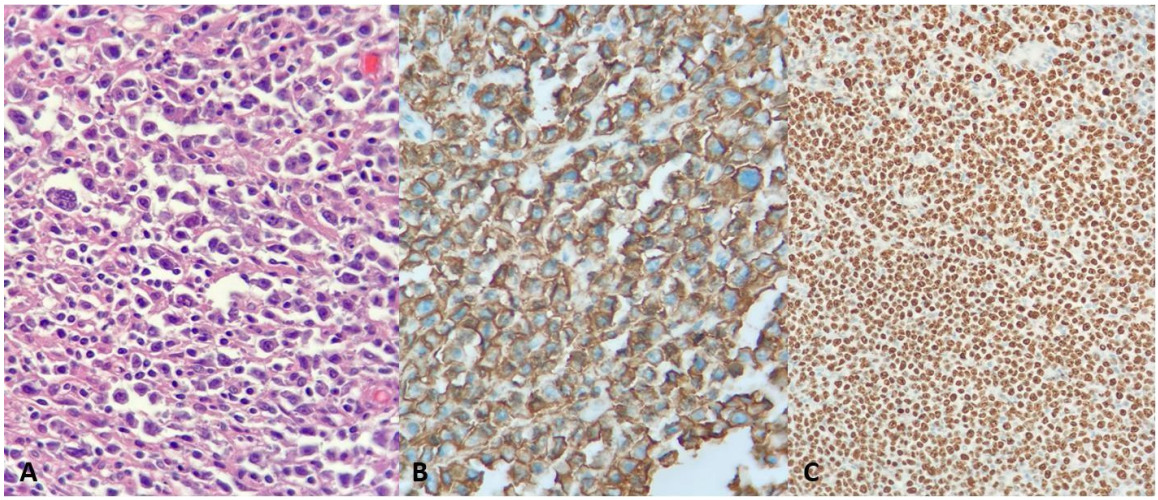

Figure 1. Large cell lymphoma. A. H&E, 20x; B. CD20, 50x; C. MIB-1, 20x.

CASE PRESENTATION

We present a case of a classic mantle cell lymphoma in close proximity to an aggressive lymphoma with diffuse large B-cell morphology.

The patient is a 71-year-old male with a history of recently diagnosed Crohn’s disease and a “mass-like thickening of the ileocecal valve protruding into the cecum with mural thickening extending proximally to involve the terminal ileum and right lower quadrant adenopathy medial to the cecum” on CT scan. He underwent a right hemicolectomy and small bowel resection. The small bowel mass (**Figure 1**) consists of a diffuse large cell lymphoma composed of pleomorphic medium to large lymphoid cells with moderate cytoplasm, irregular vesicular nuclei with large prominent nucleoli, occasional multinucleated cells, and brisk mitoses. These neoplastic cells are positive for CD20, PAX5, MUM1, BCL2 (~80%; variable intensity), BCL6 (minor subset variable intensity positive), and small subset MYC (overall ~20-30%); negative for CD3, CD5, CD21, CD23, Cyclin D1, CD138, Kappa, and lambda. Proliferation index in the neoplastic cells is high, approximately 80% MIB positive.

The ileocecal mass demonstrates a lymphoma with two distinct adjacent patterns: a diffuse large cell lymphoma that is morphologically and immunohistochemically identical to the lymphoma seen in the small bowel mass and a small cell lymphoma with a classical nodular mantle cell morphology (**Figure 2**). The small cell lymphoma is positive for CD20, PAX5, CD5, Cyclin D1, BCL2 (diffusely positive), MUM1 (weak as compared to the large cell component), low proliferative index with MIB1 5-10%; negative for CD10, BCL6, and MYC. CD21 and CD23 highlight residual fragmented FDC meshwork.

Initially, the close proximity of the classical MCL and the large cell lymphoma suggested that they were clonally the same lymphoma, despite the negative CD5 and Cyclin D1. Essentially, a diagnosis of "mantle cell lymphoma classical nodular pattern and an aggressive variant with pleomorphic morphology" was suggested. However, subsequent SOX11 immunohistochemistry revealed that the classical mantle cell lymphoma is positive for SOX11, while the diffuse large cell areas (pleomorphic morphology) are negative. Additionally, the CCND1/IGH translocation detected by FISH in the classical mantle cell lymphoma (in 84% of the nuclei) was not detected in the diffuse large cell lymphoma, which suggests that the two components are not clonally related. There was also no evidence of BCL2, BCL6, or MYC gene rearrangements. These results raise the concern of a separate distinct "diffuse large B-cell lymphoma, NOS" occurring concurrently with the classical mantle cell lymphoma.

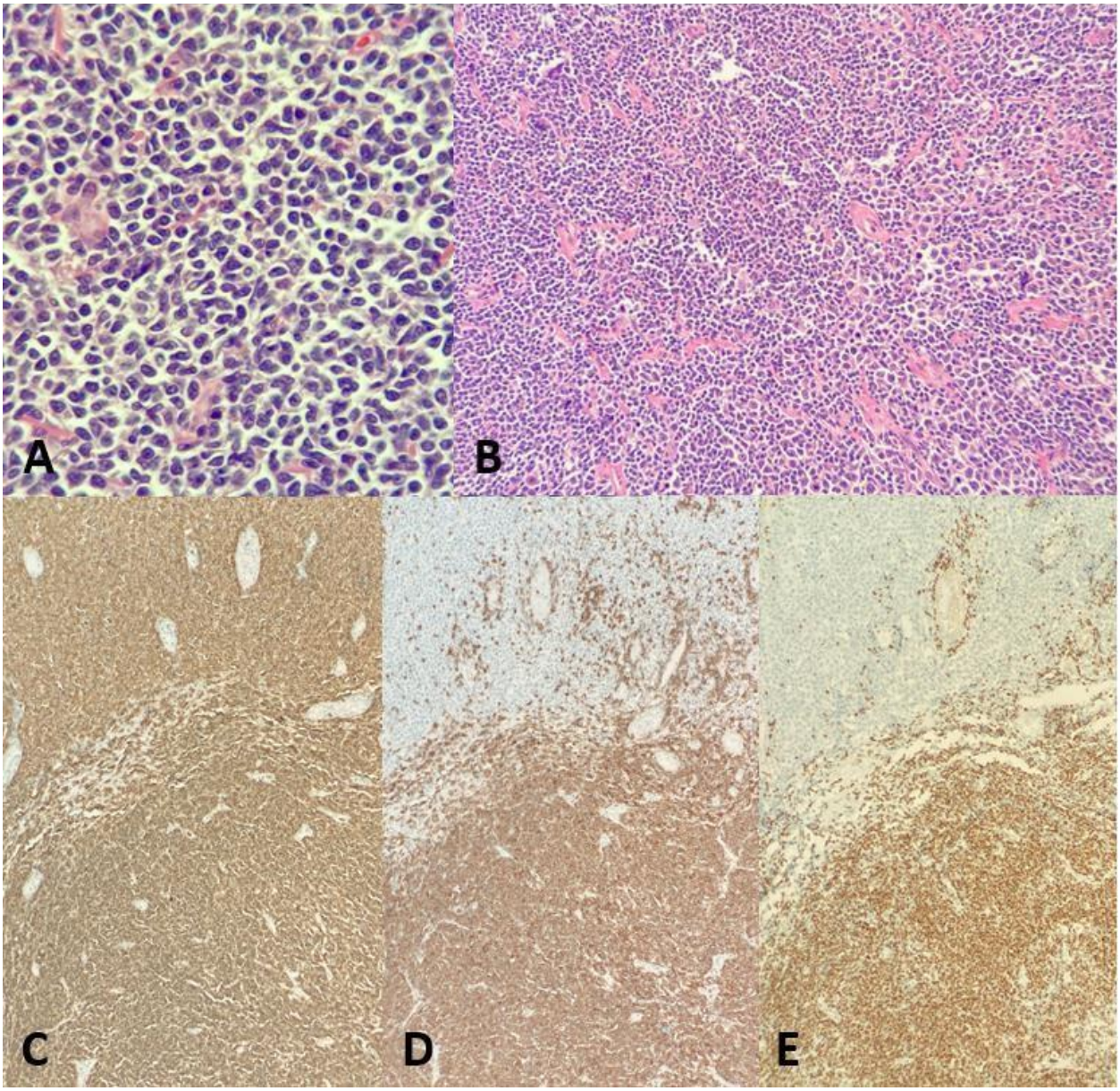

Figure 2. A. Small cell lymphoma, H&E, 50x; B. Junction of small cell lymphoma (left) and large cell lymphoma (right), H&E, 20x; C. CD20 at junction of small cell lymphoma (bottom) and large cell lymphoma (top), 10x; D. CD5 at junction of small cell lymphoma (bottom) and large cell lymphoma (top), 10x; E. Cyclin D1 at junction of small cell lymphoma (bottom) and large cell lymphoma (top), 10x.

DISCUSSION

After thorough assessment and utilization of available diagnostic tools, a diagnosis of a composite lymphoma made up of classic mantle cell lymphoma adjacent to a "diffuse large B cell lymphoma, NOS" has been made. Composite lymphoma is defined as two distinct lymphoma subtypes with distinct morphology and immunohistochemical patterns occurring concurrently in the same tissue or organ.[5]

Composite lymphomas comprise only about 1-4.7% of all lymphomas and can present a diagnostic challenge. They can be made up of various combinations of lymphoma types. While the two components of composite lymphoma are often unrelated, there are cases where they are clonally related, particularly in cases of two B cell non-Hodgkin lymphomas or a Hodgkin lymphoma combined with a non-Hodgkin lymphoma.[5]

Our particular case is a composite lymphoma composed of an unrelated DLBCL and MCL. While DLBCL accounts for about one third of lymphoma cases, MCL makes up only about 4% of cases,[5] and to have both occurring concurrently is an even rarer phenomenon, with only four cases reported previously to our knowledge.[5-7] Out of the four previously

reported cases, three were diagnosed from lymph nodes and one was a testicular primary; ours is the first arising in the bowel wall.

These composite lymphomas have additional challenges when it comes to treatment as well. Because these entities are so rare and heterogeneous, the treatment strategies are not well defined, and their management can often require a multidisciplinary approach. Generally, when there are two distinct lymphomas, it is prudent to prioritize the treatment of the more aggressive type. While DLBCL is an aggressive lymphoma, patients can be successfully treated and even cured in about 60% of patients with R-CHOP. On the other hand, MCL is also an aggressive lymphoma, but unlike DLBCL, it has a much lower cure rate, with management strategies ranging from observation to aggressive treatment, possibly followed by autologous stem cell transplantation.[5] Personalized treatment approaches should be considered for these cases.

CONCLUSION

While composite lymphomas are rare, it is important to recognize them and to accurately diagnose the separate components in order to help guide the best treatment plan for the patient. For many of these cases, a needle core biopsy may be subject to sampling bias, which could possibly lead to a composite lymphoma being missed. An excisional biopsy would help get a more accurate and complete picture of the full lesion, lowering the chance that a composite lymphoma is missed. This would be especially important in cases where there is a discrepancy between the clinical scenario and the initial biopsy diagnosis, as this could indicate that something has been missed. Additionally, further research is needed to better understand the underlying mechanisms and risk factors associated with composite lymphomas, and to guide optimal management strategies for these rare and complex cases.

CONFLICTS OF INTEREST
The authors have no conflict of interest to disclose.

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