Classifications and Treatment Outcomes of Composite Lymphomas: A Systematic Review

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Introduction

Composite lymphoma(CL) is an uncommon type of lymphoid malignancy, accounting for approximately 1.0%-4.7% of all lymphomas.[1] The presence of a minimum of two distinct pathological types of lymphomas in the same anatomical location characterizes a composite lymphoma.[2] Composite lymphoma refers to the coexistence of two or more distinct lymphomas in the same patient, as defined by Custer et al.[3] This definition was later refined by Kim et al. as simultaneous occurrence of more than one type of lymphoma in the same organ or tissue site of the same patient.[4] Although rare, composite lymphomas have been reported in multiple combinations and may consist of non-Hodgkin lymphoma (NHL) with Hodgkin lymphoma (HL)[5], B-cell NHL with T-cell NHL[6] , T-cell or B-cell NHL with other histologic type(s) of the same lineage [7] or NHL with histiocytic or dendritic cell tumors.[8] The pathophysiology behind composite lymphomas has been difficult to understand considering the reliance on case reports and previous literature for information on the nature of these entities. With the uncertainty behind composite lymphoma comes a unique diagnostic and therapeutic challenge. An individualized approach would have to be developed in each case of composite lymphomas.

Aims and Objectives

Cases in literature have varied in their approaches of treatment for composite lymphomas. Outcomes also varied drastically from complete remission to death depending on the patient, type of composite lymphoma and treatment type. Considering the rarity of composite lymphomas, it is important to monitor treatment outcomes for the cases reported to help better understand future cases and develop a synchronized approach. We herein present a systematic review of the current literature on composite lymphomas from the past 10 years, all organized by composite lymphoma type with a focus on treatments and outcomes.

Methods

The data collection was performed on the PubMed Central (PMC) archives (NCBI), using the keywords “composite lymphoma(s)”, “synchronous lymphoma(s)”, “DLBCL AND FL”, “Hodgkin AND Non-Hodgkin”, ”Treatment of composite lymphoma”, “composite lymphoma management”, with a limit on publication date in which we only included articles published from 2015 to 2025. One reviewer (B.M.) sorted through all articles choosing ones that meet the inclusion criteria.

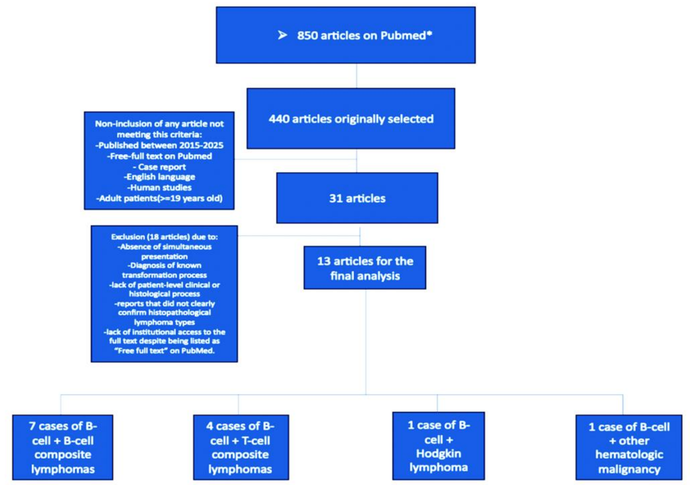

Figure 1. PRISMA-Style Flow Diagram Illustrating the Selection of Case Reports on Composite Lymphomas (2015–2025)

These 14 selected cases were subsequently categorized based on the type of composite lymphoma described. Within each subtype, individual cases were examined in detail, beginning with the patient’s clinical presentation and key findings on physical examination. Cases were categorized by composite type: B-cell + B-cell, B-cell + T-cell, B-cell + Hodgkin, and B-cell + other hematologic malignancy. Finally, patient outcomes, including treatment response, remission status, and survival, were summarized to highlight therapeutic effectiveness across different composite lymphoma types. This approach allowed for a structured comparison of disease behavior, diagnostic strategies, and management patterns among diverse composite lymphoma presentations.

Results

Thirteen articles (14 cases) were included. Patients ranged from 34 to 85 years, with a male predominance, and most presented with lymphadenopathy, though extra nodal disease was common. B-cell + B-cell composites (n=8) achieved the most favorable outcomes, with 50% attaining remission, particularly when treated with R-CHOP–based regimens. B-cell + T-cell composites (n=4) demonstrated aggressive disease with poor survival; only one patient achieved durable remission beyond 4 years. The single B-cell + Hodgkin case showed partial regression with ABVD followed by R-CHOP but no durable response. The B-cell + other hematologic case (CLL + hairy cell leukemia-variant) reflected clonal evolution, with transient responses to sequential therapies but no sustained remission.

Composite Type	Case Description	Treatment	Survival Outcome
B-cell + B-cell (n=8)	DLBCL (GCB + non-GCB, single LN)	R-CHOP ×6	Complete remission, disease-free at 2 mo
	MCL + CLL/SLL	Rituximab + ibrutinib (1 cycle)	Complete regression on CT
	Gastric SRCC + MALT	H. pylori eradication + gastrectomy + intraperitoneal chemo	No recurrence at 6 mo
	NMZL + FL	R-CHOP	Remission (duration not specified)
	FL + CLL/SLL + high-grade BCL	R-CHOP ×6 + 1	Partial remission; died 5 mo later (pneumonia)
	MCL + cHL	Supportive care only	Alive with persistent disease
	MCL + CLL/SLL	Ibrutinib 560 mg daily	Lost to follow-up
	Multifocal intestinal DLBCL (GCB + non-GCB)	Polatuzumab vedotin + R-CHP	Outcome not yet reported
B-cell + T-cell (n=4)	Breast DLBCL + T-LBL	CHOP ×1 → VDP	Rapid progression; died 2 mo
	CLL/SLL + MEITL	Partial enterectomy only	Died 12 mo
	ENKL + DLBCL	R-CHOP ×8 → relapse → CHASER ×2 + etoposide	Alive in 2nd remission at 49 mo
	PTCL-NOS + cutaneous FL BCL	Excision → PLE-DOXO ×6 → RT → salvage	No durable remission; died 28 mo
B-cell + Hodgkin lymphoma (n=1)	T-cell rich DLBCL + NLPHL	ABVD ×2 → R-CHOP ×11	Partial regression only; died 2 mo later (cardiac arrest)
B-cell + Other Hematologic (n=1)	CLL + HCL-V	BR → cladribine → cladribine + ofatumumab → ibrutinib	No durable remission; HCL-V clone dominated; lost to FU at 2.5 yr

Figure 2. Treatment and Survival Outcomes by Composite Lymphoma Type

Conclusions

Composite lymphomas represent a rare and heterogeneous group of malignancies, posing unique diagnostic and therapeutic challenges. In our review of 14 cases, patients were most often older men presenting with nodal or extra nodal masses, and treatment approaches were highly variable depending on histologic subtype. The most favorable outcomes were observed in B-cell + B-cell composites, particularly when R-CHOP–based regimens were employed, supporting existing guideline principles that therapy should be directed toward the most aggressive component. In contrast, B-cell + T-cell composites demonstrated the highest aggressiveness and the poorest survival despite multiagent chemotherapy, underscoring the refractory nature of T-cell–driven disease. B-cell + Hodgkin and B-cell + other hematologic malignancy composites were rare but showed no durable remissions, reflecting the limitations of applying standard lineage-specific regimens in dual-clone disease. Collectively, these findings emphasize the need for individualized treatment strategies guided by the dominant histology, while also highlighting the urgent requirement for collaborative studies and tailored guidelines to optimize outcomes in this rare patient population.

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