CD5⁺ diffuse large B-cell lymphoma, NOS

presenting as a relapsing mononucleosis-like syndrome with secondary hemophagocytic lymphohistiocytosis

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INTRODUCTION

BACKGROUND

CD5⁺ diffuse large B-cell lymphoma (DLBCL) is a rare, aggressive subtype, representing **5–10% of de novo DLBCL**, that may present with atypical clinical pictures, including **hyperinflammatory syndromes** such as **secondary hemophagocytic lymphohistiocytosis (HLH)**, posing important diagnostic challenges [1–3]. In adults, HLH is most often **malignancy-driven** and **lymphoma is its commonest trigger**, with **poor outcomes when recognition is delayed** [4,5].

CASE AIM

We report a case of **CD5⁺ DLBCL presenting as a relapsing mononucleosis-like syndrome complicated by secondary HLH**, highlighting diagnostic pitfalls and the need for a multimodal work-up. Clinical, laboratory, imaging, flow cytometry, histopathological and molecular data were reviewed from a single case managed at a tertiary hematology center.

CLINICAL COURSE

FIRST EPISODE · 2 MONTHS BEFORE
Self-limited episode: bicytopenia, atypical lymphocytosis, cholestatic liver injury

↓

SPONTANEOUS RESOLUTION
Attributed to **viral illness** — complete spontaneous resolution

↓

B SYMPTOMS · 2 MONTHS
Fever, drenching night sweats, anorexia, profound fatigue

↓

ADMISSION
Relapse: cachexia + massive hepatosplenomegaly, ECOG 3–4

↓

WORK-UP
Secondary HLH confirmed (HScore 225)

↓

DIAGNOSIS
CD5⁺ DLBCL, NOS
ABC subtype, Stage IV

↓

TREATMENT
Prednisolone → R-C → full **R-miniCHOP**

RESULTS

77	225	6.1%	2
years old	HScore (96–98% probability)	large immature cells in bone marrow	abnormal CD5⁺ B-cell populations

Work-up confirmed **secondary HLH** (HScore 225; 96–98% probability), with fever, ferritin ~4000 ng/mL, hypertriglyceridemia, hypofibrinogenemia, elevated soluble CD25 and bone marrow hemophagocytosis.

Bone marrow aspirate showed **6.1% large immature cells**; flow cytometry identified **two abnormal CD5⁺ B-cell populations** differing in size and CD200 expression. Biopsy confirmed **CD5⁺ DLBCL, ABC subtype, Stage IV**, without MYC/BCL2 double expression; FISH excluded double-hit lymphoma and mantle cell lymphoma.

Given the life-threatening hyperinflammatory state, **prednisolone** was started before pathological confirmation, followed by **rituximab-cyclophosphamide**, with **favorable evolution** allowing **escalation to full R-miniCHOP**.

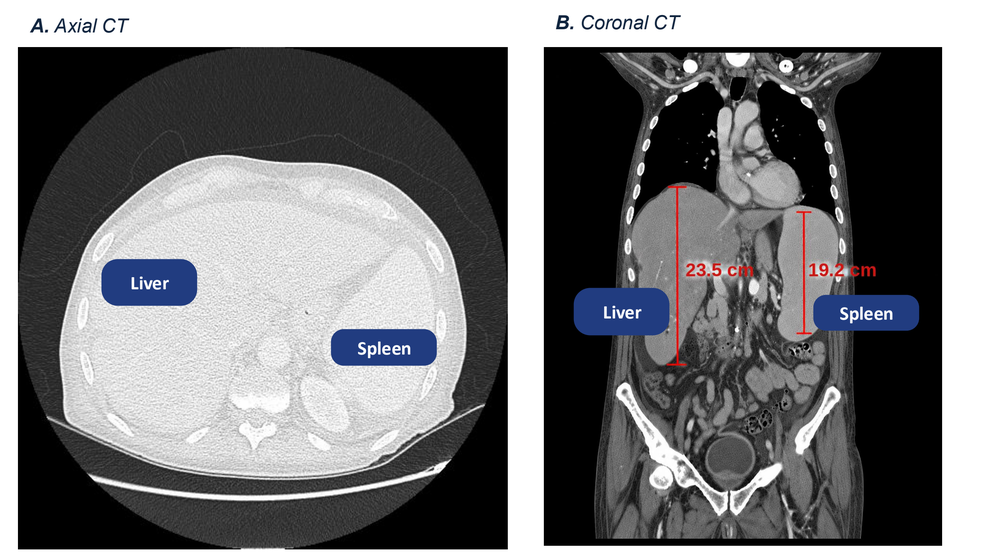

Figure 1. *Massive hepatosplenomegaly (liver 23.5 cm, spleen 19.2 cm)*

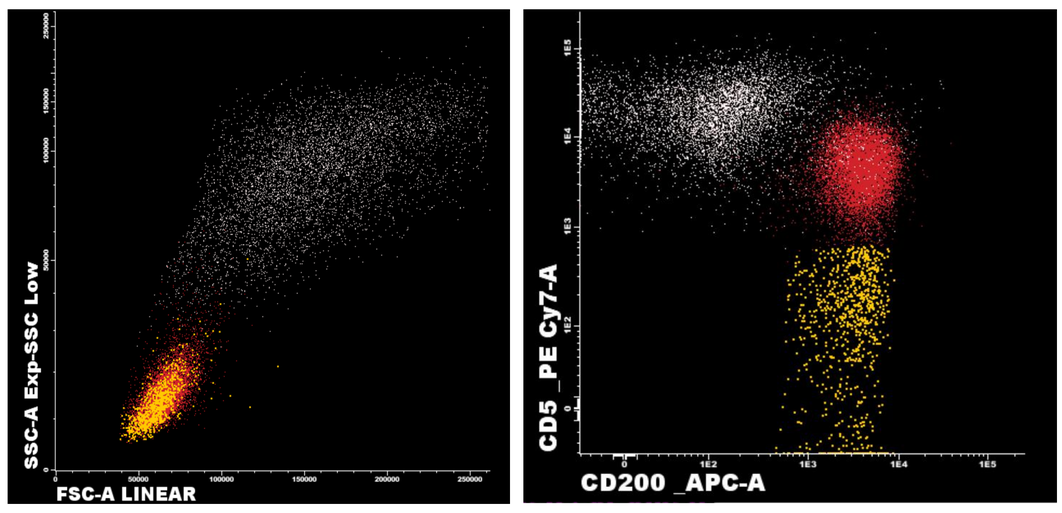

Figure 2. *Two abnormal CD5⁺ B-cell populations differing in size and CD200 expression*

TAKE-HOME MESSAGES

CD5⁺ DLBCL can mimic a **relapsing mononucleosis-like illness**.

Spontaneous resolution of cytopenias is not reassuring.

HLH is a syndrome, **not a final diagnosis** — systematic investigation of the underlying cause is essential, without delaying treatment [6,7].

Two distinct CD5⁺ B-cell populations → consider **clonal evolution or biclonality**, and integrate flow cytometry, histopathology and molecular studies.

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