

Lymphadenopathy in the time of Kaposi's and a tale of two cytopenias



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Introduction

Multicentric Castleman disease (MCD) is a polyclonal lymphoproliferative disorder arising idiopathically or secondarily. Immune dysregulation in MCD causes inflammatory symptoms and autoimmune cytopenias. We report a case of HHV-8+ MCD complicated by Evans syndrome (ES) - a rare disorder of autoimmune cytopenias of two or more cell lines.

Learning Objectives

- Evans syndrome is a rare complication of multicentric Castleman disease and can arise in both idiopathic and HHV-8+ MCD
- Direct antiglobulin testing may be negative in autoimmune hemolytic anemia (DAT-negative AIHA), enhanced DAT methods should be considered when clinical suspicion remains high despite negative DAT
- Successful treatment of underlying HHV-8+ MCD with rituximab and pegylated liposomal doxorubicin (R-Dox) can lead to resolution of immune cytopenias

Case Description

A 49-year-old man with known history of HIV previously complicated by Kaposi's sarcoma presented with one week of shortness of breath, cough, and fever.

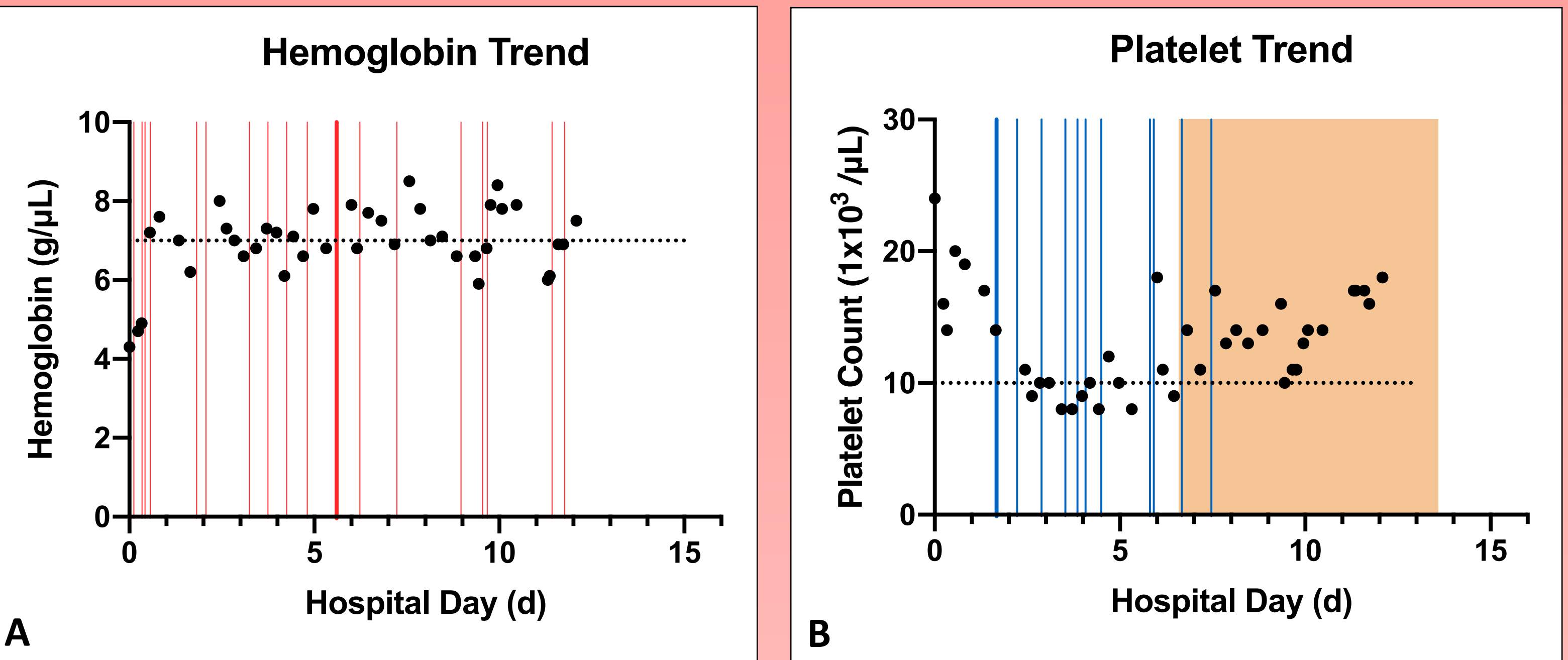
On presentation, his vitals were:
Temperature: 103°F
Heart rate: 140 beats/minute
Respiratory rate: 24 breaths/minute
Blood pressure: 94/45 mmHg

Physical examination was notable for palpable sub-centimeter cervical lymph nodes. Initial complete blood count showed:
Hemoglobin: 4.3 g/μL
WBC: 3.72 x10³ /μL
Platelets: 24 x10³ /μL

Progressive splenomegaly and diffuse lymphadenopathy were appreciated on computed tomography.

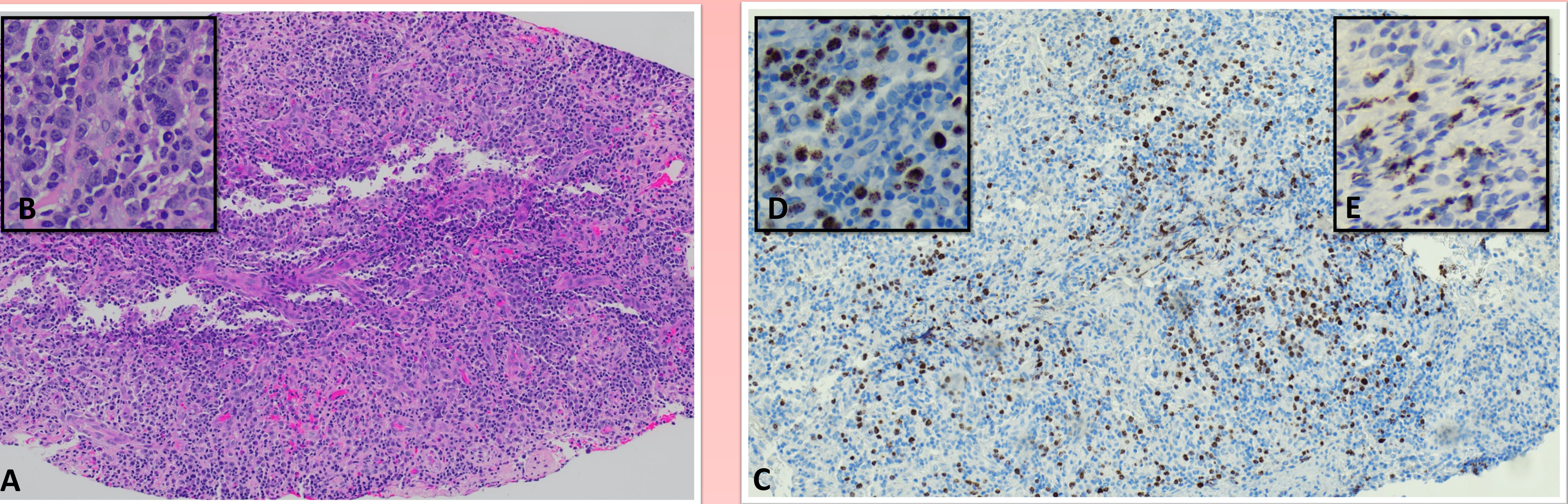
Case Description

He required significant transfusion support for severe anemia and worsening thrombocytopenia. Initial DAT was negative. Multiple units of pRBC were required to maintain adequate hemoglobin despite no signs of bleeding. His platelet count decreased to single digits with poor response to multiple platelet transfusions, refractoriness workup confirmed the presence of alloantibodies against multiple HLA antigens. He was started on weekly romiplostim and HLA-matched platelet products. There remained high clinical suspicion for AIHA despite negative DAT. Subsequent enhanced DAT detected low-titer IgG, confirming presence of auto-antibodies consistent with AIHA. A diagnosis of ES was made.



Graphical trend of hemoglobin (A) and platelet count (B) with pRBC and platelet transfusions shown by the red and blue vertical lines, respectively. Thin lines denote single unit transfusions while thick lines denote two unit transfusions. Orange shading denotes when weekly romiplostim (Nplate) was started at 125 mcg.

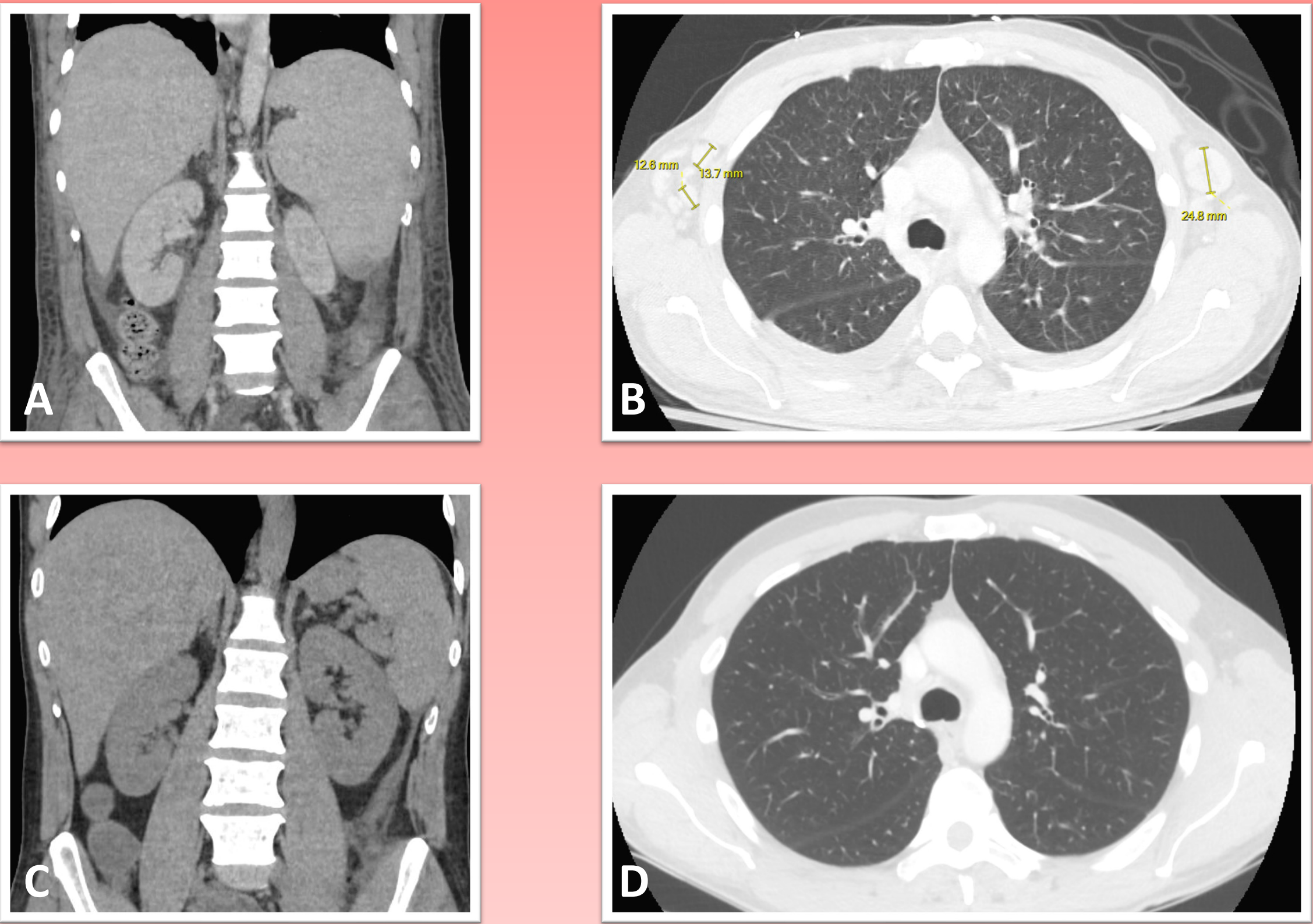
He underwent excisional lymph node biopsy of the left axilla.



H&E staining of lymph node showing atypical plasmablast expansion and architectural effacement of germinal center. There is associated thickened vasculature and prominent high-endothelial venules (A). High-magnification of atypical plasmablasts (B). HHV8 immunohistochemistry demonstrating positivity in plasmablasts (C). High magnification of HHV8+ plasmablasts (D) and morphologically distinct population of HHV8+ spindle cells (E).

A diagnosis of HHV-8+ MCD was made. He was started on a course of R-Dox and experienced significant improvement in transfusion requirements in the following days. He continued his care outpatient and completed a total of four cycles of R-Dox. He achieved complete hematologic recovery within two cycles and improvement in hepatosplenomegaly and lymphadenopathy after four cycles.

Case Description



Radiographic characterization of splenomegaly (A) and axillary lymphadenopathy (B) at presentation. Resolution of splenomegaly (C) and axillary lymphadenopathy (D) following four cycles of R-Dox.

Discussion

- To our knowledge, this is the first reported case of Evans syndrome arising secondarily to HHV-8+ multicentric Castleman disease
- Prior reported cases of Evans syndrome have involved idiopathic MCD, with treatments including rituximab, IL-6 inhibition, and combination chemotherapy
- Evans syndrome remission is achieved through treatment directed at underlying HHV-8+ MCD with R-Dox
- DAT-negative AIHA may occur in Evans syndrome, enhanced DAT methodologies offer improved sensitivity

References

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