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CASE REPORT

Multicentric Castleman Disease Following Kaposi Sarcoma in a Woman Living With HIV: A Case Report

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ABSTRACT

Background: Castleman disease comprises a heterogeneous group of lymphoproliferative disorders with shared lymph-node histopathological features. Human herpesvirus 8 (HHV8)-associated multicentric Castleman disease is strongly linked to human immunodeficiency virus (HIV) infection and may occur in patients with current or previous Kaposi sarcoma. We describe biopsy-proven multicentric Castleman disease in a virally suppressed woman living with HIV eight years after remission of Kaposi sarcoma in a resource-limited setting; HHV8 association could not be laboratory-confirmed because HHV8-specific testing was unavailable.

Case presentation: A 48-year-old woman on antiretroviral therapy, with HIV RNA <40 copies/mL and previous Kaposi sarcoma treated with six cycles of liposomal doxorubicin, presented with a one-year history of fatigue, weight loss, night sweats, abdominal distension and left lower-limb oedema. Examination showed pallor, generalised lymphadenopathy, hepatosplenomegaly and firm chronic left-leg oedema. Haemoglobin was 6.7 g/dL. Serum protein electrophoresis showed hyperproteinaemia with a markedly increased gamma fraction. Axillary lymph-node histology demonstrated regressed germinal centres, hyalinised penetrating vessels and concentric mantle-zone lymphocytes, supporting Castleman disease. Cross-sectional imaging and HHV8 LANA-1 immunohistochemistry were unavailable.

Intervention and outcome: The patient was referred for rituximab-based chemoimmunotherapy. The submitted clinical record described the planned regimen as R-EPOCH, but individual drug doses, confirmation of treatment administration and post-treatment outcomes were not available at manuscript preparation.

Conclusion: Multicentric Castleman disease should be considered in people living with HIV who develop persistent constitutional symptoms, generalised lymphadenopathy and organomegaly, including those with remote Kaposi sarcoma and suppressed HIV viraemia. Adequate lymph-node biopsy is central to diagnosis, while HHV8-specific

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testing should be obtained whenever feasible before assigning an HHV8-associated subtype.

INTRODUCTION

Castleman disease (CD) comprises a group of clinicopathological disorders that share characteristic lymph-node histopathology but differ in distribution, aetiology, treatment and prognosis.[1] Clinically, CD is classified as unicentric or multicentric; multicentric disease is further characterised by HHV8 status and associated clinical context.[1,2]

HHV8-associated multicentric Castleman disease (HHV8-MCD) occurs predominantly in immunocompromised patients, particularly people living with HIV, and is driven by HHV8-infected B-cell/plasmablast populations and cytokine dysregulation.[2,3] Kaposi sarcoma (KS) and HHV8-MCD may occur concurrently or sequentially because both are linked to HHV8 infection.[3,6]

This case illustrates the diagnostic difficulty of multicentric CD in a patient with previous KS, the value of lymph-node histology in a resource-constrained setting, and the importance of distinguishing morphological evidence of CD from laboratory confirmation of HHV8-associated disease.

CASE PRESENTATION

Patient information

A 48-year-old woman living with HIV and receiving antiretroviral therapy presented with a one-year history of fatigue, weight loss, night sweats, progressive abdominal distension and left lower-limb oedema. Her HIV viral load was <40 copies/mL. Eight years earlier, she had been treated for KS with six cycles of liposomal doxorubicin and had achieved clinical remission. She described marked anxiety about the possibility of further chemotherapy because of previous alopecia and myelosuppression.

Clinical findings

Examination showed pallor, generalised lymphadenopathy, hepatomegaly, splenomegaly and woody, firm left lower-limb oedema. The largest palpable lymph node measured approximately 6 × 5 cm. Hypopigmented oral plaques were also noted.

Differential diagnosis

The principal differential diagnoses were recurrent or disseminated KS, lymphoma, plasma-cell dyscrasia, tuberculosis and autoimmune disease.

Timeline

Table 1. Clinical timeline.

Time point	Clinical course
8 years before current presentation	Kaposi sarcoma treated with six cycles of liposomal doxorubicin; clinical remission achieved.
Approximately 1 year before presentation	Onset of fatigue, weight loss, night sweats, abdominal distension and progressive left-leg oedema.
Current presentation	Pallor, generalised lymphadenopathy, hepatosplenomegaly and firm chronic left -leg oedema documented.
Diagnostic work-up	Laboratory investigations, serum protein electrophoresis, bone-marrow aspirate, lymph-node cytology, abdominal ultrasonography and axillary lymph -node biopsy performed.
After histopathological diagnosis	Referred for rituximab-based chemoimmunotherapy and psychosocial support; post-treatment outcome was not available in the submitted record.

DIAGNOSTIC ASSESSMENT

Imaging

Abdominal ultrasonography confirmed hepatosplenomegaly, with a liver span of 18 cm and splenic length of 17.77 cm. Computed tomography and magnetic resonance imaging were unavailable.

Laboratory findings

Table 2. Selected laboratory investigations.

Investigation	Result
Haematology	
White cell count	9.17 × 10? /L
Neutrophils	4.65 × 10? /L (50.78%)
Lymphocytes	37.38%
Monocytes	11.6%
Eosinophils	0.4%
Basophils	0.0%
Red cell count	2.75 × 10^{12}/L
Haemoglobin	6.7 g/dL
Haematocrit	21.5%
Mean corpuscular haemoglobin	24.4 pg
Mean corpuscular haemoglobin concentration	31.2 g/dL
Platelets	203 × 10? /L
Chemistry / serology / microbiology	
Alanine aminotransferase	3.2 U/L
Aspartate aminotransferase	11.2 U/L
Alkaline phosphatase	85.4 U/L
Sodium	132 mmol/L
Potassium	4.4 mmol/L
HBsAg	Negative
Malaria parasite slide	No malaria parasites seen
Anti-cyclic citrullinated peptide antibody	<7 U/mL (reported as negative)
Antinuclear antibody	21.6 AU/mL
Rheumatoid factor	8.00 IU/mL
GeneXpert assay	Negative
Serum protein electrophoresis / free light chains	
Albumin	37.3%
Alpha-1 fraction	3.6%
Alpha-2 fraction	6.1%
Beta-1 fraction	4.1%
Beta-2 fraction	3.4%
Gamma fraction	45.5%
Total protein	10.33 g/dL
Free kappa light chain	196.22mg/L
Free lambda light chain	89.19mg/L
Free kappa/lambda ratio	2.20

Bone-marrow aspirate was reported as hypocellular and reactive, without clear evidence of plasma-cell dyscrasia or malignancy. Lymph-node cytology was reported as reactive and negative for malignancy.

Histopathology

Axillary lymph-node biopsy showed variably sized follicles with regressed germinal centres, hyalinised vessels penetrating the follicles and concentric layering of mantle-zone lymphocytes (Figures 1 and 2). These architectural features support CD. HHV8 LANA-1 immunohistochemistry was not available, and no blood HHV8 DNA result was documented; therefore, the HHV8 association was clinically suspected on the basis of the patient's previous KS but was not laboratory-confirmed.

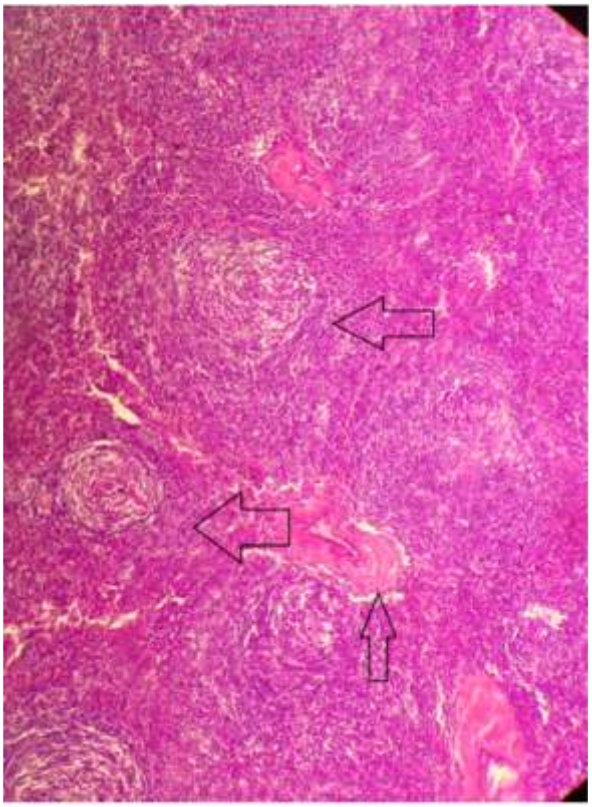

Figure 1. Low-power lymph-node histology showing variably sized follicles (horizontal arrows) and hyalinised interfollicular vessels (vertical arrow). Haematoxylin and eosin stain; original magnification approximately ×40.

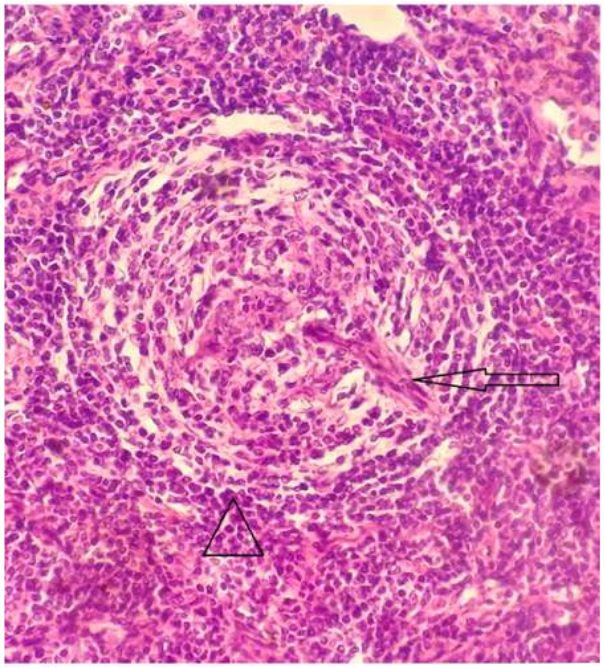

Figure 2. High-power view of a follicle showing a hyalinised vessel extending into the regressed germinal centre (arrow) and concentric mantle-zone lymphocytes producing an 'onion-skin' appearance (triangle). Haematoxylin and eosin stain; original magnification approximately ×400.

THERAPEUTIC INTERVENTION AND FOLLOW-UP

The patient was referred to haematology/oncology for rituximab-based chemoimmunotherapy. The submitted record described the intended regimen as R-EPOCH but did not provide the individual drug doses, treatment dates or confirmation that the regimen was administered. Psychosocial support was recommended because of her anxiety related to previous chemotherapy-associated alopecia and myelosuppression. At the time of manuscript preparation, no post-treatment clinical, laboratory or imaging outcome was available in the submitted record.

DISCUSSION

This case demonstrates multicentric CD presenting with constitutional symptoms, generalised lymphadenopathy, severe anaemia and

hepatosplenomegaly in a virally suppressed woman living with HIV who had remote KS. The lymph-node architecture—regressed germinal centres, hyalinised penetrating vessels and concentric mantle-zone layering—is within the recognised morphological spectrum of CD.[1,4,5]

The central diagnostic limitation is the absence of HHV8-specific testing. In HHV8-MCD, HHV8-infected plasmablasts are typically demonstrable by LANA-1 immunohistochemistry, and circulating HHV8 DNA may support the diagnosis and disease assessment.[2,4,5,9] A previous diagnosis of KS makes HHV8 infection biologically highly plausible, but it does not by itself establish that a subsequent episode of multicentric CD is HHV8-associated. For this reason, the present case is best described as multicentric CD following KS, with suspected rather than confirmed HHV8 association.

The clinical differential diagnosis is particularly important in settings where tuberculosis, HIV-associated malignancy and chronic infection are common. Zambian experience has similarly highlighted delayed or difficult recognition of CD and the importance of obtaining adequate lymph-node tissue rather than treating persistent lymphadenopathy empirically.[7]

For confirmed symptomatic HHV8-MCD, contemporary guidance supports rituximab-based therapy; etoposide or liposomal doxorubicin may be added in severe disease or when active KS is present.[2,8,9] Because the submitted case record does not provide complete treatment details or follow-up, no conclusion can be drawn regarding regimen selection, treatment response or long-term outcome in this patient.

The strengths of this report are the clear clinical phenotype, the histological demonstration of characteristic CD architecture and its relevance to a resource-limited African setting. Limitations include lack of HHV8 LANA-1 immunohistochemistry or HHV8 DNA testing, absence of computed tomography or positron-emission tomography for full disease mapping, incomplete inflammatory-marker data, uncertainty about the exact treatment delivered and lack of documented follow-up outcome. These limitations narrow the conclusions that can be drawn about viral subtype, treatment efficacy and prognosis.

Patient perspective

The patient expressed relief when recurrent KS was not identified as the explanation for her presentation, but she remained concerned about the possibility of chemotherapy-related adverse effects because of her previous treatment experience.

CONCLUSION

Multicentric CD should be considered in people living with HIV who develop persistent constitutional symptoms, generalised lymphadenopathy, anaemia and organomegaly, even when HIV viraemia is suppressed and KS has been in remission for years. In resource-limited settings, timely procurement of adequate lymph-node tissue is pivotal. Prior KS should heighten suspicion for HHV8-associated disease, but HHV8-specific immunohistochemical or virological confirmation should be obtained whenever feasible before assigning the HHV8-associated subtype.

INFORMED CONSENT

Written informed consent was obtained from the patient, including permission to publish the clinical and histopathological images.

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