



## CASE REPORT

# Multicentric Castleman's Disease with Disseminated Kaposi's Sarcoma: A Report of Prolonged Misdiagnosis

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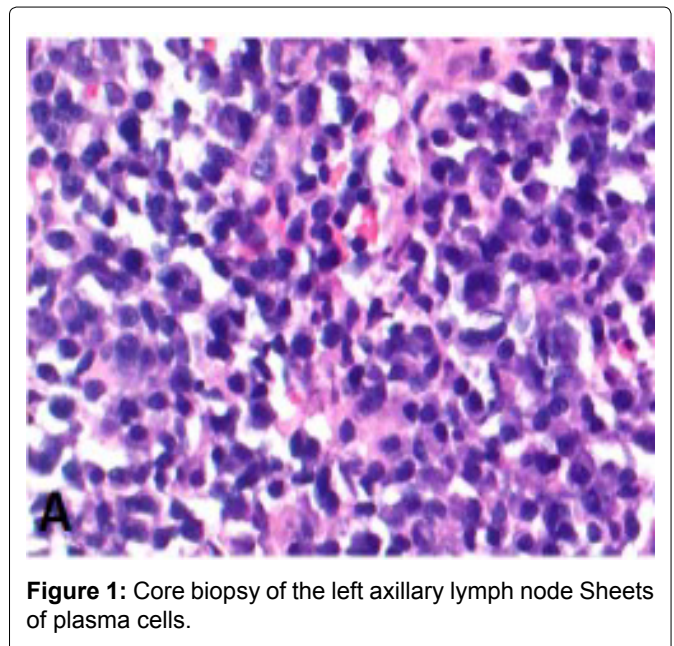


Dear Editor,

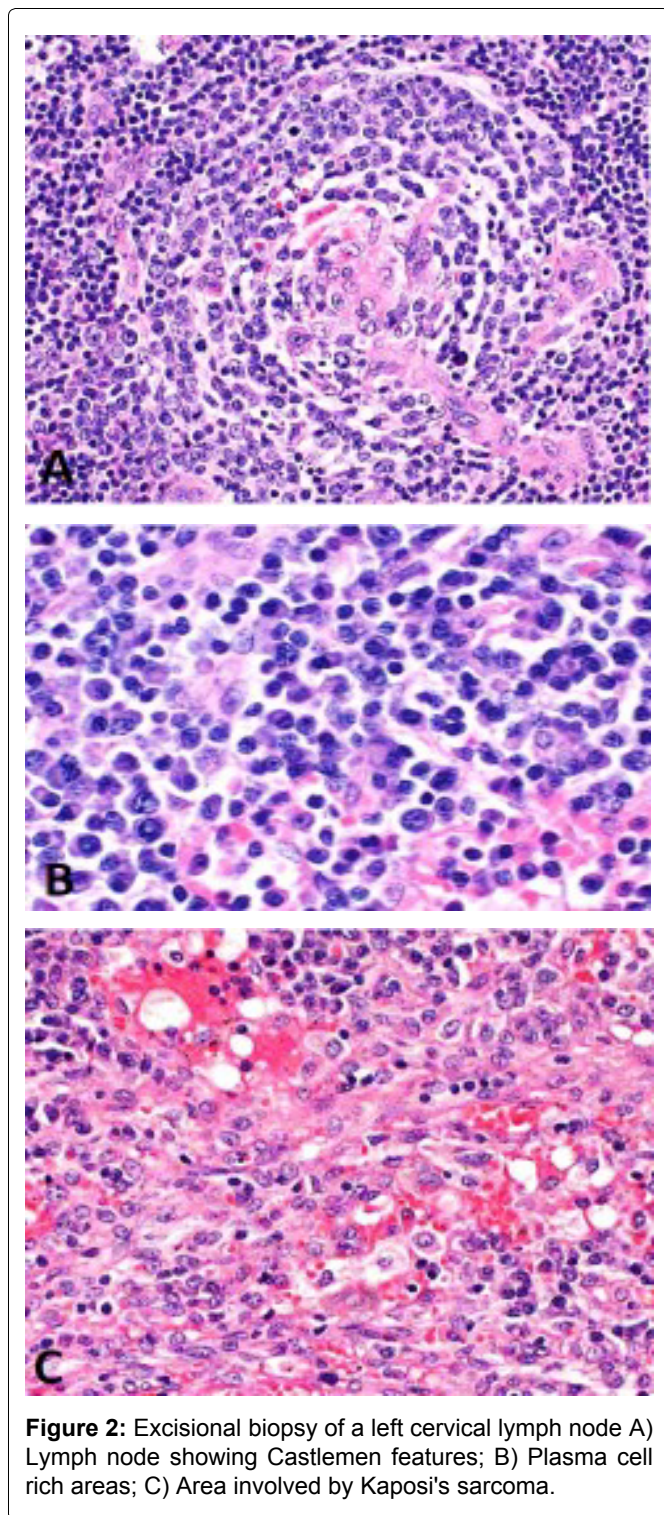
Castleman's Disease is a rare and benign lymphoproliferative disease. Human immunodeficiency virus (HIV) and human herpesvirus 8 (HHV-8) infections are highly associated with multicentric Castleman's disease (MCD) [1]. Studies suggest HHV-8 plays an important role in the pathogenesis by encoding a viral form of IL-6 [2], and MCD tends to be more common in the highly active antiretroviral therapy (HAART) era [3]. There is no standard of treatment for MCD. Many single or combined cytotoxic drugs have been reported to provide durable remissions [4,5]. Rituximab remains mainstay treatment because of its substantial safety, efficacy and survival benefit [6]. Concurrent use of liposomal doxubicin is suggested as rituximab can promote the progression of Kaposi's sarcoma (KS) [7]. The prognosis of untreated disease is poor and thus, early recognition and timely initiation of therapy are critical. Here we report a case of MCD and disseminated Kaposi's sarcoma that went unrecognized leading to unnecessary delays in initiating treatment.

A 54-year-old gentleman was diagnosed with acquired immunodeficiency syndrome (AIDS) when presenting with shingles in 2016. He was started on HAART but soon noted a very rapid increase in the size of his cervical, axillary and inguinal lymph nodes, along with profound constitutional symptoms.

**Immune reconstitution syndrome** was suspected and prednisone was tried but did not alleviate symptoms. One month later, a *core biopsy* of the left axillary lymph node was undertaken and demonstrated predominantly mature kappa-light chain restricted plasma cells (Figure 1). Flow cytometry was negative for a clonal population. One month later, the patient was referred to the Haematology department for a **plasma cell neoplasm**. Initial blood work did not reveal



**Figure 1:** Core biopsy of the left axillary lymph node Sheets of plasma cells.



**Figure 2:** Excisional biopsy of a left cervical lymph node A) Lymph node showing Castlemann features; B) Plasma cell rich areas; C) Area involved by Kaposi's sarcoma.

a monoclonal gammopathy. A bone marrow biopsy was negative for a hematologic malignancy. Computed tomography (CT) chest/abdomen/pelvis and positron emission tomography (PET) were notable for diffuse lymphadenopathy above and below the diaphragm with splenomegaly. An excisional biopsy of a left cervical node revealed nodal involvement by *MCD with metastatic KS* (Figure 2A, Figure 2B and Figure 2C). Blood work confirmed an HHV-8 level of > 10,000,000 copies/mL.

The patient was treated with liposomal doxorubicin and rituximab without a clinical response. Etoposide was added but without effect. Therapy was upgraded to cyclophosphamide, adriamycin, vincristine, and

prednisone (CHOP) with immediate resolution of symptoms. After completion of 6 planned cycles, a PET-CT confirmed a complete response and a repeat HHV-8 level was < 1000 copies/mL. Unfortunately, the patient then reported a rapidly progressive painful erythematous rash in both lower extremities. After several weeks of failing antibiotic therapy, a punch biopsy of the skin demonstrated *disseminated KS* and a repeat HHV-8 level was at > 14,000 copies/mL. Vinblastine was initiated with drastic improvement in his symptoms.

Castleman's disease is a great mimicker of multiple illnesses due to its various manifestations. In this case, the plasma cells on the core biopsy misled providers to a diagnosis of myeloma. An initial *excisional* biopsy with careful pathologic review is required to properly capture the nodal architecture. This delay led to the aggressive widespread dissemination of the disease requiring a 5-drug regimen which is an uncommon approach in this disease. The disseminated KS, presenting as rapid painful rashes instead of singular purple skin lesions, also deceived the medical team. This case illuminates the diagnostic complexity of lymphadenopathy workup in HIV+ patients and highlights the importance of pursuing ample tissue in order to make an accurate and timely diagnosis.

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### Compliance with Ethical Standards

### Funding

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### Conflict of Interest

Drs. Hu, Varga and Pilichowska have no conflicts of interest to declare.

### Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

### References

1. Soulier J, Grollet L, Oksenhendler E, P Cacoub, D Cazals-Hatem, et al. (1995) Kaposi's sarcoma-associated herpesvirus-like DNA sequences in multicentric Castleman's disease. *Blood* 86: 1276-1280.
2. Polizzotto MN, Uldrick TS, Wang V, Karen Aleman, Kathleen M Wyvill, et al. (2013) Human and viral interleukin-6 and other cytokines in Kaposi sarcoma herpesvirus-associated multicentric Castleman disease. *Blood* 122: 4189-4198.
3. Mylona EE, Barabouitis IG, Lekakis LJ, Georgiou O, Papastamopoulos V, et al. (2008) Multicentric castleman's disease in HIV infection: A systematic review of the literature. *AIDS Rev* 10: 25-35.
4. El-Osta HE, Kurzrock R (2011) Castleman's disease: From

- basic mechanisms to molecular therapeutics. *Oncologist* 16: 497-511.
5. Seo HY, Kim EB, Kim JW, Shin BK, Kim SJ, et al. (2009) Complete remission in a patient with human herpes virus-8 negative multicentric Castleman disease using CHOP chemotherapy. *Cancer Res Treat* 41: 104-107.
  6. Gerard L, Berezne A, Galicier L, Meignin, Martine Obadia, et al. (2007) Prospective study of rituximab in chemotherapy-dependent human immunodeficiency virus associated multicentric Castleman's disease: ANRS 117 CastlemaB Trial. *J Clin Oncol* 25: 3350-3356.
  7. Uldrick TS, Polizzotto MN, Aleman K, Kathleen M Wyvill, Vickie Marshall, et al. (2014) Rituximab plus liposomal doxorubicin in HIV-infected patients with KSHV-associated multicentric Castleman disease. *Blood* 124: 3544-3552.