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Castleman's disease in association with Kaposi's sarcoma of lymph node: a rare finding in an HIV negative patient. A case Reports

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Abstract

Background: Castleman's disease, is a rare disorder of unknown cause, consisting of a massive proliferation of lymphoid tissue. Two clinical types (localized and multicentric) have been described. Multicentric Castleman's disease (MCD) is manifested by generalized lymphadenopathy, hematological abnormality, and systemic symptoms.

The coexistence Kaposi sarcoma and MCD in the same tissue has been observed in some HIV infected patients, but literature reports in HIV negative patient are scant.

Case Presentation: A 60-year-old woman, HIV negative and without any relevant past medical history who presented with a multiple slowly enlarging lymphadenopathy with anorexia, fever and weight loss of six-months' duration, without any skin lesions.

Chest and abdominal tomography showed multiple lymphadenopathy in the axillar, mediastinal, inguinal, and abdominal areas suggestive of lymphoma. Histologic examination of the axillary lymph node biopsy revealed spindle-shaped cells with extravasated erythrocytes typical of Kaposi's sarcoma with many areas of Castleman's disease.

Conclusion: We report a rare co-existence of Castleman's disease with Kaposi's sarcoma in lymph node mimicking aggressive malignant lymphoma in a HIV negative patient.

Keywords: Herpesvirus 8 Human; HIV Negative; Kaposi's Sarcoma; Multicentric Castleman's Disease; Lymphoma

Abbreviations:

CRP : C-Reactive Protein
HHV-8: Human Herpesvirus 8
HIV : Human Immunodeficiency Virus
KS : Kaposi's Sarcoma
MCD : Multicentric Castleman's Disease
LANA: Human Herpesvirus 8 (HHV8) Latency Associated Nuclear Antigen
HBV : The Hepatitis B Virus
HBC : The Hepatitis C Virus
LN : Lymph Node
HE : Hematoxylin and Eosin Stain

Background

Castleman's Disease (MCD) is a rare lymphoproliferative disease, first described by Castleman et al., in 1954. and more frequent in AIDS patients.

It can be unicentric, mostly localized in mediastinum (60%), retroperitoneum (11%), and axilla (4%) [1], or disseminated (multicentric). Multicentric Castleman's disease is an aggressive condition associated with generalized lymphadenopathy, polyclonal hypergammaglobulinemia, and systemic symptoms [2].

It is known that HHV-8 is has been detected in 100% of the cases of MCD in patients HIV positive and in 40% to 50% of HIV-negative cases [3]. It presence in lymph nodes predisposes patients to other malignancies, like Kaposi's Sarcoma (KS) (13%) and lymphoma (18%) [4].

Kaposi's sarcoma is a malignant disease that develops from the vascular endothelium, and like Castleman's disease, it is observed commonly in HIV-positive patients. Both nodal and cutaneous forms of KS have been documented in MCD [5].

The association of these two diseases related to HHV-8 in the same specimen has been reported in the literature [5-10], with few cases of HIV negative patients [5,8,10,11] and one welldocumented case series [12].

We report this case with the aim of shedding light on the possibility of this rare association even in HIV negative patient, and on the fact that many diagnoses may coexist in the same sample, so pathologists must not overlook the less obvious one, particularly if it has a prognostic and therapeutic impact.

Case Presentation

The patient was a 60-year-old Moroccan woman without any other medical history. She visited our hospital for slowly enlarging peripheral lymphadenopathy. Six months prior to presentation, she began to suffer from fever, night sweats, anorexia, and weight loss (6kg). The physical examination revealed, a moderate pale conjunctiva, skin pallor with bilateral and multiple lymphadenitis in the axillar, cervical and inguinal areas without organomegaly or skin lesions. Laboratory analysis revealed anemia (hemoglobin 6.5 g/dL), thrombocytopenia (platelets 4.2 × 104/mL), polyclonal hypergammaglobulinemia and elevated CRP (120 mg/l), Erythrocyte sedimentation rate was 88 mm/hr.

Blood and sputum cultures were negative for mycobacterium. Chest and abdominal tomography showed enlarged mediastinal, axillar and abdominal lymph nodes.

Diagnostic assays for HIV-1, HBV, HCV were performed and were negative.

An axillar lymph node biopsy was performed. The histological examination showed a multifocal proliferation of atypical spindle cells forming slits with extravasated red blood cells, hemosiderin laden and numerous mitosis (Figure 1). The remainder of the lymph node showed atretic germinal centers, with thickened Mantle zones (Figure 2). There were also many plasma cells and increase vascularity and perivascular hyalinization. Follicular dendritic cells showed some dysplastic features and some giant cells. Immunohistochemical study showed that spindle cells were stained with CD31 (Figures 3) and CD34. Furthermore, CD20, CD23, CD79 and Ki-67 was strongly positive in the germinal-center-like structures, and CD23 revealed the follicular dendritic cells in the germinal centers. The Latency Associated Nuclear Antigen 1(LANA) (Figure 4) was positive in the spindle cells and only in rare plasma blasts. The diagnosis of KS associated to MCD was confirmed.

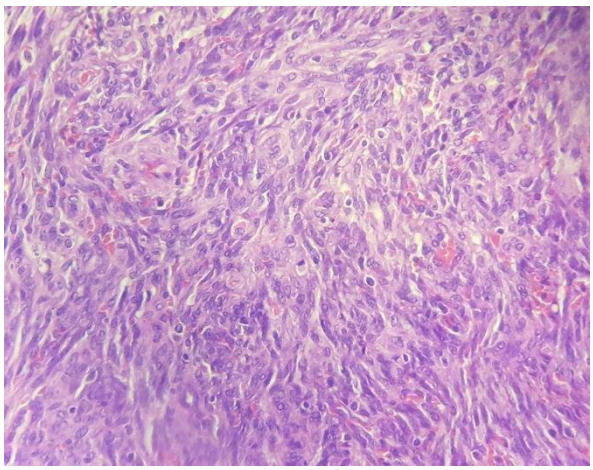

Figure 1: Low power view of the lymph node. Proliferation of atypical spindle cells forming slits with extravasated red blood cells, hemosiderin laden and numerous mitosis (HE staininstainx100).

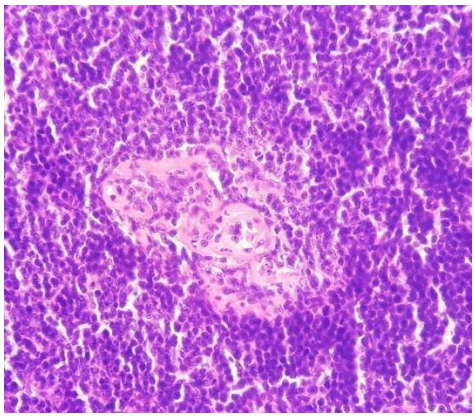

Figure 2: Spindle cells are stained with CD31.

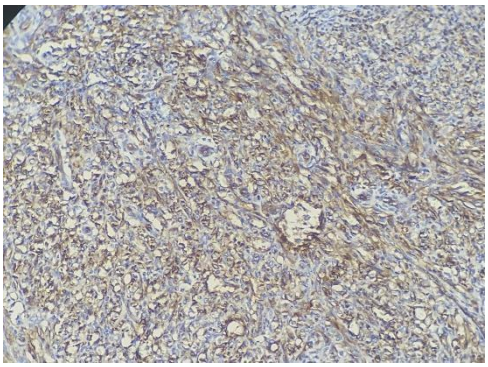

Figure 3: Nuclear staining with HHV8 anti LANA1.

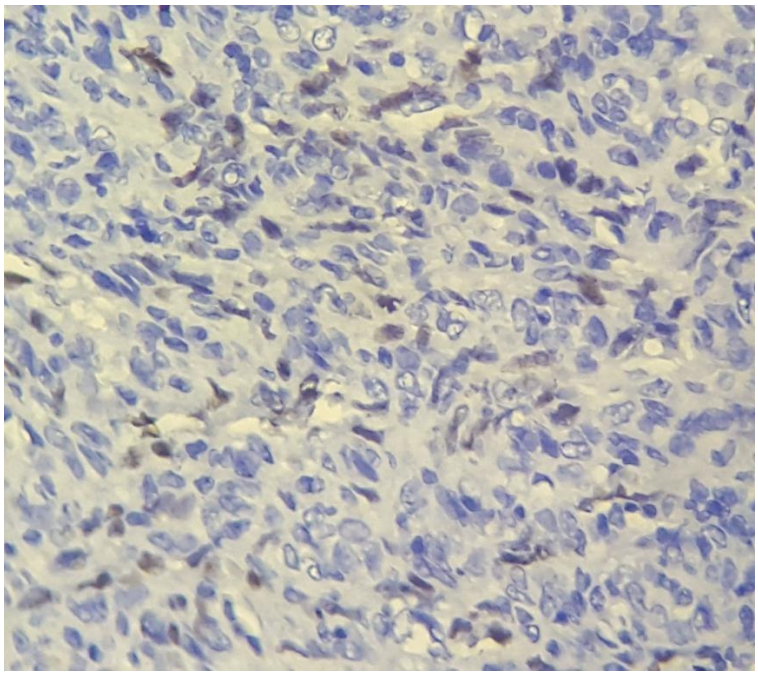

Figure 4: Atretic germinal centers, with thickened Mantle zones (HEx100).

Bone marrow biopsy revealed normocellular bone marrow showing trilineage hematopoiesis and marked polyclonal plasma cytosis. The patient was started on Rituximab with liposomal Doxorubicin for MCD and Kaposi sarcoma. Currently the patient has received 2 cycles of chemotherapy, clinical symptoms and hematologic parameters are improving.

Discussion

Kaposi Sarcoma (KS) and Multicentric Castleman Disease (MCD), are two diseases both related to Human Herpes Virus 8 (HHV8) and occurs frequently among HIV-positive patients. They are exceedingly rare among immunocompetent individuals.

The first case described in the literature about the association of KS and MCD in the same sample was by Abe et al. [6]. The patient was HIV- positive and they demonstrated, using immunohistochemistry, in a single lymph node the expression of different viral proteins in both lesions. The neoplastic cells of KS are usually positive for LANA-1, with rare expression of lytic proteins. while in MCD, both proteins of the latency and the lytic phase of HHV-8 are positive in the mantle zone cells.

In 2008, Naresh et al. [12] compare the coexistence of KS and MCD in 24 lymph nodes and five spleens from 26 HIV positive patients. 63% of lymph nodes samples showed microscopic involvement by KS in the lymph node capsule, the hilum or trabeculae in addition to MCD. They also studied 20 LN biopsies from 19 VIH positives without MCD, and among them 25% showed involvement by KS.

They concluded that infection of lymphoid cells by lytic HHV-8 expose endothelial cells in the lymph node to a high level of this virus, which produce the formation of KS tumor lets. These results suggest the importance of detecting microscopic foci of Kaposi sarcoma in HIV-positive patients lymph nodes with CD or if the microscopic examination show vascular proliferation or areas of capsular/ trabecular thickening. Immunohistochemistry for HHV-8 (LANA-1) should be performed in all these situations.

A good example of this situation was reported by Pinto et al. [7] the pathological examination of the lymph node of an HIV positive patient , showed initially a Castleman Disease and they didn't detect the microscopic focus of KS with routine H & E staining. After immunohistochemical study with HHV-8-LANA-1 they revealed a small vascular and spindle cells proliferation near to the lymph node capsule.

Otherwise, Bolen and al. [8] reported a case of a HIV-1 negative patient who developed a multicentric Castleman's disease and Kaposi's sarcoma after immunosuppressive treatment with cyclosporine A for a minimal change nephropathy. The diagnosis was made after histological examination of inguinal lymph node.

In our case, the patient was HIV negative without any medical history of immunosuppressive therapy, and she presented with diffuse lymphadenopathy and systemic symptoms suggesting malignant lymphoma. the histological examination showed the coexistence in the axillar lymph node of two different areas of Kaposi sarcoma and Castleman disease. The immunohistochemical study confirm this.

MCD has a poor prognosis. Whereas, there is no standard treatment and symptomatic cases are often treated with chemotherapy, immunomodulatory agents or monoclonal antibody against the receptor for IL-6 or anti-CD20 (rituximab). However ,pegylated-liposomal doxorubicin is the treatment of choice of KS [13]. The role of antiviral therapy in the treatment of HIVnegative HHV-8-positive patient with Kaposi's sarcoma and multicentric Castleman's disease, is not yet defined but in their experience, Murphy et al. [10] reported a five years remission by long term valganciclovir, after initial rituximab and liposomal doxorubicin.

Conclusion

The association of two HHV-8-related diseases (KS and MCD) is rarely seen in HIV-negative patients.

Since they require different treatment, pathologists should pay attention to sample of lymph node with Kaposi sarcoma or Castleman disease in patient with systemic manifestation and diffuse lymphadenopathy even the patient is HIV negative.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editorin-Chief of this journal.

Authors' Contributions

AB and NK performed the histological examination of the tumor. NK collected all patient data and were a major contributor to writing the manuscript. BH and SK analyzed and interpreted the patient data.

All authors read and approved the final version of the manuscript.

References

1. Yaghoobi R, Pazyar N, Tavakoli S (2015) Co-existence of multicentric Castleman's disease and Kaposi's sarcoma. Indian journal of dermatology 60: 323.
2. Zhao X (2011) Diffuse hyperpigmented plaques as cutaneous manifestation of multicentric Castleman disease and treatment with thalidomide: Report of three cases. Journal of the American Academy of Dermatology 65: 430-432.
3. Du M, Bacon C, Isaacson P (2007) Kaposi sarcoma-associated herpesvirus/human herpesvirus 8 and lymphoproliferative disorders. Journal of Clinical Pathology 60: 1350-1357.
4. Haque S, R van Kirk (2009) Three patients with both Hodgkin's lymphoma and Castleman's disease: Clinicopathologic correlations and lack of association with HHV-8. Indian journal of medical and pediatric oncology: official journal of Indian Society of Medical & Pediatric Oncology 30: 76-79.
5. De GR (1989) Multicentric Castleman's disease in association with Kaposi's sarcoma. Applied pathology 7: 105-110.
6. Abe Y (2006) Distinct expression of Kaposi's sarcoma-associated herpesvirus-encoded proteins in Kaposi's sarcoma and multicentric Castleman's disease. Pathology international 56: 617-624.
7. Pinto LW, Nunes EP (2011) Simultaneous lymph node involvement by Castleman disease and Kaposi sarcoma. Revista brasileira de hematologia e hemoterapia 33: 73-76.
8. Bollen J (2003) Multicentric Castleman's disease and Kaposi's sarcoma in a cyclosporin treated, HIV-1 negative patient: case report. BMC Hematology 3: 3.
9. Ali M, Rayes-Danan R (2016) Multicentric Castleman Disease and Kaposi sarcoma: Two HHV8 diseases with different prognosis and treatment: A case report and review of literature. HIV & AIDS Review 15: 127-130.
10. Murphy C (2017) Durable remission of both multicentric Castleman's disease and Kaposi's sarcoma with valganciclovir, rituximab and liposomal doxorubicin in an HHV-8-positive, HIV-negative patient. Journal of clinical pharmacy and therapeutics 42: 111-114.
11. Gaitonde SV, Vidanovic H Ni (2007) Concomitant and fatal HHV-8+ multicentric Castleman's disease and Kaposi's sarcoma in the same lymph node of an HIV–liver transplant patient. Histopathology 50: 954-958.
12. Naresh KN, Rice AJ, Bower M (2008) Lymph nodes involved by multicentric Castleman disease among HIV-positive individuals are often involved by Kaposi sarcoma. The American journal of surgical pathology 32: 1006-1012.
13. Northfelt DW (1998) Pegylated-liposomal doxorubicin versus doxorubicin, bleomycin, and vincristine in the treatment of AIDS-related Kaposi's sarcoma: results of a randomized phase III clinical trial. Journal of clinical oncology 16 p. 2445-2451.