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LETTER TO THE EDITOR

HHV-8- and EBV-positive germinotropic lymphoproliferative disorder

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Dear Editor,

A 72-year-old HIV-negative female presented with a 7-month history of palpable, non-tender left cervical lymph node. She had no fever or other systemic symptoms. No splenomegaly or hepatomegaly was present. Peripheral blood tests were within normal limits. A total body computed tomography (CT) scan confirmed a 2-cm isolated cervical lymph node, which was surgically removed. Histologically, lymph node architecture was partially effaced. Aggregates of plasmablasts partially or totally replaced germinal centers (GC) (Figs. 1 and 2). Numerous plasma cells were present in the inter-follicular areas. Some follicles showed Castleman-like features with hyalinized, atrophic GC (Fig. 3). Plasmablasts were co-infected by human herpesvirus 8 (HHV-8) and Epstein-Barr virus (EBV), being positive for HHV-8 (Fig. 1, *inset left*) and EBV by in situ hybridization (EBER) (Fig. 1, *inset right*). These cells were diffusely positive for CD38 (Fig. 2, *inset*), MUM1/IRF4, and immunoglobulin light chain lambda with a significant positivity for CD3 (Fig. 4a), and partial expression of BCL2, c-MYC, and p53. The proliferative index was elevated (ki67 about 90%). CD20 (Fig. 4b) CD79α, CD138, EMA, CD30, ALK-1, CD10, BCL6, LMO2, HGAL, CD27, IgM, and immunoglobulin light chain kappa were all negative. The inter-follicular plasma cells were polyclonal for kappa and lambda light chains. Polymerase chain reaction (PCR) analysis showed a polyclonal pattern. A germinotropic lymphoproliferative disorder (GLD) was diagnosed. Bone marrow trephine biopsy revealed a normocellular marrow. No therapy was given. The patient is free of disease, 18 months from diagnosis.

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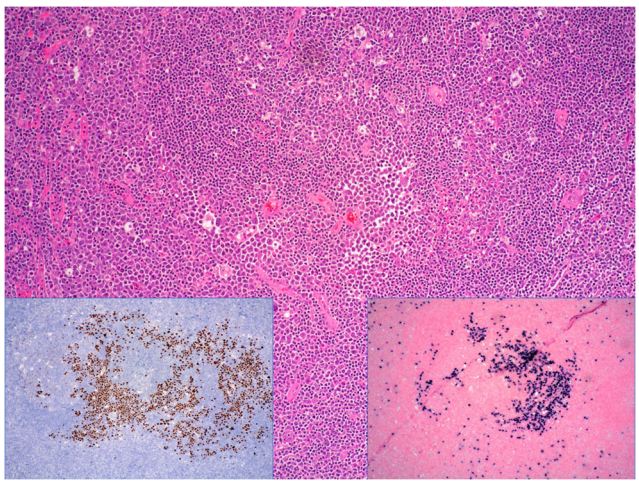

Fig. 1 Clusters of large atypical cells colonizing germinal centers (HE 20x); *inset left* HHV-8 positive staining of plasmablasts; *inset right* Epstein-Barr virus positivity of plasmablasts by in situ hybridization (EBER)

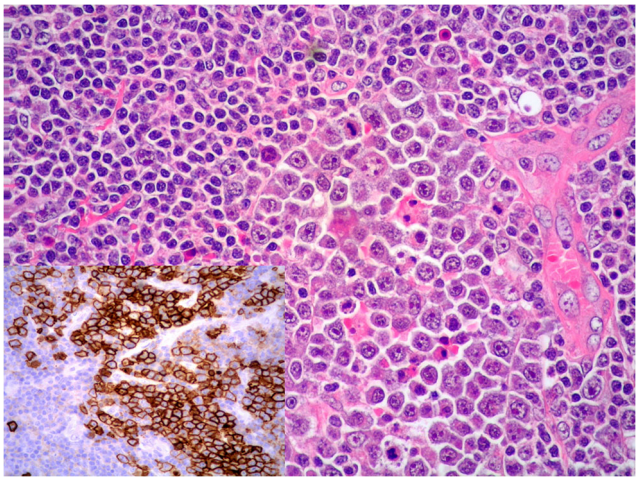

Fig. 2 High-power view of the large cells with plasmablastic morphology (H&E × 40); *inset* CD38 positive staining of plasmablasts

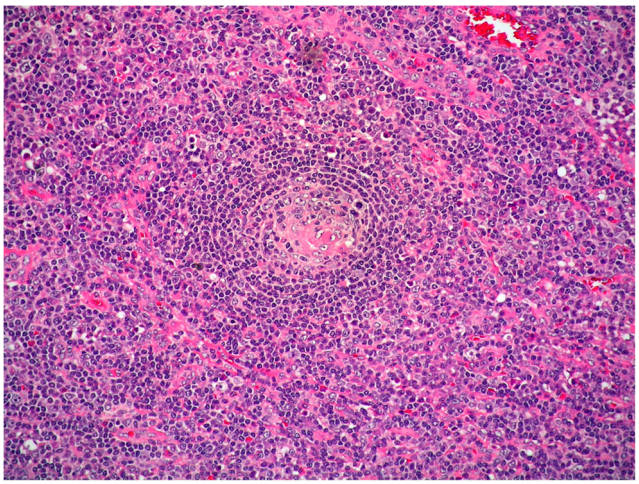

Fig. 3 Hyalinized, atrophic follicle with Castleman-like features

GLD is a rare, novel entity, presenting mainly in immunocompetent patients with isolated adenopathies and indolent behavior [1–10]. Clusters of plasmablasts show a predilection to colonize GC, hence the definition germinotropic, and are co-infected by HHV-8 and EBV [1–10].

HHV-8, also known as Kaposi sarcoma-associated herpesvirus for its role in Kaposi sarcoma etiology, is a lymphotropic virus detected in multicentric Castleman's disease (MCD), primary effusion lymphoma (PEL), HHV-8-positive diffuse large B cell lymphoma (DLBCL), and GLD [1]. Differently from GLD, the other diseases primarily occur in HIV-positive patients, with systemic symptoms, and follow a dismal course [1].

Interestingly our case showed MCD-like features as atrophic, hyalinized GC with vascular proliferation suggesting a possible overlap between GLD and MCD. Distinction may be complicated, requiring integration of clinicopathological data. In GLD, plasmablasts preferentially colonize GC, whereas in MCD, they involve the mantle zone, giving origin, in a minority of cases, to frank HHV-8-positive diffuse large B cell lymphoma [1]. In GLD, plasmablasts show monotypic kappa or lambda light chains, differently from MCD which is always IgM lambda positive [1]. Both diseases often lack molecular evidence of clonality [1]. MCD is HHV-8-positive and always EBV-negative, differently from GLD which is co-infected by HHV-8 and EBV [1–10]. The classical GLD phenotype shows negativity for B cell markers and CD138, with variable positivity for MUM1/IRF4, CD38, and CD30. The aberrant expression of a T cell marker (CD3), present in our case and rarely reported in GLD [7, 10], can be misleading particularly in absence of B cell markers. GLD mostly behave favorably either with surgery alone, as in our patient, or with additional chemotherapy or radiotherapy [1–10].

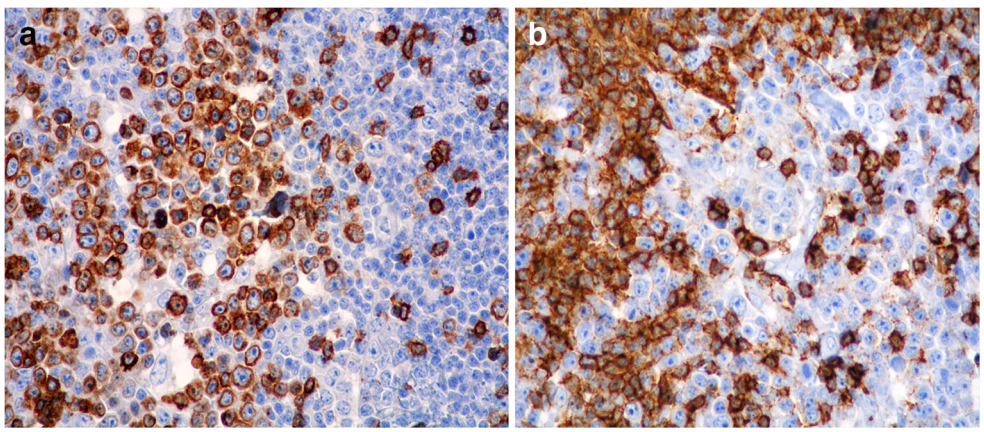

Fig. 4 **a** CD3 aberrant expression by plasmablasts. **b** CD20 negativity of plasmablasts

Compliance with ethical standards

Conflict of interest The authors declare they have no conflict of interest.

Ethical approval Local ethics committee (Comitato Etico dell'Area Vasta Emilia Nord, Italy) ruled that no formal ethics approval was required in this particular case.

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

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