CASTLEMAN DISEASE AS A LYMPHOMA MIMICKER: LESSONS FROM TWO CONTRASTING CASES

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INTRODUCTION

Castleman disease (CD) comprises a heterogeneous spectrum of rare non-clonal lymphoproliferative disorders characterized by distinctive lymph node histopathology and variable systemic inflammation. Disease may be unicentric (UCD) or multicentric (MCD), the latter including HHV-8-associated disease and HHV-8-negative idiopathic MCD (iMCD).[1]

CD may closely mimic lymphoma, particularly when patients present with generalized lymphadenopathy, constitutional symptoms, FDG-avid lesions, cytopenias and systemic inflammation. Conversely, autoimmune disorders may produce overlapping clinical and histopathological findings, creating an additional diagnostic challenge in HHV-8-negative disease.[1,2]

We present two contrasting cases illustrating the clinical spectrum of CD and highlighting the importance of adequate tissue sampling and integrated clinicopathological assessment in patients investigated for suspected lymphoma.

RESULTS

CASE 1 - LOCALIZED DISEASE WITH CURATIVE SURGERY

A 42-year-old woman was investigated for palpitations, generalized malaise and musculoskeletal pain. She had no weight loss, fever or night sweats and no relevant cytopenias. Cervical MRI demonstrated a 57-mm lesion posterior to the jugulocarotid bundle, with additional smaller cervical lesions.

Excisional lymph node biopsy demonstrated architectural distortion with regressed germinal centers, prominent mantle zones, “lollipop” follicles, follicular dendritic cell expansion, vascular proliferation and focal hyaline sclerosis. Interfollicular plasma cells were sparse, mature and polyclonal. HHV-8 and EBER were negative. The findings were consistent with hyaline-vascular Castleman disease.

PET/CT showed no evidence of metabolically active residual or distant disease. Bone marrow assessment was reactive, and echocardiography and pulmonary function tests were unremarkable. Subsequent CT showed no lymphadenopathy outside the cervical region. The patient underwent complete surgical excision and has remained clinically and analytically well under surveillance, with no evidence of recurrence.

CASE 2 - SYSTEMIC DISEASE MIMICKING LYMPHOMA

A 46-year-old woman with Sjögren syndrome presented with systemic inflammatory symptoms following an arterial thrombotic event. Initial CT demonstrated bilateral axillary lymphadenopathy, hepatomegaly and splenic enlargement. She subsequently developed persistent fever, night sweats, progressive arthralgias, profound anorexia and marked weight loss.

CT showed generalized lymphadenopathy involving supra- and infradiaphragmatic stations. PET/CT demonstrated extensive FDG-avid lymphadenopathy with splenic and axial bone marrow uptake, initially strongly suggesting disseminated lymphoma. Laboratory findings included ESR 120 mm/h, anemia, leukopenia/neutropenia, hypoalbuminemia and marked polyclonal hypergammaglobulinemia (IgG 5515 mg/dL). Serum immunofixation was negative and free light-chain ratios were preserved. IL-6 was elevated at 59. HHV-8 serology and viral load were negative. Bone marrow evaluation showed reactive changes without demonstrable lymphoid or plasma-cell clonality.

An initial image-guided core biopsy showed reactive lymphadenitis with marked plasmacytosis but no evidence of lymphoma, prompting multidisciplinary review and subsequent excisional biopsy. The excisional biopsy showed preserved nodal architecture, sinusoidal dilation, extensive interfollicular and medullary polytypic plasmacytosis, variable germinal-center involution, follicular dendritic cell prominence and mild vascular proliferation. HHV-8 and EBER were negative. The pathological differential included Castleman-like lupus lymphadenitis and iMCD.

Rheumatological reassessment favored Sjögren syndrome, with systemic lupus erythematosus considered less likely. Thus, the clinical and laboratory phenotype was highly suggestive of iMCD, although autoimmune Castleman-like lymphadenitis could not be completely excluded.

Before disease-directed therapy could be initiated, the patient developed hemorrhagic shock following rupture of an abdominal aortic aneurysm and underwent emergency surgery. Despite transient postoperative stabilization, she developed progressive multiorgan dysfunction and ultimately died.

CONCLUSION

These two cases illustrate the broad clinical spectrum of Castleman disease and its capacity to closely mimic lymphoma.

The first case represents classic HHV-8-negative hyaline-vascular UCD, in which complete surgical excision resulted in durable disease control, consistent with current consensus recommendations.[3]

The second case highlights the substantially greater diagnostic complexity of systemic HHV-8-negative Castleman-like disease. Multicentric lymphadenopathy, constitutional symptoms, marked systemic inflammation, polyclonal hypergammaglobulinemia, elevated IL-6 and characteristic lymph node changes strongly supported an iMCD phenotype. However, the coexistence of Sjögren syndrome and overlapping histopathological features prevented complete separation from autoimmune Castleman-like lymphadenitis.

These cases emphasize three clinically relevant principles:

1. CASTLEMAN DISEASE SHOULD BE CONSIDERED IN THE DIFFERENTIAL DIAGNOSIS OF LYMPHOMA, particularly in patients with inflammatory symptoms and generalized FDG-avid lymphadenopathy.

2. ADEQUATE TISSUE IS ESSENTIAL. Core biopsy may be insufficient, particularly in suspected iMCD; excisional lymph node biopsy permits assessment of architecture and the characteristic constellation of Castleman-like changes.[1]

3. HHV-8-NEGATIVE MULTICENTRIC DISEASE REQUIRES CLINICOPATHOLOGICAL INTEGRATION. Diagnosis requires characteristic histopathology, multicentric lymphadenopathy, compatible laboratory/clinical findings and rigorous exclusion of malignant, infectious and autoimmune mimics.[1,2]

Early recognition is particularly important because iMCD can progress rapidly and current consensus guidelines recommend IL-6-directed therapy, with siltuximab as preferred first-line treatment when available.[2]

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