CLINICAL VIGNETTE

Plasmablastic Lymphoma Presenting as FUO

Samir Bhalla, MD and Sidharth Anand, MD

UCLA Health and Los Robles Medical Center

Case Presentation

A 68-year-old male presented to the hospital with three weeks of recurrent nightly fevers. The fevers typically occurred in the evening and were associated with chills. He also reported progressively worsening bilateral leg swelling over several weeks. Past history is notable only for BPH and s/p TURP three months prior to admission. He was born in Gambia, but has resided locally for over 30 years, with no recent international travel. He denied any prior history of tuberculosis.

Physical examination noted a chronically ill appearing male in no distress. Vital signs included fevers of 101 in the early evening, associated with tachycardia in the 120s and relative hypotension.

Exam included 3+ bilateral lower extremity edema. There was no significant inguinal or other lymphadenopathy, and cardiopulmonary and abdominal exam were unremarkable.

Laboratory tests included significant microcytic anemia with hemoglobin 6.2 g/dL (13.5-17.7 g/dL) and MCV 72 fL (82-98 fL), white blood count of 7,700 (4,000 - 11,000 /uL) with 23% monocytes (0-11 %). Repeated urinalysis was negative for infectious markers and blood cultures did not show growth. Respiratory viral panel was negative. Quantiferon screen was negative. PSA level was undetectable. Serologies for HIV, CMV, EBV, bartonella, lyme among others were also negative for acute infection. He was initially briefly treated with empiric antibiotics, which were discontinued after negative infectious testing. CT imaging of the chest, abdomen and pelvis demonstrated mild enlargement of mediastinal and retroperitoneal lymph nodes, as well as low attenuating splenic lesions. Echocardiogram showed no vegetations or significant valvular disease. Bone marrow biopsy was negative for evidence of leukemia or lymphoma. Supraclavicular lymph node biopsy was done by interventional radiology. Pathology demonstrated plasmablastic lymphoma, EBV positive. He received cycle 1 of bortezomib with EPOCH in the hospital before discharge. He followed as outpatient, and reports resolution of fevers and improvement in lower extremity swelling. He will continue EPOCH.

Discussion

Plasmablastic lymphoma (PBL) is a rare aggressive subset of B-cell lymphoma that is typically associated with immunosuppressed states. These include: post-transplant HIV and EBV infections. Fewer than 25% of cases occur in immunocompetent individuals.[1,2] Median survival from the time of diagnosis ranges between 12-18 months.[3] A review of 135 patients reported 53% mortality within 48 months despite chemotherapy.[4] The lymphoma cells are characterized by large eccentric nucleoli with abundant cytoplasm, thus resembling plasmablasts.[1] Extranodal masses can occur, most commonly in the oral mucosa and GI tract, and musculoskeletal symptoms, are the most common presentation of PBL.[2] B symptoms including fevers are rare, however HIV positive patients more commonly reported associated B symptoms.[2] This patient was not immunocompromised, and tested negative for HIV by both serology and PCR.

The pathogenesis of PBL is not fully understood. *MYC* gene rearrangements in addition to EBV infection are thought to be important to pathogenicity. Immunohistological study typically shows PBL cells with expression CD38, CD138, IRF4/MUM1, BLIPM1, and cytoplasmic immunoglobulin light chain restriction, with Ki-67 proliferation and MYC overexpression. EBV-associated PBL accounts for 70% of cases with CD30 and programmed cell death-ligand 1 (PD-L1) expressions, as was in our patient's immunostaining.[1,2]

Regimens such as CHOP and EPOCH which are commonly used for NHL have traditionally been treatment options for PBL.[1] Recently promising response results and improved 2-year survival were noted with initial bortezomib infusion in addition to EPOCH.[3,5] Our patient will continue EPOCH with monitoring for clinical response and hopeful remission.

Summary

This rare presentation of an immunocompetent, HIV negative patient presented with B-symptoms of recurrent fevers and was diagnosed with plasmablastic lymphoma. PBL traditionally portends a poor prognosis, although new treatment lines offer hope for our patient. Occult malignancies like lymphoma must be considered on the evaluation of fever once infections are ruled out.

REFERENCES

1. **Bailly J, Jenkins N, Chetty D, Mohamed Z, Verburgh ER, Opie JJ**. Plasmablastic lymphoma: An update. *Int J Lab Hematol*. 2022 Sep;44 Suppl 1(Suppl 1):54-63. doi: 10.1111/ijlh.13863. Erratum in: *Int J Lab Hematol*. 2022 Dec;44(6):1121. doi: 10.1111/ijlh.13981. PMID: 36074710; PMCID: PMC9545967.
2. **Castillo JJ, Bibas M, Miranda RN**. The biology and treatment of plasmablastic lymphoma. *Blood*. 2015 Apr 9;125(15):2323-30. doi: 10.1182/blood-2014-10-567479. Epub 2015 Jan 30. PMID: 25636338.
3. **Castillo JJ, Guerrero-Garcia T, Baldini F, Tchernonog E, Cartron G, Ninkovic S, Cwynarski K, Dierickx D, Tousseyn T, Lansigan F, Linnik Y, Mogollon R, Navarro JT, Olszewski AJ, Reagan JL, Fedele P, Gilbertson M, Grigoriadis G, Bibas M**. Bortezomib plus EPOCH is effective as frontline treatment in patients with plasmablastic lymphoma. *Br J Haematol*. 2019 Feb;184(4):679-682. doi: 10.1111/bjh.15156. Epub 2018 Mar 12. PMID: 29527667.
4. **Tchernonog E, Faurie P, Coppo P, Monjanel H, Bonnet A, Algarte Génin M, Mercier M, Dupuis J, Bijou F, Herbaux C, Delmer A, Fabiani B, Besson C, Le Gouill S, Gyan E, Laurent C, Ghesquieres H, Cartron G**. Clinical characteristics and prognostic factors of plasmablastic lymphoma patients: analysis of 135 patients from the LYSA group. *Ann Oncol*. 2017 Apr 1;28(4):843-848. doi: 10.1093/annonc/mdw684. PMID: 28031174.
5. **Dittus C, Grover N, Ellsworth S, Tan X, Park SI**. Bortezomib in combination with dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) induces long-term survival in patients with plasmablastic lymphoma: a retrospective analysis. *Leuk Lymphoma*. 2018 Sep;59(9):2121-2127. doi: 10.1080/10428194.2017.1416365. Epub 2018 Jan 5. PMID: 29303024.