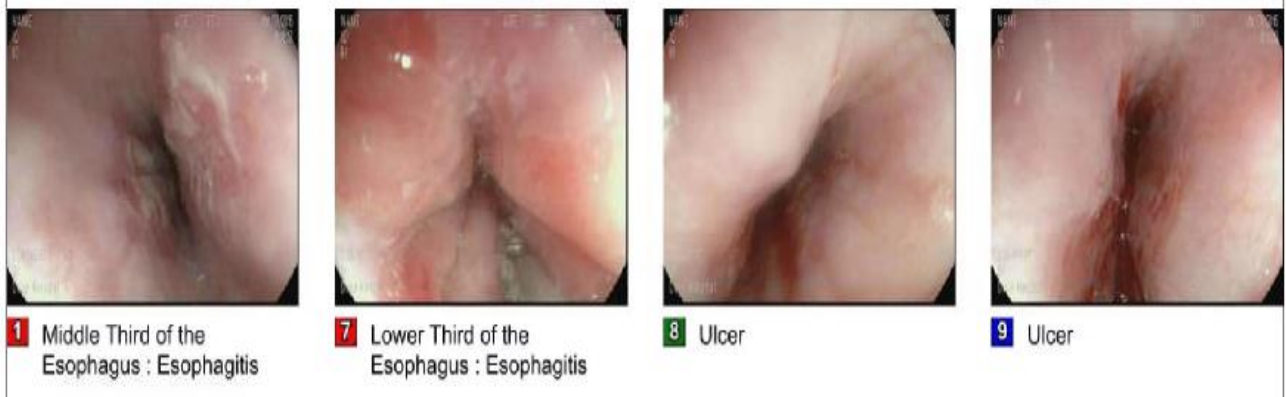
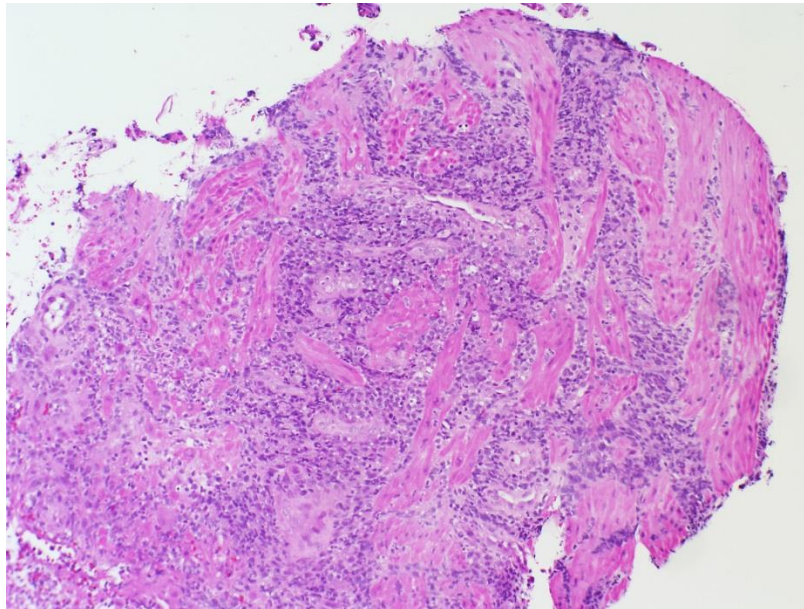


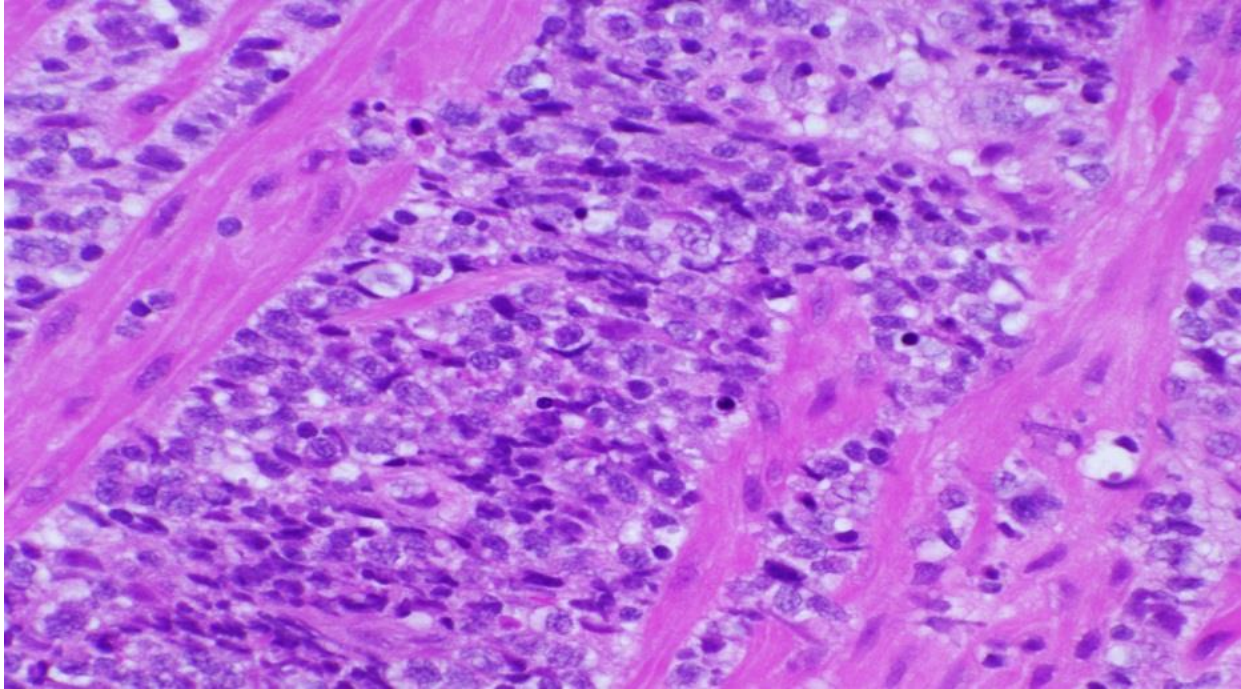
CASE HISTORY

A 59-year-old male with a history of glioblastoma multiforme requiring chronic steroid therapy was admitted for multiple medical complications prior to craniotomy during which time he developed decreased oral intake and worsening dysphagia over the course of several weeks. He underwent an esophagogastroduodenoscopy which showed two linear esophageal ulcers and severe esophagitis. Endoscopic images are shown below.



Representative histologic sections of the biopsy are provided below for your review.





The immunohistochemical profile is provided below:

Negative in Neoplastic Cells: Cytokeratin, MPO, CD3, CD68, and CD56.

Weak/Focally Positive: CD45, CD20.

Diffuse and Strongly Positive: CD79a and CD138.

The Ki-67 proliferation rate was markedly high (>90%).

What is your diagnosis?

- Plasmablastic plasma cell myeloma
- Burkitt Lymphoma
- Immunoblastic diffuse large B-cell lymphoma
- Plasmablastic Lymphoma
- Kaposi's sarcoma-associated lymphoproliferative disorder

What test would you order next to confirm the correct diagnosis?

- HHV8 PCR
- EBV in situ hybridization
- HIV PCR
- FISH for ALK gene rearrangement
- Serum protein electrophoresis

(SCROLL DOWN FOR ANSWERS AND DISCUSSION)

Answers and Discussion:

D. Plasmablastic lymphoma

B. EBV in situ hybridization

Plasmablastic lymphoma (PBL) is an uncommon, aggressive subtype of diffuse large B-cell lymphoma (DLBCL) which is characterized by a proliferation of neoplastic cells that resemble immunoblasts, but in which all tumor cells have the immunophenotype of plasma cells. It was first described in 1997 as a mass occurring in the oral cavity of an HIV+ male. While it is most commonly seen in HIV positive individuals, it can also be seen in patients with iatrogenic immunosuppression or other immune deficiencies as well as in the elderly. It may also occur in patients with a prior plasma cell neoplasm; however, such cases should be considered a plasmablastic transformation of myeloma rather than a primary lymphoma. In addition to the oral cavity, it can occur in other extra-nodal sites including sinonasal cavity, orbit, skin, bone, soft tissues, and the GI tract. Nodal involvement is rare and is generally seen in NON HIV-positive patients. No significant bone marrow involvement is seen.

Morphologically, PBL has a diffuse growth pattern and effaces the architecture at the site of invasion. The neoplastic cells are large and predominately resemble immunoblasts with moderate cytoplasm, a central, vesicular nucleus, and prominent nucleoli. However, there can be a spectrum with some cells also having plasmacytic differentiation with basophilic cytoplasm, a paranuclear hof, and an eccentric large nucleus. Necrosis, karyorrhexis, increased mitotic figures, and a “starry sky” pattern with frequent tangible body macrophages are common

The immunophenotype is similar to that in plasma cell neoplasms, positive for CD79a, IRF-4/MUM-1, BLIMP-1, CD38, and CD138. The neoplastic cells are negative or weakly positive for B-cell markers CD20 and PAX-5 and a subset may be dim positive for CD45. CD56 can be positive or negative, and, if it is positive, it should raise suspicion for underlying plasma cell myeloma. Ki-67 proliferation index is typically very high (>90%). MYC is expressed in about 50% of cases and correlates with MYC translocations or amplification. About 70% of cases express EBV-encoded RNA (EBER), which is the most sensitive methodology for detecting EBV infection within the malignant cells.

The main differential diagnosis of PBL is plasmablastic myeloma which may be morphologically and immunophenotypically nearly identical. Features that favor PBL include association with immunodeficiency and EBER positivity. Features favoring myeloma include the presence of monoclonal paraproteinemia, hypercalcemia, renal dysfunction, and lytic bone lesions. One study found that the only significant difference in the immunophenotype between the two was the presence of EBV-encoded RNA, which was positive in all PBL cases tested and negative in all plasmablastic myelomas.

The prognosis of patients with PBL is extremely poor with an estimated 1-16 month survival rate. Interestingly, some studies have shown that HIV+ patients have a slight survival advantage which may be due to the significant improvements in HIV management. Given the dismal prognosis, there is no definitive standard of care, although the use of CHOP is considered inadequate therapy and current guidelines recommend more intensive regimens.

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