Primary Bone Marrow Hodgkin Lymphoma in an HIV-negative patient complicated by Hemophagocytic Lymphohistiocytosis

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Introduction

Classical Hodgkin Lymphoma is an uncommon clinicopathological entity, often diagnosed by morphological and immunophenotypic findings seen on lymph node biopsy. When the malignancy is isolated to the bone marrow, this presents a significant barrier to making a timely diagnosis. Furthermore, primary bone marrow Hodgkin lymphoma (PBMLH) in an HIV-negative patient is extremely rare.

Not only do we present a case of PBMLH in an HIV-negative patient, but this rare clinical presentation was complicated by malignancy-induced hemophagocytic lymphohistiocytosis (HLH). Her complex presentation led to a significant delay in her diagnosis, primarily due to her constitutional B symptoms, refractory fevers despite broad spectrum antibiotics, persistent hypotension, and multi-organ dysfunction.

Case Presentation

51-year-old Somali-speaking female with a history of chronic hypertension and presumed polymyalgia rheumatica presented with acute onset altered mental status, generalized weakness, and myalgias. On arrival, she was febrile to 38.9°C, hypotensive to 91/63 mmHg, tachycardic to 120s, tachypneic to the mid-30s, only intermittently responsive to questions, and profoundly weak in all extremities. There was no lymphadenopathy on physical examination. See Table 1 for significant admission laboratory findings. Figure 1 includes notable imaging findings. Our patient was admitted to the medical intensive care unit (MICU) for symptomatic hypotension to 117 and systemic inflammatory response with unclear infectious etiology. Extensive infectious workup including lumbar puncture studies were unremarkable besides positive Epstein-Barr virus serology. Thoracentesis of the enlarging moderate-sized bilateral pleural effusions revealed a transudative process. Patient had several days of persistent high grade fevers despite broad spectrum antimicrobial coverage. On hospital day 13, patient acutely decompensated with persistent fevers and tachycardia over 160 BPM, requiring MICU readmission for intubation given her hypoxemia and respiratory distress, along with vasoactive medications for hypotension and rising lactate greater than 7. HLH Labs resulted with minimal function of NK cells (2%), elevated IL-2, and increased CXCL9 activity.

Sternal bone marrow biopsy: atypical lymphohistiocytic infiltrate and occasional Reed-Sternberg type cells diagnostic of primary bone marrow Classic Hodgkin Lymphoma without associated adenopathy and mediastinal masses. Discharged on hospital day 27 after receiving 5 days of Dexamethasone 40 mg daily and induction chemotherapy of Cyclophosphamide and Vinristine.

Case Presentation (Cont.)

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Table 1: Significant labs on admission

- WBC: 5.2 K/uL
- Hb: 8.3 g/dL
- Platelets: 40 K/uL
- INR: 1.8
- Lactic acid: 2.5 (H)
- AST: 223 (H)
- ALT: 103 (H)
- ALP: 196 (H)
- Fibrinogen: 49 (H)
- Coombs Test: Negative
- DIC panel: + Schistocytes <500ng/mL
- D-dimer: 2312 (H)
- LDH: 397 U/L

Figure 1: Notable imaging findings

- Magnetic resonance imaging brain: concerning for central pontine myelinolysis.
- Computed tomography chest/abdomen/pelvis with contrast: Lymph nodes: No axillary, supraclavicular, mediastinal, hilar retroperitoneal or mesenteric, illigual or pelvic side wall lymphohistiocytosis.
- Thorax: Moderate to large bilateral pleural effusions.
- Spine: Normal in size.
- Abdomen: significant anasarca, small volume ascites.
- Osseous Structures: Mild spondylotic changes involving the impinged spine. No aggressive osseous lesion seen.

Discussion

Our case is unique for the following reasons:

- PBMLH in an HIV-negative patient is extremely rare
- 5th case in medical literature to report PBMLH in an HIV-negative patient
- 2nd female to date and youngest patient to be diagnosed; other patients were >55 years old
- Previous cases of HLH secondary to EBV and Hodgkin lymphoma have been reported
- Only patient with HLH-associated PBMLH to survive hospital admission to receive post-diagnosis chemotherapy

- Diagnosis of PBMLH was significantly delayed due to myriad of constitutional and infectious symptoms from malignancy induced HLH, initially presenting as septic shock
- Initial concern for HLH considered (elevated ferritin, pancytopenia, recurrent high grade fevers, refractory hypotension). However, triglycerides were normal, no splenomegaly, bone marrow biopsy with no overt hemophagocytosis
- Histologic hemophagocytosis is absent in up to 30% of HLH cases; whereas soluble CD25 is very specific for HLH (4-5)
- Did not initially meet criteria for diagnosis as esoteric labs take days/weeks to result. Ultimately our patient met criteria for HLH (B7) due to minimal function of serum Natural Killer Cells (2%), an elevated IL-2 (84250), and increased CXCL9 activity >1100
- However, this was after bone marrow biopsy discovered PBMLH on HLH treatment was deferred
- Unclear data on whether morbidity/prognosis of patient suffered from delay in diagnosis of PBMLH or HLH, or if diagnosing and treating the HLH (high dose steroids/chemotherapy/allergic bone marrow transplant) would have led to missed diagnosis (steroids associated with false negative bone marrow biopsy results)
- Obtaining an early bone marrow biopsy when esoteric HLH labs are pending are of utmost importance in clinically deteriorating patients such as our patient, due to the possibility of aggressive, rapidly-progressive malignancies

References