HIV-Associated Burkitt Lymphoma: More than a starry sky appearance

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Introduction

- People with HIV infection are at least 50 times more likely to get cancer compared to the general population.
- 25-40% of these lymphomas will be Burkitt Lymphoma (BL)—an aggressive B cell malignancy with a high proliferative rate and potentially fatal within months if not diagnosed and treated in a timely manner.
- This translates to a 10-20% individual lifetime risk of BL for an HIV infected person.
- The incidence of BL declined after the introduction of highly active antiretroviral therapy (HAART), but to a lesser extent than other HIV-associated malignancies.
- Epidemiologic studies suggest the incidence of BL will increase as the HIV-infected population ages.

Case Presentation

A 24 yo woman with known HIV presented with 1 month of intermittent fevers, chills, nausea and diffuse abdominal pain most notable in the epigastric region. Her symptoms acutely worsened in the last week, prompting her visit to the Emergency Department.

Past Medical History:
- HIV diagnosed in 2014. Last on ART Feb-May 2019 while in jail. CD4 count 596 (low at 26%) and HIV RNA viral count 26,400 prior to ART initiation.
- CD4 count improved to 33% with an undetectable viral load in April.
- Chronic hepatitis C
- Active IDU – heroin, methamphetamines
- Tobacco dependence

Exam:
- Vitalis: HR 135, RR 22, Temp 30.2±0.6, normotensive, SpO2>95% on room air
- Profuse sweating, notably uncomfortable
- New 2/6 holosystolic heart murmur in LUSB with no radiation
- Left lower quadrant and epigastric tenderness, negative Murphy’s sign

Labs on admission:
- High Hgb 9 (baseline: 11)
- Blood cultures negative
- CT abdomen pelvis obtained the night of admission demonstrated diffuse gastric thickening with evidence of osseal seeding with nodularity and splenomegaly
- Endoscopy completed the following day found a large nonbleeding gastric ulcer and diffuse gastric inflammation.
- Pathology of endoscopic biopsies of the gastric antrum identified Diffuse Large B cell Lymphoma (DLBCL) and H.pylori.
- Immunohistochemistry test positive for Epstein Barr Virus

Hospital Course:
- Started on broad spectrum antibiotics for presumed endocarditis in the setting of active IDU
- TTE revealed no vegetations, blood cultures negative
- CT abdomen pelvis obtained the night of admission demonstrated diffuse gastric thickening with evidence of osseal seeding with nodularity and splenomegaly
- Endoscopy completed the following day found a large nonbleeding gastric ulcer and diffuse gastric inflammation.
- Pathology of endoscopic biopsies of the gastric antrum identified Diffuse Large B cell Lymphoma (DLBCL) and H.pylori.
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The patient was started on Bactrim (last use 1-3 months prior)
- PET scan was done for staging revealed advanced disease with a diffuse tumor burden
- MYC rearrangement detected on FISH analysis, consistent with high grade Burkitt lymphoma
- She completed 1 cycle of Short Course EPOCH-R with a guarded prognosis. There was high concern for TLS and gastric perforation due to the extensive abdominal tumor burden. Fortunately, neither happened.

- Thus far, she has tolerated 3 of the anticipated 6 chemotherapeutic cycles with relatively minor complications by comparison including bradycardia, frequent NSVT and neutropenia necessitating adjustments to her chemotherapy regimen and schedule delays.
- Her pain control has remained a challenge in light of her ongoing IV substance use.

Discussion

- Lymphoma in the leading cause of cancer-related deaths among HIV-infected patients in the anti-retroviral therapy era.
- Burkitt lymphoma (BL) is a highly proliferative NHL deriving from B cells and with characteristic oncogenic pathways, including translocation in the MYC gene—a gene that normally plays a role in controlling cell proliferation, differentiation and apoptosis.
- The WHO classifies 3 different clinical variants of BL: endemic, sporadic and immunodeficiency-associated.
- Unlike other HIV-associated lymphomas, BL is frequently noted in patients with CD4 cell counts <200 and viral loads suppressed by ART.
- HIV-associated BL typically presents with extra-nodal disease, mostly commonly the stomach.
- Intra-abdominal BL may present with abdominal pain, nausea, vomiting, GI bleeding, bowel obstruction; fever, night sweats, weight loss (B symptoms), fatigue and malaise are also common.
- Approximately 70% will present with wide spread disease (stage III or IV), in addition to elevated LDH and uric acid levels.
- The classic “starry sky appearance” is not often seen in the histological examination of HIV-associated BL. Most are positive for Epstein Barr Virus (EBV).
- Recent studies suggest the pathobiology of HIV-associated lymphomas is distinct from non-HIV lymphomas. HIV may directly induce B-cell activation. Further oncogenic viruses, as EBV, are more prevalent in HIV-associated lymphomas.
- Survival with HIV-associated BL is approaching that of HIV-negative BL thanks to the development of short duration, dose intensive combination chemotherapy with aggressive CNS prophylaxis, the availability of rituximab and the implementation of effective ART.
- Rare cases of IRIS-associated Burkitt Lymphoma have been reported, typically within 6 months after the initiation of HAART. It is unclear if that was the case with our patient.

Take Home Points

- This case emphasizes the importance of considering lymphomas in the HIV positive patient presenting with subacute abdominal symptoms. CT abdomen pelvis with contrast, possibly endoscopy, should be considered as part of the work up.
- HIV-associated BL, unlike other lymphomas, can develop in HIV patients well controlled on ART.
- BL is an aggressive malignancy that can be fatal within months if not appropriately diagnosed and treated.
- The impact of HIV, oncogenic viruses and HAART on the lymphoma microenvironment is still unclear.
- IRIS associated BL appears to be rare.

References