

An Unusual Presentation of HIV-Related Burkitt Lymphoma as Leptomeningeal and Bone Marrow Disease

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Introduction

Burkitt lymphoma (BL) is an aggressive B-cell neoplasm characterized by a short doubling time which most often presents at extranodal sites. The World Health Organization (WHO) clinically subdivides BL into three categories: endemic, sporadic, and immunodeficiency-associated. Immunodeficiency-associated BL represents 25 to 40% of all acquired immunodeficiency syndrome (AIDS)-related non-Hodgkin lymphomas. It is almost exclusively related to human immunodeficiency virus (HIV) and is one of the AIDS defining illnesses. Immunodeficiency-associated BL often has nodal localization and frequent bone marrow involvement. In adult type BL, bone marrow may be involved up to 70% of the time and leptomeningeal involvement may be present 40% of the time. We report an unusual case of HIV-related BL with leptomeningeal and bone marrow involvement in the absence of a primary CNS mass.

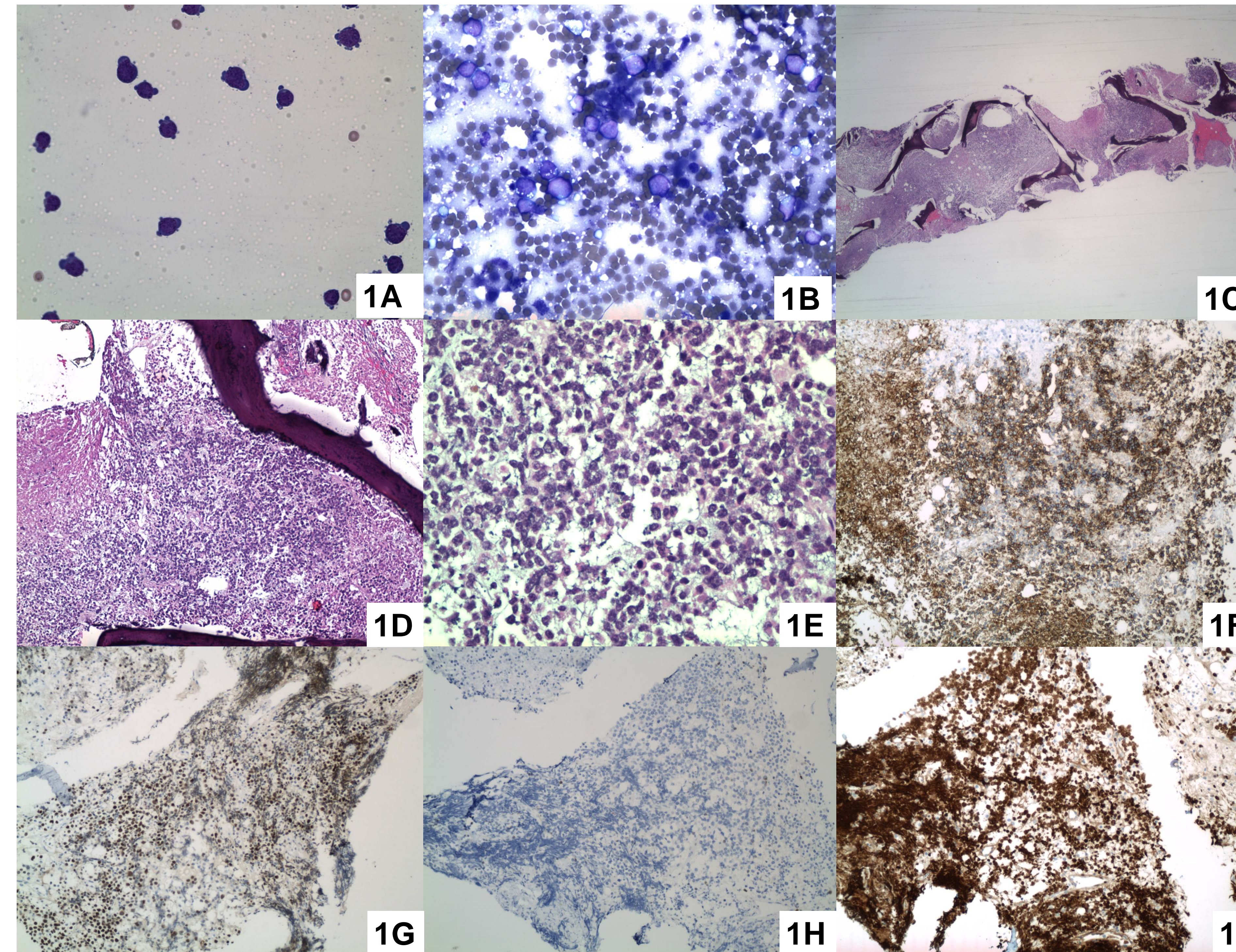


Figure 1. Burkitt Lymphoma A. CSF B. Bone marrow touch prep C. Bone marrow core biopsy, 20x D. Bone marrow core biopsy 100x E. Bone marrow core biopsy 400x F. CD20 G. Bcl-6 H. Bcl-2 I. Mib-1 (Ki-67).

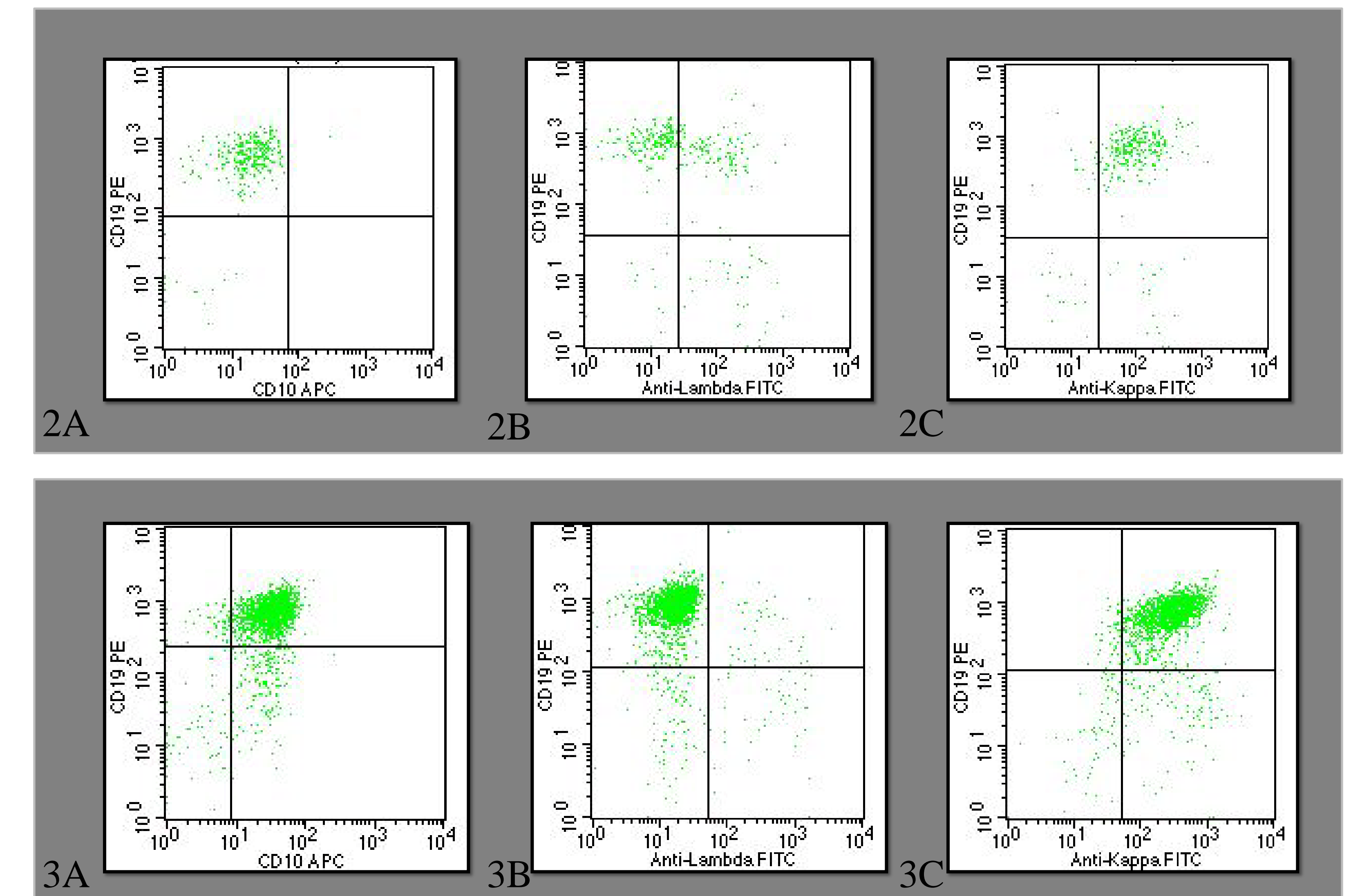


Figure 2. (CSF) **Figure 3.** (Bone marrow):. Flow cytometry demonstrating CD19/CD10 coexpression (A), B cell population with absence of lambda expression (B), and B cell population with kappa restriction (C).

Clinical History

A 36 year old male with a 9 month history of HIV, non-compliant with medications, and a past medical history of pneumonitis presented to an outside hospital with a one week history of severe headache, diplopia, and bilateral lower extremity weakness. His review of symptoms was pertinent for fever, night sweats, and weight loss. Physical exam demonstrated a cachectic male with ptosis of the left eye and no lymphadenopathy. At the outside hospital, he had a working diagnosis of aseptic meningitis after a cerebral spinal fluid (CSF) analysis revealed a total white blood cell count of 148 cells with a differential of 100% lymphocytes. Antigens for common microbial causes of meningitis were negative. Magnetic resonance imaging (MRI) of the spine demonstrated thickening of the L4 and L5 nerve roots. His polyneuropathy symptoms became progressively worse; he was then transferred to our facility for higher level of care. Upon admission, laboratory results included a white blood cell count of 3.2 K/CMM with an absolute lymphopenia (0.5 K/CMM, 17.5%), hemoglobin of 10.4 g/dL, and a platelet count of 273K/CMM. A lumbar puncture demonstrated a CSF with a white cell count of 154K/CMM with 98% lymphocytes and some atypical lymphoid cells. The lymphoid cells had large nuclei with inconspicuous nucleoli present, a high nucleo-cytoplasmic ratio, and basophilic cytoplasm without vacuoles. Based on the histology of the CSF smear, flow cytometry was ordered. The patient underwent extensive imaging studies including: MRI, computed tomography (CT) scan, and a positron emission tomography-computed tomography (PET-CT) whole body scan. MRI of the head was negative, but an MRI of the spine showed evidence of an infiltrative process of the iliac crest with either tumor or an infectious process. However, a CT scan failed to reveal any specific lesion. Oncology was consulted and a bone marrow biopsy was performed.

Results

Flow cytometry of the CSF revealed a kappa light chain restricted monoclonal B cell population. Due to a dry tap, bone marrow touch prep was used for the bone marrow cell count differential and showed greater than 95% abnormal intermediate lymphoid cells with high nucleo-cytoplasmic ratio, finely dispersed chromatin, and basophilic cytoplasm with small clear cytoplasmic vacuoles. Bone marrow core biopsy showed almost complete replacement of the marrow spaces with sheets of intermediate cells with high nucleo-cytoplasmic ratio, finely dispersed chromatin, and inconspicuous nucleoli, alternating with areas of necrosis and apoptotic debris. By immunohistochemistry, the neoplastic cells demonstrated positivity for bcl-6, CD20, CD79a, and focal positivity for CD10. The neoplastic cells are negative for CD3, MPO, and bcl-2. Mib-1 (Ki-67) proliferation index was greater than 95%. Analysis of the cell suspension by flow cytometry revealed a predominant B cell population coexpressing CD19/CD10 with a kappa:lambda ratio of 88:3. The cells were negative by flow cytometry for MPO, TdT, CD117, T cell and myeloid markers. The fluorescence in situ hybridization (FISH) was positive for *MYC* gene rearrangement, confirming the diagnosis of Burkitt lymphoma. PET-CT imaging demonstrated no extraosseous disease.

Discussion

HIV-related Burkitt Lymphoma (BL) is an aggressive B cell neoplasm presenting clinically as bulky disease with a high tumor burden. The peripheral blood is rarely involved, whereas nodal and extranodal involvement including presentation at unusual sites is common. Although leptomeningeal disease and central nervous system root involvement have been previously described in HIV-related BL, they are very rare in the absence of a primary CNS mass. Bone marrow involvement confers a poor prognosis. Since the diagnosis of BL requires the demonstration of *MYC* translocation, prompt recognition of this unusual clinical presentation may lead to early diagnosis and therapy initiation.