Isolated CNS Relapse in a Case of Pancreatic Plasmablastic Lymphoma

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Summary

Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL). With features overlapping with myeloma and lymphoma coupled with its relapsing, aggressive clinical course and lack of consensus regarding standard treatment in the upfront and relapsed setting, PBL poses a diagnostic and therapeutic challenge and has a dismal prognosis with multi-agent chemotherapy. An isolated central nervous system (CNS) relapse of plasmablastic lymphoma associated with HIV infection in a 28 year old patient is reported here. He presented with altered sensorium and quadriparesis. He was evaluated outside with fluorodeoxyglucose positron emission tomography (FDG-PET) and magnetic resonance imaging (MRI) of brain which showed multiple parenchymal metastases in left cerebral hemisphere. He underwent whole brain radiotherapy (WBRT) outside and was referred to our institute for further management. He was treated with salvage chemotherapy regimen comprising of dexamethasone, cytarabine and cisplatin (DHAP). Despite best efforts, the patient succumbed after receiving one cycle. Our objective is to report the unusual site of disease coupled with the unique nature of relapse and review the complexity in diagnosis and treatment.

Keywords: Plasmablastic lymphoma; relapse; unusual; HIV

Introduction

Plasmablastic lymphoma (PBL), first described in the oral cavity of a patient infected with human immunodeficiency virus (HIV) in 1997,[1] is a rare and aggressive lymphoma. It was recognized by World Health Organization (WHO) as a variant of diffuse large B-cell lymphoma eleven years later.[2] The B cell nature and clonal origin along with an immunophenotype of a plasma cell with cells showing an immunoblast morphology makes the diagnosis of PBL challenging.[3] Since the original report, PBL has been described in a variety of both sites and clinical settings. It occurs predominantly in HIV infected population but it can also affect immunocompetent individuals, post-transplant patients and patients with other immuno deficiencies.[3] There are no standard guidelines in the management of PBL due to the rarity of this disease. Due to its aggressive and relapsing natural history, along with lack of standard treatment guidelines and difficulty in diagnosis, PBL is a challenging disease to treat and has a dismal outcome.[3]

Case Report

A 28 year old male was diagnosed with HIV infection in December 2021 and was started on antiretroviral therapy. His CD4 count at diagnosis was 53/uL. He presented with abdominal pain and vomiting since 2 months. A contrast enhanced computed tomographic (CECT) scan of abdomen and pelvis revealed a 9.6 x 6.6 x 8.9 cm mass involving head and uncinate process of the pancreas along with liver and bony metastases as shown in figure (Figure 1).

A tru-cut biopsy of the pancreatic mass and subsequent histopathological examination showed medium to large round plasmacytoid cells. Immunohistochemistry (IHC) showed atypical cells positive for CD-138, CD79A, c-MYC, CD10, MUM-1 and negative for Bcl-2, Bcl-6, CD30, CD3, Tdt, kappa and lamba light chains with Ki-67 of 80-85%. A chromogenic in situ hybridization (CISH) showed Epstein Barr virus–encoded RNA(EBER) positive.

He received treatment at a tertiary care hospital and his treatment record revealed that he was started on pulse dose of prednisolone followed by 6 cycles of Dose-adjusted EPOCH (etoposide, prednisone, vincristine, doxorubicin and cyclophosphamide). A FDG PET/CT dated 17th august 2022 showed complete metabolic response. After a disease free interval (DFI) of 4 months, a FDG PET/CT done on 27th December 2022 showed multiple hypermetabolic lesions involving left cerebral cortex (Figure 1). He received WBRT (10#/30Gy) till 23rd January 2023 and was referred to

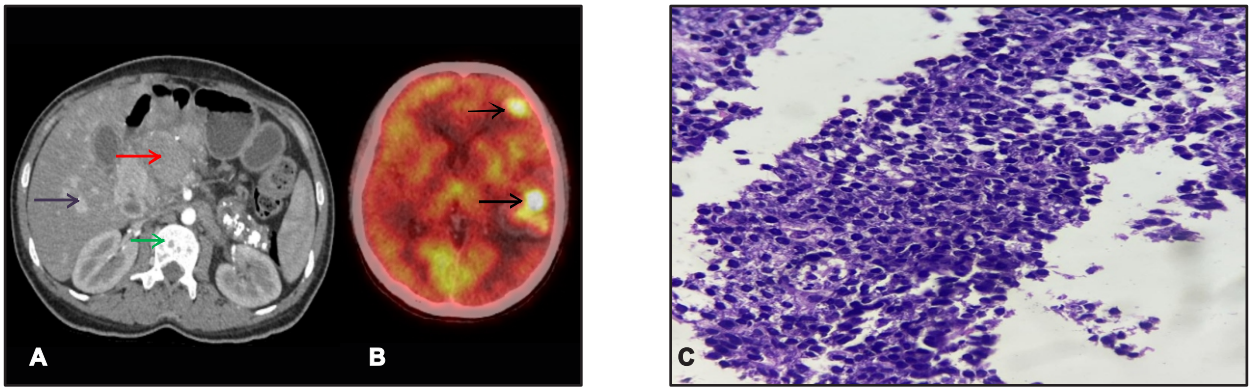
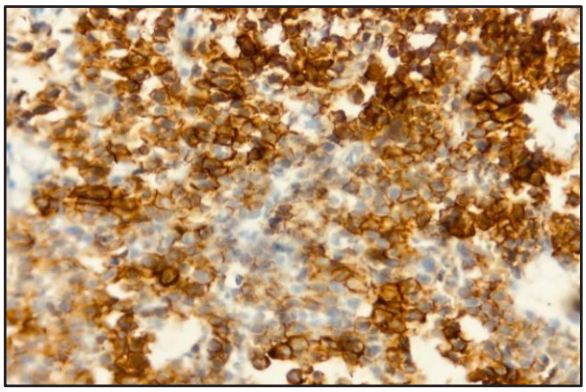
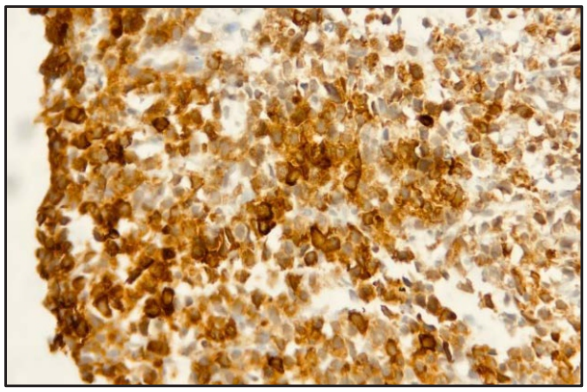


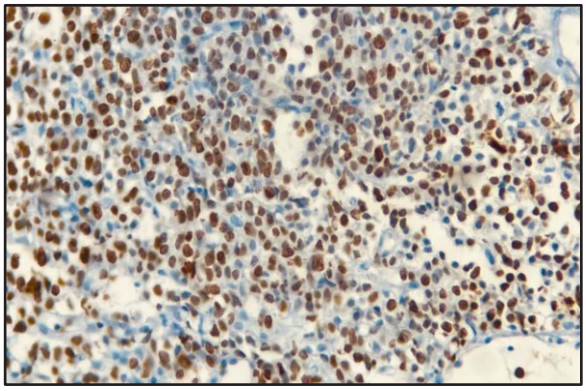
Figure 1: Clockwise from top left- **A)** CT imaging of the abdomen showing pancreatic mass (red arrow), hyperdense liver lesions (purple arrow) and lytic lesions in vertebral body (green arrow) **B)** FDG-PET showing hypermetabolic lesion in left cerebral hemisphere (black arrows) after DFI of 4 months **C)** Histopathology of pancreatic biopsy shows sheets of atypical medium sized to large cells with round nuclei displaying vesicular chromatin and distinct nucleoli with moderate amphophilic cytoplasm and brisk mitotic activity



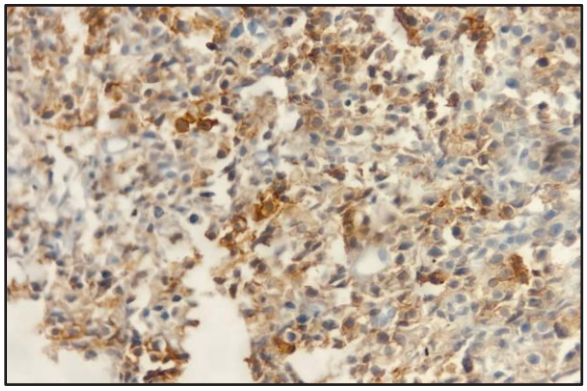
A) CD138 positve



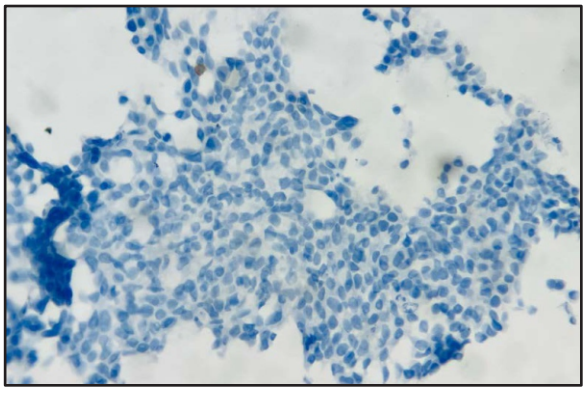
B) CD79a positive



C) MUM 1 positive (nuclear)



D) CD38 positive



E) CD20 negative

Figure 2:IHC showing cells positive for A)CD138, B) CD79a, C) MUM 1, D) Cd38 and negative for E) CD20

our institute for further management. Blood investigations including complete blood count, liver function tests, renal function tests and lactate dehydrogenase were within normal limits. The pancreatic biopsy and histopathology review was done at our institute (Figure 1). IHC showed cells that were positive for CD79a, CD38, CD138, MUM-1 and negative for CD20, CD3, PAX 5, AE1, synaptophysin (Figure 2). His cerebrospinal fluid examination was haemorrhagic. Bone marrow aspiration and trephine bone biopsy, serum protein electrophoresis, immunofixation and free light chain assay done to rule out plasmablastic myeloma were found to be normal.

He was started on DHAP as a salvage regimen but unfortunately the patient died of infectious complications secondary to neutropenia despite prophylaxis with pegylated granulocyte stimulating factor.

Discussion

PBL accounts for 2% of HIV-related lymphomas in incidence. The association of PBL with HIV and EBV coinfection occurs commonly, but its occurrence in patients with autoimmune disorders, lymphoproliferative disorders and in those who have undergone solid organ transplantation has also been described.[4] PBL has a tendency to involve extra medullary sites like oral cavity (most common), lung, bone, sinus, testicles and gastrointestinal tract.[5] At first presentation, our patient had a pancreatic mass and at relapse, he had involvement of left cerebral hemisphere.

PBL is thought to originate from plasmablast, an activated B cell that has undergone somatic hypermutation and class switching recombination.[4] The cells in PBL show an immunoblastic morphology with an immunophenotype suggestive of plasmacytic differentiation with CD38, CD138, IRF-4/MUM-1 and BLIMP-1and negative for B-cell markers CD19, CD20 and PAX-5.[4] EBER is expressed in 70% of the cases & it is the most sensitive method of detecting EBV infection within malignant cells and is more commonly seen in HIV-positive patients (75%). Plasmablastic or anaplastic multiple myeloma is the closest differential as they may be morphologically and immunophenotypically identical to PBL.[4] Features that are in favour of PBL include an association with HIV infection and EBER positivity in neoplastic cells while monoclonal paraproteinemia, hypercalcemia, renal dysfunction and lytic bone lesions favour myeloma.[4] Our patient's investigations showed EBER positivity but also had multiple lytic lesions. But further investigations such as protein electrophoresis, immunofixation, trephine bone biopsy showed absence of monoclonal protein and absence of bone marrow plasmacytosis.

Cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) is not considered adequate therapy[4,5] and current guidelines favour more aggressive regimens such as infusional EPOCH,[6] cyclophosphamide, vincristine, doxorubicin, methotrexate alternating with ifosfamide, etoposide, and cytarabine (CODOX-M/IVAC),[7] or hyper fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with methotrexate and cytarabine (hyper-CVAD).[8] There is a high risk of CNS progression at time of initial treatment or during relapse which makes intrathecal CNS prophylaxis essential.[4,9] Although our patient had complete remission post EPOCH, he did not receive intrathecal CNS prophylaxis while being treated elsewhere which could explain the isolated disease recurrence in the CNS within three months.

Conclusion

PBL is a rare disease, typically extranodal in nature, can have unusual presentations both at diagnosis and at relapse. Differentiating this entity from myeloma is important. Intrathecal CNS prophylaxis is an essential component in the management of PBL. The disease poses challenges in diagnosis, treatment and has a dismal outcome. Ideal management strategy has not been established in the relapsed setting.

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