Extra oral Plasmablastic lymphoma with Pleural Effusion- Rare Case

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Abstract

Plasmablastic lymphoma is extremely uncommon. Mostly they are found in HIV positive/immunodeficient patients. Fine needle aspiration cytology (FNAC) is increasingly used as a primary diagnostic procedure to diagnose lymphoma. But FNAC alone cannot differentiate between Plasmablastic lymphoma (PBL) and extramedullary plasmacytoma (EMP) and biopsy with histopathological examination/other ancillary techniques are used for confirmation. The distinction is important as the latter have a completely different therapy and a better prognosis than PBL. We are reporting a case of PBL in a HIV positive 40 year old male patient, presenting initially with a primary scalp swelling and later on with a soft tissue neck swelling with left sided pleural effusion. The patient was initially erroneously diagnosed as extramedullary Plasmacytoma. The diagnostic dilemma that we faced along with a review of literature is added to help other cytopathologists to avoid misdiagnosis of this rare lymphoma.

Keywords: Extramedullary Plasmacytoma, Fine needle aspiration cytology (FNAC), Plasmablastic lymphoma

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Introduction

Plasmablastic lymphoma (PBL) is an uncommon(2.6% of NHL in HIV positive patients)[1] aggressive B-cell non Hodgkin's lymphoma(NHL) arising mostly in the jaw and oral mucosa in HIV-infected patients, as described initially in 1997 by Delecuse et al.[2] Since then, it has been encountered in other extra oral sites (Gastrointestinal, orbit, skin, bone, soft

tissues) in HIV positive and lymph nodes mainly in HIV negative patients.[3] A recent study by Hansra D et al[4] has shown two distinct subtypes of PBL-oral and extra oral . The oral PBL (80% associated with HIV) , as already described by Delecuse et al [2] shows a monomorphic plasmablastic morphology without plasmacytoid differentiation(large cells with scanty cytoplasm, prominent nucleoli, fine reticular chromatin) and has a better prognosis.[3] The extraoral PBL (30-50%associated with HIV) displays a plasmacytoid differentiation with a bimorphic population (large cells with increased cytoplasm, eccentric nucleus, small nucleoli, clumped chromatin and smaller cells with plasmacytic differentiation).[4] Although both show the same characteristic phenotype[3] of PBL (i.e. positive for plasma cell markers (CD38, CD138, MUM-1) and negative for B-cell markers(CD19,CD20,CD45, PAX-5)), they differ slightly in the expression of ki67, CD56 and EBER. While the oral subtype is CD56 negative and has high expression of ki-67 and EBER, the extraoral may express CD56, but has a variable expression of ki-67 and EBER.[4] FNAC is now increasingly used as a 1st line investigation in the diagnosis of lymphoma. As the PBLs have a varied cytologic spectrum, FNAC findings are also varied. As reported in earlier case reports and case series, FNAC in PBL shows heterogeneous cytological findings- ranging from large immature tumour cells (immunoblasts, plasmablasts) to cells with a mature plasmacytic differentiation, which present in a variable and somewhat overlapping maturity range.[5, 6]

Case summary

A 40 year old asymptomatic male presented with a complaint of single localized swelling on the scalp (occipital region) measuring 5x4x3 cm2 (Figure 1a). An FNAC was performed from the swelling (Figure 1b), and was initially diagnosed as extramedullary plasmacytoma. Bone marrow aspiration performed at that time showed only 2% plasma cells, with no M-protein band in serum and urine electrophoresis.

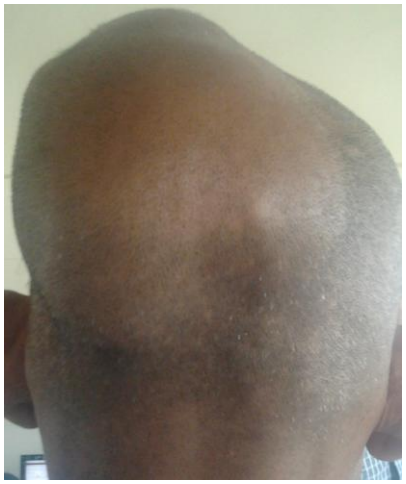


Figure1a: Scalp swelling

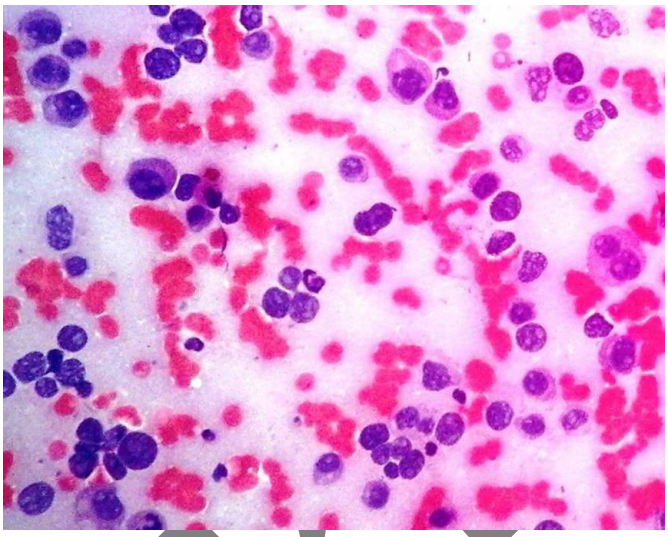
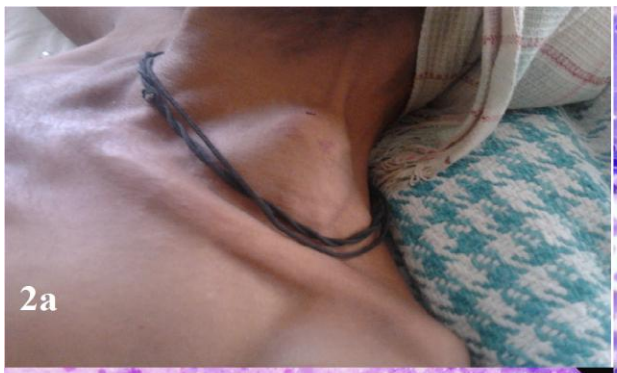
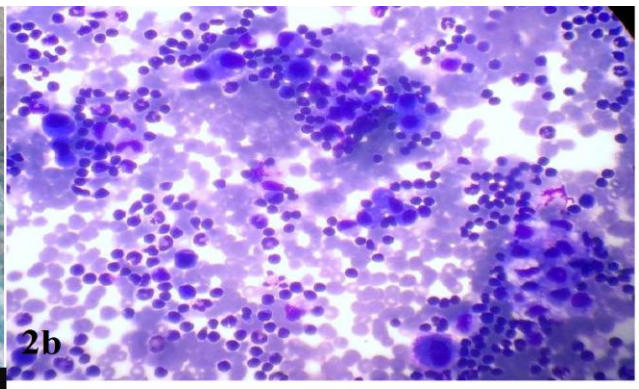


Figure1b:FNAC from scalp swelling showing Plasmacytoid cells and atypical lymphoid cells

The patient was lost in follow up and was admitted 6 months later with a complaint of exertional dyspnoea, fever with chills ,vomiting and a left supraclavicular swelling(3x3 cm2, firm ,nontender). Further investigations revealed that the patient was HIV +ve, had a left sided massive pleural effusion with no hepatosplenomegaly or lymphadenopathy. Peripheral smear was unremarkable. Renal function tests were normal. FNAC was performed from the left supraclavicular swelling (Figure 2a), which showed two cell populations (plasmacytoid and round cells) predominantly singly scattered. The round cells showed heterogeneous population with high N: C ratio, irregular nuclear membrane, coarsely granular chromatin, prominent multiple 2-3 nucleoli and scanty cytoplasm.The plasmacytoid population consisted of mature and immature plasma cells, with central/eccentric nucleus, coarsely granular chromatin, single/multiple prominent nucleoli and variable amount of basophilic cytoplasm. Bi/multinucleated plasmacytoid cells were also seen.Background showed chunk of hyaline material, typical and atypical mitosis, and foamy/tingible body macrophages (Figure 2b). Pleural fluid examination showed the same cytological features as seen in the supraclavicular FNAC (Figure 2c).





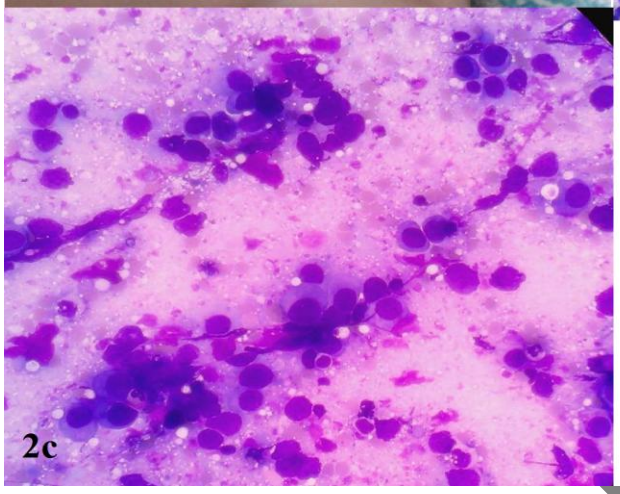


figure 2a,left supraclavicular swelling

2b.Fnac from left supraclavicular swelling showing atypical plasmacytoid cells.

2c. pleural fluid examination from showing same cytologfy as in left supraclavicular swelling.

Considering the clinical history and cytological findings, possibility of Plasmablastic lymphoma was offered, with a 2nd possibility of NHL with plasmacytoid differentiation.

A subsequent biopsy showed a tumour composed of plasmablasts with atypical lymphoid cells and plasma cells. The cells expressed CD138 and EMA and were immune-negative for LCA, CD56, CD20 and inconclusive for EBV which confirmed the cytological diagnosis of plasmablastic lymphoma (Figure 3)

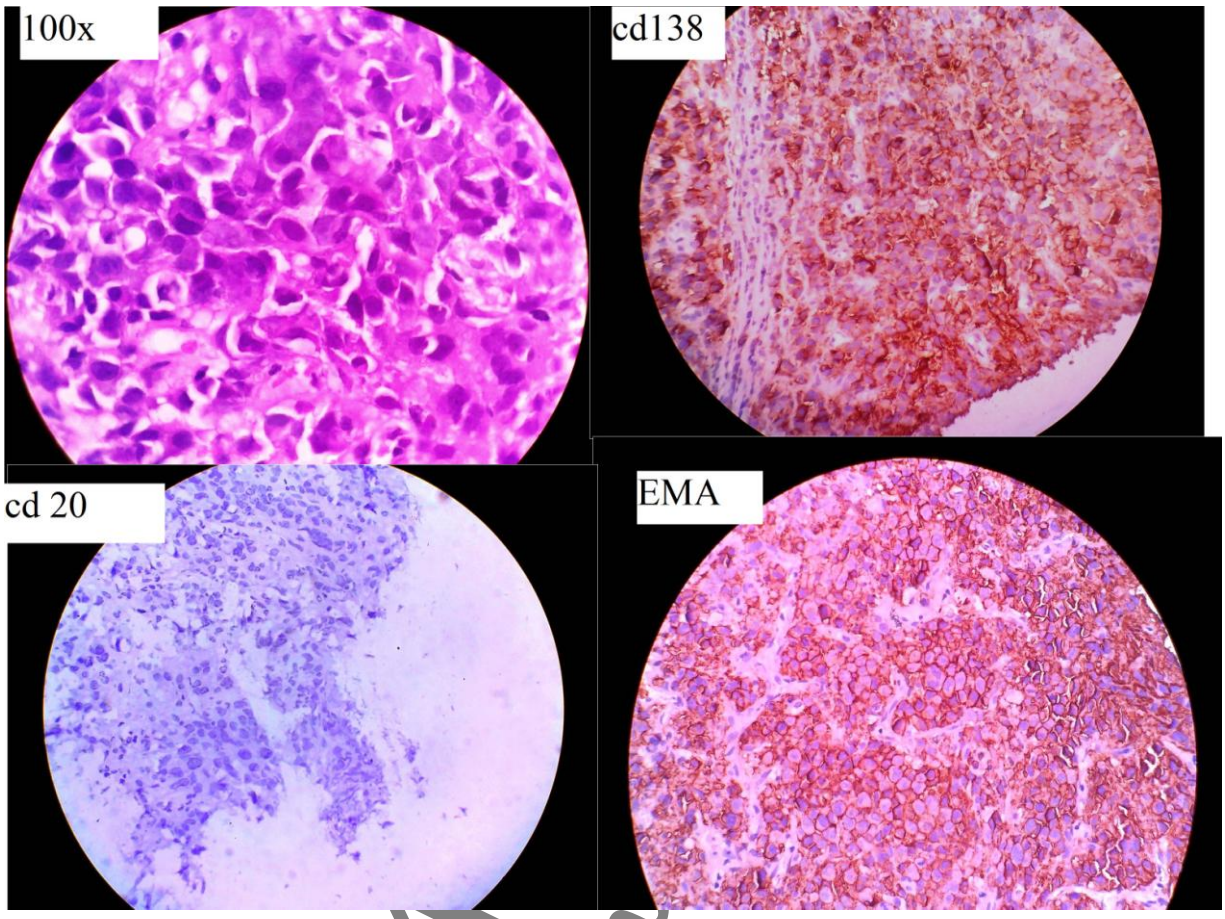


Figure 3: (biopsy and ihc findings)-The picture to the topmost left is H/E section showing plasmacytoid cells arranged in sheets. The plasmacytoid cells are CD 138+ve and EMA +ve and are negative for CD20. EBV was inconclusive (not shown in picture).

Discussion

HIV positive patients have a higher incidence of haematopoietic malignancies. The most common HIV-associated lymphomas include Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBCL) (often involving the central nervous system), Primary effusion lymphoma (PEL), and plasmablastic lymphoma (PBL).[7]

The important differential diagnoses that we considered in our case were a) Plasma cell neoplasm (extramedullary plasmacytoma) (EMP) b) PBL c) B-cell NHL with plasmacytoid differentiation.

Out of these, it is clinically important and critical to differentiate EMP and PBLs, as the treatment for these two diseases is significantly different, with the former having a better prognosis. EMP is very difficult to distinguish from PBL

(extraoral) on FNAC because both show a plasmacytoid differentiation. Clinical history is also not helpful, as neither show any bone marrow involvement, any M-protein, or any symptoms of myeloma. However, unlike PBL(extraoral), which consists of a dual population of cells(large plasmablastic cells and small cells with plasmacytoid differentiation)[3], a plasmacytoma typically consists of mature plasma cells without a high rate of mitotic activity.[5] Immunophenotypically, both express CD38, CD138 and often express CD56 (more in plasma cell myeloma and in PBL with plasmacytoid differentiation-extraoral type and rarely in extramedullary plasmacytoma).[8] EBER may help in differentiating the two, as PBL is usually EBER +ve(more in oral type than extraoral plasmacytoid variant).[4] Only the expression of μ rather than γ heavy chain favours the diagnosis of lymphoma over plasmacytoma.[9] However, clinical history and biochemical investigations can easily differentiate between PBL and plasmablastic/anaplastic myeloma. The detection of paraproteinaemia in blood and/or excess light chains (Bence- Jones proteins) in urine, lytic bone lesions(on CT/PET scan), and hypercalcaemia or anaemia favours the diagnosis of a plasma cell myeloma over PBL.[9] Also ,the proliferative fraction highlighted by MIB-1 is much higher in PBLs (range,75-100%) compared with anaplastic plasmacytoma(60%) and myelomas (5%).[6] Therefore, a combined clinical, morphologic, immunophenotypic, and laboratory data are necessary to distinguish PBL from blastic transformation of a plasma cell neoplasm.

A dual immunostaining of CD56 and CD19 can differentiate between B-cell NHL with plasmacytoid differentiation and myeloma/plasmacytoma(detection of CD19 expression by neoplastic plasma cells in an individual plasmacytic neoplasm would increase the likelihood of its being a B-cell NHL, and the absence of CD19 and/or presence of bright CD56 expression favours myeloma/plasmacytoma).[10]

In our case, the solitary presentation of scalp swelling in an asymptomatic patient initially led us to the erroneous diagnosis of EMP. An absence of bone marrow involvement and M-Protein band in electrophoresis ruled out MM/plasmablastic myeloma. However, when the patient later presented with a

neck mass and massive left sided pleural effusion, and with the additional history of being HIV positive, a provisional diagnosis of lymphoma was thought off. The characteristic FNAC finding of dual population of cells (plasmacytoid and round cells) favoured a diagnosis of Plasmablastic lymphoma, considering the fact that the patient was HIV positive.

Possibility of PEL was also considered as the patient presented with a malignant effusion with cells showing plasmacytoid morphology. PEL usually presents with serous effusions without any tumour mass in HIV positive patients, but may rarely present with extranodal tumour mass. They have almost the same immunophenotype as that of PBL (expression of CD38, and CD138, and negative for CD19, CD20, CD79a, and immunoglobulin expression), except for CD45 which is positive in PEL only.[11] However clinically, the differential diagnosis of extracavitary PEL from PBL may not be crucial because both represent high-grade lymphomas, which can be treated in a similar fashion. As our patient 1st presented with scalp swelling and later with pleural effusion, possibility of PEL was excluded.

Conclusion:

The clinical features of PBL, which include its association with HIV, the male gender and predilection for the oral cavity, may help in the differential diagnosis, however, an extra-oral location with an inadequate clinical history makes it more difficult to diagnose on cytology alone. This case highlights an unusual presentation of PBL which presented as a soft tissue mass along with pleural effusion. Hence, PBL should be included in the differential diagnosis of soft tissue masses in HIV positive patients. A proper history should be taken(HIV status, myeloma symptoms) and proper biochemical(M-protein, renal function tests) and haematological investigations(bone marrow investigations) should be carried out in any patient presenting with an unusual soft tissue mass showing malignant plasma cells on fnac. As Extramedullary plasmacytoma and Plasmablastic lymphoma are extremely difficult to differentiate on cytology alone, the cytological findings should be interpreted in the light of the clinic-patho-radiological findings to come to a correct diagnosis.

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