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CASE REPORT

Plasmablastic Lymphoma of the Endometrium: A Rare Site for Primary Presentation

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Abstract

Global incidence of non-Hodgkin's lymphoma (NHL) is 3% of which 1% occurs in extranodal lymphoma. Plasmablastic lymphoma (PBL) is a rare and aggressive variant of diffuse large B-cell lymphoma (DLBCL). It is usually seen in human immunodeficiency virus (HIV) infected patients. PBL occurring in extranodal site, particularly female genital tract, is very rare, and only few case reports have been reported. Here, we report a unique rare case of uterine PBL in an HIV/Epstein–Barr virus-negative patient that was initially diagnosed as endometrioid carcinoma.

Introduction

Global incidence of non-Hodgkin's lymphoma (NHL) is 3% of which 1% occurs in extranodal lymphoma [1]. Among them, diffuse large B-cell lymphoma (DLBCL) is the most common subtype, accounting for 50% of the cases [2]. Plasmablastic lymphoma (PBL) is a rare and aggressive variant of DLBCL with plasmablastic features, commonly occurs in the oral cavity of human immunodeficiency virus (HIV) infected patients. Primary female genital system lymphoma (PFGSL) is a rare disease, accounting for 0.21–1.1% of extranodal lymphoma [2, 3]. It usually involves ovary, uterus, vagina and vulva.

Case Report

A 29-year-old female (gravida2, para 2) presented with complaints of irregular menstrual bleeding since 6 months. She consulted a gynaecologist where she was advised removal of the Copper T inserted 3 years back in view of infection diagnosed on TVUS, following which she was prescribed medication for 3 months for regularisation of the menstrual cycle. She developed heavy bleeding during the next cycle. She had no other systemic complaints. No other comorbidities were present. On examination, polypoidal growth felt coming from uterus and cervix appeared normal.

USG pelvis revealed bulky uterus with endometrial thickness of 29 mm. Endometrial curettage was done and sent for histopathological examination (HPE) which was suggestive of poorly differentiated adenocarcinoma favouring

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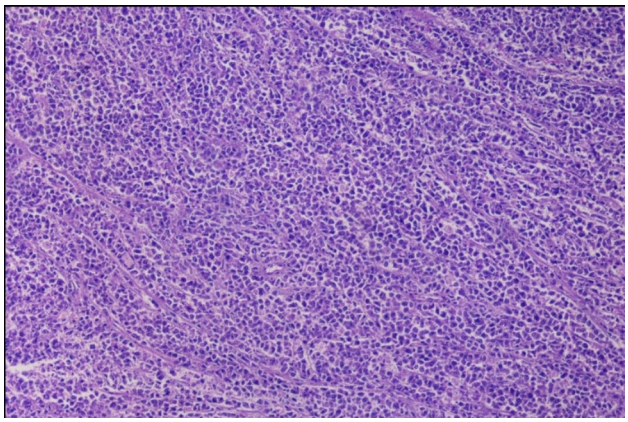

Fig. 1 Section studied shows a tumor arranged in sheets within the myometrium. Individual cells are large atypical lymphoid cells having vesicular nuclei multiple prominent nucleoli and moderate cytoplasm

endometrioid carcinoma. Following this, patient was referred to surgical oncologist for further management. CECT abdomen and pelvis showed soft tissue density growth in the endometrial cavity measuring 2.8(TR) × 1.7(AP) × 4.6(CC) with no involvement of growth outside myometrium and no obvious cervical growth or enlarged pelvic nodes. She underwent radical hysterectomy with pelvic lymphadenectomy, intraoperatively endometrial lesion was seen protruding through the cervix. HPE showed poorly differentiated neoplasm suggested for immunohistochemistry (IHC), and all pelvic nodes were reactive, Fig. 1.

On IHC tumour cells were strongly positive for CD138 (Fig. 2a) and showed kappa light chain restriction and were positive for MUM-1, Pax-5, CD79A (focal) and had 90% Ki-67 proliferation index (Fig. 2b), but were negative for CD3, CD56 and CD20 (Fig. 2c). The Epstein–Barr virus (EBV) encoded small RNAs in situ hybridisation revealed negative findings (Fig. 2dD). This IHC profile was consistent with PBL.

Discussion

PBL is an aggressive type of lymphoma, and it is very rare. It was first seen in 1997 in the oral cavity of HIV patient. PBL is an aggressive, uncommon subtype of DLBL with

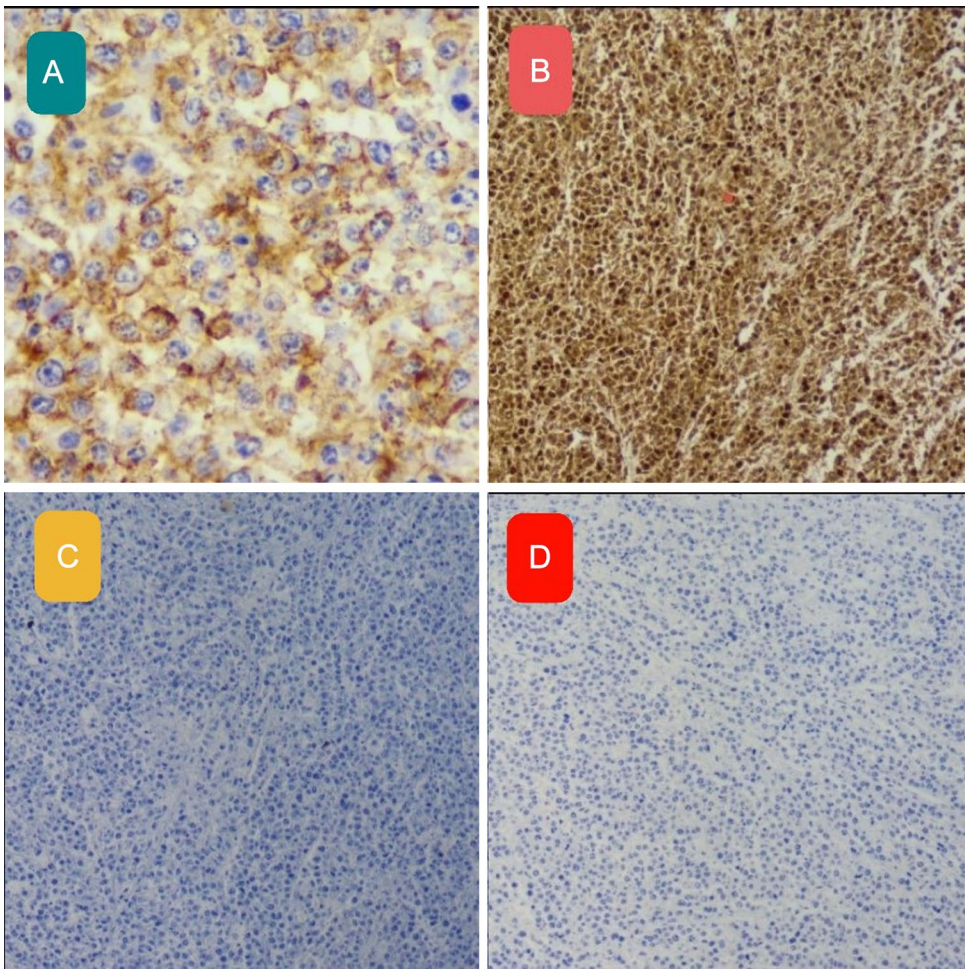

Fig. 2 Then, patient underwent definitive staging workup with whole body PET-CT scan and bone marrow biopsy which was normal. Patient received 6 cycles of EPOCH chemotherapy (Etoposide, vincristine, doxorubicin, endoxan, prednisolone). Her follow-up PET-CT scan after 6 months did not show any residual disease

relapse common after chemotherapy. PFGSL accounts for only 0.21–1.1% of extranodal NHL [2, 3] and can involve ovary, uterus, vagina and vulva. PBL occurring in female genital tract is very rare, and only few case reports have reported of PBL involving endometrium. DLBCL accounts for 35% of NHL. DLBCL will be either CD20 positive (98%) or negative (2%), and DLBCL with CD20 negative has complex genetics, histopathology and therapeutic resistance. Most common subtype of CD20-negative DLBCL is PBL, accounting for 75% cases [4]. PBL is common in men commonly occurring in 4th decade. PBL commonly involves extranodal sites like the oral cavity, gastrointestinal tract and skin, and other less common sites include the central nervous system, paranasal sinus, mediastinum, lungs, liver, retroperitoneum and soft tissues. In 30% of cases, bone marrow involvement is seen.

Its difficulty to diagnose uterine lymphoma preoperatively as patients does not have classical symptoms like abdominal pain, distension, per vaginal bleeding or haematuria or gastrointestinal symptoms. Physical symptoms like fever, night sweats or weight loss in only in 17% of NHL.

Viral serologies like HIV or EBV must be included in the workup as PBL is commonly seen in them; however, it was negative in our case. If biopsy is suggestive of poorly differentiated neoplasm, it is better to IHC to know the definitive diagnosis. PBL is also seen in association with immunocompromised states like high-dose steroid therapy, pre-existing lymphoproliferative diseases and advanced age.

Differential diagnosis for PBL is poorly differentiated carcinomas, gastrointestinal stromal tumours, multiple myeloma, Burkitt's lymphoma, anaplastic large cell lymphoma and leukaemia.

Long-term intrauterine device implantation and poor intrauterine environment may lead to chronic inflammation which resulted in DLBCL because of chronic inflammation [5]; similar history was seen in our case.

Histopathology is mandatory in the diagnosis. On histopathology, PBL cells exhibit a typical high-grade tumour. As they lack the expression of B-cell markers (CD19, CD20, PAX5) with focal expression of leukocyte common antigen (CD45), it is very difficult to diagnose PBL. They frequently express CD79a, BLIMP-1, IRF4/MUM1, CD38 and CD138, thus adding B-cell lymphoma and multiple myeloma to the list of differentials. Similarly, in our case, CD38, CD138 and MUM1 markers were positive, and CD20 and CD79 were negative. Usually, PBL exhibits a high proliferation index as detected by high Ki-67 levels same was seen in our case that Ki67 was 90%, which is poor prognostic factor.

There are no standard treatment guidelines in PFGSL and are often treated with surgery and chemotherapy combined with radiotherapy according to the patient's situation. There is no standard treatment regimen for PBL. CD20 negativity confers lack of responsiveness to rituximab and other conventional drugs, thereby posing a unique challenge. Present guidelines recommend against the use of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) due to poor outcomes. Few studies have shown favourable outcomes with the following regimens: EPOCH (infusion etoposide, vincristine and doxorubicin along with bolus cyclophosphamide and prednisone), CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, methotrexate alternating with ifosfamide, etoposide, cytarabine) and hyper-CVAD (cyclophosphamide, vincristine, doxorubicin and dexamethasone alternating with high-dose methotrexate and cytarabine).

Role for transplant in these patients is not clear. Interestingly, due to the plasmacytic nature of PBL, drugs from the myeloma line like bortezomib have been tried with limited success. Case reports advocating the use of a combination of bortezomib and EPOCH, lenalidomide and brentuximab in PBL are also present.

The overall prognosis is poor with many systematic reviews reporting median overall survival ranging between 9 and 15 months, 19 months in HIV negative patients compared with 15 months in HIV-infected patients.

Conclusion

Lymphomas of the female genital tract are rare and uterine PBL being even more uncommon. Our case demonstrates a rare presentation of PBL and the challenges faced in diagnosing and treating these patients, because of the paucity of reported cases and the absence of a standard therapy. This may facilitate early diagnosis and implementation of treatment of the patient.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Informed consent was obtained from the patient mentioned in the case report.

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