CASE REPORT

Rare presentation of orbital plasmablastic lymphoma with oral cavity involvement in an HIV-negative patient

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SUMMARY

Plasmablastic lymphoma is described as a subtype of non-Hodgkin's lymphoma under the category of diffuse large B-cell lymphoma. It is classified by WHO as HIV-associated lymphoma of the oral cavity. Several cases have been reported in non-HIV patients with extra-oral involvement. The characteristic immunohistochemical markers are generally positive for CD138, CD38 and MUM1/IRF4, and negative or weakly positive for pan B-cell markers CD20, CD79a, PAX-5 and BCL-6. We report a rare case of orbital plasmablastic lymphoma with oral and oropharyngeal involvement where the immunohistochemical markers were positive for CD138, CD43, CD45, CD79a and MUM1. A small subset of markers was weakly positive for CD20, CD30 and κ , and negative for CD10, BCL-6, CD4, CD56 and Epstein-Barr virus-encoded small RNA (EBER). Our case reinforces the fact that plasmablastic lymphoma is a different entity of non-Hodgkin's lymphoma that cannot simply be classified under diffuse large B-cell lymphoma. It demands modification of the WHO classification.

BACKGROUND

Plasmablastic lymphoma (PBL) is an entity of diffuse large B-cell lymphoma (DLBCL) having morphological resemblance to B-cell immunoblasts. It has an immune profile similar to plasma cells, with absence of monoclonal protein and bone marrow involvement. PBL was first described by Delecluse *et al*¹ in 1997, when they reported a series of patients with highly malignant DLBCLs of the oral cavity in association with HIV-positive patients.

Later, in 2001, the WHO described PBL as a variant of DLBCL.² A literature review suggested that PBL accounts for 2.6% of HIV-associated non-Hodgkin's lymphomas and is commonly seen in the oral cavity.³ Scheper *et al*⁴ first presented a PBL in a non-HIV patient in 2004. Tavora *et al*⁵ tabulated 33 extra-oral cases of patients with PBL in 2006. Among these 33 extra-oral cases, lymph node involvement—6; anus involvement—6; skin involvement—5; maxillary sinus involvement—5; nose involvement—2; skull involvement—2; soft tissue involvement (unspecified)—2; stomach involvement—1; small bowel involvement—1; nasopharynx involvement—1; lung involvement—1; and spermatic cord involvement—1, were reported. Several other PBLs in non-HIV with extra-oral cases have been described in the English language literature.⁶

In the published cases, treatment mostly consisted of a chemotherapy regimen using prednisone, cyclophosphamide, adriamycin and/or vincristine, or local excision followed by radiotherapy.⁴ The clinical course of PBL has often been described as very aggressive and with a poor prognosis. Death usually occurs within 1–24 months after diagnosis; the median average survival is 6 months.⁷

We report a case of PBL with left orbital involvement and loss of vision in an HIV-negative patient.

CASE PRESENTATION

A 71-year-old man from Nigeria presented with swelling and protrusion of the left eye for a period of 6 months. Initially, he had diminished vision in the left eye and, subsequently, the eyeball began to gradually protrude, with complete loss of vision. He also had throat discomfort, which was associated with palatal swelling and narrowing of the oropharyngeal pathway leading to oropharyngeal dysphagia. Symptoms of dysphagia permitted the patient to take liquid food only. His social history was negative for smoking and alcohol abuse. The medical history was significant only for hypertension. Family history was negative for any malignancy.

On physical examination, vitals including oxygen saturation were normal. The patient was found to have severe proptosis of the left eye: a fleshy visible mass protruded anteriorly, superiorly, inferiorly and laterally around the eye (figure 1). Three superior cervical lymph nodes (two on the left and one on the right), the largest being 2 cm in size, were palpable. Narrowing of the oropharyngeal airway was noted, with mild palatal bulging. Eye examination revealed visual acuity with +2.5 readers 20/60 in the right eye and no light perception in the left eye.

Figure 1 Patient's face at presentation.

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The extraocular muscle in the left eye 2/4 adduction, 0/4 supra-duction, and abduction, 1/4 infraduction and right eye findings were normal. The pupils were round and reactive bilaterally, with an afferent pupillary defect in the left eye. The chest was clear on auscultation. Cardiovascular, abdominal and remaining neurological examinations were normal.

INVESTIGATIONS

Initial laboratory tests were significant for microcytic anaemia with haemoglobin/haematocrit: 9.9/31.1, mean corpuscular volume: 76 and elevated blood urea nitrogen/Cr: 57/2.5 suggestive of dehydration owing to decreased fluid intake. Imaging was performed to evaluate the eye and oral cavity. CT scan demonstrated left orbital, palatal, sublingual and oral floor cavity masses with enlarged adenoids and lymphadenopathy. Further MRI was carried out to better characterise the lesions, demonstrating a lobular mass within the superolateral quadrant of the left orbit. This mass displaced the globe, optic nerve, superior rectus and lateral rectus muscles. The mass appeared central to the lacrimal gland, measured 5.9 cm anteroposteriorly, 2.6 cm in width and 2.9 cm craniocaudally, and eroded the roof of the orbit. There was no intracranial extension (figure 2A–F).

Enlarged nasopharyngeal soft tissue was seen slightly eccentric towards the right. Enlarged retropharyngeal lymph nodes were also present. Additionally, there was an abnormal lobulated soft tissue palatal mass measuring 4 cm anteroposteriorly, 4.7 cm in width and 2.5 cm craniocaudally, which appeared to extend to the retromolar space on the right (figure 3A, B). There were also small multiple mental, submental and retropharyngeal lymph nodes noticed in the imaging.

Relative decreased signal in T-2 imaging suggested diagnosis towards lymphoma. Cerebrospinal fluid analysis was negative for malignant cells and total white cell count was 1/hpf.

Subsequently, a biopsy was performed from the soft palate lesion. Histopathology revealed a uniform population of large cells with a moderate amount of cytoplasm and nuclei (figure 4A, B). Immunohistochemical study revealed large atypical cell phenotype: CD45 positive, CD79a positive, CD138 positive and MUM-1 positive (figures 4C, D and 5E–H). Some of the large cells showed weak cytoplasmic κ positivity. A small subset of large cells showed weak positivity for CD30 and CD20,

Figure 2 MRI of the brain and face: lobular mass within the superolateral quadrant of the left orbit. This mass displaced the globe and optic nerve. Relative decreased signal in T-2 imaging suggested diagnosis of a lymphoma. (A) Axial diffusion-weighted imaging (DWI); (B) axial T1 post; (C) coronal view; (D) 3D susceptibility-weighted angiography (SWAN); (E) axial T2 and (F) coronal thin post fat.

Figure 3 MRI of the neck and soft tissue: lobulated soft tissue palatal mass appeared to extend to the retromolar lesion on the right; (A) sagittal view and (B) coronal view.

which is, overall, characteristic of PBL. Epstein-Barr virus (EBV) serology and HIV study were negative.

While waiting for the biopsy results, the patient's airway was severely compromised and he needed intubation to protect the airway.

DIAGNOSIS

A diagnosis of plasmablastic lymphoma was confirmed.

TREATMENT

The patient was started on chemotherapy, in an intubated state, with an R-CODOX regimen, which is composed of cyclophosphamide, doxorubicin, vincristine, leucovorin, methotrexate, cytarabine and rituximab (a monoclonal antibody).

OUTCOME AND FOLLOW-UP

The patient tolerated the first cycle of chemotherapy very well. There was significant response to the therapy and the patient was subsequently extubated after a weaning trial. His tumour size clinically decreased with clinical remission in 1 week. He was discharged home with outpatient follow-up. Later, he was administered a second cycle of chemotherapy with an IVAC regimen, which includes ifosfamide with mesna, etoposide, cytarabine and methotrexate. His vision in the left eye started to improve and subsequently returned to normal. The throat and proptosis of the eye were stable during follow-up (figure 6).

Figure 4 (A and B) Plasmablastic differentiation showing uniform population of large cells with a moderate amount of cytoplasm and a nucleus (H&E staining). (C and D) Markers: (C) CD8 positive cells and (D) CD45 positive cells (immunohistochemical staining).

Figure 5 Immunohistochemical staining. (A) CD 79a positive cells; (B) CD138 positive cells; (C) MUM1 positive cells; (D) high proliferation index of ki67.

DISCUSSION

PBL is a rare entity of non-Hodgkin's lymphoma, initially described with involvement of the oral cavity in an HIV-positive patient. However, it has subsequently been reported in non-HIV patients with extra-oral site involvement. Extra-oral sites reported involved the skin, lymph node, stomach, small intestine, anus, skull, maxillary sinus, nose, nasopharynx, lung and spermatic cord. It is reported to be a very aggressive lymphoma with median survival of 6 months.⁶

Our patient had a complicated presentation with left orbital swelling along with oral cavity, oropharyngeal, cervical and retropharyngeal lymphadenopathy. Neoplastic cells in PBL express a plasma cell phenotype including positivity for CD138, CD38, Vs 38c and MUM1/IRF4. Also, several others plasma cell markers such as CD56, CD10 and CD4 are observed aberrantly in PBL.⁸ The proliferation Ki67 index is usually very high in >90% of cases, with EBV EBER in situ hybridisation positive in 60–75% of cases.² Unlike DLBCL, the pan B-cell antigens CD20, CD79a, PAX-5 and BCL-6 are negative or weakly positive.

Colomo *et al*⁸ categorised PBL into two major subtypes. The first conforms PBL of the oral cavity with immunoblastic morphology, a high rate of association with HIV and EBV, and an unfavourable outcome. The second subtype, PBL with plasmacytic differentiation composed of plasmablasts and immunoblasts, shows more mature plasma cell differentiation. These cells are negative for CD20 and show variable expression for CD79a.

The immunophenotype marker for our patient was positive for CD138, CD43, CD 53, MUM1, CD45 and CD79a. It did

not fit either of the two subtypes, because of positivity for CD79a, weak positivity for CD20 and negativity for EBER. Based on the immunophenotype markers aforementioned, it has been proposed that considering PBL as a variant of DLBCL, as laid down in the WHO classification, is not appropriate.⁹

Our patient has received two cycles of chemotherapy to date, and has shown remarkable improvement in the physical findings. He received R-CODOX in the first cycle and IVAC therapy in the second cycle. Treatment has not been standardised and is presently given on a case-by-case basis. Our case report showed marked improvement, reinforcing the fact that PBL needs further revision for identification of prognostic criteria. We expect standardised treatment for PBL patients based on the prognostic criteria in a non-HIV patient. We also suggest the revision of the WHO classification, as PBL is not only an HIV-associated lymphoma, and extra-oral site involvement is not a rare presentation. Further meta-analysis should be performed to formulate treatment and prognosis guidelines in non-HIV patients.

Learning points

- ▶ Plasmablastic lymphoma (PBL) is characterised by immunoblastic morphology and plasma cell phenotype. These lymphoid cells morphologically resemble B-cell immunoblasts but have acquired a plasma cell immunophenotype. The absence of monoclonal serum protein with no bony involvement favours the diagnosis of PBL.
- ▶ PBL was initially described as an HIV-associated lymphoma. Several cases in non-HIV patients have been reported. Extra-oral presentation of PBL has also been reported. PBL therefore represents a new distinct subtype of diffuse large B-cell lymphoma.
- ▶ The morphological, immunophenotypic and clinical features should be taken into consideration to diagnose PBL and treatment should be individualised.

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Contributors SP contributed to writing of the manuscript, and in the selection of images and pathological slides. PK helped in reviewing the report and in the literature search, and aided in gathering the reference materials. SS was involved in direct patient care and management, and provided ideas towards the writing of the manuscript. KM was directly involved in patient care and contributed to the writing of the manuscript.

Competing interests None declared.

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Figure 6 Post-treatment facial appearance.

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