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Case Report

Plasmablastic lymphoma of nose and para-nasal sinuses in an immunocompetent patient

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ABSTRACT

Plasmablastic lymphoma (PbL) is a rare and aggressive neoplasm with heterogeneous clinical, histological and genetic features. It has been reported in both immuno-compromised and immuno-competent patients and commonly presents in the extra-nodal regions, but it is more heterogeneous in immuno-competent patients. Its clinical course is aggressive with early dissemination and poor response to therapy. A 61 year old male presented with left sided nasal bleeding and nasal obstruction for last 6 months, snoring and disturbed sleep for last 2 months. On examination, there was fullness over left side of nose and obliteration of left naso-facial groove. A mass lesion was seen in the left nasal cavity on endoscopy. There was bulge in the soft palate and the mass extended into the oropharynx. CECT showed a locally aggressive sino-nasal mass. Histopathology and immuno-histo-chemistry (IHC) of the biopsy were suggestive of plasmablastic lymphoma. A debulking surgery was done to relieve his obstructive symptoms. The patient received 3 cycles of EPOCH chemotherapy and radiotherapy to local site. At 9 months of follow up he presented with recurrence of the mass. Plasmablastic lymphoma presents in patients other than those with HIV. Awareness about its unique characteristics is crucial for establishing a correct diagnosis. Currently available treatments are ineffective in achieving long term remission and prognosis remains unfavourable with high incidence of recurrence

Keywords: Plasmablastic lymphoma, Sino-nasal, Neoplasm, Immuno-competent, Chemotherapy, Radiotherapy

INTRODUCTION

PbL is a rare and aggressive neoplasm with morphologic and immunophenotypic characteristics that overlap with aggressive large B-cell lymphomas and plasma cell neoplasms. It constitutes a sub-group of lymphomas with heterogeneous clinical, histological and genetic features. The diagnosis of PbL is a challenge to the pathologist and clinician due to its rarity and lack of specific and optimal treatment guidelines.

It was first described in 1997 by Delecluse et al in patients with human immuno-deficiency virus (HIV).[1] It has later been reported in patients with solid organ transplantation, other immune-suppressed states and even in immuno-competent patients.[2] The incidence of PbL is estimated in 2-12% of all HIV-associated lymphomas. However, the incidence in the immune-competent population is still unknown due to its rarity.[3] PbL commonly presents in extra-nodal regions, the most frequent being the oral cavity, the digestive tract and the skin. Most patients present at an advanced stage (III or IV), with frequent bone marrow involvement and presence of B-symptoms (40% of patients).[4] Its location in HIV-negative patients is more heterogeneous than in HIV-positive patients and bone marrow involvement, as well as B-symptoms are less frequent.[4] Its clinical course is regarded aggressive, associated with early dissemination and poor response to therapy, with overall survival rate between 4-12 months.

Here, we present a case of left sino-nasal plasmablastic lymphoma in an immuno-competent patient because of its clinical rarity.

CASE REPORT

A 61 year old male patient presented with chief complaints of left sided nasal bleeding and nasal obstruction for last 6 months. He also had complaints of snoring and disturbed sleep for last 2 months. He reported no complaints of decreased vision, fever, night sweats or weight loss.

On clinical examination, there was fullness over the left side of nose with obliteration of naso-facial groove (Figure 1). There was no proptosis or diplopia and visual acuity was 6/9 bilaterally. Nasal endoscopy revealed a mass lesion completely obscuring the left nasal cavity. There was appreciable bulge on the soft palate and the mass could be seen extending into the oropharynx. Rest of the ear and throat examination was unremarkable. He had no peripheral lymphadenopathy, organomegaly or any other notable findings.

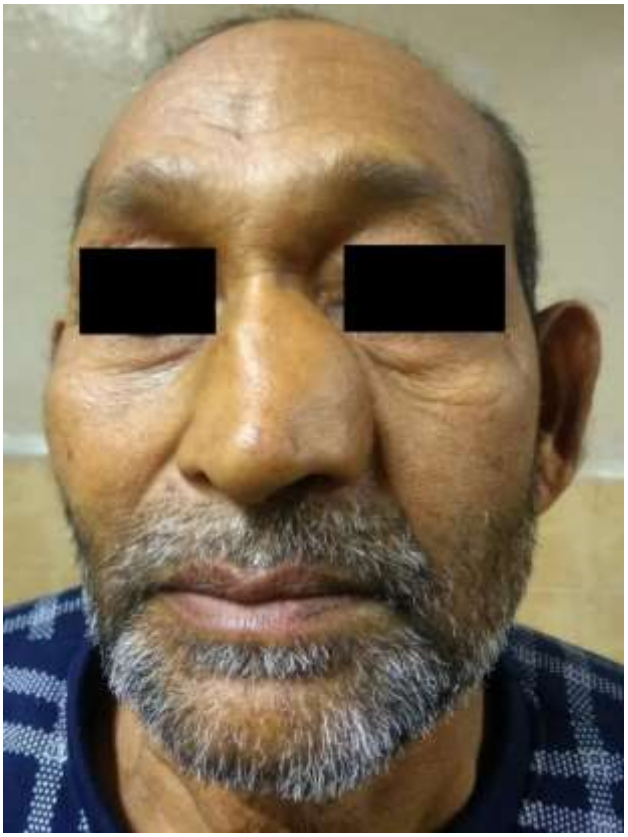

Figure 1: Clinical presentation with fullness over left side of nose.

CECT of nose and para-nasal sinuses (PNS) showed locally aggressive sino-nasal mass lesion of size 4.9×4.5×2.4 cm, involving left side of nasal cavity, maxillary sinus and adjacent ethmoidal sinus with associated post-obstructive frontal sinus opacification, extending to the nasopharynx, with marked adjacent bony erosion. There was no intra-cranial or intra-orbital extension (Figures 2 a and b).

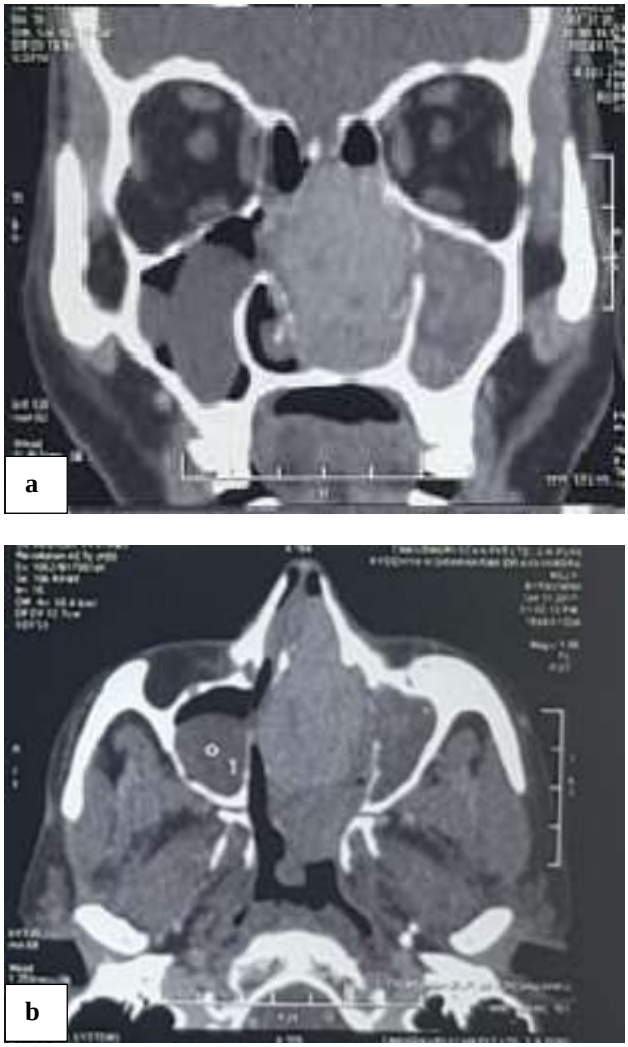

Figure 2: Pre-operative CECT scan showing extent of the mass in nasal cavity and nasopharynx; (a) coronal view; (b) axial view.

Histo-pathological examination of the biopsied specimen showed tissue lined by pseudo-stratified ciliated columnar cells and nuclear atypia at places with multi-nucleation. IHC staining demonstrated reactivity for CD 138, CD 45 and kappa light chain, but no reactivity to CD19, CD20, epithelial membrane antigen (EMA) and lambda light chain. These findings were suggestive of PbL. The patient was further investigated and his haemogram was within normal range, serum lactate dehydrogenase (LDH) was normal, serum and urine electrophoresis revealed no immunoglobulins. Tests for HIV (ELISA) and Epstein-Barr virus (EBER) were negative. A complete radiographic skeletal survey was unremarkable. Bone marrow biopsy was free of lymphoma. Cerebro-spinal fluid was free of malignant cells.

Since, the patient had severe sleep apnoea because of nasal obstruction, a debulking surgery was done via lateral rhinotomy under general anaesthesia and the mass was removed from the left nasal cavity, left ethmoid and maxillary sinuses and naso-pharynx (Figure 3). The histopathological examination of the excised specimen showed diffuse sheets of plasmablasts with starry sky pattern. The tumour cells were large with eccentric nuclei, single central prominent nucleolus and abundant basophilic cytoplasm. Mitotic activity and apoptosis were prominent. The findings further confirmed the diagnosis of PbL.

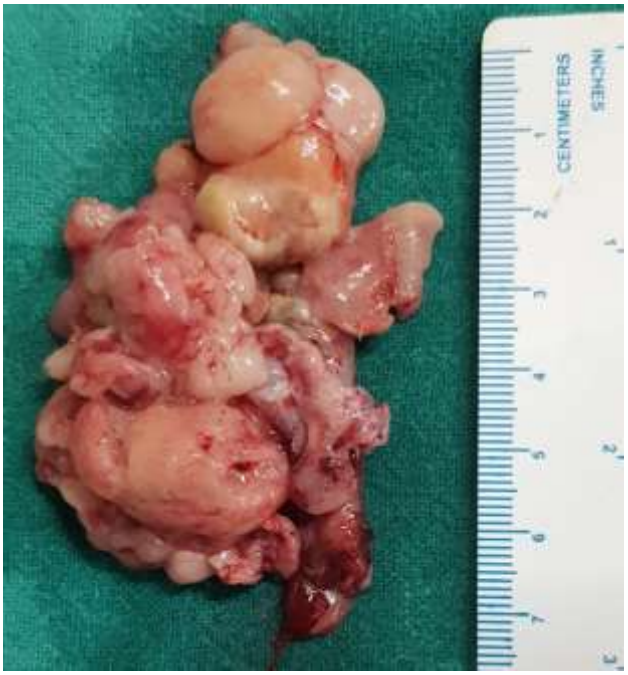

Figure 4: Entire mass after the debulking surgery.

The patient was started on a chemotherapy regime of EPOCH (etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin hydrochloride). After receiving 3 cycles of chemotherapy and radiotherapy to the local site he was free of disease. On follow-up at 9 months he presented with recurrence of nasal mass.

DISCUSSION

PbL is a rare neoplasm, has been strongly associated with HIV infection and other conditions of immuno-deficiency, but it has also been diagnosed in immuno-competent patients. Considering the immune status, patients usually are classified into three groups; HIV-positive patients, post-transplant patients and immuno-competent patients.[5]

The disease is more predominant in males (75% of the cases). Its prevalence in HIV-positive and HIV-negative cases is not well-defined and ranges from 63% in some case reviews to 44% in the case registry of the national cancer data base.[6,7] The median age at diagnosis is around 50 years. However, the age of presentation is lower in HIV-positive patients, with a median age of 40 years, than in non-HIV patients, where the median age is above 50 years. In the present case too, the patient was of 61 years, which is in accordance with the concept that age-related senescence can play a relevant role in a proportion of HIV-negative cases.[4]

Clinical presentation is commonly in extra-nodal regions, the most frequent being the oral cavity, the digestive tract and the skin.[4] In immuno-competent patients, the site of lesions is variable as in the present case where the mass was involving the left nasal cavity, left ethmoid and maxillary sinuses. Diagnosis of PbL is a challenge requiring high degree of clinical suspicion. Unilateral sino-nasal symptoms including facial pain, swelling, numbness, orbital symptoms of compression (e.g. diplopia, vision acuity changes) with or without blood-stained discharge should point toward a suspicion of neoplastic pathology until proven otherwise.[8]

Thorough clinical examination, hematological investigations, radiological investigation, histopathological evaluation including immune-phenotyping and bone marrow biopsy is needed to confirm the diagnosis. PbL has characteristic immune-phenotype staining features. It is constantly immunoreactive to CD-138 which is a well-differentited plasma cell marker. It has minimal expression of leukocyte common antigen CD 45. B-cell antigens like CD-19, CD-20 are weakly positive or negative. Similar immunoreactivity was noted in the present case as well.

A very high percentage of PbL cases show an association with Epstein–Barr virus (EBV) infection. EBV-encoded small RNA expression has been described in 80% of the HIV-positive cases and ~50% of the HIV-negative cases.[6,7] Laurent et al proposed that EBV infection induces antiviral cytotoxic immunity, inhibits B-cell apoptosis and promotes the tolerogenic tumour microenvironment of PbL.[9,10] However, there is a proportion of EBV-negative cases as well. The present case too, was EBV and HIV negative. Therefore, neither HIV status nor EBV seem to confer probability of PbL.[11]

The range of treatments delivered to PbL patients has been extensive, from local control with radiotherapy in patients with localized disease to a variety of chemotherapy combinations.[12] Patients with localized disease have a better prognosis. In these cases, disease control has been achieved with radiotherapy or combining doxorubicin-based chemotherapy with radiation therapy.[12] There are no standards of care defining the optimal therapeutic approach. Treatment regimens have been largely varied without established consensus, although literature suggest overall response of PbL to chemotherapy.[13] CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) has been the most common regimen used in PbL.[4] However, CHOP is not considered efficacious enough to be considered

adequate therapy, and national comprehensive cancer network (NCCN) guidelines recommended chemotherapy regime is etoposide, prednisone, vincristine (oncovin), cyclophosphamide, and doxorubicin hydrochloride (EPOCH).[3]

Considering the lack of standard treatment guidelines, new therapeutic strategies with various chemotherapeutic agents are being tried in different studies. Bortezomib, a proteasome inhibitor, is the most reported new drug for PbL. It is used as a single agent as well as in combination chemotherapy.[14] Other agents to which PbL has shown response are lenalidomide (an immunomodulatory agent), brentuximab vedotin (an antibody-drug conjugate of anti-CD30), siltuximab, tozilizumab (anti-IL6 and IL6R antibodies).[4]

The prognosis of patients with PbL is generally poor and no clear differences between HIV-positive and HIV-negative patients has been noted.[5] Survival is variable ranging from 4 to 12 months.[3]

CONCLUSION

PbL is a rare and aggressive neoplasm, which WHO recognizes as most commonly occurring with HIV infection. However, it extends beyond patients with HIV, with a significant proportion of cases occurring in post-transplant and immuno-competent patients. Awareness of this entity and its unique characteristics and correlation with clinical findings as well as immuno-histochemistry are crucial for establishing a correct diagnosis. Currently available chemotherapy regime with or without radiotherapy has failed to achieve long term remission. The prognosis is generally unfavourable with high incidence of recurrence. Further studies investigating the role of newer drugs and standardisation of treatment guidelines is needed for better management of this rare clinical entity.

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