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Case report

Plasmablastic lymphoma in a previously undiagnosed human immunodeficiency virus-positive patient: a case report

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Abstract

Plasmablastic lymphoma (PBL) is a rare and aggressive non-Hodgkin lymphoma subtype associated with human immunodeficiency virus (HIV) infection. PBL is extremely aggressive and has a poor response to treatment. Clinically PBL resembles a periodontal disease, Kaposi sarcoma, or melanoma. Delayed diagnosis adversely affects the treatment and life expectancy. A 52-year-old male presented with a firm intraoral mass causing a slight elevation noticeable extraorally. Radiologically, loss of lamina dura around the first premolar and loss of both vertical and horizontal bone height around the dental implant replacing the second premolar were present. The biopsy confirmed a diagnosis of PBL. Further evaluation revealed that the patient was positive for HIV. The chemotherapy regimen included etoposide, vincristine, hydroxydaunorubicin, cyclophosphamide, and prednisolone, followed by an autologous hematopoietic stem cell bone marrow transplant. This article attempts to describe the clinical presentation and histopathological evaluation of PBL, and emphasize the paramount role of biopsy, early clinical suspicion, and correct diagnosis.

Keywords: **Plasmablastic lymphoma; human immunodeficiency virus; gingival overgrowth; oral cavity**

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[Abstract in Turkish is at the end of the manuscript]

Introduction

Plasmablastic lymphoma (PBL) is a rare and aggressive non-Hodgkin lymphoma (NHL) subtype associated with human immunodeficiency virus (HIV) infection, constituting 2% of all HIV-associated lymphomas.[1,2] Although this type of lymphoma is of large B-cell origin, it differs from other subtypes by having weakly positive B-cell markers and strongly positive plasma cell markers.[3,4] It may also be associated with the Epstein-Barr virus (EBV). PBL is extremely aggressive and has a poor response to treatment.[5]

Plasmablastic lymphoma often affects middle-aged people but may also occur in the pediatric population.[6] Classic triad of symptoms including fever, weight loss, and night sweats are usually present in PBL whereas lymphadenopathy is not among the common symptoms.[7] Clinically PBL may resemble periodontal disease, Kaposi sarcoma, or melanoma.[6]

Even though PBL is difficult to diagnose and distinguish from myeloma or other types of lymphomas, a biopsy is essential in the diagnosis.[7] Delayed diagnosis adversely affects the treatment and life expectancy.[3] Patients who reject any treatment have a median survival of three months after their diagnosis.[8] This case report aims to emphasize the paramount role of biopsy, early clinical suspicion, and correct diagnosis.

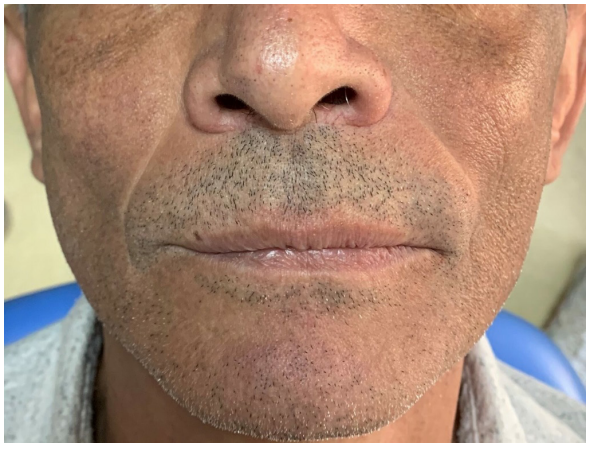

Figure 1. *Extraoral examination – a slight elevation on the left side of the face is noted, giving a subtle asymmetrical appearance to the nasolabial folds.*

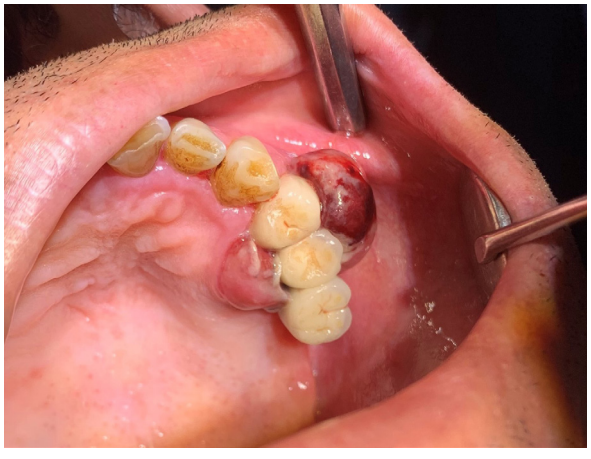

Figure 2. *Intraoral examination – a firm hemisphere-shaped mass is noted both on the buccal and palatal sides enclosing two premolar teeth of the left maxilla.*

Case Report

A 52-year-old male was referred to the Department of Oral and Maxillofacial Surgery due to an intraoral mass with an initial differential diagnosis of periimplantitis. He did not recall when the lesion initially started to develop.

The patient's medical history was unremarkable, and he stated no use of any medication. He had no alcohol drinking or smoking habits. During his extraoral examination, a slight elevation on the left side of his face was noted, giving a subtle asymmetrical appearance to the nasolabial folds (Figure 1). No lymphadenopathy was detected. His intraoral examination revealed a firm hemisphere-shaped mass both on the buccal and palatal sides enclosing two premolar teeth of the left maxilla. The buccal part of the lesion was 18 mm in length and 9 mm in width. The smaller palatal part of the lesion measured 9 mm in length and 7 mm in width (Figure 2). The lesion surface had minor ulcerations and areas of hemorrhage which accounted for the reddish surface. The orthopantomogram revealed loss of lamina dura around the first premolar and loss of both vertical and horizontal bone height around the dental implant replacing the second premolar (Figure 3). Both the tooth and the implant were asymptomatic during percussion, and he reported no pain in general. Patient consent was obtained, and an excisional biopsy was performed with a differential diagnosis of giant cell granuloma. The first premolar was extracted, and the dental implant was explanted due to increased mobility.

The histopathological report revealed neoplastic hematologic cell infiltrations with high mitotic activity, eccentric nuclei and large prominent nucleoli infiltrating the non-keratinized squamous epithelium, and the patient was diagnosed with PBL. Histopathological images were unavailable due to patient's request for paraffin blocks and pathology slides to get a secondary consultation at an external center.

Immunohistochemistry showed CD38, CD138, CD10, and MUM-1 positivity, and lambda, kappa, EMA and CD45 focal positivity. Ki-67 proliferation index was 95-100%. Negative markers were listed as CD20, CD79a, Pax 5, CD3, ALK-1 CD30, Bcl-6, Pan CK, high molecular weight keratin, p53, desmin, caldesmon, HMB-45, and vimentin. Mucin was not detected.

Accordingly, the patient was advised to take an enzyme-linked immunosorbent assay due to the high possibility of an HIV-infection. During his recall one week after the biopsy, he tested positive for HIV and a

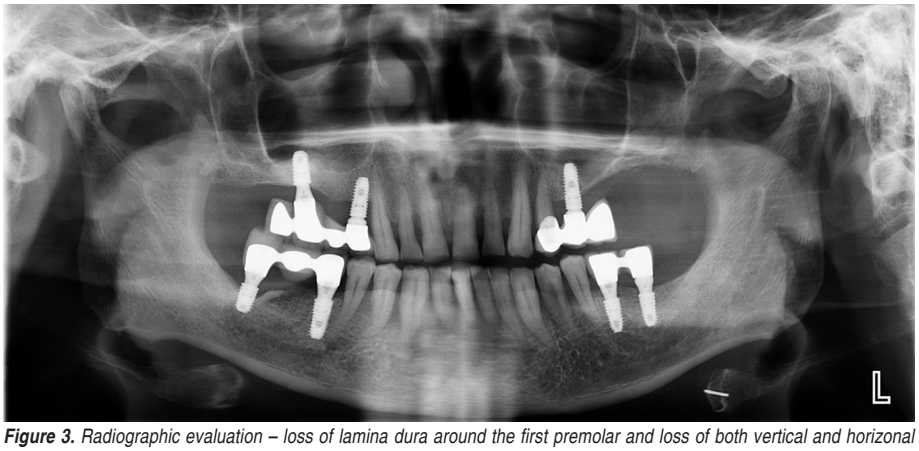

Figure 3. *Radiographic evaluation – loss of lamina dura around the first premolar and loss of both vertical and horizonal bone height around the dental implant replacing the second premolar.*

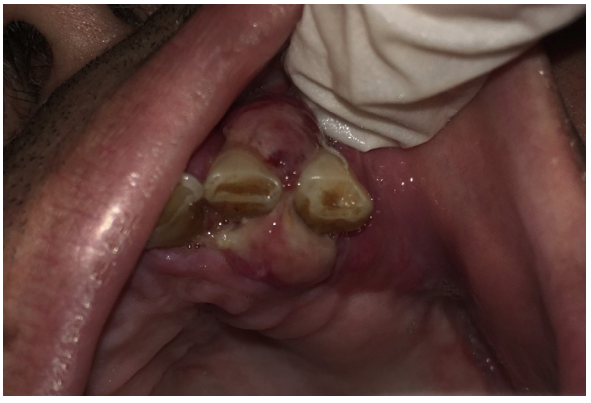

Figure 4. *Recall intraoral examination – a new lesion mesial to the biopsied region is noted with similar characteristics.*

new oral lesion was present like the previously biopsied lesion (Figure 4). He was referred to both hematologic oncology and infectious diseases departments for his further evaluation and treatment.

He completed six cycles of chemotherapy including etoposide, vincristine, hydroxydaunorubicin, cyclophosphamide, prednisolone (EPOCH), and mesna. This was followed by an autologous hematopoietic stem cell bone marrow transplant. He was additionally prescribed filgrastim and ondansetron for neutropenia and emesis, respectively, during the course of his treatment. During chemotherapy, he tested positive for Anti-HBc total and daily entecavir treatment was started.

He remains on remission for six months and continues his antiviral therapies for HIV and for prophylaxis of HIV-related complications.

Discussion

Plasmablastic lymphoma was first defined by Delecluse in 1997 as a large B-cell lymphoma of the oral cavity unique to HIV-positive patients.[9] Although this relatively new disease was first identified in patients with an HIV-infection, recent reports have confirmed PBL in either immunosuppressed or immunocompetent patients, and in patients who underwent solid organ transplantations.[10] Still, a diagnosis of PBL often serves as an HIV-defining illness due to the high rate of HIV-positive PBL patients.[9] Moreover, even though its original definition mentions the oral cavity, PBL is also reported in the nasopharynx, stomach, intestines, anus, lungs, and skin.[6]

PBL is an aggressive type of lymphoma especially in immunocompromised patients. A co-infection of Epstein-Barr Virus (EBV) intensifies its aggressive nature.[9] The prognosis of PBL is very poor without any treatment and life expectancy is between 1-24 months.[6] The difference in prognosis between HIV-negative and positive patients is uncertain.[11]

PBL has a male predominance of 75%, which also coincides with our case. PBL presents at a median age of 40 in HIV-positive patients and the patient presented in this report was within the early 50s of his life.[11]

Oral cavity is commonly involved in HIV-positive PBL patients with a rate of 58%. This is followed by the bone marrow. Less common sides include the central nervous system, paranasal sinuses, mediastinum, lungs, liver, and testes.[12]

Immunohistochemical profile of PBL shows variability. Although listed as a subtype of large B cell lymphoma, PBL does not express the mature B cell marker CD20, as seen in our case.[13] On the other hand, PBL shows positive expression in at least one of the plasma cell markers such as CD38, CD138 and MUM1, as well as a very high Ki-67 expression.[14] Similarly, this reported case shows positivity in all three plasma cell markers and a very high rate (95-100%) of Ki-67 expression.

Currently, there are no standard guidelines for PBL treatment, instead there are different chemotherapeutic options, most of which include the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone, or the combination of etoposide, prednisone, vincristine, cyclophosphamide and hydroxydaunorubicin, shortly known as CHOP and EPOCH, respectively.[13] Autologous or allogeneic hematopoietic stem cell transplantation is another option for PBL; however, its benefit is unclear and is generally used as a consolidation or salvage therapy.[15] Several reports claim that autologous hematopoietic stem cell transplantation after the first complete response results in improved remission in PBL and treatment reinforcement in refractory or relapsed PBL patients.[16] The literature is supportive of the use of EPOCH, followed by autologous hematopoietic stem cell transplant in eligible patients, due to its better outcomes than CHOP.[17] A similar treatment plan was followed for the present case, as well.

Conclusion

PBL is a hard-to-diagnose and hard-to-treat disease with an aggressive clinical course. Like many other oral lesions, PBL may mimic other gingival enlargements. Correct differentiation between PBL and other malignant, benign, or reactive lesions relies on an accurate histopathological and immunohistochemical examination. It is a rare and aggressive type of B-cell lymphoma often coinciding with an HIV-infection. This case aims to underline how a diagnosis of PBL may manifest as the first clinical sign of HIV.

References

1. Said J, Cesarman E, Rosenwald A, Harris NL. Lymphomas Associated with HIV Infection. In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H *et al.* editors. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. France: International Agency for Research on Cancer; 2008. p. 451–2.

2. Carbone A. AIDS-related non-Hodgkin's lymphomas: from pathology

and molecular pathogenesis to treatment. Hum Pathol 2002;33:392–404.

3. Riedel DJ, Gonzalez-Cuyar LF, Zhao XF, Redfield RR, Gilliam BL. Plasmablastic lymphoma of the oral cavity: a rapidly progressive lymphoma associated with HIV infection. Lancet Infect Dis 2008;8:261–7.

4. Delecluse HJ, Anagnostopoulos I, Dallenbach F, Hummel M, Marafioti T, Schneider U, *et al.* Plasmablastic lymphomas of the oral cavity: a new entity associated with the human immunodeficiency virus infection. Blood J Am Soc Hematol 1997;89:1413–20.

5. Delecluse HJ, Feederle R, O'Sullivan B, Taniere P. Epstein–Barr virus-associated tumours: an update for the attention of the working pathologist. J Clin Pathol 2007;60:1358–64.

6. Bagul N, Mamatha GS, Mahalle A. Plasmablastic Lymphoma of Gingiva Mimicking a Reactive Lesion: A Case Report. Case Rep Dent 2012;2012:1–4.

7. Bhatt R, Desai DS. Plasmablastic Lymphoma. [Updated 2022 Apr 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532975/

8. Yamada T, Kitamura N, Sasabe E, Yamamoto T. Plasmablastic lymphoma of the upper gingiva in an HIV-negative elderly patient. Oral Maxillofac Surg Cases 2015;1:19–24.

9. Vieira FO, El Gandour O, Buadi FK, Williams GB, Shires CB, Zafar N. Plasmablastic Lymphoma in a Previously Undiagnosed Aids Patient: A Case Report. Head Neck Pathol 2008;2:92–6.

10. Morscio J, Dierickx D, Nijs J, Verhoef G, Bittoun E, Vanoeteren X, *et al.* Clinicopathologic comparison of plasmablastic lymphoma in HIV-positive, immunocompetent, and posttransplant patients: single-center series of 25 cases and meta-analysis of 277 reported cases. Am J Surg Pathol 2014;38:875–86.

11. Lopez A, Abrisqueta P. Plasmablastic lymphoma: current perspectives. Blood Lymphat Cancer Targets Ther 2018;8:63–70.

12. Sapkota S, Priyadarshini M, Hazarika D, Swamy S, Naik R. Plasmablastic Lymphoma Involving Kidney in an HIV Positive Patient: A Case Report with Review of the Literature. Indian J Nephrol 2021;31:176–8.

13. Fonseca FP, Robinson L, van Heerden MB, van Heerden WFP. Oral plasmablastic lymphoma: A clinicopathological study of 113 cases. J Oral Pathol Med 2021;50:594–602.

14. Castillo JJ, Furman M, Beltrán BE, Bibas M, Bower M, Chen W, *et al.* Human immunodeficiency virus-associated plasmablastic lymphoma. Cancer 2012;118:5270–7.

15. Rong C, Sheng L, Wu A, Sun Y, Ouyang G. Allogeneic hematopoietic stem cell transplantation in a patient with HIV-negative recurrent plasmablastic lymphoma. Medicine (Baltimore) 2021;100:e24498.

16. Tchernonog E, Faurie P, Coppo P, Monjanel H, Bonnet A, Génin MA, *et al.* Clinical characteristics and prognostic factors of plasmablastic lymphoma patients: analysis of 135 patients from the LYSA group. Ann Oncol 2017;28:843–8.

17. Jayachandran PK, Rajan AK, Karunakaran P, Mehra N, Selvarajan G, Kesana S, *et al.* Plasmablastic lymphoma – single centre experience with infusional EPOCH chemotherapy. Leuk Res 2020;95:106391.

Daha önce tanı almamış insan immün yetmezlik virüsü pozitif hastada plazmablastik lenfoma: bir olgu sunumu

Özet

Plazmablastik lenfoma (PBL), insan immünyetmezlik virüsü (HIV) enfeksiyonu ile ilişkili, nadir ve agresif bir Hodgkin olmayan lenfoma alt tipidir. PBL son derece agresiftir ve tedaviye yanıtı zayıftır. Klinik olarak PBL; periodontal hastalığa, Kaposi sarkomuna veya melanomaya benzeyebilir. Geç tanı, tedaviyi ve yaşam beklentisini olumsuz etkilemektedir. 52 yaşında erkek bir hasta, ekstraoral olarak da belirgin hafif bir asimetriye neden olan, sert bir intraoral kitle şikayetiyle kliniğimize başvurmuştur. Radyolojik olarak birinci premolarda lamina dura kaybı ve ikinci premolara denk gelen implant çevresinde dikey ve yatay kemik kaybı izlenmiştir. Biyopsi PBL tanısını doğrulamıştır. İleri tetkikler, hastanın HIV pozitif tanısını doğrulamıştır. Hasta, etoposid, vinkristin, hidroksidaunorubisin, siklofosfamid ve prednizolon içeren kemoterapi rejimi almıştır ve ardından otolog hematopoietik kök hücre kemik iliği nakli gerçekleştirilmiştir. Bu makale PBL'nin klinik sunumu ve histopatolojisini tanımlamaya ve biyopsi, erken klinik şüphe ve doğru tanı koymanın önemli rolünü vurgulamaya çalışmaktadır.

Anahtar Kelimeler: Plazmablastik lenfoma; insan immünyetmezlik virüsü; diş eti aşırı büyümesi; oral kavite