J Oral Med Oral Surg 2024;30:27
https://doi.org/10.1051/mbcb/2024036

https://www.jomos.org

JOMOS
Journal of Oral Medicine and Oral Surgery

Case Report

Oral plasmablastic lymphoma: at the origin of the discovery of an HIV infection

Nurhayu Ab Rahman[1,2*], Faezatul Arbaeyah Hussain[2,3], Kam Chuan Eng[4]

[1] Oral Medicine and Oral Pathology Unit, School of Dental Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian 16150, Kelantan, Malaysia
[2] Hospital Universiti Sains Malaysia, Universiti Sains Malaysia, Kubang Kerian 16150, Kelantan, Malaysia
[3] Department of Pathology, School of Medical Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian 16150, Kelantan, Malaysia
[4] Oral and Maxillofacial Surgery Unit, School of Dental Sciences, Universiti Sains Malaysia Health Campus, Kubang Kerian 16150, Kelantan, Malaysia Kelantan, Malaysia

(Received: 25 July 2024, accepted: 10 November 2024)

Keywords:
Oral plasmablastic lymphoma / gingiva / histopathology / HIV testing / prognosis

Abstract – Introduction: Plasmablastic lymphoma is a rare and aggressive malignancy derived from a B cell lineage. It has a predilection for extranodal sites, particularly arises de novo in the oral cavity. Underlying immune deficiency is a well-established factor, as most cases are associated with HIV infection or posttransplant patients. **Observation:** A 55-year-old man presented with a large, painful, multi-lobulated, bluish-purplish mass on the right posterior maxillary gingiva and was initially misdiagnosed as a dental abscess. He was married with three children and had no known risk for immune deficiency. The histopathological diagnosis revealed a plasmablastic lymphoma lesion, which subsequently led to the establishment of the patient's HIV positive status. **Conclusions:** From a histopathology perspective, HIV testing is warranted in a patient who has been diagnosed with plasmablastic lymphoma despite having a negative history of HIV, transmission risk or exposure to further establish the clinicopathological correlation. Clinically, this testing is necessary to determine the patient's overall therapy, with a focus on counselling of the individual patient and family members to prevent the disease from spreading further.

Introduction

Plasmablastic lymphoma (PBL) is a rare, aggressive B cell neoplasm accounting for ~1% of large B cell lymphomas. It features large cells resembling immunoblasts and plasmablasts, but lacks mature B cell markers like CD20 and PAX5, while expressing plasma cell markers MUM1 and CD138 [1,2]. First reported by Delecluse *et al.* (1997), PBL predominantly affects males (M:F ratio 3:1) and is often associated with HIV (75% of cases) [3]. It typically manifests at extranodal sites (>90%), especially in the oral cavity (~50%) [1,2]. Other sites include the respiratory and gastrointestinal tracts, skin, and bone. In post-transplant settings, up to 30% show nodal involvement [1,2]. Here, we report a case of PBL arising from the gingiva in a patient with previously undiagnosed immune deficiency.

Observation

A 55-year-old man presented with painful swelling in the upper right gum, first noted in early September 2023. Initially diagnosed with a dental abscess and pyogenic granuloma, his incision and drainage procedure was postponed due to high blood pressure. He was prescribed Augmentin 625 mg twice daily for 5 days, Paracetamol 1g four times daily for one week, and chlorhexidine gluconate mouthwash 0.2% twice daily for one week. Two weeks later, his condition worsened with severe gum pain and was admitted to hospital for suspected upper gastrointestinal bleeding and sepsis.

He had lost over 20 kilograms in the past year and experienced a loss of appetite a month before the gingival mass was discovered. He had hypertension, diabetes mellitus, and a history of cerebrovascular accidents, but was compliant with his medications. He also suffered from chronic rhinorrhoea, post-nasal drip, and nasal congestion for over ten years. Five years ago, he had a difficult extraction of the upper right wisdom tooth. Socially, he was married with three healthy children and had no known risk factors for immune deficiency

* Correspondence: nurhayu@usm.my

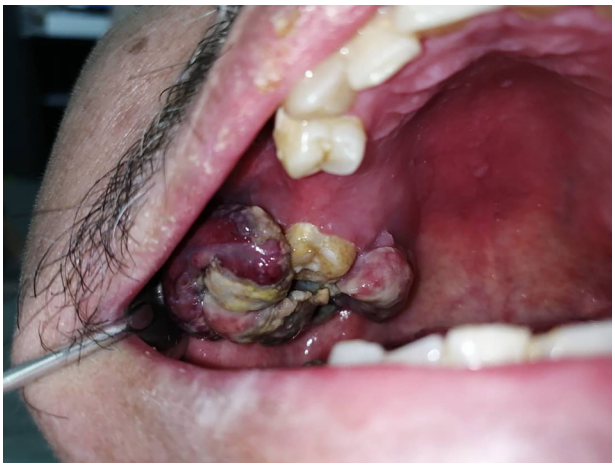

Fig. 1. Intraoral photograph of the lesion. Large, exophytic, multi-lobed, bluish-purplish mass on the right posterior maxillary gingiva with ulcerated surface.

such as history of intravenous drug injection, multiple sexual partners (homo- or heterosexual), needle prick injuries, blood or blood product transfusion, or organ transplant. He worked as a counsellor for a local government agency and did not smoke, consume alcohol, or chew betel quid.

Upon examination, the patient appeared unwell, pale, lethargic, and cachexic. No cervical lymphadenopathy was noted. His blood pressure was 134/71 mmHg, heart rate 121 bpm, temperature 37.1°C, and capillary blood sugar 11.9 mmol/L. Intraorally, a large, fungating, dark bluish-purple mass was observed on the upper right posterior gingiva near teeth 17 and 18 (Fig. 1). The mass was multi-lobulated, partly ulcerated with yellowish fibrinous exudate, extending beyond the right maxillary tuberosity, measuring approximately 4 × 4 cm. Tooth 18 was missing, and tooth 17 was sound with grade I mobility.

A dental panoramic tomograph showed the upper right maxillary alveolar bone was intact (Fig. 2). A biopsy a month later revealed neoplastic proliferation beneath the ulcerated surface, with immunoblastic and plasmablastic cells, and tingible body macrophages, creating a starry sky appearance. Frequent abnormal mitotic figures (3-4 per high power field) were noted (Fig. 3). Immunohistochemistry (IHC) showed strong positivity for MUM1 in both cell types, and negativity for CD20, CD79a, PAX5, CD3, CD5, CD25, BCL2, CK AE1&3, S100, and Melan A. Plasmablastic cells showed weak CD138 reactivity, while immunoblastic cells were non-reactive. Both cell types had focal CD56 reactivity (Fig. 4). Plasmablastic cells were strongly positive for CD30, CD45, and EMA, while immunoblastic cells showed focal CD30 reactivity and weak CD45 and EMA staining. CD10 was moderately positive in plasmablastic cells and strongly positive in immunoblastic cells. The Ki-67 index was high (>90%), and neoplastic cells exhibited lambda light chain restriction, indicating B cell clonality (Fig. 4).

These findings confirmed the microscopic diagnosis of plasmablastic lymphoma. During a follow-up, the diagnosis and need for further investigations, including HIV testing,

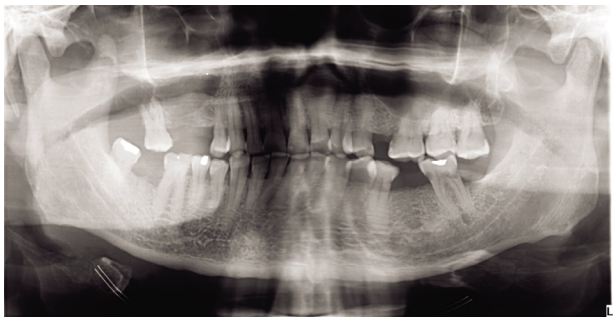

Fig. 2. Dental panoramic tomograph of the patient. No evidence of alveolar bone resorption was noted at the right maxilla in the area where the mass was located.

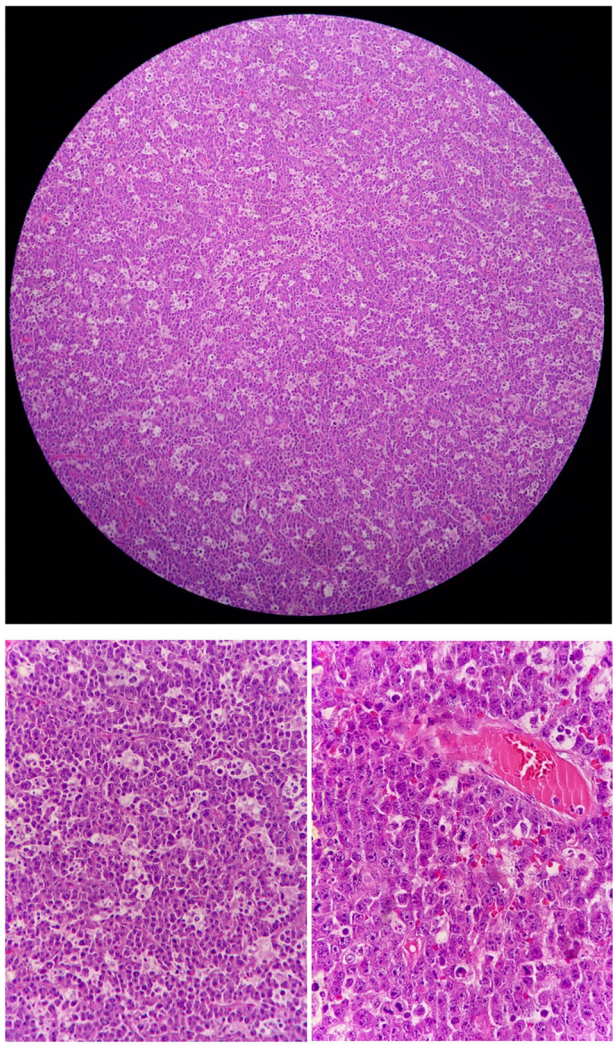

Fig. 3. Histopathological examination of the haematoxylin-eosin stained specimen. The starry-sky appearance (upper, 10X) comprised sheets of immunoblast-like cells, with a few notable plasmablast-like cells in between, and interspersed tangible body macrophages (lower left, 20X and right, 40X). Abnormal mitotic figures were frequently seen (lower right, 40X).

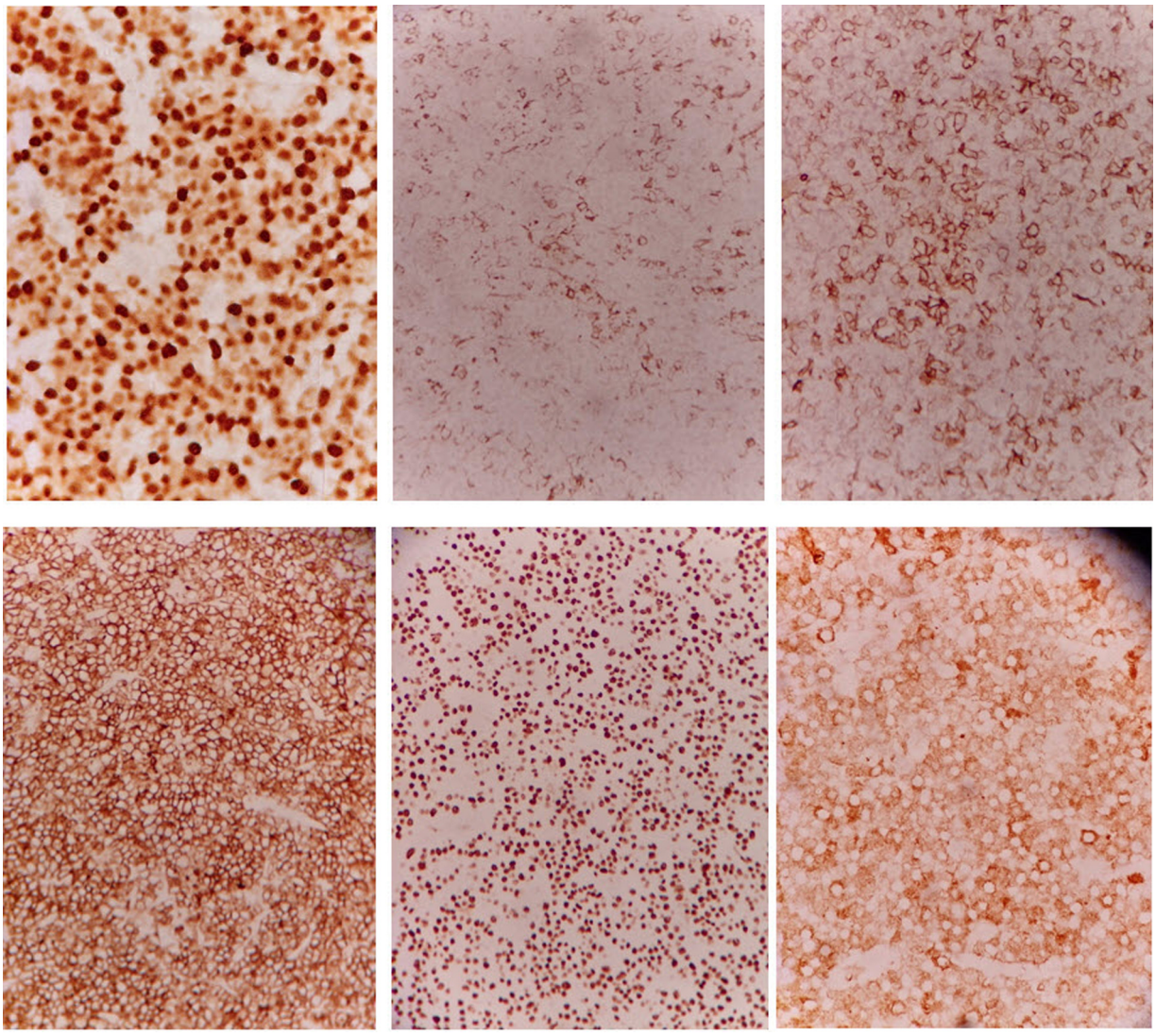

Fig. 4. Immunohistochemical staining of the lesion. Strong staining for MUM1(upper left, 40X), weak staining for CD138 (upper middle, 20X), focal strong staining for CD56 (upper right, 20X) and strong membranous staining for CD10 (lower left, 20X). The tumour cells showed strong nuclear staining for Ki-67 (lower middle, 20X). The tumour cells exhibit monoclonality as shown by positive lambda stain (lower right, 20X) and negative kappa stain (not shown).

were explained to the patient and his wife. The patient consented, and an enzyme immunoassay (EIA) returned positive results, confirmed by a second EIA. In-situ hybridization (ISH) on the biopsied tissue detected Epstein-Barr virus and c-myc gene rearrangement, both positive (Fig. 5). The district health office was notified, and the case was referred for counselling. Social, psychological, and financial support was provided to the patient and his family.

A CT scan revealed a lobulated mass with heterogeneous enhancement, measuring $3.5 \times 4.6 \times 5.3$ cm, in the right maxillary antrum, causing expansion (Fig. 6). The mass extended into the subcutaneous layer of the right cheek, right buccal space, right nasal cavity, right ethmoidal sinus, and approached the right orbital floor, with bone thinning. It also extended into the oral cavity, destroying the right maxillary bone and alveolar processes. Bilateral subcentimeter lymph nodes were involved at levels Ib, IIa, IIb, IVa, Va, and Vb, with the largest node measuring 1.2 cm at right level IIa. Additional findings included multiple liver lesions, possible pulmonary involvement, and lytic lesions on the iliac bones and vertebral bodies.

He was referred to haematology medical oncology for combined radiation therapy and medication. By December 2023, he became bed-bound and developed septic encephalopathy from orthostatic pneumonia and suspected toxoplasmosis. He received IV Ceftriaxone 2 g stat. His white cell count was 15.78 μl, and platelet count was 365×10^9/L. He experienced severe tachypnea and an altered mental state. At his wife's request, he was discharged at his own risk (AOR) and died at home 24 days later.

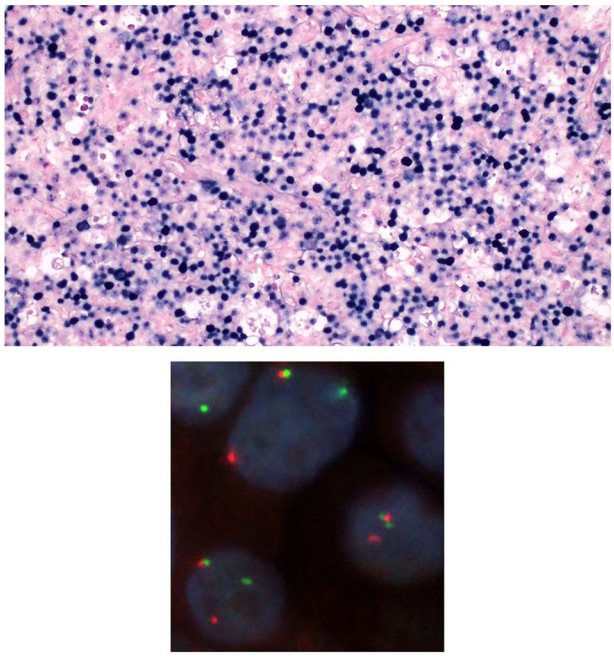

Fig. 5. In-situ hybridisation (ISH). The tumour was positive for Epstein-Barr virus-encoded small RNA (upper, 20X) and exhibited many nuclei with split signals indicating the presence of c-myc gene rearrangement (lower).

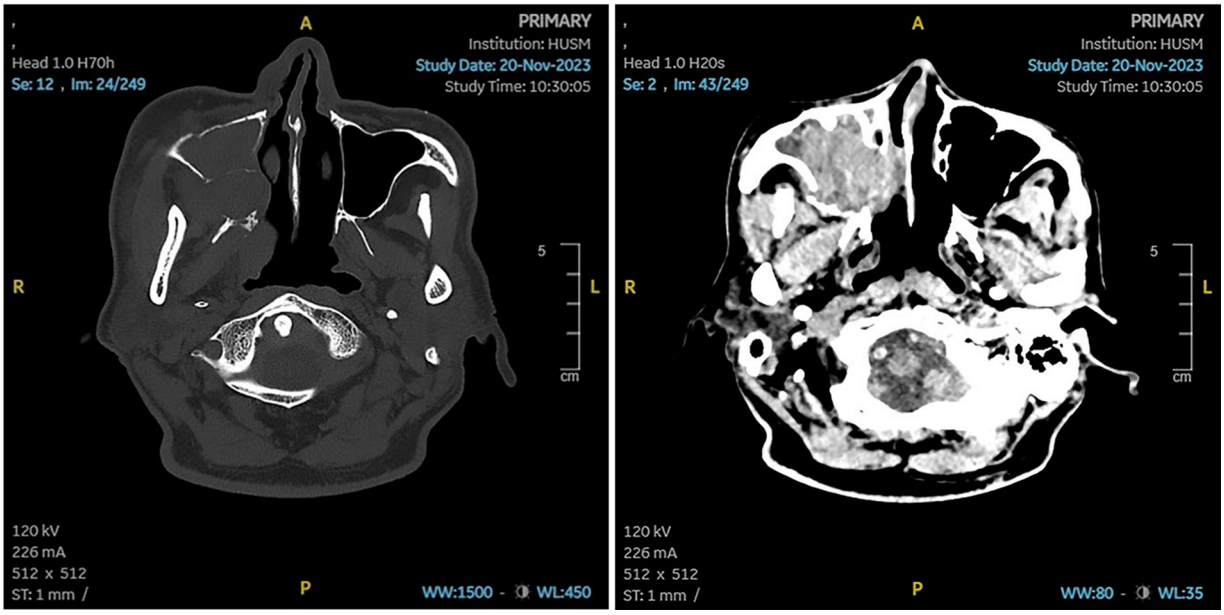

Fig. 6. CT-scan (axial) images of the patient. A large tumour mass was noted, without contrast (left), occupying and causing expansion in the right maxillary antrum, and more tumour delineation was observed upon enhancement with contrast (right).

Discussion

In a dental setting, dental abscesses are the most frequent diagnosis. Severe pain and an ulcerated surface with a yellowish pseudomembrane might suggest an abscess. Additionally, benign gingival growths like pyogenic granulomas are common. However, these are usually small (<2 cm), bleed easily, and are painless unless irritated. Diffuse large B cell lymphoma (DLBCL), a rare reddish-blue oral growth >2 cm, is the most common lymphoma in the head and neck region [4]. It often presents with nasal obstruction and has a predilection for the gingiva, typically accompanied by B-type symptoms and affecting men in their sixth to seventh decade of life [4,5].

In this case, without a history of immune deficiency or exposure risk, the diagnosis of PBL was based on HPE showing immunoblastic and plasmablastic-like cell morphology. IHC

findings supported this with MUM1 and weak CD138 positivity, and negative CD20 and PAX5 expression, distinguishing PBL from DLBCL with a partial plasmablastic phenotype [6]. The lesion showed strong CD45 and CD56 positivity, unlike most oral PBL cases [2]. These findings, along with CD10 positive expression, were common aberrancies found in plasma cell neoplasms [7]. ISH tests confirmed Epstein-Barr virus (positive in 60% of cases) and c-myc rearrangement, the latter indicating a poorer prognosis [1,8]. The main treatment for PBL is conventional chemotherapy.

The patient's management was complicated by a positive HIV status discovered after an advanced PBL tumor mass was found. This late HIV diagnosis led to multiple organ involvement and a poor prognosis, with an overall survival rate of 6–32 months [8,9]. The patient had been generally ill for a year before diagnosis, presenting with non-specific symptoms like rhinorrhea, lethargy, and upper gastrointestinal bleeding, as well as weight loss. He did not have fever, night sweats, or lymphadenopathy. Medically and socially, he had no prior history of HIV, RVD transmission risk, or transplant.

Common oral lesions associated with HIV/AIDS include acute pseudomembranous candidiasis, chronic hyperplastic candidiasis, erythematous candidiasis, herpes zoster, oral hairy leukoplakia, lingual gingival erythema, and necrotising ulcerative gingivitis and periodontitis [10]. None of these lesions were seen in this patient. Less commonly, non-Hodgkins lymphoma and Kaposi sarcoma may present as gingival swelling, indicating advanced disease [9].

PBL is commonly associated with HIV-positive individuals, as reported by Delecluse *et al.* (1997), but up to 28% of cases are HIV-negative [11]. The prognosis is generally poor, with a median overall survival (OS) of 15 months and a 25% survival rate at 3 years. Despite combined antiretroviral therapy (cART), the prognosis remains poor, as shown by Castillo *et al.* (2012) [12]. Small study cohorts have shown conflicting evidence regarding OS in HIV-positive PBL treated with ART; some reported better responses to chemotherapy [13], while others reported similar OS outcomes with ART-naïve cases [11,14].

Conclusion

A larger cohort of studies is needed to establish the standard of care for PBL patients. This should include public health strategies involving trained healthcare professionals engaging with patients and their families. Proper counselling, psychological support, and recommended HIV testing are crucial for early ART treatment, better outcomes, and preventing the spread of HIV in the community.

Acknowledgments

The authors would like to thank the Director of the Hospital Universiti Sains Malaysia (USM), Kubang Kerian, Kelantan, the staff of the Medical Records Department Hospital USM, Oral Pathology Laboratory, School of Dental Sciences USM and Diagnostic Service Department, Hospital Canselor Tuanku Muhriz for their help.

Funding

This work did not receive any specific source of funding from agencies in the public, commercial, or not for profit sectors.

Conflicts of interest

The authors declare that they have no conflict of interest.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

Author contribution statement

N. A. Rahman: Conceptualisation, Writing original and final draft. F.A. Hussain: Data interpretation and analysis. K. C. Eng: Data acquisition, Investigation.

Ethics approval

The ethical approval was obtained from the Human Research Ethics Committee Universiti Sains Malaysia (USM/JEPeM/KK/24060553). This work conformed to the principles of the Helsinki Declaration of 1975,1983 and 2002.

Informed consent

Written informed consent was obtained from the patient prior to the preparation of the case report, and the author(s) have omitted personal and nonessential details to ensure anonymity.

References

1. Montes-Moreno S, Leoncini L, Miranda R, Louissaint JA, Sengar M. Plasmablastic lymphoma. In: Ott G, Jong D, Dave SS, editors. WHO Classification of Haematolymphoid Tumours (Online), Lyon: International Agency for Research on Cancer, 2022. https://tumourclassification.iarc.who.int/chaptercontent/63/154 (Accessed on 30th January 2024)
2. Leoncini L, Siebert R, Ferry JA, Boy S. Plasmablastic lymphoma. In: Khoury JD, Chan JKC, editors. WHO Classification of the Head and Neck Tumours (Online), Lyon: International Agency for Research on Cancer, 2022. https://tumourclassification.iarc.who.int/chaptercontent/52/244 (Accessed on 30th January 2024)
3. 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 1997;89:1413–1420.
4. Medeiros LJ, Ferry JA, Martinez LQ. Diffuse large B-cell lymphoma. In: Khoury JD, Chan JKC, editors. WHO Classification of the Head and Neck Tumours (Online), Lyon: International Agency for Research on Cancer, 2022. https://tumourclassification.iarc.who.int/chaptercontent/52/242. (Accessed on 21st June 2024)

5. Rodrigues-Fernandes CI, de Souza LL, Santos-Costa SFD, Pontes HAR, de Almeida OP, Vargas PA, *et al.* Clinicopathological analysis of oral diffuse large B-cell lymphoma, NOS: A systematic review. J Oral Pathol Med 2019;48:185–191.
6. Montes-Moreno S, Gonzalez-Medina AR, Rodriguez-Pinilla SM, Maestre L, Sanchez-Verde L, Roncador G, *et al.* Aggressive large B-cell lymphoma with plasma cell differentiation: immunohistochemical characterisation of plasmablastic lymphoma and diffuse large B-cell lymphoma with partial plasmablastic phenotype. Haematologica 2010;95:1342–1349.
7. Bailly J, Jenkins N, Chetty D, Mohamed Z, Verburgh ER, Opie JJ. Plasmablastic lymphoma: An update. Int J Lab Hematol 2022;44:54–63. Erratum in: Int J Lab Hematol 2022;44:1121.
8. Valera A, Colomo L, Martínez A, de Jong D, Balague O, Matheu G, *et al.* ALK-positive large B-cell lymphomas express a terminal
B-cell differentiation program and activated STAT3 but lack MYC rearrangements. Mod Pathol 2013;26:1329–1337.
9. 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;38:875–886.
10. Classification and diagnostic criteria for oral lesions in HIV infection. EC-Clearinghouse on Oral Problems Related to HIV Infection and WHO Collaborating Centre on Oral Manifestations of the Immunodeficiency Virus. J Oral Pathol Med 1993; 22:289–91.
11. Castillo JJ, Bibas M, Miranda RN. The biology and treatment of plasmablastic lymphoma. Blood 2015;125:2323–30.
12. Castillo JJ, Furman M, Beltrán BE, Bibas M, Bower M, Chen W, *et al.* Human immunodeficiency virus-associated plasmablastic lymphoma: poor prognosis in the era of highly active antiretroviral therapy. Cancer 2012;118:5270–5277.
13. Castillo JJ, Winer ES, Stachurski D, Perez K, Jabbour M, Milani C, *et al.* Clinical and pathological differences between human immunodeficiency virus-positive and human immunodeficiency virus-negative patients with plasmablastic lymphoma. Leuk Lymphoma 2010;51:2047–53.
14. Vaughan J, Perner Y, Mayne E, Wiggill T. Plasmablastic lymphoma in Johannesburg, South Africa, in the era of widescale antiretroviral therapy use. HIV Med 2021;22:225–30.

Cite this article as: Rahman NA, Hussain FA, Eng KC. 2024. Oral plasmablastic lymphoma: at the origin of the discovery of an HIV infection. *J Oral Med Oral Surg*. 30, 27: https://doi.org/10.1051/mbcb/2024036.