Radiological Features of Oral and Maxillofacial Plasmablastic Lymphomas

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Abstract

Objective: The purpose of the current study was to report on the clinical presentation and radiological features of 72 cases of oral and maxillofacial Plasmablastic lymphomas (PBL).

Methods: Histologically confirmed cases of PBL were retrospectively reviewed over a 10-year period. Demographic and clinical data were retrieved from the patient's records. Radiologic information was obtained from the available radiographic examinations.

Results: The prevalence of PBL was 0.6% of diagnosed head and neck lesions. PBL presented at a mean age of 39 years, demonstrating a strong male predominance. All patients with a known retroviral disease (RVD) status were HIV-positive. PBL had a maxillary predilection (78%), with posterior regions of both jawbones most commonly affected (76%). Most cases had bony involvement (95%), with poorly-demarcated bony borders seen in the majority of cases (93%). PBL had a tendency to cause a loss of cortical integrity (96%), either via cortical erosion or destruction, rather than cortical expansion (2%).

Conclusion: Most of the current literature on PBL focuses on demographics, anatomical location, and histopathological profile, with radiological features only reported in isolated case reports. This study is the first of its kind to report on the clinicoradiological appearance of PBL in a large sample. These findings may assist clinicians in the clinical diagnostic work-up of patients, including the acquisition and assessment of appropriate advanced radiographic imaging.

Keywords: Maxillofacial Pathology, Maxillofacial Radiology, Malignant neoplasms, Lymphomas, Plasmablastic lymphomas

Introduction

Plasmablastic lymphoma (PBL) is an aggressive, fast-growing hematolymphoid neoplasm occurring most commonly in the head and neck region [1,2]. PBL is classified as a subtype of non-Hodgkin lymphoma, being first described as a distinct entity in 1997 by Delecluse *et al* [3]. The neoplasm is strongly associated with human immunodeficiency virus (HIV)-related immunosuppression. Additionally, Epstein-Barr virus (EBV) is considered an important aetiological factor. The exact mechanism of EBV association has not been fully elucidated, however, more than 90% of PBL cases are positive for EBV on appropriate testing [1,4–6].

Globally, the incidence of HIV infection has decreased over the past three decades. Despite these improvements in disease burden, Southern Africa still has the highest HIV prevalence and mortality rates in the world [7]. In HIV-affected individuals, PBL is considered an AIDS-defining neoplasm [2], with most cases diagnosed in patients with CD4 counts of less than 200 cells/mm^3 [4]. PBL presents on average five years after the diagnosis of HIV [4]. In rare instances, they may also present in HIV-negative individuals, particularly iatrogenically immunosuppressed patients such as transplant recipients [8]. These patients often present at an older age with a decreased male predominance, as well as lower rates of oral cavity involvement and EBV positivity [4,8]. PBL in immunocompetent patients is rare, being reported in patients older than 50 years of age in the background of immunosenescence [9–11].

PBL presents at a mean age of 38 years (range 7-65 years) with a strong male predilection (3:1 ratio) [1,4,6,12]. They typically occur extranodally, with a predilection for the head and neck region [1,4,10]. Most head and neck PBLs occur in the oral cavity (83%), with the remainder located in extraoral regions including the sinonasal complex, orbit, and parotid region [9,12–14]. PBLs often present as painful facial swellings [15,16], with accompanying B-symptoms including fever, night sweats, and weight loss [1,6,17].

Histologically, PBL shares similar cytological features to plasmablasts, often displaying neoplastic cells with frequent mitotic figures, apoptotic cells, and occasional tingible body macrophages. The neoplastic cells express plasma cell markers (CD38, CD138 and MUM1), with subsequent loss of expression of mature B-cell markers (CD20/PAX5) [1]. They have a high proliferation index (via Ki-67), usually greater than 90%, but ranging between 50-100% [4,12].

The ideal treatment modality of PBL has not been established, with reports of chemotherapy or a combination of surgery and/or chemoradiotherapy being advocated [15]. PBL has a poor prognosis, with most patients succumbing to the disease within one year of diagnosis. The rate of disease-related death is roughly 60%, following a mean period of 10 months after diagnosis [15]. The prognosis

seems to be unaffected by location or HIV status [10,15]. In HIV-positive patients, the prognosis may be improved with the initiation of highly active antiretroviral therapy (HAART) [6,15].

Radiologically PBL often presents as a poorly-demarcated osteolytic lesion on conventional imaging and as a hypodense or soft tissue lesion on CBCT/CT imaging. [16, 18]. Most of the currently available literature on PBL focuses on demographics, anatomical location, and histopathological profile, with radiological features only reported in isolated case reports. The current study focuses on the clinical presentation and radiological features of a large sample of oral and maxillofacial PBLs.

Materials and Methods

The study was conducted following approval by the University of Pretoria, Faculty of Health Sciences Research Ethics Committee (Reference number: 410/2021). All procedures followed the ethical standards of the Helsinki Declaration of 1975, as revised in 2008.

Histologically confirmed cases of PBL were retrospectively reviewed over a 10-year period (2011-2021). Cases were collected from the histopathological archives of the Department of Oral Pathology and Oral Biology, University of Pretoria. An experienced Oral and Maxillofacial Pathologist confirmed the diagnosis of all included cases. Cases with insufficient clinical data were excluded from the study. Demographic and clinical data, including mean age, gender, retroviral disease (RVD) status, mean duration, clinical signs, and the affected site were retrieved from the patient's records.

Conventional radiographs, including panoramic radiographs, and specialised imaging, consisting of computerised tomography (CT) and cone-beam CT (CBCT), were utilised for radiological evaluation. For the purposes of describing the presenting radiological features, positron emission tomography (PET) studies were not included in this study. The panoramic radiographic equipment utilised in the study included: Instrumentarium Dental, Orthopantomograph®/Orthoceph® OP200D/OC200D, Finland, and Sirona Dental Systems, Orthophos XG, Germany. The exposure settings were based on the recommended dose from the manufacturer for an adult (66 kVp, 6.3 mA and 14.1 s and 64 kVp, 16mA and 14s, respectively). The CBCT unit utilised in the study was a Planmeca ProMax 3D Max CBCT scanner, Helsinki, Finland, paired with Romexis 6.0 R software used for evaluation. The CT unit utilised was the Phillips Ingenuity Core 129 CT scanner, Koninklijke Philips N.V, Amsterdam, Netherlands. The exposure settings were based on manufacturers instructions and differed based on the size of the patient and the requested field of view, as well as additional settings such as metal artefact removal.

Radiologic information, including location, borders, radiodensity, and effects/encroachment of the surrounding structures were obtained from the available radiographic examinations. Lesions confined

anterior to and including the canine region were classified as anterior, whereas lesions located posterior to the canine region were classified as posterior. The radiological features were analysed by the first two authors (CN and LR), who have experience in the field of Maxillofacial Radiology, with any disagreements resolved by consensus and/or consultation with the third author (WvH).

The results of the radiological examinations were recorded using Microsoft Excel (Version 2016) with subsequent statistical analysis of the categorical data performed using SPSS software 26.0 (IBM Corporation, New York, NY). All data was deemed to be categorical in nature given the 'either-or' fashion of classification, for example: the borders of the lesion were classified as being either 'well-demarcated, 'poorly-demarcated' or with 'soft tissue involvement'. A univariate frequency table was constructed for each categorical variable, showing the percentage breakdown and distribution of the cases according to the variable parameters. Multivariate 2x3 tables, which highlighted the interaction between the location in the jaws and other variables, were constructed prior to determining the statistical significance thereof. The association between independent, categorical, variables were evaluated using Pearson's Chi-Squared test, along with the Fishers Exact test being used as a reasonability check when the underlying assumptions of Chi-Squared were violated. Correlations with a two-sided Asymptotic Significance (p-value) of less than 0.05 were considered to be statistically significant.

Results

Clinical Features

During the 10-year study period, a total of 11 664 lesions involving the oral and maxillofacial region were diagnosed at the institution, from which 106 PBLs were diagnosed. Thirty-four (34) cases were excluded from the study due to insufficient clinical data, leaving a total of 72 cases included in the final sample. The prevalence of PBL was therefore determined as 0.6% in the current study. Table 1 summarises the main demographic and clinical features. The mean age of presentation was 39 years with a peak incidence in the 4th and 5th decades of life (Fig. 1). The overall sample demonstrated a strong male predominance.

Table 1: Summarised demographic and clinical features of PBLs

Clinical features	N=72	%
Age, years (range)	39	(8-70)
Gender	55M:17F	(3.2:1)
HIV status	50 positive: 22 unknown	
Gender of HIV positive cases	38M:12F	(3.2:1)
Duration, months (range)	5	(0.25-36)
Clinical signs[1]		
Rapid growth	12	25%
Painful swelling	16	33%
Ulcer	19	40%
Fungating	9	19%
After extraction	5	10%
Mobile teeth	9	19%
Proptosis	7	15%
Vision loss	5	10%
Other[2]	4	08%
Subsite[3]		
Maxilla	44	61%
Mandible	17	24%
Sinonasal complex	37	51%
Orbit	14	19%
Hard/soft palate	30	42%
Buccal mucosa	25	35%
Gingiva	25	35%
Other[4]	8	11%

[1]Information only available for 48 patients with some presenting with more than one symptom
[2]Other symptoms included: nerve fallout, otalgia, and epistaxis
[3]Extensive lesions involved multiple regions
[4]Other sites included: retromolar trigone, tonsil and tongue base, midface, and supraorbital region

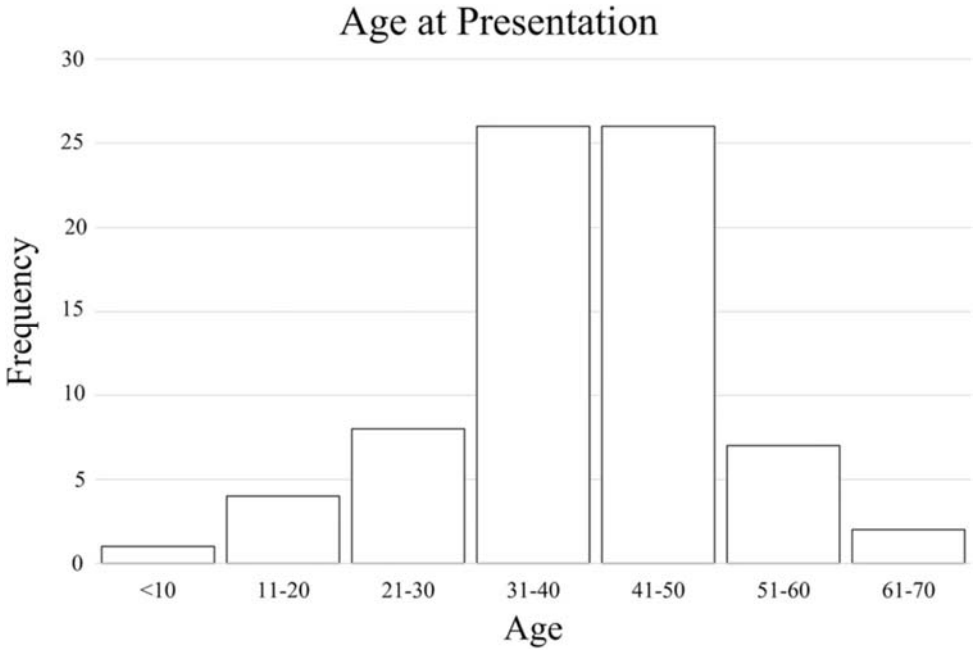

Figure 1. Age distribution in the current sample

From: Radiological features of oral and maxillofacial plasmablastic lymphomas

Fifty patients with a known RVD status were HIV-positive, comprising of 38 male and 12 female patients. The mean reported duration of clinical signs was 5 months, with all patients presenting with facial swellings. A significant number of patients (33%) presented with pain, with 25% of patients reporting rapid growth. Intraoral lesions presented as erythematous ulcerative (40%) or fungating (19%) soft tissue masses (Fig. 2). Five cases (10%) presented following tooth/teeth extraction, while tooth mobility was seen in 19% of cases. Other common clinical signs included proptosis (15%) and vision loss (10%), while epistaxis, nerve fallout and otalgia were rare presentations. Many PBLs reached a considerable size involving multiple regions simultaneously. This resulted in difficulty determining the epicentre of the lesion. The maxilla (61%) and sinonasal complex (51%) were the most frequently affected subsites. The mandible was involved in 24% of cases. Fourteen cases (19%) extended to involve the orbit. Intraorally, the palate (42%) followed by the buccal mucosa (35%) and gingiva (35%) were the most commonly affected subsites.

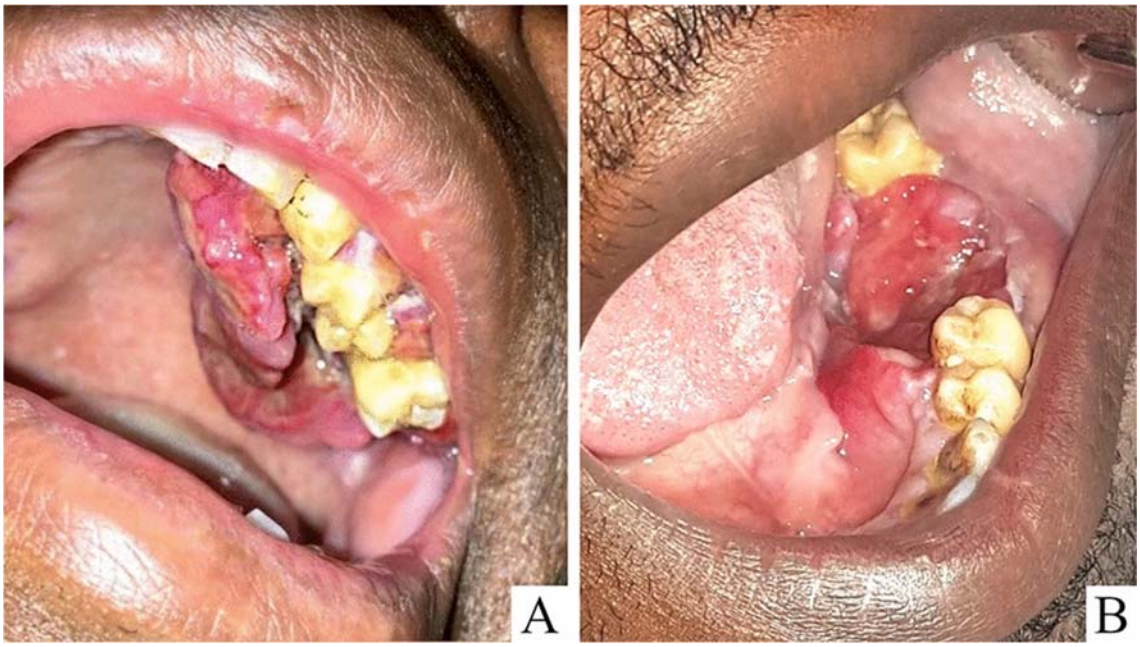

Figure 2. a, **b** Clinical presentation of PBL. Erythematous fungating soft tissue masses with areas of overlying ulceration

Radiological Features

Radiographic examinations were available for 45 patients, including 31 cases with panoramic radiographs and 21 cases with CT/CBCT imaging. Three cases presented with concurrent maxillary and mandibular lesions. Unfortunately, only the maxillary lesions were biopsied with a confirmed diagnosis, and the mandibular lesions were therefore not be included in the final sample. The diagnosed maxillary lesions were included in the final analysis. One case had extensive left facial involvement with radiological signs of erosion of both the left maxilla and left mandible. An

additional poorly-demarcated radiolucent lesion was noted in the posterior right mandible, which was unfortunately not biopsied and therefore this region was not included in the final analysis (Fig. 3). Considering this, the radiological features of a total of 46 lesions from 45 patients were analysed in the study. The radiological features are summarised in Table 2.

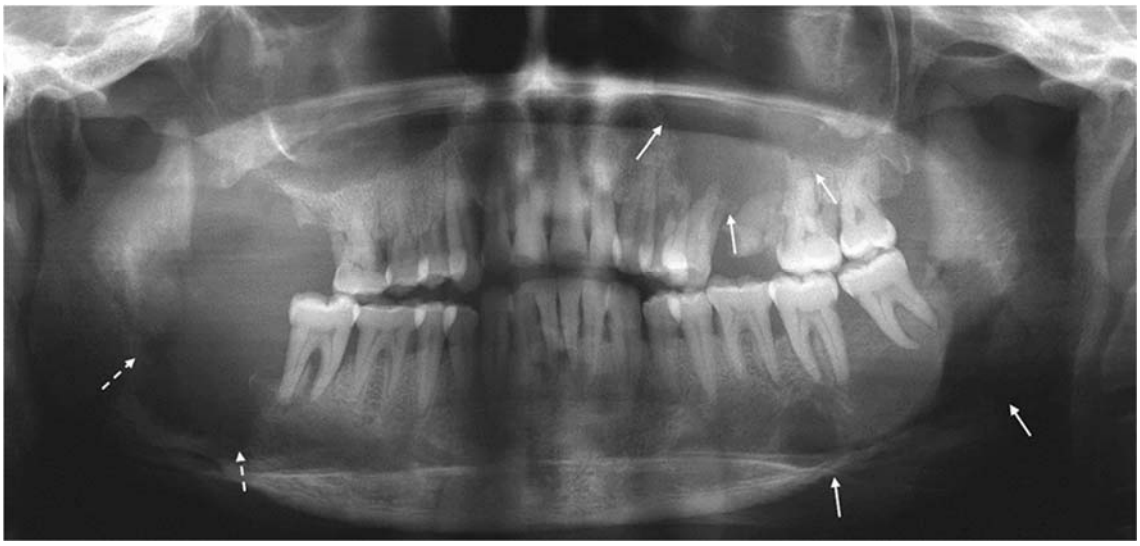

Figure 3. Panoramic radiograph of a PBL primarily affecting the left facial region. There was infiltration into the left maxillary sinus and mandible showing poorly demarcated osteolytic changes (solid arrows). An additional poorly demarcated radiolucent lesion was also noted on the right (interrupted arrows)

Cases with available radiographic examinations had a maxillary predilection (78%), with only 10 cases (22%) involving the mandible. The posterior regions of both jawbones were most commonly affected (76%). All mandibular lesions occurred in a posterior location (Fig. 4), whilst only 69% of maxillary lesions occurred in the posterior region. This result was found to be statistically significant. Due to the large size and extension of lesions in the current sample, both the anterior and posterior regions were affected simultaneously in a significant number of cases (17%). Only two cases were confined to the soft tissues with no radiological signs of bone involvement. Both cases were found in the mandible, which proved to be statistically significant. Most cases had bony involvement (95%), with poorly-demarcated bony borders seen in the majority of cases (93%) and isolated cases exhibiting demarcation (2%). The radiodensity of all cases was osteolytic (radiolucent) on conventional imaging, and hypodense, resembling soft tissue, on advanced imaging. An overlying soft tissue outline could be visualised in 28% of cases.

Table 2: Summarised radiological features of PBLs

Radiological features	**N=46**						
	Maxilla		**Mandible**		**Total**		**P-Value**
Location[5]	**36**	**78%**	**10**	**22%**	**46**	**100%**	
Anterior	3	8%	0	0%	3	7%	0.345
Posterior	25	69%	10	100%	35	76%	0.045*
Anterior and Posterior	8	22%	0	0%	8	17%	0.101
Borders							
Well-demarcated	1	3%	0	0%	1	2%	0.594
Poorly-demarcated	35	97%	8	80%	43	93%	0.115
Only soft tissue involvement	0	0%	2	20%	2	4%	0.043*
Radiodensity							
Osteolytic	27	75%	9	90%	36	78%	0.309
Hypodense	9	25%	1	10%	10	22%	0.309
Effects							
Soft tissue outline	9	25%	4	40%	13	28%	0.351
Cortical expansion	0	0%	1	10%	1	2%	0.055
Cortical erosion/destruction	36	100%	8	80%	44	96%	0.055
Loss of teeth	18	50%	6	60%	24	52%	0.575
Tooth displacement[6]	6	19%	2	17%	8	17%	0.806
Root resorption[6]	5	16%	0	0%	5	11%	0.212
Encroachment of anatomical structures							
Maxillary sinus	27	75%					
Nasal cavity and ethmoid sinus	21	58%					
Orbit	15	42%					
Frontal sinus	7	19%					
Sphenoid sinus	10	28%					
Cranial vault	7	19%					

[5]One case had both maxillary and mandibular lesions

[6]Four cases presented in edentulous maxillae

*A statistically significant relationship exists between the variables at a 95% confidence interval ($p<0.05$)

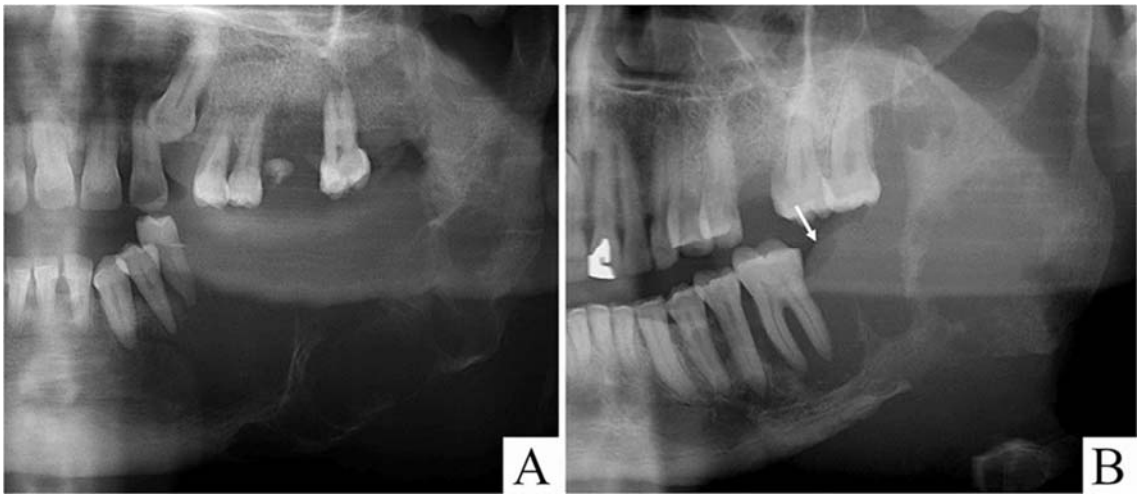

Figure 4. a, **b** Two cases of mandibular PBL with a multilocular-like appearance on panoramic radiography. The lesions appeared non-corticated and poorly demarcated. In addition, a soft tissue outline could be visualised in image B (arrow)

PBL tended to cause a loss of cortical integrity (96%), either via cortical erosion or destruction, rather than cortical expansion (2%). Loss of teeth in the affected region was common (52%), with tooth displacement (17%) and root resorption (11%) being rarer findings. Maxillary lesions resulted in the invasion of adjacent structures, with the maxillary sinus (75%), nasal-ethmoid complex (58%) and orbit (42%) being commonly affected (Fig. 5). On conventional panoramic radiography often the only visible signs of maxillary PBLs were sinus opacification and loss of sinus borders (33%) (Fig. 6). Additionally, infiltration into the cranial vault was seen in 19% of cases involving the upper facial skeleton (Fig. 7).

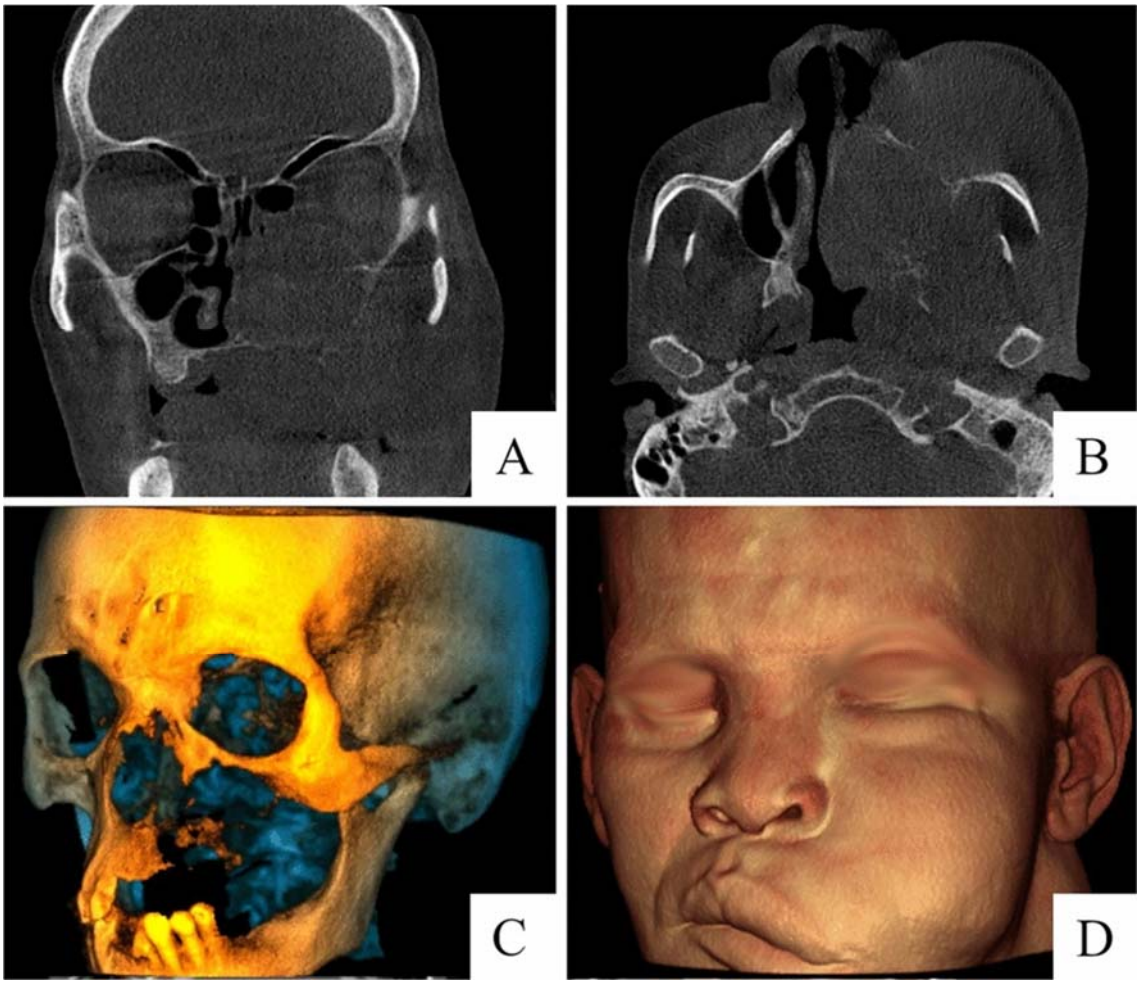

Figure 5. a–d PBL affecting the left side of the face. CBCT imaging showed extensive infiltration of the left maxillary sinus, nasal cavity and orbit, with a loss of teeth in the affected region

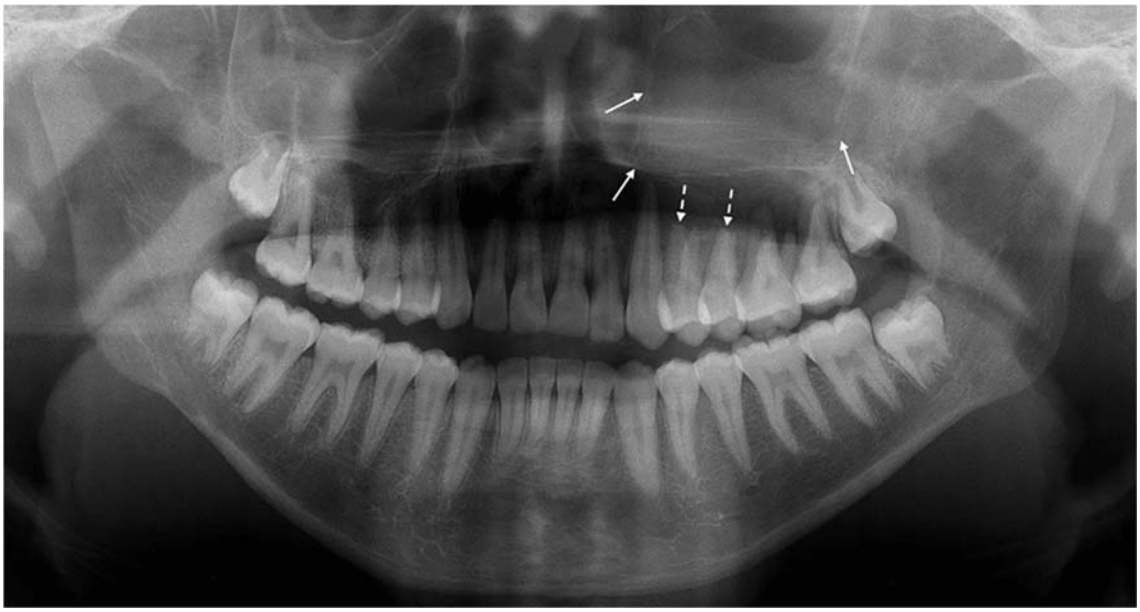

Figure 6. Maxillary PBL showing opacification of the left maxillary sinus with associated cortical destruction of sinus borders (solid arrows) and mild root resorption of teeth in the affected region (interrupted arrows)

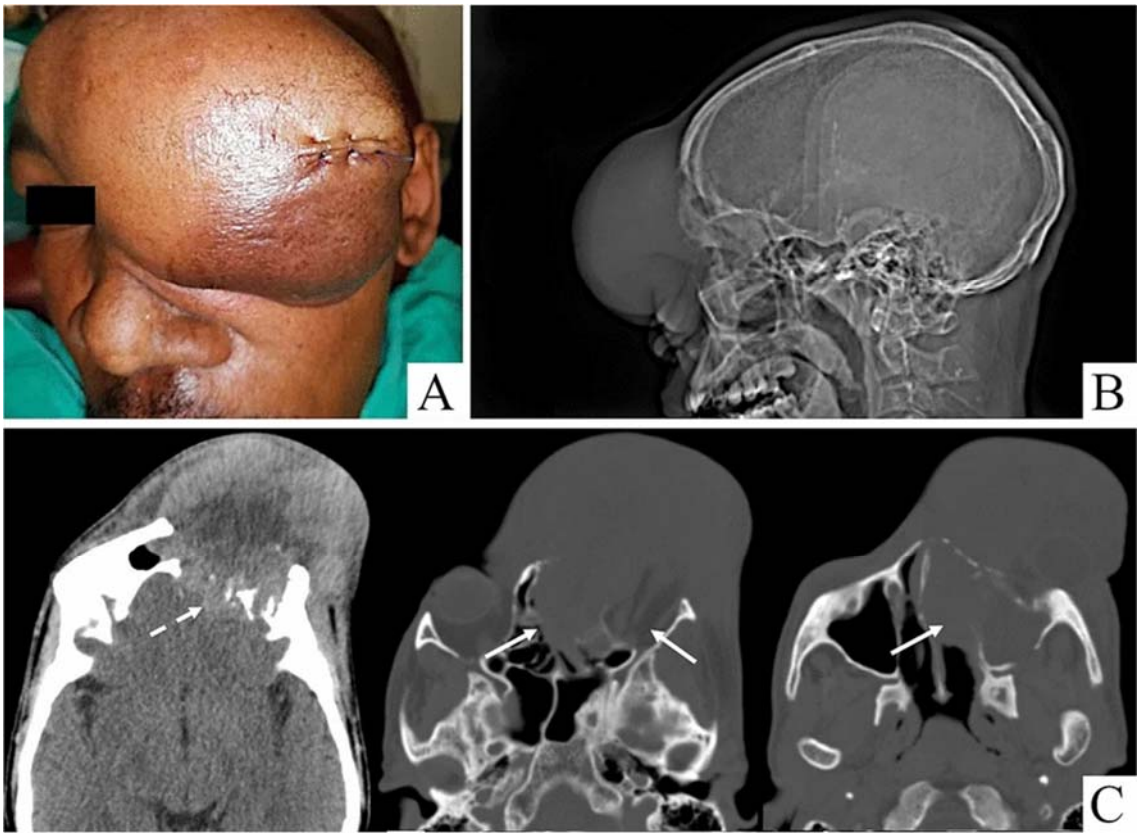

Figure 7. a–c Upper facial PBL presenting radiologically with an enhancing soft tissue mass infiltrating the maxillary and frontal sinuses, nasal-ethmoid complex and orbit (solid arrows), with intracranial extension (interrupted arrows)

Discussion

The prevalence of head and neck PBLs was recently reported as 0.7% in the South African population, with almost all cases (99%) seen in HIV-positive individuals [13]. These results mirrored the findings of the current study. Although the global prevalence of PBL is low, South Africa has a high burden of HIV infection and associated neoplasms, which translates to large absolute numbers of PBLs in the population group. A recent publication from our institution documented the largest single centre sample of oral PBLs to date, mainly focusing on the histopathological characteristics of the entity [1]. In this study, all cases tested positive for EBV infection, with all included patients with a known HIV status being HIV-positive [1]. The current study differs in that the region of interest was extended to involve the maxillofacial regions, with a focus on the clinical presentation and radiological features.

In the current study, PBLs presented at a mean age of 39 years with a strong male predilection, which is consistent with the literature [1,4,6,12]. The male predominance seen in PBL may be explained by more men being HIV-positive [1,10]. This was also seen in the current study, which included three times more HIV-positive males. PBLs are rare in children, with only 21 cases being reported to date in the literature [19]. The current study included a single case presenting during the first decade of life and four cases presenting at the age of 16 years or younger.

PBLs typically present with a high proliferation index, which correlates with their rapid growth rate and short reported clinical duration. They often present as painful facial swellings [15,16], a common finding in the current sample. Intraorally they present as ulcerative or fungating lesions. Dental-related pain or tooth mobility are common presenting features in cases of oral PBL [5,9,16]. Additionally, PBLs are often first identified following tooth extraction [9]. These dental-related symptoms were noted in the current sample, with the loss of teeth in the affected region being a common finding. This presentation may be explained by the extraction of teeth in the affected region due to associated pain, swelling or tooth mobility. Additionally, the radiographic features of the affected region could be mistaken for periapical or periodontal inflammatory diseases.

The extensive nature of PBL cases often results in multiple regions being frequently involved, with infiltration into adjacent structures being a common finding. The findings of involvement of multiple regions have also been reported in the literature [5,20]. Consistent with the literature, a predilection for the oral region was also noted in the current study [13]. The hard and soft palate, followed by the buccal mucosa and gingiva, were the most frequently involved subsites. Other intraoral locations reported in the literature included the floor of the mouth, tonsillar region and retromolar trigone [9]. These subsites were also only involved in a minority of cases in the current study. A single case showed extensive supraorbital involvement. Extraoral head and neck PBLs may occur in the sinonasal

complex, orbit, and parotid region [9,12,14]. In the current study, PBLs had a predilection for the maxilla and sinonasal complex. Maxillary lesions frequently infiltrated adjacent structures, which was best appreciated on advanced imaging.

The radiological features of PBL need to be analysed taking into account the aggressive biological course of the neoplasm as primarily a soft tissue lesion. All lesions in the current study presented with an epicentre involving soft tissue, with subsequent erosion or infiltration into the adjacent bony structures. Radiologically, PBLs present as soft tissue masses with cortical destruction and encroachment of the neighbouring structures or expansile, poorly-demarcated osteolytic lesions [11,15,16,18]. After evaluation of all current radiographic images, a predilection for the posterior region of the jaws was noted. All mandibular cases in the current study were limited to the posterior region. The majority of PBLs showed extensive growth and bony involvement. In isolated cases, the mass was limited to the soft tissue without bony involvement. Consistent with the aggressive nature of these neoplasms, the bony borders were often poorly-demarcated having a so-called 'moth-eaten' appearance. Due to the soft tissue nature of PBLs, all cases had hypodense or osteolytic radiographic appearances. A soft tissue mass, or the outline of a mass, could often be discerned on radiological evaluation. Bony expansion generally points to indolent behaviour or slow growth. In contrast, lesions perforating anatomical planes or borders are often associated with malignant or aggressive behaviours. Most cases of PBL showed a loss of cortical integrity in the vicinity of the mass. The low frequencies of reported tooth displacement or root resorption can be attributed to the majority of cases presenting with prior tooth loss. These findings correlate with the aggressive reported biological behaviour of PBLs.

Maxillary lesions frequently infiltrated the nasal cavity and paranasal sinuses, with the maxillary sinus being involved in 75% of cases. With involvement of the maxillary sinus, panoramic radiography may reveal a soft tissue mass or diffuse opacification of the sinus [16]. In 33% of maxillary cases, sinus opacification was the only visible sign on panoramic radiography. The orbit was involved as the primary site in 19% of cases, with orbital infiltration seen in 42% of cases with available radiographic imaging. It is not surprising with the incidence of radiological evidence of orbital involvement that vision loss and proptosis were common clinical signs. Ocular involvement with associated symptoms, albeit rare, have been previously reported in the literature [11,21,22]. Infiltration of the cranium was also noted radiologically in seven cases in the current study. Central nervous system involvement by PBL, either as the primary site or secondary extension, has been reported in the literature [23].

The histological distinction between PBL and other plasma cell neoplasms with plasmablastic features, including plasmacytoma/multiple myeloma, may be challenging. Adjunct clinical and radiological findings may assist in distinguishing these entities. Plasmacytomas usually present

clinically with slower growth patterns due to their lower proliferation index [1]. They show a predilection for the nasopharynx rather than the oral cavity [14]. Kane et al. emphasise the role of radiological investigations to help distinguish between a plasmacytoma and PBL [14]. Plasmacytomas frequently occur intraosseously, whereas PBLs typically present as soft tissue tumours causing destruction of the adjacent bone [14]. Multiple myeloma usually presents as multiple, multifocal well-demarcated bony radiolucencies [15]. These clinical and radiological features are not pathognomonic for any of these entities, but function as an important adjunct in reaching a final diagnosis. Most PBL studies focus on the clinicopathological profile of PBL, with radiological features only reported in isolated case reports. The current study focused on the clinical presentation and radiological features of PBLs involving the oral and maxillofacial region. Although not entirely pathognomonic, a painful rapidly growing maxillary soft tissue mass in an HIV-positive patient that infiltrates the maxillary sinus and nasal-ethmoid complex should raise suspicion for PBL. Additionally, the findings of the current study indicate that if PBL is diagnosed in an individual, investigations regarding the immune status of the patient are warranted.

Limitations of the current study included the limited availability of advanced imaging, with not all cases having CBCT/CT imaging for evaluation. The majority of available radiographic imaging was limited to panoramic images. This implies that certain radiographic features may have been underreported. Additionally, due to the retrospective nature of the study, some of the clinical information may have been missing and therefore not included in the final analysis. Estimations around prognosis were not available as a significant number of patients were lost to subsequent follow-up. This study is however the first of its kind to report on the clinicoradiological appearance of PBL in a large sample. These findings may assist clinicians in the clinical diagnostic work-up of patients, including the acquisition and assessment of appropriate advanced radiographic imaging.

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