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The development of Proliferative Verrucous Leukoplakia on a background of oral lichen planus: A case series

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ABSTRACT

Oral Lichen Planus (OLP) and Proliferative Verrucous Leukoplakia (PVL) are oral potentially malignant disorders with large differences in rates of malignant transformation (1–2% and 60–100% respectively). They share a number of clinicopathological features, particularly in the early stages of the diseases. Seven patients from one Oral Medicine and one Oral and Maxillofacial Surgery Department in the UK are described, who have developed PVL with a background of OLP. All patients were female, non-smokers and fulfilled diagnostic criteria for both conditions in their disease course. Patients initially presented with reticular striae and subsequently developed plaque-like and verrucous oral lesions. There are three cases of oral cancer development to date, with mean follow up time of 13 years. Our case series reinforces the importance of clinicopathological correlation for the diagnosis of both conditions and periodic review of patients with OLP to allow early-detection of PVL.

1. Introduction

Oral Lichen Planus (OLP) and Proliferative Verrucous Leukoplakia (PVL) are classified as Oral Potentially Malignant Disorders (OPMD), with reported malignant transformation rates of 1–2% [1] and 60–100% respectively [2]. Case series with a total of 44 patients with OLP who subsequently developed PVL have been published [3,4]. The present paper describes a further seven patients with an apparent transition from OLP to PVL; three have developed oral cancer during follow up.

2. Materials and methods

Patients with a final clinical diagnosis of PVL or verrucous carcinoma and a background of OLP, under follow-up from 2015 to 2020, were identified from hospital databases at Liverpool University Dental Hospital (UK) and Leeds Dental Institute (UK). Patients were included if their diagnosis of OLP fulfilled modified WHO criteria (2003) [5] and preceded the diagnosis of PVL according to requirements of Cereo-Lapiedra criteria [6]; both diagnoses were corroborated by clinical photographs. Data were collected on year of birth, sex, smoking history, clinical and histological diagnostic details of OLP and PVL, oral subsites affected, follow-up and development of oral cancer.

3. Results

Table 1 shows the clinical details of seven patients with an initial diagnosis of OLP, who all developed PVL during follow-up. Five patients displayed typical clinical and histological features of OLP. Two were diagnosed with Type 1 Oral Lichenoid Lesions (OLL), both with typical clinical features and compatible histological features of OLP. All patients presented with classical reticular striae and all patients developed plaque-like areas on the oral mucosa; further histological examination confirmed verrucous hyperkeratosis in all cases. Time between OLP and PVL diagnoses ranged from 2 to 18 years. Three patients have developed oral cancer, with time from PVL diagnosis to malignant transformation

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Abbreviations

Oral Lichen Planus – OLP
Proliferative Verrucous Leukoplakia – PVL

ranging from 2 months to 2 years. Figs. 1 and 2 show malignant transformation of case 5. Case 3 was diagnosed with a pT2N0 Squamous Cell Carcinoma (SCC) of the right buccal mucosa (depth of invasion 0.4 mm), which was managed surgically (excision, right selective neck dissection and reconstruction with medial sural artery perforation flap). Case 5 has been diagnosed with T2N0M0 oral cancers of the buccal mucosa, lower lip, alveolar mucosa, hard and soft palate and upper lip/labial mucosa between 2019 and 2021, all managed with surgical laser excision; depth of invasion ranged from 0.8 mm to 2.6 mm. Case 6 was diagnosed with pT4apN1M0 SCC of the right buccal mucosa/maxillary alveolar mucosa

Table 1
Clinical Details of Patients with Oral Lichen Planus (OLP) who developed Proliferative Verrucous Leukoplakia (PVL) and Oral Cancer.

Case Number	Sex (M/F) and year of birth	Ever smoker (Y/N)	Clinical and histological diagnosis of OLP: WHO definition; site involved	Site and year of OLP biopsy	PVL: Sites involved	Site and year of PVL biopsy	Clinical and pathological diagnosis of PVL according to Cerero-Lapiedra criteria; sites involved		Time interval from OLP to PVL diagnoses	Oral cancer diagnosis (Y/N; if yes, histological subtype, oral site and year)	Time from PVL to Oral Cancer diagnosis (months)
1	F 1944	Y (ex)	Typical OLP; L + R BM, left tongue	BM; 1999	Plaque-like area R tongue 2013; White plaque left tongue 2018	R Lateral tongue: 2017 (PVL 4/10)	Major Minor	B, E A, B, C, D	18 years	N (to June 2021)	N/A
2	F 1931	Y (ex)	Typical OLP: L + R BM & DG.	Lateral tongue; 2002	Bilateral tongue, buccal sulci, BM; new plaque like area hard palate 2017	Right posterior hard palate; 2017 (PVL 3/10)	Major Minor	B, E A, B, C	15 years	N (to June 2021)	N/A
3	F 1954	N	Typical OLP, L + R BM	Buccal mucosa; 2008	Verrucous area upper right gingivae, right buccal mucosa, upper lip 2017	2017: Upper right buccal gingivae and upper right lip; verrucous HKT	Major Minor	A, B, C, E A, B, C, D	9 years	**Y; SCC; R BM, 2019.**	24
4	F 1974	Y (ex)	OLL type 1 (typical clinical; compatible histological); buccal sulci/gingivae	L buccal sulcus; 2013	Verrucous area lower right attached gingivae – size increasing: 2014–2020	2015: Lower right attached gingivae LR premolar: PVL 5/10	Major Minor	B, C, E B, C, D	15 months	N (to June 2021)	N/A
5	F 1945	N	Typical OLP; BM and DG	BM; 2007	BM/hard + soft palate, lips, lower alveolar ridge.	R BM; March 2019 Papillary squamoproliferative lesion	Major Minor	A, B, E B, C	12 years	**Y; multiple verrucous ca:R BM March 2019; lower lip May 2019 & Dec 2020; papillary SCC right alveolus Nov 2019**	4
6	F 1940	N	Typical OLP; L + R BM	R BM; 2011	R BM, anterior mandible, anterior and lateral tongue	R BM: 2016; PVL 4/10 + severe oral epithelial dysplasia	Major Minor	A, B, E A, B, C	5 years	**Y; SCC; R BM/tongue/maxillary alveolus**	5
7	F 1958	N	OLL Type 1. Typical clinical; compatible histological; L + R BM	BM; 2010	BM and hard palate	BM/hard palate: 2011; Verrucous hyperplasia/PVL 4/10	Major Minor	A, B, E B, C	2 years	N	N/A

Table 1. Clinical Details of Patients with OLP and PVL. Cerero-Lapiedra criteria: **Major Criteria**: a: leukoplakia lesion with more than two different oral sites b: existence of a verrucous area c: lesions have spread or engrossed during development of disease d: recurrence of a previously treated area; e: histopathology shows simple hyperkeratosis to verrucous hyperplasia, verrucous carcinoma or OSCC, whether in situ or infiltrating. **Minor Criteria**: a – oral leukoplakia at least 3 cm (sum of all affected areas), b-female patient, c-non-smoker, d-disease duration greater than 5 years. A PVL diagnosis is supported with either 3 major (one of which must be histopathology) OR 2 major and 2 minor criteria (one of which must be histopathology). **Bold; patients developing OSCC/verrucous Ca.**
L – left; R-right; BM-buccal mucosa; DG- Desquamative Gingivitis; OLL – Oral Lichenoid Lesion; OLP – oral lichen planus.

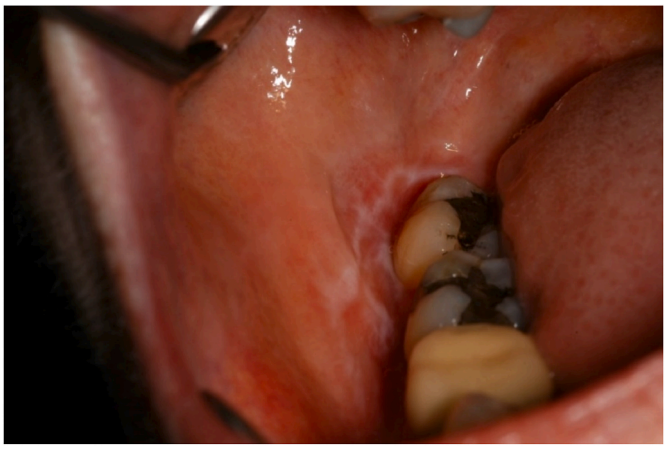

Fig. 1. Clinical Photograph of Right buccal sulcus (case 5; Table 1) demonstrating classic reticular striae of OLP (taken 2008). (Published with the patient's consent).

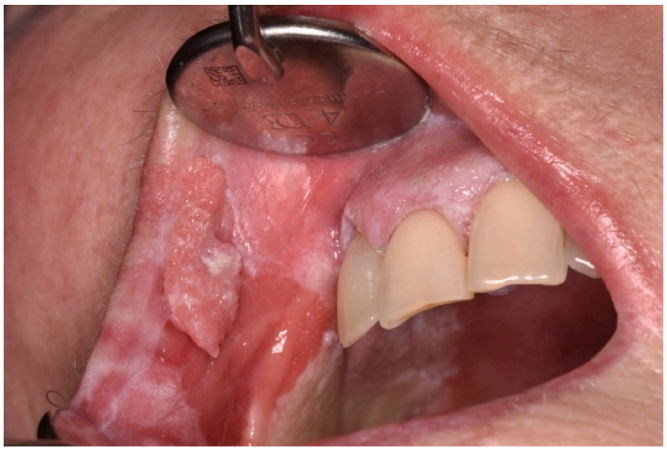

Fig. 2. Verrucous carcinoma of the right inner commissure/buccal mucosa with proliferative verrucous changes of the oral mucosa evident on the gingivae and palate (case 5; Table 1); taken 2019. (Published with the patient's consent).

and right tongue/mandible. The disease was managed surgically (excision of lesion right buccal mucosa in continuity with palatal maxillary mucosa, mandibular rim resection with associated dentition, right lateral tongue, right selective neck dissection and reconstruction with right ALT flap); the disease recurred rapidly following adjuvant radiotherapy and the patient died 4 months later.

4. Discussion

PVL is an OPMD with rates of malignant transformation around 49.5% on meta-analyses [2]. It is characterised by multifocal oral leukoplakias with a progressive course despite treatment [7]. McParland and Warnakulasuriya [4] reported 30 cases of PVL that were preceded by OLP in their retrospective review; all patients presented with roughly symmetrical, reticular white lesions and 20 of these displayed histological features of lichen planus, lichenoid reaction or lichenoid inflammation: six (30%) developed oral cancer. Garcia-Pola et al. described the development of PVL in 14 patients with OLP, over a period of 6–24 years [8]. They reported a significant female:male ratio (11:3) and a malignant transformation rate of 28% (n = 4) with a mean time to transformation of 9 years. Unlike our cohort, who presented with typical reticular striae of OLP, 12 of their 14 reported cases had plaque-like oral lichen planus at presentation, which may have been an early presentation of PVL, with lichenoid features.

Both OLP and PVL are more common in females and non-smokers and these characteristics feature in the diagnostic criteria for PVL [6]. The overlap with OLP both clinically and epidemiologically necessitates careful clinical judgement when confirming a diagnosis of PVL; diagnostic criteria should be employed as a guide together with expert clinical and histological assessment to avoid misclassification.

We have reported seven cases of patients with a diagnosis of OLP and PVL, with 3 cases of malignant transformation. The molecular basis for this apparent transition from OLP to PVL is unclear and warrants further exploration to identify markers of genetic instability and genetic/epigenetic aberrations that may be potential predictors of malignant transformation in both diseases [9,10].

This case series reinforces the importance of careful follow-up of patients with OLP who develop white, plaque-like areas of the oral mucosa as they may represent development of PVL where more frequent surveillance would be indicated [7].

Data statement

Data available on request from corresponding author.

Ethics statement/confirmation of patient permission

Ethics approval not applicable. Patient photographs included: patient has consented to publication in journal.

Conflict of interest

The authors declare no competing interests.

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