

Evaluation of MYC status in oral lichen planus in patients with progression to oral squamous cell carcinoma

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Background

Malignant transformation of oral lichen planus (OLP) to oral squamous cell carcinoma (OSCC) is a matter of debate, ranging from 0.4% to 12.5%. Despite the controversy, a regular screening for malignant transformation is generally recommended and the World Health Organization classifies OLP as a premalignant condition¹. C-MYC is a proto-oncogene involved in various solid tumours, including OSCC².

Objectives

To determine MYC status by florescence *in situ* hybridization (FISH) and immunohistochemistry (IHC) in OLP lesions from 10 patients with progression to OSCC (Group I, Table 1, Fig. 1) and to compare with OLP lesions from patients without progression to OSCC (Group II, Table 2).

Table 1. Clinical features of patients with OLP and OSCC (Group I)

Case	Sex	Age	Site OSCC	Time evolution OLP (months)	Location OLP	Clinical features OLP	Severity OLP	HCV serology	Smoking	Evolution
1	M	63	tongue	6	buccal mucosa	WRP, erosions	moderate	negative	ex smoker	alive
2	F	48	tongue	120	tongue	WRP, erosions	moderate	negative	no	deceased
3	M	81	buccal mucosa, gingiva	1	buccal mucosa	WRP	moderate	negative	ex smoker	deceased
4	M	69	gingiva	24	buccal mucosa	WRP, erythematous plaques, erosions	severe	positive	yes	alive
5	M	50	buccal mucosa, buccal mucosa,	120	buccal mucosa	WRP, erosions	severe	negative	no	deceased
6	F	59	buccal mucosa,	180	buccal mucosa	WRP, erosions	moderate	negative	no	alive
7	F	86	buccal mucosa,	6	gingiva	WRP	mild	positive	no	alive
8	F	64	tongue	48	buccal mucosa	WRP, erythematous plaques, WRP	moderate	negative	no	alive
9	M	33	buccal mucosa,	6	buccal mucosa	WRP, erythematous plaques, WRP	severe	negative	yes	alive
10	M	41	retromolar trigone	36	lip	WRP	mild	negative	no	alive

M: male; F: female; OSCC: oral squamous cell carcinoma; OLP: oral lichen planus; HCV: hepatitis C virus; WRP: white reticulated plaques

Table 2. Clinical features of OLP controls (Group II)

Control	Sex	Age	Follow up (years)	Location OLP	Clinical features	Severity OLP	HCV serology	Smoking
1	F	59	5	buccal mucosa,	WRP	mild	negative	no
2	M	71	5	tongue	WRP	mild	negative	yes
3	M	63	5	buccal mucosa,	WRP	mild	negative	ex smoker
4	F	44	5	tongue	WRP	mild	negative	ex smoker
5	F	52	3	tongue	WRP	mild	negative	no
6	F	70	3	buccal mucosa	WRP	mild	negative	no
7	M	57	3	buccal mucosa	WRP	mild	negative	ex smoker
8	M	68	5	buccal mucosa	WRP, erosions	moderate	negative	yes
9	F	67	5	gingiva	WRP, erosions	moderate	negative	no
10	M	73	10	buccal mucosa	WRP	moderate	negative	ex smoker
11	M	75	10	tongue	WRP, erosions	moderate	negative	no
12	M	66	8	buccal mucosa	erosions	moderate	negative	no

M: male; F: female; OSCC: oral squamous cell carcinoma; OLP: oral lichen planus; HCV: hepatitis C virus; WRP: white reticulated plaques

Methods

We constructed two tissue microarray with 11 OSCC samples (Group IA), 17 OLP samples from those patients (Group IB) and 13 OLP specimens from 12 control patients (Group II). FISH evaluation of the MYC gains were determined in 100 non-overlapping nuclei per sample. IHC evaluation was determined by calculating percentage C-MYC expression in the epithelial cells.

Results

Clinical data from patients included in the study are shown in Table 1 (group I) and Table 2 (group II). OSCC showed MYC copy number gains and C-MYC overexpression in 91% and 73% of cases, respectively (Fig. 2). MYC gains were detected in 47% of samples from group IB (Fig. 3c) and were absent in all samples from group II (Fig. 4c). C-MYC was overexpressed in 87% of cases from group IB (Fig. 3d) and in only 44% of control specimens (group II)(Fig. 4d). The differences in MYC status between group IB and II were statistically significant (Table 3).

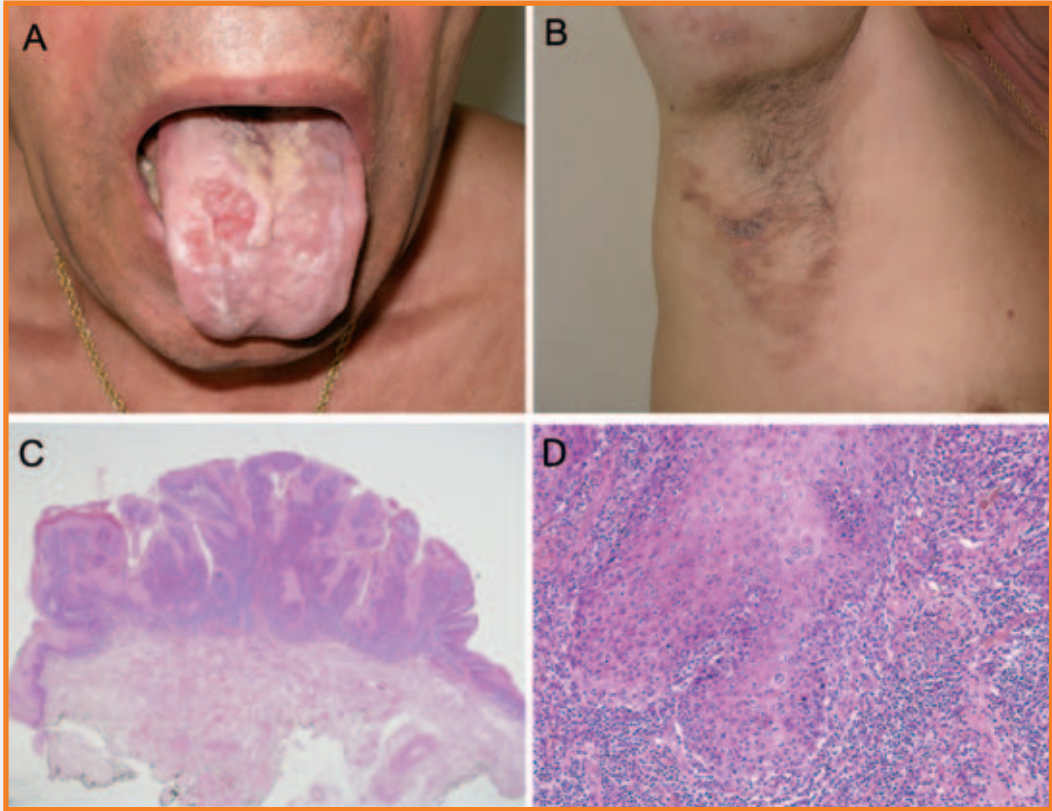


Figure 1. Case 1, 63 year old man with and history of oral and cutaneous lichen planus. A, Clinical image showing oral lichen planus lesions on the tongue and associated verrucous plaque suggestive of OSCC. B, Clinical lesions of cutaneous lichen planus; C, H&E 20x, Low magnification preparation of a verrucous tumor with associated dermal inflammatory infiltrate; D, H&E 200x, histopathological section of the tumor showing dermal nests of squamous cell carcinoma associated to lichenoid inflammatory infiltrate.

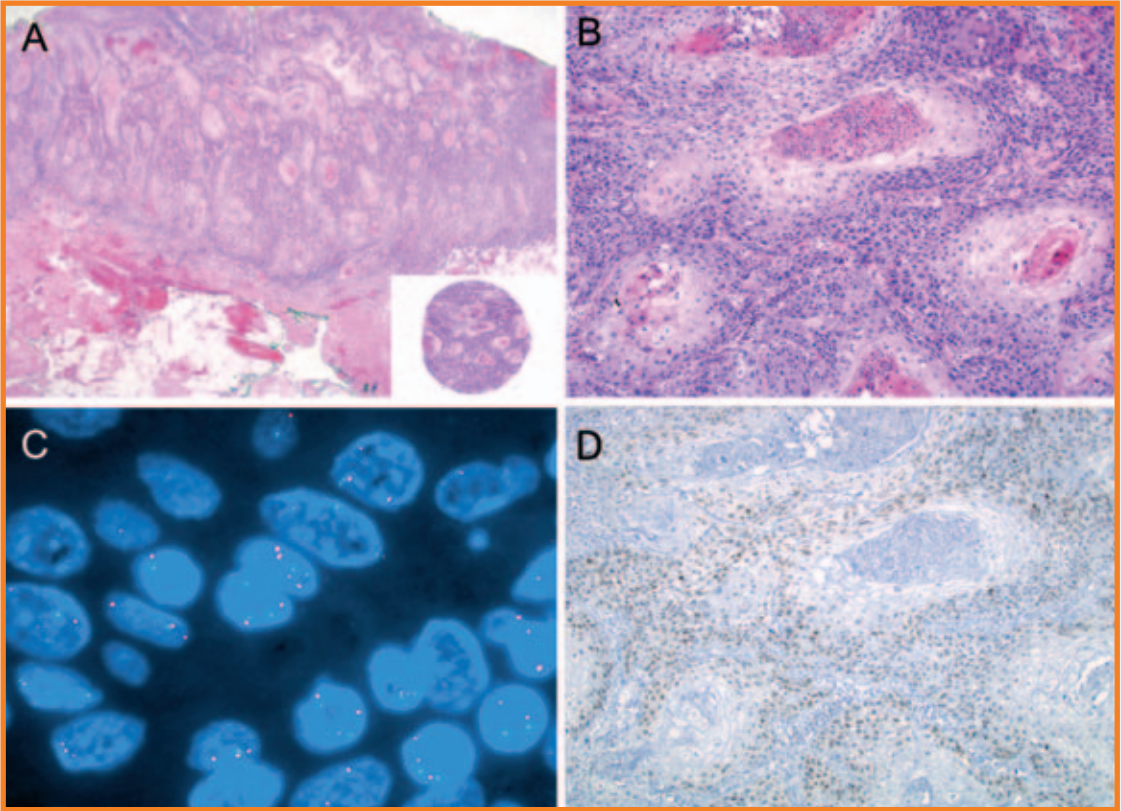


Figure 2. Oral squamous cell carcinoma in a patient from group I. A, H&E 20x, low magnification section showing irregular epithelial hyperplasia with cords of cells penetrating in the submucosa. Inset: H&E 40x, 1 mm punch of the tumor used in the tissue microarray. B, H&E 100x, close up image of the studied area showing nests of atypical squamous cells with areas of keratinization. C, Fluorescence *in situ* hybridization image showing 3 to 4 copy number gains of MYC (red signal). D, C-MYC immunostaining, 100x. Nuclear expression of C-MYC in more than 50% epithelial cells.

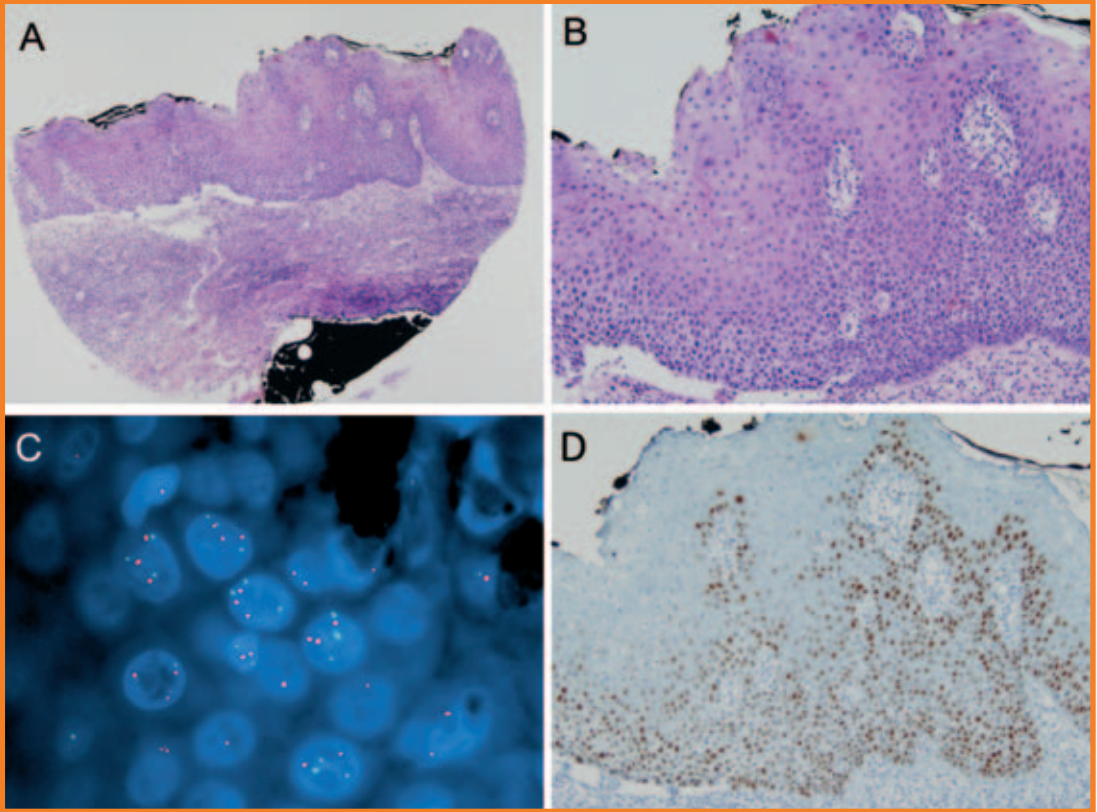


Figure 3. Oral lichen planus in a patient from group I. A, H&E 40x, low magnification image showing epithelial hyperplasia and lichenoid inflammatory infiltrate at the submucosa. B, H&E 100x, epithelial hyperplasia without cytological atypia. C, Fluorescence *in situ* hybridization image showing copy number gains of MYC (red signal). D, C-MYC immunostaining.

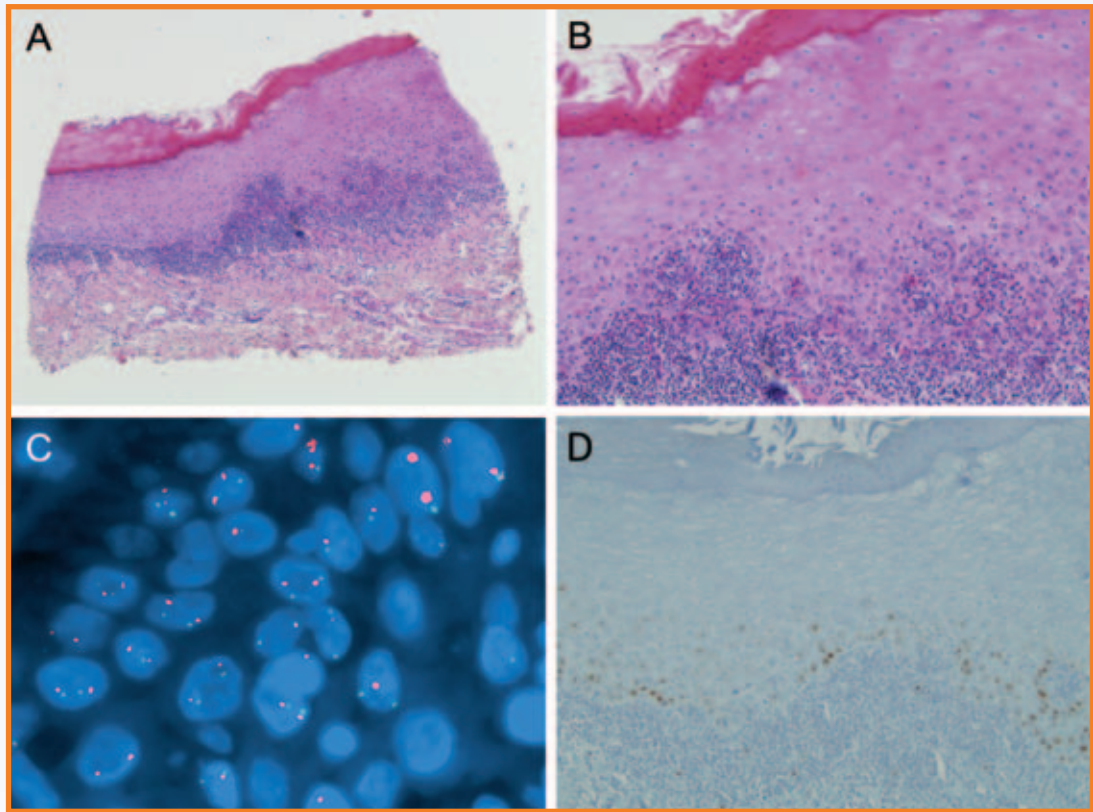


Figure 4. Oral lichen planus in a patient from group II. A, H&E 40x, low magnification image showing epithelial hyperplasia with band-like infiltrate at submucosa. B, H&E 100x, close up image revealing lymphocytic infiltrate obscuring mucosa-submucosa union, with presence of colloid bodies. C, Fluorescence *in situ* hybridization image shows an absence of copy number gains of MYC. D, C-MYC immunostaining, 100x. Mild C-MYC nuclear expression is confined to basal and parabasal layers.

Table 3. Fluorescence *in situ* hybridization and immunohistochemistry results

	GROUP I OSCC samples (Group IA)	OLP samples (Group IB)	GROUP II OLP controls	p value
MYC gains (%)	10/11 (90.9)	7/15 (46.7)	0/9 (0)	0.019 *
C-MYC over expression (%)	8/11 (72.7)	13/15 (86.7)	4/9 (44.4)	0.003**

Group I: patients with OLP and progression to OSCC / Group II: patients with OLP with no progression to OSCC (OLP controls) / OSCC: oral squamous cell carcinoma; OLP: oral lichen planus / *Fisher's exact test comparing group IB and group II / **Mann-Whitney test comparing group IB and group II

Conclusions

OLP lesions in patients with progression to OSCC show MYC gains and C-MYC overexpression. In patients with severe OLP determining MYC status may predict a subgroup of subjects with higher risk to progress to OSCC.

References

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- Martín-Ezquerria G, Salgado R, Toll A, et al. Multiple genetic copy number alterations in oral squamous cell carcinoma: study of MYC, TP53, CCDN1, EGFR and ERBB2 status in primary and metastatic tumours.Br J Dermatol. 2010;163:1028-35.