Malignant Transformation of Esophageal Lichen Planus

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Since the first reports of squamous cell carcinoma arising from oral lichen planus lesions, it is accepted that these lesions may represent precancerous conditions that must be closely monitored [1-3]. However, it is still not known whether ELP should be considered a premalignant lesion as very few cases of esophageal SCC deriving from ELP have been reported [4,5].

PATIENT DESCRIPTION

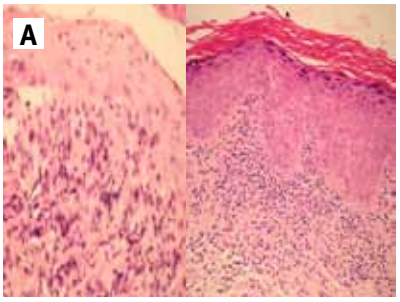
In 2001, a 61 year old woman was referred to our department because of odynophagia, weight loss, sore mouth and progressive dysphagia to solids. An oral inspection revealed erythema and plaques on the buccal mucosa. An upper gastrointestinal endoscopy showed a moderate stricture with exudate and erythema in the upper esophagus. Biopsies from both lesions confirmed the diagnosis of lichen planus [Figure A]. Dilatations of the esophageal stricture with through-the-scope dilation balloons (controlled radial expansion 12–15 mm, 15–18 mm, Boston Scientific, Natick, MA, USA) were successful but short-lived.

On high doses of oral steroids (prednisolone 60 mg/day), replaced later by azathioprine 100 mg/day, the stricture and the inflammatory lesions disappeared. Clinical remission was maintained for the next 6 years and during that period the patient underwent repeated endoscopic examinations, which were all normal. In 2007, the patient complained of weight loss and progressive dysphagia. Upper endoscopy revealed an asymmetric tumorous stenosis located within a stricture in the proximal esophagus. Biopsies obtained from the esophageal mass [Figure B] showed several degrees of dysplasia in the biopsy and carcinoma in situ. No clear invasive tumor was demonstrated, but it could not be ruled out.

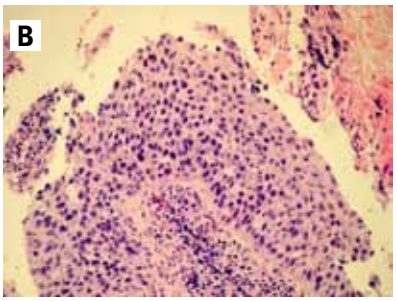
Computerized tomography scans of the thorax and upper abdomen showed no signs of metastatic disease. Treatment included chemoradiotherapy followed by trans-hiatal esophagectomy. Biopsy obtained after chemoradiation [Figure C] from the surgical specimen (hematoxylin & eosin, magnification x20) showed mostly denuded epithelium with no residual tumor; the preserved areas showed features compatible with lichen planus, with a band-like lymphocytic infiltrate and saw-tooth appearance of the epithelium.

COMMENT

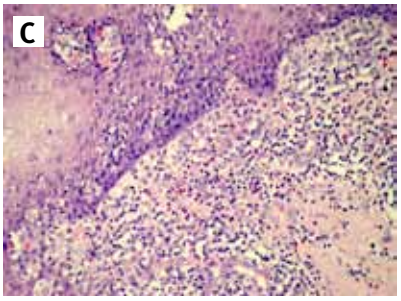
It has been suggested that lichen planus is a risk factor for esophageal SCC. However, the evidence in support of this suggestion is poor as most of the published cases have described buccal or vaginal lesions [2,3]. In lichen planus, carcinogenesis may be related to chronic irritation by scratching (cutaneous lichen planus) and to smoking, alcohol abuse and infection by human papillomavirus (oral lichen planus). In the esophagus, little is known about the malignant potential of lichen planus. SCC may be the result of the chronic inflamma-



[A] Left panel: biopsy from the esophageal stricture at diagnosis (H&E magnification x20) shows superficial dense lymphocyte infiltrate in the lamina propria, mild lymphocytic infiltrate into the squamous epithelium, numerous individual degenerated squamous cells, variable vacuolation of the squamous mucosa, and variable thinning and acanthosis of the squamous epithelium. Right panel: concomitant biopsy of the oral mucosa



[B] Biopsy from the esophageal mass (H&E magnification x20)



[C] Biopsy from the surgical specimen

ELP = esophageal lichen planus
SCC = squamous cell carcinoma

tory process that results in increased turnover of basal cells, or it may be attributed to the long use of immunosuppressive agents. Our patient did not smoke and reported no alcohol consumption. Infection with human papillomavirus was ruled out by the biopsy specimens at diagnosis

To date, only two case reports of esophageal SCC arising from esophageal lichen planus have been described [4,5]. In 2006, Schwartz et al. [5] reported esophageal SCC in two sisters who suffered from esophageal lichen planus. In that case report SCC developed more than 20 years after the diagnosis of ELP. In our patient, SCC developed 6 years after diagnosis of esophageal lichen planus, which may indicate a more aggressive nature of the tumor or a late diagnosis due to the asymptomatic nature of ELP in its early stage. In our patient, a malignant transformation occurred despite close follow-up, as repeated biopsies failed to demonstrate malignancy in the ELP. This highlights the difficulty pathologists experience in interpreting biopsy specimens of such a rare disease. One of the main problems they encounter is to differentiate dysplastic and malignant mucosa from the inflammation and hyperkeratosis [4]. The presence of a thick parakeratosis layer of cells may make the identification of dysplastic or malignant cells within the lichenoid lesions difficult, and this is markedly compounded by the difficulty of obtaining suitably deep biopsy specimens. Schwartz and co-authors [5] suggested the use of chromoendoscopy to differentiate areas of hyperplasia, or low grade dysplasia, from areas of severe dysplasia and SCC.

In conclusion, this case report increases awareness that esophageal lichen planus may represent a premalignant disease and thus should be considered for a surveillance program. The latter, used in conjunction with chromoendoscopy, may enable us to better diagnose and understand the natural history of esophageal lichen planus and, hopefully, to detect early-stage tumors. Esophageal lichen planus is a very rare disease and as such the role of endoscopic surveillance to detect early malignant transformation remains to be established by future and larger studies.

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Capsule

NLRP4 negatively regulates type I interferon signaling by targeting the kinase TBK1 for degradation via the ubiquitin ligase DTX4

Stringent control of the type I interferon signaling pathway is important for maintaining host immune responses and homeostasis, yet the molecular mechanisms responsible for its tight regulation are still poorly understood. Cui and group report that the pattern-recognition receptor NLRP4 regulated the activation of type I interferon mediated by double-stranded RNA or DNA by targeting the kinase TBK1 for degradation. NLRP4 recruited the E3 ubiquitin ligase DTX4 to TBK1 for Lys48 (K48)-linked polyubiquitination at Lys670, which led to degradation of TBK1. Knockdown of either DTX4 or NLRP4 abrogated K48-linked ubiquitination and degradation of TBK1 and enhanced the phosphorylation of TBK1 and the transcription factor IRF3. These results identify a previously unrecognized role for NLRP4 in the regulation of type I interferon signaling and provide molecular insight into the mechanisms by which NLRP4-DTX4 targets TBK1 for degradation.

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Eitan Israeli

Flatter me, and I may not believe you. Criticize me, and I may not like you. Ignore me, and I may not forgive you. Encourage me, and I will not forget you

William Arthur Ward (1921-1994), American college administrator and writer and one of the most quoted writers of inspirational maxims