ONCOLOGY

Soluble Fas Antigen in the Serum of Women with Oral Lichen Planus

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 143, No. 6, pp. 672-674, June, 2007
Original article submitted April 18, 2007

Enzyme immunoassay showed that soluble Fas antigen is significantly more often detected in the serum of patients with oral lichen planus (72.5%) and oral squamous-cell cancer (75%) than in healthy postmenopausal women (36%). The level of soluble Fas antigen was significantly higher in patients with squamous-cell cancer and erosive ulcerative and exudative hyperemic lichen planus than in healthy women.

Key Words: *lichen planus; cancer; mucosa; soluble Fas antigen*

The incidence of pretumor processes and cancer of the oral mucosa increased in recent years [3,14]. Lichen planus is the most incident nosological forms of pretumor processes in the oral mucosa [6]. The incidence of lichen planus increased 2-fold during the latest 30 years [2,4].

The detection rate of oral lichen planus is 0.5-2.5% in the entire adult population (male to female ratio 1:4) [7], women of postmenopausal age suffering more often [5]. Oral lichen planus undergoes malignant transformation in 0.07-3.20% cases, particularly its erosive ulcerative form [4,9]. The risk of malignant transformation increases to 20% in infiltrative lichen planus [5].

Despite numerous clinical, morphological, and experimental studies of oral lichen planus, its pathogenesis remains not quite clear. The problem of apoptosis attracted special attention of scientists investigating the pathogenesis of lichen planus in recent years. Significant differences in the apoptosis index in patients with lichen planus were revealed by the immunohistochemical method and a relationship between high expression of Fas, its ligand, and granzyme B, on the one hand, and disease progress, on the other, was established [13]. Expression of Fas was detected in oral mucosa keratinocytes and foci of lichen planus, and a correlation between Fas expression index differentiation degree of oral squamous cell cancer was demonstrated. Destruction of basal cells in oral lichen planus is linked with the apoptosis mechanisms [12], namely, with high expression of Fas and its ligand in the basal layer in comparison with the suprabasal layer and infiltration of the foci by some cell populations (CD3, CD4, and CD6). Apoptosis processes are more pronounced in the epithelium of lichen planus foci than in normal oral mucosa [8,12].

We compared the concentrations of Fas-dependent apoptosis inhibitor, soluble Fas antigen (sFas), in the sera of patients with oral lichen planus and squamous-cell carcinoma and in healthy women (control group); the results were expected to show the relationship between sFas and clinical features of these diseases.

MATERIALS AND METHODS

The concentration of sFas was measured by enzyme immunoassay in the sera from 40 postmeno-

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0007-4888/07/1436-0727

pausal women (age 50-67 years, 2-16 years postmenopause duration) with different clinical forms of lichen planus: typical (n=10), exudative hyperemic (n=16), and erosive ulcerative (n=14). Concomitant chronic somatic diseases were detected in 67% patients with lichen (chronic gastrointestinal, cardiovascular diseases, and diseases of the reproductive system).

Twelve patients with oral squamous-cell cancer (stage III) aged 52-67 years (postmenopause of 4-14 years) were examined.

Control group consisted of 25 healthy women aged 50-65 years (postmenopause duration 4-12 years).

Serum level of sFas was measured after overnight fasting in patients with lichen planus before therapy and in healthy women by enzyme immunoassay, developed at M. M. Shemyakin and Yu. A. Ovchinnikov Institute of Organic Biochemistry and N. N. Blokhin Oncological Center [1].

RESULTS

Soluble Fas was detected in the sera of 29 of 40 patients with lichen (in 72.5% cases; Table 1). Dispersion analysis showed that the mean level of sFas in patients with lichen planus was higher (3.37± 0.50 ng/ml) than in healthy women and virtually did not differ from the level in patients with oral squamous-cell cancer.

Soluble Fas was rarely detected in the control group compared to patients with oral lichen and oral squamous cell cancer. The differences in the incidence of sFas in the serum between patients with lichen and cancer and in healthy women were statistically significant (p=0.0025).

The incidence and levels of sFas in patients with lichen planus did not depend on patient's age and disease duration.

Soluble Fas was detected 1.9-2.2 times more often in the sera of patients with various clinical forms of oral lichen planus (except typical form) than in controls (Table 1).

The incidence of sFas values corresponding to the control group was minimum in patients with erosive ulcerative lichen planus (0%) and squamous-cell cancer (11.1%), being somewhat higher in patients with exudative hyperemic lichen (27.3%). Serum levels of sFas corresponding to the control level were significantly (p=0.004) more often de-

TABLE 1. Serum sFas in Female Patients with Different Clinical Forms of Oral Lichen Planus and Oral Squamous Cell Cancer and in Healthy Women

Group	Incidence of sFas		sFas concentration, ng/ml		
	abs.	%	$M\pm m$	range of values	median
Healthy women (n=25)	9	36	1.31±0.06	0.70-1.38	1.26
Oral lichen planus of the oral mucosa					
exudative hyperemic form (n=16)	11	68.8	2.8±0.4*++	1.1-5.0	2.8
erosive ulcerative form (n=14)	11	78.6	4.9±0.8*+	1.8-8.6	5.0
typical form (n=10)	7	70	1.9±0.3	1.1-3.0	1.4
Oral squamous-cell cancer (n=12)	9	75	3.7±0.8*+	1.3-8.0	2.6

Note. *p<0.05 compared to healthy women; +p<0.01 compared to typical lichen planus; ++p<0.05 compared to erosive ulcerative form.

TABLE 2. Serum sFas in Patients with Oral Lichen Planus of Different Location of foci

Group	n	Incidence of sFas		sFas concentration, ng/ml		
		abc.	%	$M\pm m$	range of values	median
Buccal mucosa	10	6	60	2.9±0.5	1.1-5.4	1.8
Tongue mucosa	6	5	83.3	3.9±0.8	2.0-7.2	3.1
Mucosa of oral cavity bottom	11	9	81.8	4.7±1.0	1.1-8.6	4.6
Gingival mucosa	8	4	50	1.9±1.0*	1.2-8.0	1.8
Buccal and tongue mucosa	5	4	80	2.4±0.1*	1.2-3.0	2.4

Note. *p<0.05 compared to oral cavity bottom mucosa.

tected in patients with typical forms of oral lichen planus (42.9%).

Analysis of dispersions showed significantly higher level of sFas in the sera of patients with all forms of lichen planus (except typical form) compared to the control (Table 1).

Multiple comparisons (Scheffe's test) showed that sFas content in erosive ulcerative lichen planus was significantly higher than in exudative hyperemic (p=0.018) and typical forms of lichen planus (p=0.004). No differences between sFas levels in patients with squamous-cell cancer and typical lichen planus were detected.

Hence, the incidence and degree of the increase in serum sFas concentration directly depend on clinical form of oral lichen planus.

Analysis of the incidence and level of serum sFas in patients with lichen of different location on the mucosa showed that sFas was least incident in patients with lichen located on the buccogingival mucosa (Table 2). sFas was more often detected in patients with lichen planus located on the mucosa of the bottom of the oral cavity.

Analysis of dispersions of sFas levels in the sera of patients with lichen planus showed significantly higher values in cases with lichen located on the mucosa of the oral cavity bottom than on the buccogingival and lingual mucosa (Table 2).

Normal sFas levels were detected in 33.3% patients with lichen located on the buccal mucosa, 28.6% patients with involvement of the gingival mucosa, and 11.1% patients with foci on the oral cavity bottom. The content of soluble Fas in patients with lichen planus foci located on the lingual and buccal mucosa were above the control in all cases.

Only a trend to difference in sFas levels (p=0.09) was detected in patients with lichen planus with and without history of concomitant chronic somatic diseases (2.9±0.5 and 4.4±0.6 ng/ml, respectively).

No correlation between sFas level and patients' age and between sFas and duration of the disease in the total group of patients with lichen planus was detected. No significant correlation between serum sFas level and disease duration was detected in patients with exudative hyperemic (r=0.55; p=0.08), erosive ulcerative (r=0.5; p=0.12), and typical lichen (r=0.5; p=0.14).

Hence, serum levels of sFas in patients with oral lichen planus depend on clinical form of the disease; the highest sFas levels were detected in patients with foci on the oral fundus mucosa. Serum sFas level in lichen planus patients did not depend on the presence of concomitant chronic somatic diseases, patients' ages, and disease duration.

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