Langerhans' Cells in Cervical Condyloma and Intraepithelial Neoplasia in Smoking and Non-smoking Adolescents

Sir,

Papillomavirus infection, early sexual activity and smoking are considered independent risk factors for cervical neoplasia. However, there is no consensus on the correlation between smoking and the development of cervical condyloma and intraepithelial neoplasia in sexually active young women (1–4). The results of a recent case-control study in Brazilian adolescents concluded that smoking was a significant independent risk factor for cervical condyloma associated or not with cervical intraepithelial neoplasia (CIN) (5). Zanninetti et al. (6) and Moscicki et al. (3) found no statistically significant relationship between smoking and human papillomavirus (HPV) infection in female adolescents with altered Pap smear or DNA-HPV positive hybridization. On the other hand, a positive association between cervical invasive cancer and smoking has been established, with a relative risk of 1.8 to 10 (4).

The oncological mechanism triggered by smoking is not well understood, but it may involve changes in cellular immunity, since it has been stated that cervical biopsies show a reduced number of Langerhans' cells and an increased frequency of morphological alterations in the epithelium (7). The aim of this study was to compare the number of epithelial Langerhans' cells in cervical biopsies of sexually active smoking and non-smoking adolescents, who had cervical condyloma with or without CIN. It was intended to clarify the effect of smoking on these accessory immunological cells and on the predisposition of cervix epithelium to undergo viral infection with corresponding morphological changes.

SUBJECTS AND METHODS

Langerhans' cells were counted in cervical biopsies of 49 sexually active adolescents aged 14–19 years (median =18 years) with cervical condyloma. Sixteen patients had never been pregnant, while 33 had had one to three pregnancies. Twenty-three patients had only one sexual partner, while the remaining 26 had 2 to 5 partners (overall mean 2 sexual partners). Twenty patients were smokers and 29 non-smokers. The 20 smokers had been smoking 3 to 40 cigarettes a day (mean = 13 cig./day) for 6 to 96 months (mean = 42 months). Cervical biopsies obtained through colposcopy were formalin-fixed and paraffin-embedded for analysis. Langerhans' cells were detected by an immunohistochemical reaction using the polyclonal antibody to S-100 protein (DakoPatts). Previous enzymatic digestion with trypsin was performed on sections, and incubation with the antibody (dilution 1:1000) took place overnight at 4°C. Reaction was revealed using the streptavidin-biotin-peroxidase method. The number of labeled cells per mm² was determined by light microscopy. Prevalence of CIN and number of Langerhans' cells per mm² were correlated with smoking × non-smoking, number of sexual partners (one × two or more), number of pregnancies and use of oral contraceptives. Univariate analysis was performed using chi-square test and Student's unpaired t-test to compare the means.

RESULTS

Twenty-nine patients had pure cervical condyloma, while in 20 this lesion was associated with intraepithelial neoplasia (9 CIN I; 6 CIN II and 5 CIN III). The number of sexual partners and the use of oral contraceptives were not statistically associated with CIN. The number of Langerhans' cells per mm² was 2.6 ± 2.1 in pure condyloma vs. 1.9 ± 1.8 in condyloma plus CIN (not significant, p = 0.38). In non-smoker adolescents, counts were 2.6 ± 2.3 vs. 1.8 ± 1.4 for smokers. This difference was not statistically significant (p = 0.159), nor could we detect differences in cell counts according to duration of smoking, previous pregnancy, use of oral contraceptives, or number of sexual partners.

DISCUSSION

In cervical neoplasia, HPV probably acts as an epigenetic factor. During adolescence cervix has a high biological activity, which favours faster viral replication leading to preneoplastic cell changes. However, in only 1% of infected women will this condition progress to invasive cancer. In the present study 23 patients were also studied for HPV. HPV genome could be detected in 16 of 23 patients by in situ hybridization on paraffin sections: 2 types 6/11, 3 types 16/18, 2 types 31/33/51, and 9 of them were infected by more than one HPV type (unpublished data). The association between CIN and condyloma in 41% of our cases strongly suggests that the two lesions may have a common pathogenetic agent. The presence of CIN II and III in 22% of these young women evidences the noxious participation of HPV infection leading to potentially neoplastic changes of epithelial cells in such a short period of time.

Certain factors appear to facilitate neoplastic transformation, such as vaginal secretions and immunological status (7). However, in our series data do not support the statement that smoking may be associated with a significant decrease in Langerhans' cells counts. In addition, Langerhans' cells counts were not significantly different among patients with or without CIN. In spite of the high frequency of CIN associated with condylomatous lesions in such a young population, which has been sexually active for only a short time, this parameter remained unaltered in both groups, smokers and non-smokers. Whether smoking will alter the progression of the disease in these girls must be further investigated.

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Serum Levels of Soluble CD14 in Scleroderma

Sir,

The course of the immunological dysregulations in systemic sclerosis (SSc) is still unknown. Our group has documented that miners exposed to silica dust over decades can develop scleroderma indistinguishable from the idiopathic disease (1, 2). Furthermore, we were able to show that monocytes after incubation with silica crystals release fibrogenic cytokines like IL-6 (3). In the inflammatory stage of SSc, monocytes are found in the perivascular infiltrates of the dermis. CD14 is a marker of these cells and shed into circulation after activation (4). Soluble CD14 (sCD14) in serum has been used as a marker of monocyte activation in atopic dermatitis and psoriasis (5, 6). In view of these data, we were interested in knowing whether a general and widespread activation of monocytes/macrophages in SSc patients could be detected using the sCD14 ELISA.

We measured the serum level of soluble CD14 using an ELISA from Immuno Biological Laboratories (IBL), Hamburg, Germany, with a normal range: <3.5–250 ng/ml. The concentration was measured in 20 sera of scleroderma patients with the following characteristics: 15 female, 5 male. Skin involvement limited to the hands and face: 5 patients; sclerosis ascending the limbs: 12 patients; generalised involvement of the skin including the trunk: 3 patients. In 3 patients the joints were affected. Involvement of internal organs was: oesophagus: 12 patients; lung: 9 patients; kidney: 0 patients. Disease activity was classified as either “active SSc” (n = 11) or “inactive SSc” (n = 9) according to the following criteria: active SSc: elevation of C reactive protein, ESR and/or immune complexes, leukocytosis, ANF titre > 1,024, clinical skin aspect of inflammation: oedema, redness and terness, inactive SSc: ANA titre < 512, indurated but not oedematous or atrophic skin, ESR and C reactive protein in the normal range.

Serum levels of sCD14 were in the normal range in SSc patients. Only 1 SSc patient showed a slightly raised sCD14 value of 4.21 ng/ml. No correlation with clinical findings was observed.

Even if there is an activation of macrophages in the tissue microenvironements, this does not seem to result in elevated serum levels.

REFERENCES


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