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CASE REPORT

Very early cytological and DNA-cytometric diagnosis of *in situ* carcinoma in an immunosuppressed liver transplant recipient

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BACKROUND: We describe a patient with an *in situ* carcinoma with the clinical presentation of an erythroplakia of the tongue in an area where DNA-aneuploidy was detected by means of exfoliative cytology (EC) and DNA-image-cytometry 32 months before.

METHODS: Brush- and scalpel biopsies were obtained from a suspicious lesion of the right border of the tongue prior to scalpel biopsy. After Feulgen restaining of the specimens on glass slides, nuclear DNA-contents were measured using a TV image analysis system.

RESULTS: A small reddish lesion of the tongue was diagnosed as malignant through EC and DNA-image-cytometry, whereas the synchronous histology from the same area showed only mild dysplasia. A subsequent scalpel biopsy 32 months after the first examination showed an *in situ* carcinoma.

CONCLUSIONS: Non-invasive brush biopsies are of great importance for the very early identification of mucosal areas with a high risk for malignant transformation through cytological and DNA-cytometric examination.

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Keywords: DNA-image-cytometry; liver transplantation; oral erythroplakia; oral exfoliative cytology

Description of the case

In January 2002, a 62-year-old Caucasian male contacted the department of oral surgery for a focus examination before liver transplantation. The patient did not report any complaints from the oral cavity and was a non-smoker, but he used to drink alcohol until the diagnosis of liver cirrhosis due to alcohol abuse. After a thorough clinical and radiological examination of the teeth and oral mucosa, a reddish, elevated, non-ulcerated, painless oral lesion was found on the right lateral border of the tongue (Fig. 1). Two brush biopsies for cytological examination were obtained from the lesion and the adjacent normal appearing oral mucosa, which revealed the diagnosis of severe dysplasia (Fig. 2). Because of this fact a DNA-image cytometry was performed, which showed DNA-aneuploidy with abnormal DNA-stemlines around 4c and 8c and 12 cells with DNA-content greater than 9c (Fig. 3). Furthermore, an incisional biopsy was performed from the reddish lesion, which showed discrepancies of the histological diagnoses of four pathologists, but mainly revealing mild dysplasia (Fig. 4) (1). Because of the urgent need for liver transplantation, it was decided – after detailed discussion with the physicians of the patient – not to excise the lesion, but to keep the patient in follow-up. Four brush biopsies for cytological examination, taken from the reddish lesion and the adjacent normal appearing oral mucosa 32 months after the first examination (August 2004) revealed once more severe dysplasia and

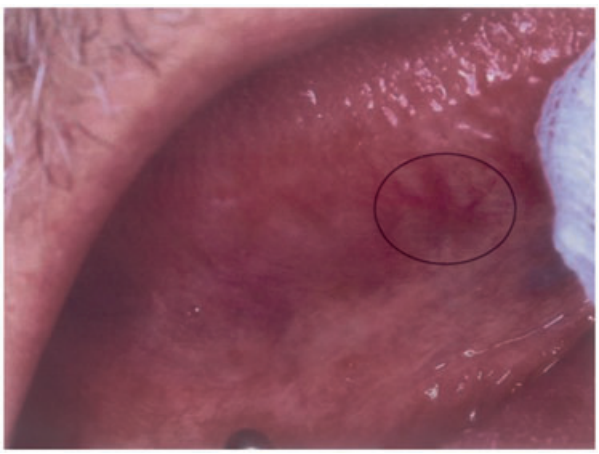

Figure 1 Erythroplakia of the lateral border of the tongue.

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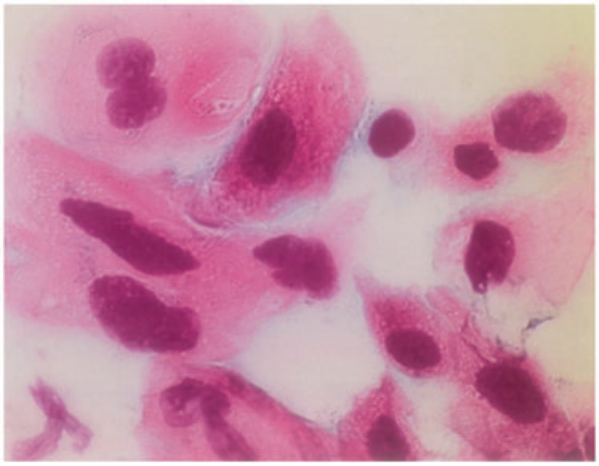

Figure 2 Cytological specimen of the erythroplakia above, showing severe dysplasia.

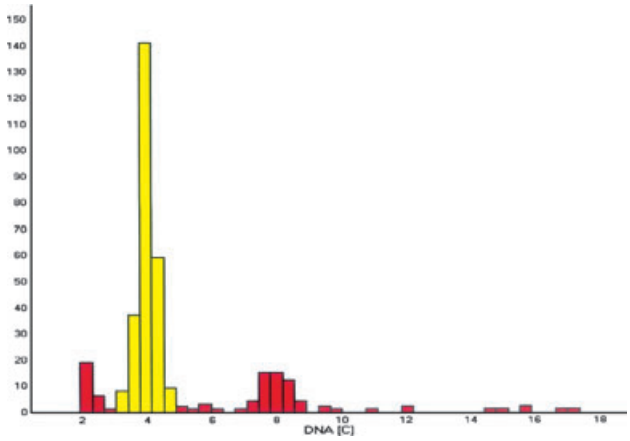

Figure 3 DNA-histogram of an erythroplakia revealing DNA-aneuploidy (abnormal stemlines at 4c and 8c/12 cells with DNA-content greater than 9c).

DNA-cytometry showed DNA-aneuploidy. Synchronous histology showed a progression of the lesion with a severe dysplasia with the final diagnosis of *in situ* carcinoma (Fig. 5). The polymerase chain reaction (PCR) examination of the histological specimen showed no signs of HPV infection. In particular, literature shows that immunosuppressed patients with severe dysplasia or in situ carcinoma, as observed in our case, show a fast progression to an invasive carcinoma. Therefore, we decided for an immediate operation in the clinic for oral and maxillofacial surgery, in order to excise the whole lesion.

Comments

As already proven in clinical practice, exfoliative cytology combined with DNA-image cytometry can early detect oral cancer and its recurrence and also specify the prospective behaviour of oral dysplastic lesions (1, 2). Moreover, Hernandez et al. (3) described a rapid progression of a leukoplakia to squamous cell

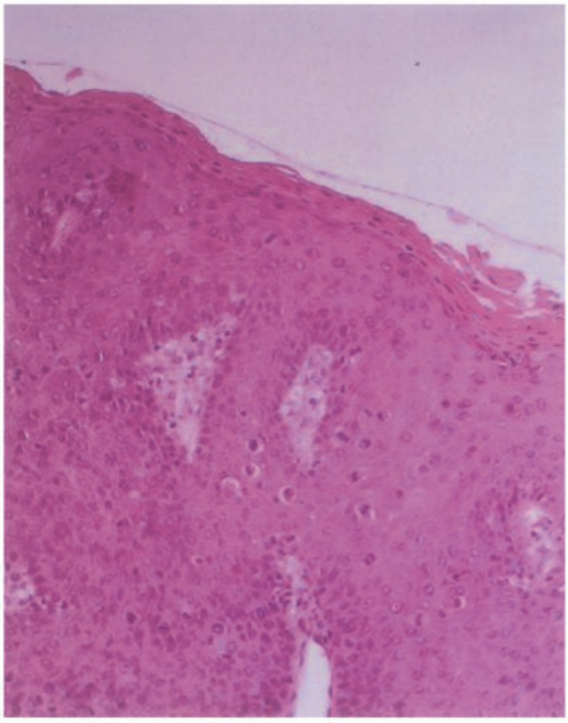

Figure 4 Histological specimen of the erythroplakia (January 2002), showing the diagnosis of mild to severe dysplasia (200×).

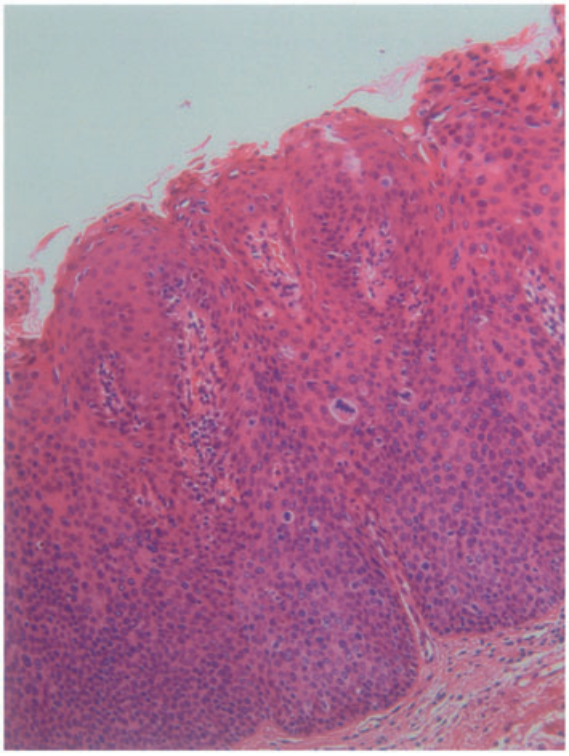

Figure 5 Histological spcimen of the same erythroplakia in August 2004, revealing an *in situ* carcinoma (200×).

carcinoma in an immunosuppressed patient 4 months after liver transplantation. With regard to alcohol consumption, the authors mentioned that oropharyn-

geal squamous cell carcinoma exclusively occurs in alcoholics, who received liver transplantation, when compared to non-alcoholics. In view of the cases mentioned above, we underline the importance and need for a very early diagnosis of oral cancer, especially in immunosuppressed recipients, who show a faster progression of dysplasia in comparison to normal, healthy patients (3). Sudbø et al. (4, 5) could show on archived material that 84% of DNA-aneuploid oral leukoplakias and 92% of DNA-aneulpoid erythroplakias developed histologically evident malignant transformation after a mean time of 35 months and 53 months, respectively following initial histological examination. In our opinion, DNA-aneuploidy is the cause of malignant transformation in a very early cellular level, which cannot yet be distinguished by synchronous histology (1). Therefore, we accept – as a gold standard for the examination of DNA-aneuploid oral lesions – the histopathological diagnosis of the follow-up, which has been confirmed in the course of many years. Our case report reveals a very early diagnosis of malignant transformation of an oral erythroplakic lesion, through exfoliative cytology and DNA-image cytometry, 32 months prior to histological confirmation of an *in situ* carcinoma and supports once more the proven hypothesis, that oral lesions which show DNA-aneuploidy should be immediately excised completely and sent for a histological examination, in order to remove epithelial areas with very early malignant transformation.

Incisional biopsies bear principally the risk of sampling errors. In order to minimize this risk in our case, we made a photo-documentation both before taking a brush and an incisional biopsy, which enabled us, to compare the areas biopsied. Furthermore, the size of the second incisional biopsy (August 2004) was at least 2×1 cm, so that the borders of this histological specimen were beyond the area biopsied the first time. Additionally, in order to further minimize sampling errors, we use as a routine examination exfoliative cytology and DNA-image cytometry, which are suitable not only for the early diagnosis of oral cancer, but also for screening large mucosal lesions.

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