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Are Acquired Nevi Oestrogen-dependent Tumours?

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Jemec GBE, Bhogal BS, Wojnarowska F. Are acquired nevi oestrogen-dependent tumours? Acta Derm Venereol (Stockh) 1987; 67: 451–453.

Twelve benign acquired nevi were studied for the possible specific binding of the ER D5 monoclonal antibody. The ER D5 monoclonal antibody identifies the p29 protein, which is found in the cytoplasm of oestrogen-sensitive cells and which is present in a higher concentration than nuclear oestrogen receptors. No staining was seen in nevoid cells, and the results are taken to support the hypothesis that acquired nevi are not oestrogen-dependent tumours. (Received January 23, 1987.)

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Acquired benign nevi are known to grow in puberty and pregnancy, and biochemical investigations using radio-labelled oestrogens in competitive binding studies have implied that nevi may be oestrogen-sensitive tumours (1, 2, 3, 4). In immunofluorescence studies using FITC-labelled oestrogens (5, 6, 7) these findings could only be reproduced in part, and it would seem that acquired nevi do not bind fluorescent labelled oestrogen (6). Because of the possible association between malignant melanoma and nevi, it was decided to test acquired nevi for the presence of p29 protein. The p29 protein is found in the cytoplasm of all normal oestrogen-sensitive cells, and is present in a higher concentration than actual nuclear oestrogen receptors (8, 9). The p29 protein is identified with the ER D5 monoclonal antibody, and the technique offers the advantage of not crossreacting with tissue enzymes as does labelled oestrogen (10), thereby eliminating false-positive results.

MATERIALS, METHODS AND RESULTS

Acquired and obviously benign nevi excised for cosmetic reasons at the request of the patients were used in this study, with the permission of the patients. The patients were all in good health, and not on treatment with oestrogens or steroids. Twelve nevi were excised from eight patients (7 female, 1 male), the average age of the patients was 38.9±14.1 years and histologically seven nevi were of the compound type, one junctional and four intradermal.

ER D5 monoclonal antibody and normal mouse serum were obtained from Amersham International

plc. The FITC-labelled anti-mouse link antibody was obtained from DAKO (U.K.) Ltd. Normal human vaginal tissue and myometrium were used for positive controls.

Immediately after excision the tissue was fixed in PLP-fixative (11) for one hour at 4°C. Maintaining the same temperature the tissue was then transferred to Phosphate-Buffered-Saline (PBS) and stored before further processing. The tissue was dehydrated through ethanol and xylene, and imbedded in paraffin at a temperature not exceeding 60°C. Sections were cut at 4 microns. Prior to staining the sections were rehydrated through xylene, ethanol and PBS. The staining itself was a two-step indirect immunofluorescence technique, with all incubations taking place at 37°C and lasting 45 min each.

The results were identical in all samples stained. There was a strong specific staining in all the epidermal structures as expected from previous studies. This staining correlates well with the specific staining seen in known oestrogen-sensitive tissue such as vaginal tissue and myometrium. In none of the sections any specific staining was seen of the nevoid cells or the surrounding tissue.

DISCUSSION

In states of hyperoestrogenism such as pregnancy and use of high dose oestrogens for contraceptive purposes, changes in nevus size and pigmentation have been seen, suggesting a causal relationship between oestrogen levels in blood and growth of nevi. Similarly reports of increased mortality from melanoma in pregnancy (12, 13) have suggested that malignant melanoma may be an oestrogen-influenced tumour. These observations have led to a search for specific oestrogen-binding proteins in both malignant melanoma and benign nevi. The techniques used have been competitive binding studies using labelled hormone, and the results have generally indicated that these tumours did contain oestrogen receptors and hence were likely to be oestrogen-dependent. Later studies have disputed this (10) and showed that interaction between tissue tyrosinase and tritium-labelled oestrogen causes a significant false-positive result in such studies. In studies using FITC-labelled hormone (7) specific binding was shown to be reproducible even when levodopa was added to block the tissue tyrosinase. Recently studies using monoclonal antibodies against nuclear oestrogen receptor have not been able to show an increased presence of these receptors in malignant melanoma (14). Since as many as 20 % of all malignant melanomas have adjacent elements of nevoid tissue, it has been suggested that a portion of malignant melanomas do arise from preexisting nevi, and this has led to a natural interest in the possible oestrogen sensitivity of nevi.

Biochemically oestrogen has been shown to bind to nevi in studies using the same biochemical techniques as the studies of malignant melanoma referred to above, and therefore with the same risk of false-positive results. Studies using FITC-labelled hormone have however been able to show increased uptake of oestrogen in congenital nevi, but not in acquired nevi (6). No studies have been made using monoclonal antibodies against nuclear oestrogen receptor. The monoclonal antibody used in the present study is purely cytoplasmic in its staining and bind specifically to the p29 protein, which is found in the cytoplasm of all normal oestrogen-sensitive cells. It is not binding to nuclear oestrogen receptor, which is present in much smaller concentrations than is the p29 protein. Therefore one may conclude that the ER D5 antibody is suitable for the study of oestrogen-sensitivity in various tissues, and the results obtained in this study taken to support the hypothesis that acquired nevi are not oestrogen-sensitive or oestrogen dependent tumours.

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Common Warts Suggestive of Allergy to Metals: A Case Report

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Kokelj F. Common warts suggestive of allergy to metals: A case report. Acta Derm Venereol (Stockh) 1987; 67:453–455.

This report describes the case of a woman positive to nickel and cobalt patch tests and presenting common warts in the sites of contact with metals. *Key words: Patch test; Nickel sulphate; Cobalt sulphate.* (Received February 27, 1987.)

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A patient who was allergic to metals—nickel and cobalt—had as main symptom an eruption of multiple common warts in the sites of contact with metal bracelets.

CASE REPORT

The patient (G. B.) is a 33-year-old woman employee. The physiological and remote history did not reveal any significant feature apart from the fact that the 10-year-old daughter had repeatedly presented common warts on her hands and on her right knee. The patient came to our observation, when multiple warts appeared on her left wrist, particularly on the volar side. We noticed numerous (about 40) small papules with smooth surface, neat border and average diameter of 4–6 mm. The colour was similar to that of the surrounding skin and neither itching nor pain were reported. The patient told us that the lesions appeared after wearing a bracelet of non-precious metal for some time