Lack of Progesterone Receptor Expression in Extramammary Paget's Disease

Sir,

Extramammary Paget's disease occurs either in the anogenital region, in the axilla, or most commonly in the vulva (1). It occurs more frequently in women than men and usually occurs in the fifth decade or later. In some cases, an underlying sweat gland adenocarcinoma or a primary carcinoma of other organs, such as the rectum, urethra or cervix uteri is found; however, in other cases it occurs primarily in the epidermis as carcinoma in situ. Although a number of studies have been performed concerning the expression of oestrogen receptor (OR) and/or progesterone receptor (PR) in breast carcinoma (2, 3), little is known about the expression of OR or PR in extramammary Paget's disease. A recent study showed OR to be negative in extramammary Paget's disease specimens (4). In this study, we examined PR expression in extramammary Paget's disease using an immunohistochemical method.

MATERIALS AND METHODS

Surgical specimens from 4 men and 5 women (aged 59-92 years) with extramammary Paget's disease were examined for PR expression, 6 were of *in situ* and 3 of invasive carcinoma, of which 2 had lymph node swelling. One breast carcinoma specimen was used as a positive control. The PR content in this control was measured with enzyme immunoassay (5), which revealed 468 fmol/mg protein, and this specimen was thus used as a positive control. None of the 9 extramammary Paget's disease patients had either underlying sweat gland adenocarcinoma or a primary carcinoma of other organs.

The formalin-fixed, paraffin-embedded tissue specimens and positive control specimens, were cut into 5- μ m sections and then deparaffinized. The sections were incubated for 30 min in 1% hydrogen peroxide to block any endogenous peroxidase activity. After blocking with normal goat serum, the sections were incubated with rabbit polyclonal anti-PR antibody (C-19, Santa Cruz, CA, USA) or mouse monoclonal anti-OR antibody (C-314, Santa Cruz, CA, USA) at a concentration of 2 μ g/ml. The sections were subsequently treated with secondary antibody using the Vectastain ABC-Peroxidase kit (Vector, CA, USA) followed by staining with the Vector VIP peroxidase substrate kit (Vector, CA, USA), and were then counterstained with methyl green.

RESULTS AND DISCUSSION

The positive control breast carcinoma section showed positive staining for PR, according to the immunohistochemical method using rabbit polyclonal anti-PR antibody. However, no positive staining was observed when the 9 extramammary Paget's disease specimens were stained for either PR or OR.

Lloveras et al. (4) examined OR expression in extramammary Paget's disease specimens and normal skin appendages, such as the eccrine and apocrine sweat glands, by an immunohistochemical method using a monoclonal antibody to OR. They failed to detect any OR expression. Based on these results, they concluded that extramammary Paget's disease, as well as normal skin appendages, either do not express OR or contain OR in undetectable amounts by immunohistochemical methods. They also speculated that OR may appear in breast tissue as a step in selective differentiation distinct from normal skin and appendages. Our results seem to correlate closely with their findings (4). The absence of both PR or OR expression in extramammary Paget's disease may therefore indicate that extramammary Paget's disease has an essentially different nature from that of breast carcinoma.

REFERENCES

- MacKie RM. Extramammary Paget's disease. In: Champion RH, Burton JL, Ebling FJG, editors. Textbook of dermatology, 5th edn, Vol. 2. Oxford: Blackwell Scientific Publication, 1992: 1487– 1488.
- Allegra JC, Lippman ME, Thompson EB, Simon R, Barlock A, Green L, et al. Distribution, frequency, and quantitative analysis of estrogen, progesterone, androgen, and glucocorticoid receptors in human breast cancer. Cancer Res 1979; 39: 1447–1454.
- 3. Wittliff JL. Steroid-hormone receptors in breast cancer. Cancer 1984; 53: 630-643.
- Lloveras B, Googe PB, Goldberg DE, Bhan AK. Estrogen receptors in skin appendage tumors and extramammary Paget's disease. Modern Pathol 1991; 4: 487–490.
- Jordan VC, Jacobson HI, Keenan EJ. Determination of estrogen receptor in breast cancer using monoclonal antibody technology: results of a multicenter study in the United States. Cancer Res 1986; 46 (Suppl): 4237–4240.

Accepted February 21, 1999

Sumihisa Imakado¹, Hisae Satomi¹, Yoshiyuki Ishii¹, Yuji Aiyoshi² and Fujio Otsuka¹

Departments of ¹Dermatology and ²Surgery, Endocrinology and Metabolism, Institute of Clinical Medicine, University of Tsukuba, 1-1-1 Ten-nodai, Tsukuba, Ibaraki 305-8575, Japan.