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Prognostic Significance of TGF-β2 Expression in Female Breast Cancer

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A VARIETY of polypeptide growth factors may have a potential role in breast cancer cell growth [1], one of which is transforming growth factor beta (TGF-β) [1]. In fact, TGF-β is a family of five different peptides, three (TGF-β1, 2 and 3) being expressed by human cells [1]. The different TGF-β isoforms share 70–80% amino acid sequence homology, and also have partly similar activities *in vitro* [2]. TGF-β has a role in controlling cellular differentiation, but it also affects cell proliferation, angiogenesis, stroma formation and immunosuppression [3]. *In vitro* TGF-β stimulates the growth of fibroblast cell lines, but inhibits the growth of most epithelial cells, including breast cancer cell lines [4].

We studied the expression of TGF-β2 in 273 breast cancer biopsies and analysed its expression in relation to other well established prognostic factors and patient survival.

The material of the present study consists of 273 consecutive women undergoing surgery for invasive breast cancer at Kuopio University Hospital between July 1979 and December 1984, and who were subsequently followed-up until June 1990. The expression of TGF-β2 in 273 formalin-fixed, paraffin-embedded breast cancer sections was examined immunohistochemically with polyclonal TGF-β2 antibody (Santa Cruz Biotechnology, Santa Cruz, California, U.S.A.), showing no cross-reactivity with other TGF-β isoforms. The immunoreactivity of the tumours was assessed using light microscopy and the TGF-β2 expression was classified as negative or positive.

Altogether, 110/273 (40%) tumours were positive for TGF-β2. The expression of TGF-β2 was mostly localised in the cytoplasm of cancer cells, but was ocassionally also expressed in stromal connective tissue. Positive TGF-β2 expression was related to low histological grade ($P = 0.04$) and diploid DNA ($P = 0.05$). TGF-β2 negativity was associated with severe nuclear pleomorphism ($P = 0.02$) and extensive tumour necrosis ($P = 0.07$).

In univariate survival analysis, the TGF-β2 positive cases had a higher survival probability than the TGF-β2 negative ones. Survival probability in the entire cohort at 10 years was 66% in the TGF-β2 positive cases and 55% in the TGF-β2 negative cases ($P = 0.09$) (Figure 1). In axillary lymph node negative (ANN) tumours, the survival probability at 10 years was 82% in the TGF-β2 positive cases and 63% in the TGF-β2 negative cases ($P = 0.06$). The recurrence-free survival was also better in the TGF-β2 positive cases, but the difference was not statistically significant. In multivariate analysis, TGF-β2 was not an independent prognostic factor. Tumour diameter ($P = 0.0073$) and ANN status ($P = 0.0001$) were superior to other prognostic factors.

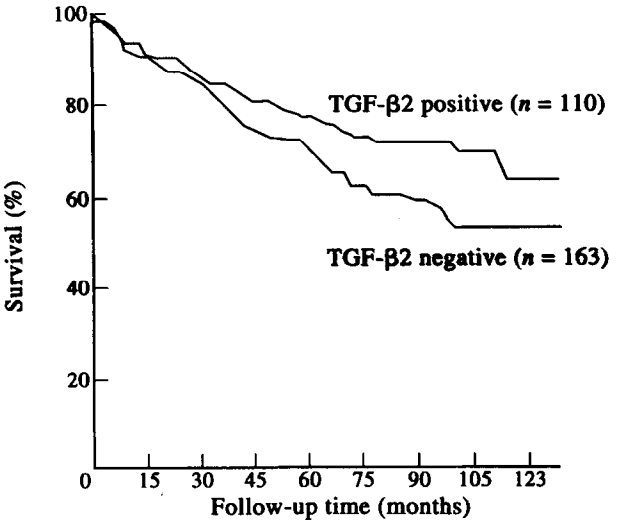

Figure 1. Survival of all the patients categorised according to TGF-β2. The difference in survival between the curves was 11% ($P = 0.09$).

The results indicate that the expression of TGF-β2 is related to some favourable histological features of breast cancer and favourable disease outcome with a borderline statistical significance. However, the expression of TGF-β2 does not have an independent prognostic value over the well-established prognostic factors. The results of the present study are in agreement with some previous clinical reports [4, 5] and also consistent with the data of most experimental studies [6, 7].

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