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Adjuvant Tamoxifen: 5 Year Control of Dormant Disease?

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TAMOXIFEN HAS been accepted as an adjuvant treatment of breast cancer patients, having either advanced age, being postmenopausal, or with positive oestrogen or progesterone receptors. Adjuvant treatment with tamoxifen, 20 mg/day has been shown to improve the overall survival of patients [1] and reduce the local-regional relapse and the rate of distant metastases, as reflected by a longer disease-free survival [2]. Tamoxifen also constitutes a milestone in the treatment of hormone-sensitive metastatic disease, and has been suggested for breast cancer patients with a continuously increasing serum tumour marker level, in the absence of clinical or radiological evidence of disease [3]. The optimal duration of adjuvant tamoxifen treatment has not been determined. It is not yet clear whether treatment for longer than 5 years is better than 5 or even 2 years. A dilemma is commonly raised whenever an out-protocol patient reaches the end of the preplanned period of tamoxifen treatment, especially when the treatment was well tolerated, and the patient is still disease-free.

Here, we describe two breast cancer patients who received adjuvant tamoxifen for 5 years, following which treatment was interrupted. Within a relatively short period, the disease relapsed. Re-introduction of tamoxifen re-controlled the disease for a long period thereafter. Case 1 was a 64 year old female who underwent a modified radical mastectomy in November 1985, for a T1N0M0 infiltrating ductal carcinoma. The oestrogen receptor level was 42 fmol/g and progesterone receptor level was 0 fmol/g. Tamoxifen 10 mg three times daily was started. Thirteen months later, in the absence of clinical, radiological or biochemical evidence of recurrent disease, or a contralateral breast primary tumour, tamoxifen was stopped. Six months later, the MCA (mucin-like carcinoma antigen) level increased from 14 U/ml to 16.5 followed by 17.89 U/ml, without any clinical signs of relapse. Tamoxifen was re-introduced. The MCA level decreased to 12.9 U/ml on February 1992. Over the following 3 years, the disease and the marker levels were within the normal range. Case 2 is a 59 year old female who underwent a modified radical mastectomy in February 1989, for a T1mN0M0 medullary carcinoma of the left breast. The oestrogen receptor level (ER) was 121 fmol/g and that of progesterone was unknown. Tamoxifen 10 mg twice daily was introduced for the following 5 years, and then interrupted. Eight months later, an enlarged left supraclavicular lymph node was palpated. Fine needle aspiration from the node yielded malignant cells compatible with medullary carcinoma of breast. No other sites of disease were revealed on systemic work-up, including bone marrow biopsy. CEA, MCA and CA15.3 levels were within the normal range. Tamoxifen 10 mg twice daily was re-started. The node completely disappeared within the next 3 months.

Both our patients belong to the low risk group characterised by node-negative, ER-positive breast cancer. Our patients seemed to benefit from the adjuvant treatment, although it is not clear whether it was necessary, in view of the good prognostic factors. In both cases, the relapsing cells were hormone-sensitive, instead of hormone-resistant, as might be expected following 5 years of exposure to tamoxifen.

Our observations point to a possible advantage for longer than 5 year duration adjuvant tamoxifen treatment in breast cancer patients. In both patients, metastatic disease developed after discontinuing adjuvant treatment after 5 years. In one case, an overt metastasis appeared in a supraclavicular lymph node, while in the other elevation of the MCA level probably reflected growth of metastases [3–5]. In both cases re-introduction of tamoxifen resulted in regression of the node and a decrease of the marker level back to the normal range.

Since no clear guidelines exist, the oncologist should assess the cost, risk and benefit of interruption or continuation of tamoxifen treatment whenever a breast cancer patient reaches the end of the adjuvant course. However, our cases demonstrated that the relapsing disease was well controlled by re-introduction of tamoxifen, and this approach may be adopted instead of "tamoxifen for life". The twilight zone of the timing for cessation of adjuvant tamoxifen treatment may be illuminated by results of prospective, controlled, randomised studies comparing 5 year with longer period treatment.

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1. Early Breast Cancer Trialist's Collaborative Group. Systemic treatment of early breast cancer by hormonal cytotoxic or immune therapy: 133 randomised trials involving 31 000 recurrences and 24 000 deaths among 75 000 women. *Lancet* 1992, **339**, 1–15, 71–85.
2. Fisher B, Costantino J, Redmond C, *et al.* A randomized clinical trial evaluating Tamoxifen in the treatment of patients with node-negative breast cancer who have estrogen-receptor positive tumors. *N Engl J Med* 1989, **320**, 479–484.
3. Kovner F, Merimsky O, Hareuveni M, Wigler N, Chaitchik S. Treatment of disease-negative but marker-positive breast cancer patients by Tamoxifen: preliminary results of a prospective controlled randomized trial. *Cancer Chemother Pharmacol* 1994, **35**, 80–83.
4. Merimsky O, Inbar M, Hareuveni M, Witenberg B, Wolman Y, Chaitchik S. Serial MCA measurements in the follow-up of breast cancer patients. *Eur J Cancer* 1991, **27**, 1440–1444.
5. Merimsky O, Hareuveni M, Inbar M, *et al.* Increasing serum levels of mucin-like carcinoma associated antigen and mucinous antigen H23 in clinically disease-free breast cancer patients. *Diagn Oncol* 1993, **3**, 61–66.