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Development of Breast Cancer during Long-term Tamoxifen Therapy for Lymphangioleiomyomatosis

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TAMOXIFEN BLOCKS the effects of oestrogen on the breast, but does not act as a pure antioestrogen [1] and is an effective palliative therapy for a proportion of women with advanced breast cancer. In addition tamoxifen can improve survival in certain subgroups of women when used as adjuvant treatment following initial surgery [2]. These data combined with its low incidence of side-effects has lead to proposals in the UK and the USA to investigate its use as a primary prevention in women judged to be at risk of developing breast cancer [3, 4] and pilot studies have commenced [5]. However, as tamoxifen is usually given to women with established breast cancer, there is no information on the development of breast cancer in women given it for other reasons. We have recently observed such a case.

A 49-year-old woman was investigated in January 1988 for pulmonary fibrosis with recurrent pneumothoraces and pleural effusions and was found to have pulmonary lymphangioleiomyomatosis following open lung biopsy. Because of anecdotal reports of tamoxifen use in this rare condition [6] she was given tamoxifen 20 mg each day continuously and over the next 2 years her chest X-ray and pulmonary function assessments remained stable and she symptomatically improved and suffered no further pneumothoraces. In December 1989 she was found to have a 2 cm left breast carcinoma, predominantly intraduct carcinoma but with foci of microinvasion. The intraduct component extended to the deep resection margin of the lumpectomy but the patient refused to proceed to mastectomy and the axillary nodes were not sampled and hormone receptor status was unknown. Local radiotherapy was thought inadvisable because of the risk of worsening the underlying pulmonary fibrosis. Over the ensuing 12 months there has been no evidence of recurrence and mammography of the contralateral breast is normal. The tamoxifen has been continued and the lymphangioleiomyomatosis remains stable. The patient had a hysterectomy many years previously but had no menopausal symptoms and serum leutinising hormone and follicle stimulating hormone levels are in the premenopausal range. She has no family history of breast cancer.

The growth rates of primary breast cancers are highly variable. In a study using serial mammography the mean tumour doubling time was 325 days but varied from too rapid to be measured to no apparent growth [7]. As 20–30 doublings are normally required to produce a clinically evident tumour, in our patient the initial malignant event probably occurred at a considerable time prior to the commencement of tamoxifen. However, the administration of tamoxifen did not prevent the progression to clinically overt breast cancer.

This case illustrates that breast cancer can develop during continuous tamoxifen given for illnesses other than breast cancer. This, however, should not deter the important studies [5] in progress which attempt to determine if tamoxifen can reduce the risk of breast cancer among healthy women with a family history of breast cancer. The use of family history as a selection criterion for preventative tamoxifen therapy in healthy women has been questioned [1], but the lack of this factor in our patient who developed breast cancer despite continuous tamoxifen tends to support the restriction of this prophylactic therapy to healthy women with a close family history of breast cancer.

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Combined Goserelin and Tamoxifen in Premenopausal Advanced Breast Cancer: Duration of Response and Survival

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THE ENDOCRINE effects and efficacy of the luteinising hormone releasing hormone (LH-RH) agonist goserelin as initial hormone therapy for premenopausal advanced breast cancer patients have been reported [1–3]. In an early study [2] of 53 patients we reported a response rate of 31%, comparable to our experience with surgical ooporectomy [4]. Whilst LH-RH agonists reduce ovarian activity they do not interfere with peripheral oestradiol production, a factor believed to play a role in promoting hormone

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