American Thyroid Association Statement on Breast Cancer and Thyroid Hormone Therapy

It has recently been reported [1] that among patients undergoing mammography at a hospital in Detroit, Michigan, the prevalence of breast cancer was higher in women receiving thyroid hormone therapy than in those who were not. Prevalence of breast cancer was said to increase with increasing duration of thyroid hormone treatment, particularly in nulliparous women. Since the time that this report appeared and was widely publicized by the news media, many patients have expressed concern that the thyroid hormone they are taking may be dangerous, and they have inquired as to whether such treatment should be stopped.

The American Thyroid Association, whose membership comprises physicians and basic scientists interested in the thyroid and its diseases, views the aforementioned article with concern, because of both its implication of a possible basic relationship between thyroid therapy and breast cancer and its potential impact on the treatment of patients who require thyroid hormone therapy.

Several aspects of the study reported from Detroit require clarification before the findings can be properly evaluated. The authors of the report did not provide information about any of the following important questions: the nature of the patient's underlying thyroid disease, if any; the dosage of thyroid hormone being taken; the duration of therapy and whether it was intermittent or continuous; whether thyroid hormones were being taken at the time of the study or only in the past; and whether any patient had received radioiodine, antithyroid agents, or other medications, including other hormones. Referral patterns to the hospital, the racial and ethnic mixture of the patients in the groups treated with thyroid hormone and in the control groups, and the frequency and type of coexistent diseases were not stated. We were also not told how the diagnosis of breast cancer was confirmed. Most important, even granted that a valid relationship between thyroid hormone therapy and breast cancer had been established, the central question would remain whether breast carcinoma is associated with thyroid hormone therapy per se, as the authors of the article strongly imply, or with the disease for which thyroid hormone treatment was being employed.

The many data already in the literature, though in themselves inconclusive, give reason to question the inference that might be drawn from the article in question. A relationship between thyroid dysfunction and breast carcinoma has been sought since 1896 when Doctor George Beatson [2] observed objective remissions from metastatic breast carcinoma in two patients given thyroid substance as an adjunct to surgical castration. Definition of the exact relationship has been difficult. Not only do changes in thyroid hormone levels influence the breast directly, but they also cause alterations in the production of other hormones which have been implicated to some degree in the pathogenesis of breast tumors. These include thyroid stimulating hormone [3,4] and prolactin [5-7] as well as estrogenic [8] and androgenic [9,10] steroids. Furthermore, iodine deficiency, which is a cause of thyroid disease, is apparently associated with an increased prevalence of breast carcinoma in humans [11-13] and breast dysplasia in rats [14].

Studies dealing directly with the incidence of breast cancer in patients with thyroid disease have given conflicting results. Attempts to link autoimmune thyroid disease to breast cancer in British and American women [15,16] were unsuccessful, although a significant association seemed to exist in Japanese women [17]. An association between hypothyroidism and the development of breast carcinoma has been both suggested [4,18-21] and denied [22-24]. Recently, Mittra and Hayward [4] used sensitive testing methods to identify early hypothyroidism and reported that breast cancer patients as a group have a lower level of thyroid function than age-matched controls. Nevertheless, among a group of Caucasian women studied by Schottenfeld [23], a history of thyroid disease or thyroid medication was no more frequent among breast cancer patients than among those with benign breast disease, those with other cancers, or those who had an unconfirmed suspicion of cancer. Hyperthyroidism, too, has been linked to breast tumors. In women who had both hyperthyroidism and cancer, Wanebo, Benua, and Rawson [25] found that 56 per cent had breast cancer, an incidence significantly higher than the 36 per cent incidence of breast cancer among all women at that center with malignant neoplasms.
Apart from disorders of thyroid function, thyroid cancer and breast cancer were statistically linked in a series of 100 patients with thyroid cancer who had an 8.7 per cent incidence of breast cancer as opposed to less than 0.2 per cent among the general population of England and Wales [26]. In the area of experimental tumorigenesis, hypothyroidism increased the incidence of tumors induced by 7,12-dimethylbenz[a]anthracene [27], and thyroid feeding reduced the incidence of tumors induced by 3-methylcholanthrene from 92 per cent in euthyroid rats to 36 per cent in hyperthyroid rats [28]. These effects could be related to differences in the rate of metabolism and excretion of the carcinogens rather than a direct effect of thyroid hormones at the level of the breast.

These selected references from an extensive literature indicate that it is difficult to draw meaningful conclusions from a survey demonstrating in one series that there is an association between thyroid hormone treatment and breast carcinoma. Unless precise information is available on the other factors mentioned which may influence the emergence of breast tumors, attention may be focused inappropriately on the thyroid hormone treatment rather than on the conditions it is being used to treat.

Indeed, in contrast to the highly tenuous nature of the relationship between thyroid hormone therapy and breast cancer, the adverse and often serious effects of withholding specific therapy in patients with hypothyroidism are unquestioned. The American Thyroid Association recommends, therefore, that patients who are taking thyroid hormones for well-established indications continue to take their medication. In addition, the Association recognizes the need for and urges strong support for carefully designed and controlled studies of a possible relationship between the thyroid and cancer of the breast in humans.

References


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