



Examination of the breast in women treated for nodular thyroid disorders

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Summary

The relationship between various mammary gland diseases and thyroid disorders has been the focus of interest at many research centres. What has been investigated are various genetic and hormonal underlying factors and conditions as well as the co-existence diseases of both organs.

The aim of the work was to examine the mammary gland in women treated for nodular thyroid disorders.

Material and methods: An analysis is presented comprising 269 patients with a diagnosed nodular thyroid disorders. The diagnosis of the breast included palpation, mammography, ultrasonography. In cases of suspected lesions additionally fine-needle aspiration and surgical biopsy were performed.

Results: Breast cancer, benign lesions and no pathology were found in 2%, 23% and 75% of all patients.

Conclusions: A significantly greater incidence of breast cancer was observed, which justifies especially careful diagnosis of the breast in patients with a well-diagnosed thyroid disorder.

Key words: breast cancer, thyroid disorders.

Ocena gruczołu piersiowego u kobiet leczonych z powodu choroby guzkowej tarczycy

Streszczenie

Związek pomiędzy różnymi schorzeniami gruczołu piersiowego i chorobami tarczycy wzbudza zainteresowanie licznych ośrodków badawczych. Analizowane są uwarunkowania genetyczne, hormonalne, jak również współistnienie chorób obu narządów.

Celem pracy jest ocena gruczołu piersiowego u kobiet leczonych z powodu choroby guzkowej tarczycy.

Materiał i metoda: W pracy przedstawiona jest analiza 269 chorych z rozpoznaną chorobą guzkową tarczycy. Diagnostyka gruczołu piersiowego obejmowała: badanie palpacyjne, mammografię, ultrasonografię, a w przypadku stwierdzenia zmiany dodatkowo: punkcję cienkoigłową i biopsję chirurgiczną.

Wyniki: U 2% badanych rozpoznano raka gruczołu piersiowego, u 23% stwierdzono zmiany łagodne, a u 75% nie wykryto żadnej patologii.

Wnioski: Stwierdzono wyraźnie zwiększoną zachorowalność na raka piersi, co uzasadnia szczególnie wnikliwą diagnostykę gruczołu piersiowego u chorych z rozpoznaną chorobą tarczycy.

Słowa kluczowe: rak gruczołu piersiowego, choroby tarczycy.

Introduction

Epidemiological studies

Among the most important epidemiological studies on the relationship between thyroid disorders and breast diseases are those by Chen et al. [1] using the database from the Surveillance, Epidemiology and End Results (SEER) study by US National Cancer Institute collected from 11 regional cancer registers covering about 14% of the total US population. In 1973-94, 365 women patients suffering from thyroid and breast carcinomas were registered. In 113 cases the thyroid carcinoma was primary (RR,0,99:P=0.57), whereas in 252 cases, breast cancer was detected as a primary tumour (RR,1.18:P=0.007). The conclusion was that in the group of white women before menopause thyroid cancer significantly predisposes the patients to breast cancer (RR,1.42:P=0.001). Vassilopoulou et al. [2] investigated 41.686 patients with breast cancer and 3662 women with thyroid tumours. Using statistical analysis they found that young women with diagnosed thyroid cancer run an increased risk of carcinoma of the breast. Li et al. [3], also on the basis of SEER, reported an increased risk of breast cancer following the diagnosis of thyroid cancer, particularly in women before 45 year of age.

Extensive epidemiological studies based on the Osaka Cancer Registry, were carried out by Japanese researchers. Tanaka et al. [4] determined the so-called O/E (observed/expected) index in women patients who were found to have primary breast cancer. Considerably higher risks of thyroid cancer (O/E=3.7; CI [95% confidence interval]=1.8-12.9) and ovarian cancer (O/E; 95% CI=2.4) were observed, particularly in a group of patients treated with hormones for breast cancer (O/E =5.5; 95% CI=1.8-12.9).

In Russian investigations [5], using a database of 15.627 women with breast cancer, it was statistically proved that the risk of breast cancer in patients with any other carcinomas of the mammary gland, endometrium, thyroid, lung and skin detected earlier was increased.

The most frequently studied problems

Cowden's disease

It is a hereditary autosomal dominant syndrome forming various lesions in the mucosa and skin associated with frequent co-existence of thyroid, breast and endometrium carcinomas. The disease is conditioned by the PTEN gene mutation in chromosome 10 (10q22-23) [6].

Ruvalcaba-Myhre-Smith (Bannayan-Riley-Ruvalcaba) syndrome

This is another hereditary autosomal dominant syndrome also involving PTEN gene mutation. Among the symptoms

and signs of macrocephaly, intestinal polyps, lipomas or "milky" spots there also appear breast and thyroid carcinomas.

Mastopathy vs. simple goiter

Mizia-Stec et al. of the Śląsk Medical Academy [7] have investigated this problem with the use of ultrasonography. They found goiter in 80% of patients with mastopathy. In premenopausal women the levels of prolactine were increased and the triiodothyronine concentrations were normal. On the other hand, in post-menopausal women, in addition to higher prolactine levels, triiodothyronine concentrations were lower.

Autoimmune thyroid diseases vs. breast carcinoma

Thyroid autoimmune diseases associated with breast carcinoma were observed in Greek studies [8]. As many as 43.9% of patients with breast cancer were found to have thyroiditis of immunologic origin.

Hormonal disorders vs. breast and thyroid carcinomas

Women suffering from breast cancer often manifest hormonal disorders or disturbances. Higher estrogen and lower gestagen in the luteal stage are often observed. Lack of melatonin and thyroid hormones as well as an excess of prolactine have been noted. This is the reason why the relationship between the hormonal state and its effect on organs has been subjected to investigations. It was found that triiodothyronine leads to a decrease in mammary epithelial cell proliferation. It also has an estrogen-like effect on the cell cycle by elevating p53 protein levels. Consequently, it leads to hyperphosphorylation of pRb proteins. Interactions between cell lines in breast and ovarian cancers and non-physiological hormone levels are explained by disturbances in the binding ability of thyroid hormones receptors [10].

The aim of the work

The aim of the present work is the examination of the breast in women treated for nodular thyroid disorders.

Material

The study comprised a total of 269 patients treated for thyroid nodular cancer. The largest group was that of women aged 46 and 55 years (32%), and the smallest group was that of less than 35 years of age (18%). 23 percent of patients were those between 36 and 45 years of age, whereas 56-year-olds and older constituted 27% of the total (Figure 1). Two groups were distinguished:

Group I (230 patients) had thyroid cancer, of which 77%

was found to be papillary carcinoma, and Group II (39 patients) treated for non-malignant thyroid diseases such as nodular goiter (67%), Hashimoto's disease or other forms of thyroiditis (23%), and Graves' disease (10%) (Figure 2, 3).

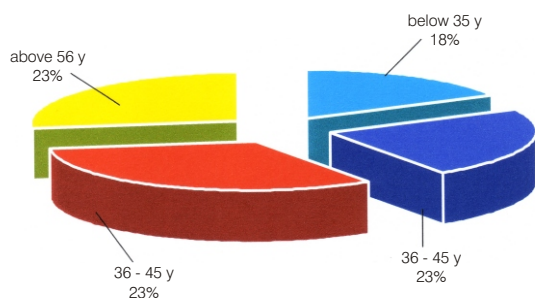


Figure 1. Age distribution of patients with nodular thyroid disorders.

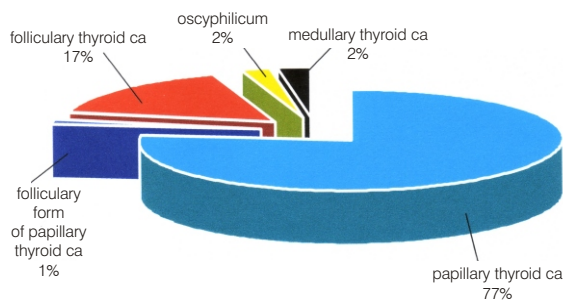


Figure 2. The group of 230 women treated due to thyroid CA.

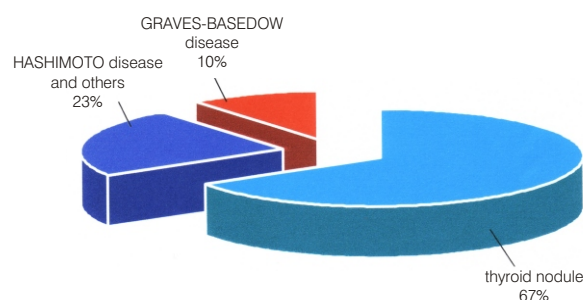


Figure 3. Distribution of nodular thyroid disorder patients vs. microscope diagnosis for the group of 39 PTS with diagnosis of non-malignant disease.

Method

Each patient included in the study had a full spectrum of medical examinations and tests of the mammary gland carried out. These included:

- palpation,
- mammography,
- ultrasonography,
- fine needle biopsy when lesions were found in diagnostic imaging,
- surgical biopsy with the aim of excising the lesion and obtaining complete histopathologic diagnosis.

Results

As a result of the study no pathologic lesions in the breast were found in 75% of patients, whereas 23% women were found to have benign tumours. Breast carcinoma was detected in 2% of the total and radical oncological treatment was initiated.

The incidence of breast cancer in the total of 269 patients was 2.298 per hundred thousand, which is much higher than the age-related morbidity rate of 36 per hundred thousand of the population in Poland (Figure 4).

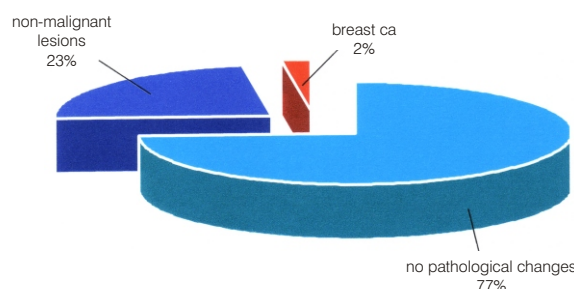


Figure 4. Results of distribution of breast examinations in the group of 269 patients investigated.

Discussion

Breast diseases as well as thyroid disorders are among the most common diseases in women. Their prevalence gives rise to the question whether or not they are inter-related. Breast carcinoma is thought to be the most common malignant tumour and cause of death of cancer origin in women in Poland. Thyroid cancer, albeit much more infrequent, also presents an important medical problem. The high thyroid cancer morbidity rate in women implies that estrogens and/or progesterone may have a role in the progression of the disease of both organs. Immunohistopathologic tests have confirmed the existence of steroid receptors in the thyroid tissue. Benign tumours, however, have been far more frequently observed. In mammary glands these are mostly fibrocystic disease and fibroid adenoma, whereas hormonally non-active adenomas are found in the thyroid gland. In our group under investigation as many as 25% of patients had breast diseases, of which 23% with thyroid nodular tumour had benign forms of breast pathology. Like other authors in most cases we found fibrocystic disease, in less frequent cases intratubular papillomas and in younger patients adenomafibromas were observed. In our study of the invasive mammary glands carcinoma was found in 2% of patients with thyroid nodular tumours detected histologically. This result, reflecting higher morbidity rate than that of the total population, has not so far been unequivocally accounted for, although epidemiological studies cited in medical literature have reported its existence [1,2,3,4].

The mammary gland is among the organs which are fully controlled by hormones, whereas breast cancer is a ma-

lignant tumour dependent on hormones, which can be classified in three categories: reproductive hormones such as estrogen, progesterone, placental lactogen, prolactin and oxytocin, metabolic hormones such as growth hormones, corticosteroids, thyroid hormones and insulin, and recently discovered hormones produced by the mammary gland such as growth hormone, prolactin, PTHrP and leptin. The protective role of pregnancy and breast feeding in reducing the risk of breast cancer is well known. Knowledge of the mechanism of the contributions by various substances, thyroid hormones included, to the cellular differentiation may play a role in the prevention of breast carcinomas [11]. The following are the most common hormonal disorders observed in breast cancer patients: excess of estrogens, low activity of progestins in the luteal phase, deficit of adrenal androgens, excess of ovarian androgens, deficit of melatonin, excess of prolactin and deficit of thyroid hormones [12].

Many authors concur on the opinion that the relationship between the thyroid and its disorders and mammary gland diseases is not clear out. The report by Slivy et al. seem to indicate that disturbances of thyroid hormonereceptor genes, TRalpha and TRbeta have an effect on the progression of breast cancer [13]. Triiodothyronine (T3) lowers the T1 gene expression, the overexpression of which is observed in breast adenocarcinoma cells and is induced by mitogenes and numerous oncogenes and cytokins. According to Gonzales-Sancho et al. T3 lowers the proliferation of mammary cells and inhibits the expression of T1 and D1 cyclin genes [9]. In *in vitro* studies an increase in p53 protein levels in the presence of T3 was also observed [10]. On the other hand, in clinical investigations a significant increase in thyroid disorders in women with breast cancer was noted in the form, among other things, of subclinical deficit of thyroxine and autoimmunologic disturbances [14].

Our results are only preliminary and seem to indicate the need for further investigations of the factors underlying the relationships observed.

Conclusions

In a group of patients with thyroid disorders a greater incidence of mammary gland pathologies has been observed. These results emphasize the need for routine examination of the women patients' breasts by endocrinologists.

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