

## CASE REPORT

# HASIMOTO'S THYROIDITIS AND BREAST CANCER: COINCIDENCE OR CORRELATION?

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### SUMMARY

**Introduction:** Associations between breast cancer and thyroid disease have been reported but no convincing evidence exists regarding the causal role for overt thyroid diseases in breast cancer. In this context, we present the case of a middle-aged female patient with breast cancer and chronic autoimmune thyroiditis in an attempt to establish a correlation between the two disorders.

**Case report:** A 58-year old non-smoking female was diagnosed and treated for right breast cancer at age of 55. Mammogram and ultrasound pointed out one suspicious mass of the right breast of 2 centimeter. There was no evidence of abnormalities of the left breast on physical exam and radiological examinations. Core needle biopsy of breast mass revealed ductal carcinoma without infiltrations in surrounding structures. A unilateral mastectomy with sentinel node excision was performed. Radiotherapy and three cycles of chemotherapy were added. One year later, the patient presents marked fatigue, daytime sleepiness and bowel disorders. Thyroid function and autoimmunity profile showed: an increase of thyroid antibodies and hypothyroidism, and hypoechoic pattern on ultrasound, suggesting autoimmune thyroiditis. Therapy with daily levothyroxine was recommended. The subject associated metabolic risk factors as obesity, hypercholesterolemia, and hypertriglyceridemia. Bone assessment found osteoporosis with low 25-hydroxyvitamin D. Hypolipemiant therapy, injectable yearly 5 mg zoledronic acid, calcium and vitamin D supplements were recommended. The patient will be further followed-up by a multidisciplinary team regarding the thyroid, bone and oncologic profile.

**Conclusions:** There is still controversy regarding the potential correlations between breast cancer and thyroid disease by sharing common cytokine anomalies interactions between thyroid hormone

### RÉSUMÉ

**La thyroïdite de Hashimoto et le cancer de sein: coïncidence ou corrélation?**

**Introduction:** Les associations entre le cancer du sein et les maladies de la thyroïde ont été rapportés mais, il n'y a aucune preuve convaincante concernant le rôle causal des maladies de la thyroïde manifesté dans le cancer du sein. Dans ce contexte, nous présentons le cas d'une patiente d'âge moyen avec un cancer du sein et une thyroïdite auto-immune chronique en essayant d'établir une corrélation entre les deux affections.

**Présentation de cas:** Une femme âgée de 58 ans, non-fumeuse, a été diagnostiquée et traitée pour un cancer du sein droit à l'âge de 55 ans. La mammographie et l'échographie ont révélé une masse suspecte de 2 cm au sein droit. Il n'y avait aucune preuve d'anomalies du sein gauche aux examens physique et radiologiques. La biopsie à l'aiguille fine de la masse tumorale a montré un carcinome canalaire sans infiltrations dans les structures environnantes. Une mastectomie unilatérale avec l'excision du ganglion sentinelle a été effectuée. On a ajouté de la radiothérapie et trois cycles de chimiothérapie. Un an plus tard la patiente présente de la fatigue marquée, une somnolence diurne et des troubles intestinaux. La fonction thyroïdienne et le profil de l'auto-immunité ont montré: une augmentation des anticorps thyroïdiens et de la l'hypothyroïdisme et le modèle hypo-échogène à l'échographie, ce qui suggère la thyroïdite auto-immune. On a recommandé le traitement par la lévothyroxine chaque jour. La patiente a associé les facteurs de risque métaboliques comme l'obésité, l'hypercholestérolémie, l'hypertriglycéridémie. L'évaluation osseuse a trouvé de l'ostéoporose avec une thérapie hypolipémiant faible, de l'acide zoledronique de 5 mg injectable annuellement. Ont été recommandés des suppléments de calcium et de la vitamine D. La patiente sera suivie par une

and estrogens in hormonally-responsive tissues. In our patient, the development of autoimmune thyroiditis with hypothyroidism after breast cancer seems incidental.

**List of abbreviations:** TPO = Antithyroperoxidase antibodies TSH = Thyroid Stimulating Hormone, TgAb= Anti-thyroglobulin antibodies, Free T4 = free levothyroxine, DXA = Dual-Energy X-Ray Absorptiometry, BMD = Bone Mineral Density, 25-OHD = 25-hydroxyvitamin D, PTH= Parathyroid Hormone, cm = centimeter

**Key words:** breast cancer, autoimmune thyroiditis, hypothyroidism, antithyroperoxidase antibodies, Thyroid Stimulating Hormone

## INTRODUCTION

**A**utoimmune thyroiditis (AI), also known as Hashimoto's disease, represents a chronic inflammatory disorder of the thyroid gland which is caused by abnormal blood antibodies finally causing thyroid hormone deficiency. AI presents various combinations of symptoms, making diagnosis difficult, and sometimes multiple autoimmune disorders are associated. (1,2,3,4,5) The increased incidence of Hashimoto's thyroiditis in women raised the suspicion of the estrogen involvement in its etiology. (1,2,3,4,5) Even the relationship between the level of serum estrogens and thyroid or systemic autoimmune diseases is incompletely elucidated, it is well known the role of estrogen level in breast cancer etiology. (6,7,8,9) Although associations between breast cancer and thyroid disease have been reported in the literature, no clear evidence exists regarding the causal role for overt autoimmune thyroid conditions in breast cancer. (6,7,8,9) There are some endocrine stimuli identified in thyroid products that exert a simultaneous action on the breast as thyroid antibodies, cytokines which could interact with receptors on breast tumors. (7,8) This association is not surprising as both diseases are female predominant with a similar postmenopausal peak incidence. (8,9,10) Overall, the relationship between breast cancer and thyroid disease is still controversial.

In this context, we present the case of a middle-aged female patient with chronic autoimmune thyroiditis and breast cancer.

This is a case report presentation. Thyroid, breast, metabolic and bone evaluation is described. Thyroid profile is based on ultrasound, autoimmunity (circulating antithyroperoxidase antibodies or TPO, circulating anti-thyroglobulin antibodies or TgAb), and function assess-

équipe multidisciplinaire en ce qui concerne la thyroïde, les os et le profil oncologique.

**Conclusions:** Il y a encore une controverse sur les éventuelles corrélations entre le cancer du sein et les maladies de la thyroïde en distribuant les interactions des anomalies des cytokines communes entre l'hormone de la thyroïde et les oestrogènes dans les tissus hormono-sensibles. Chez notre patiente, le développement de la thyroïdite auto-immune à l'hypothyroïdie suite au cancer du sein semble accidentel.

**Mots clés:** cancer du sein, thyroïdite auto-immune, hypothyroïdie, anticorps anti-thyréoperoxidase, hormone de stimulation thyroïdienne

ment (Thyroid Stimulating Hormone or TSH, Free Thyroxine or FT4). Breast evaluation included ultrasound, mammogram, and histological exam. Metabolic complications were reflected by biochemistry tests: lipid and glucose profile. Skeleton was evaluated performing central Dual-Energy X-Ray Absorptiometry (DXA, GE Lunar Prodigy device). Bone Mineral Density (BMD) provided provided T-score. The vitamin D status is reflected using the blood 25-hydroxyvitamin D (25-OHD) and parathormone (iPTH). The informed written consent was obtained by the patient.

## CASE REPORT

A 58-year old non-smoking female was diagnosed and later on treated for right breast cancer. Her medical family history was negative. At age of 55, a breast lump was discovered accidentally by self physical exam. Mammogram reveled one highly suspicious mass of the right breast and ultrasound determined mass size of 2 centimeters (cm). There was no evidence of abnormalities of the left breast neither on physical exam nor on radiological examinations. Additionally, there were no palpable or radiological suspicious axillaries lymph nodes. Core needle biopsy of breast mass revealed ductal carcinoma without infiltrations in surrounding structures. A unilateral mastectomy with sentinel node excision was performed. The final pathology report demonstrated a ductal carcinoma of 2 cm (T2N0M0). Estrogen and progesterone receptor immune-staining of tissue sample were negative. Treatment was completed with radiotherapy and three cycles of chemotherapy. One year later, the patient presents marked fatigue, daytime sleepiness and bowel disorders. Physical exam of thyroid was irrelevant. Thyroid function and autoimmunity were tested and found highly suggestive for Hashimoto's thyroiditis and hypothyroidism. (Table 1) Thyroid ultra-

Table 1 - The endocrine and biochemical parameters of a female patient previously diagnosed and treated for breast cancer which established the diagnosis of autoimmune hypothyroidism

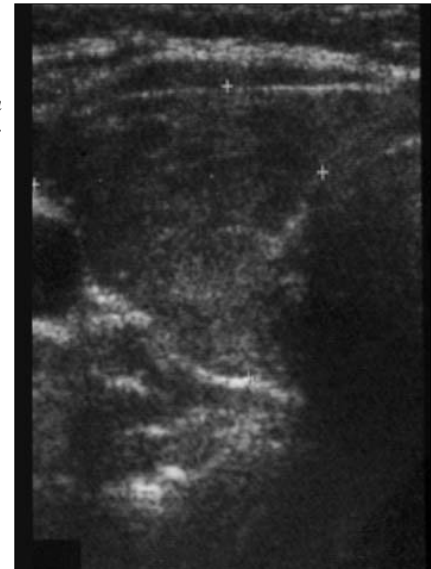
Parameter	Patient's value	Normal limits	Units
Thyroid stimulating hormone (TSH)	22.5	0.27-4.20	μUI/mL
Free Levothyroxine (FT4)	8.9	12-22	pmol/L
Anti-thyroperoxidase antibodies (TPO)	312	0-34	UI/mL
Anti-thyroglobulin antibodies (TgAb)	157	0-115	UI/mL
Total Plasma Cholesterol	264	< 200	mg/dL
Plasma triglycerides	197	< 150	mg/dL
Fasting Plasma Glucose	89	70-110	mg/dL

sound showed: right thyroid lobe of 1.96 by 2.59 by 4.16 cm, left lobe of 2.31 by 2.37 by 3.89 cm with hypo-echoic pattern, suggestive for autoimmune thyroid condition. (Fig. 1) Metabolic risk factors profile revealed: obesity (body mass index of 34 kg/sqm), hypercholesterolemia (total cholesterol level of 264 mg/dL, with normal ranges less than 200 mg/dL), hypertriglyceridemia (197 mg/dL, with normal ranges less than 150 mg/dL), and normal fasting glucose (of 89 mg/dL, with normal levels between 70 and 110 mg/dL). (Table 1) The patient was treated with daily levothyroxine and statin and followed-up. One year later, TSH was normal and a bone assessment was done. The serial imagery scans revealed no metastases. Vitamin D deficiency was found (25-OH D of 24.2 ng/mL, with optimal levels above 30 ng/mL) without secondary hyperparathyroidism (iPTH of 58.6 pg/mL with normal ranges between 15 and 66 pg/mL). DXA results established the diagnosis of osteoporosis: L1-4 BMD of 0.82 g/sqcm, T-score of -3 SD, Z-score of -2.3 SD; femoral neck BMD of 0.884 g/sqcm, T-score of -1.3 SD, Z-score of -0.2 SD. (Fig. 1) No vertebral fractures were found at profile thoracic-lumbar X-Ray. IV 5 mg yearly zoledronic acid was introduced together with calcium and vitamin D supplements. Long time follow-up is recommended by a multidisciplinary team related to the thyroid, bone and oncologic profile.

**DISCUSSIONS**

Some studies showed the higher incidence of autoimmune thyroid diseases in breast cancer patients than in control individuals. (10) Generally, there are recognized some genetic correlations regarding the autoimmune disorder and thyroid cancer. (11,12,13) Immune system disorders with concomitant induction of breast cancer and autoimmune thyroiditis may be a possible responsible mechanism for both diseases but not all the studies agree on this matter. (14,15,16) Some reports have shown that the presence of high TPO is associated with a significant improvement

Figure 1 - Thyroid ultrasound: hypo-echoic pattern highly suggestive for Hashimoto's thyroiditis



of breast neoplasia outcome as other prognostic factors like axillary nodes and tumor size. (16,17) In our case the diagnosis of autoimmune thyroiditis was established because of symptomatic hypothyroidism as marked fatigue, daytime sleepiness and bowel disorders.

The possible interactions between thyroid gland and breast tissue are based on the common property of the mammary and thyroid epithelial cell to concentrate iodine by a membrane active transport mechanism as well as on the presence of TSH receptors in fatty tissue, which is abundant in mammary gland. (18,19,20)

It has been suggested a better prognosis for breast cancer among patients with increased levels of TPO, although high TPO level has been shown to be a very important factor in antibody-dependent cell cytotoxicity in the thyroid, there is no agreement on the significance of its association with breast cancer. (20, 21) In our case the high TPO level was associated with mild hypothyroidism and limited ductal

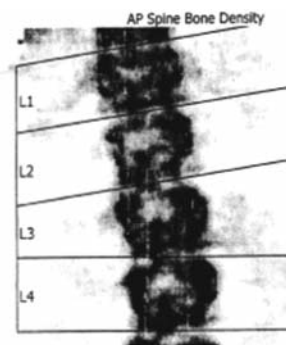
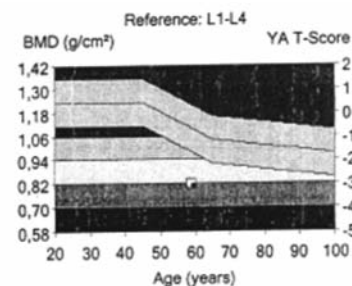


Figure 2 - DXA examination : Osteoporosis based on lumbar T-score



Region	BMD (g/cm <sup>2</sup> ) <sup>1</sup>	Young-Adult T-Score <sup>2</sup>	Age-Matched Z-Score <sup>3</sup>
L1	0,752	-3,1	-2,5
L2	0,743	-3,8	-3,1
L3	0,852	-2,9	-2,2
L4	0,921	-2,3	-1,7
L1-L2	0,748	-3,4	-2,7
L1-L3	0,785	-3,2	-2,5
L1-L4	0,820	-3,0	-2,3
L2-L3	0,800	-3,3	-2,7
L2-L4	0,841	-3,0	-2,3
L3-L4	0,886	-2,6	-2,0

breast cancer without local lymph nodes involvement.

It has been demonstrated that breast cancer and thyroid tissue share common properties, as they both express TPO and the sodium iodide symporter gene. (21,22,23) For this reason the immune response might be mediated both by tumor and by thyroid tissue or by other autoimmune reactions as seen in lupus erythematosus (22,23)

In this case, the short time interval from the diagnosis of breast cancer to Hashimoto's thyroiditis discovery may not reflect interdependence between the two disorders. Some studies found that primary hypothyroidism may be correlated with a lower incidence of mammary cancer. (23) Other observations found no association between breast cancer and thyroid antibody level, neither of the lymphocytic infiltrates in environment of the mammary cancer. (24,25)

### CONCLUSIONS

There is still a matter of debate related to the clinical correlations between breast cancer and thyroid disease but common pathogenic pathways are involved. In this particular case the development of Hashimoto's thyroiditis-associated hypothyroidism one year later after the diagnosis of unilateral breast cancer seems incidental but highlights the clinical significance of the interactions between thyroid hormones and estrogens in hormonally-responsive tissues.

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