



Paper Accepted*

ISSN Online 2406-0895

Case Report / Приказ случаја

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Thyroid Gland Metastasis from Breast Cancer: A Rare Case Report and Literature Overview

Метастазе карцинома дојке у штитастој жлезди: редак приказ случаја и преглед литературе

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Received: May 4, 2017

Revised: July 6, 2017

Accepted: July 7, 2017

Online First: July 11, 2017

DOI: <https://doi.org/10.2298/SARH170504143I>

* **Accepted papers** are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the *Serbian Archives of Medicine*. They have not yet been copy edited and/or formatted in the publication house style, and the text may be changed before the final publication.

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SUMMARY

Introduction The thyroid gland is a rare site for metastatic lesions from non-thyroid cancers. Due to the fact that achieving a thyroid gland metastasis from a breast cancer diagnosis prior to an operation is challenging, a diagnosis thereof is mainly based on a pathological biopsy and immunohistochemical staining.

The aim of this study was present a rare case of thyroid gland metastasis from lobular breast cancer.

Case Outline The patient was a 33-year-old female who had already had a five-year history of lobular cancer of the right breast and was thereafter found to have two suspicious tumors in the left breast as well as a thyroid mass diagnosed as metastatic breast carcinoma.

Conclusion Patients who have a thyroid lesion and a history of malignancy also are at a higher risk for metastasis and require additional caution during diagnosis and treatment.

Keywords: thyroid metastasis; breast cancer; diagnosis; treatment; histopathological analysis

САЖЕТАК

Увод Штитасте жлезде је ретко место метастатских лезија из нетироидних карцинома. Постављање дијагнозе метастаза у штитастој жлезди порекла карцинома дојке пре операције је ретко, јер се заснива на патолошкој биопсији и имунохистохемијском бојењу.

Циљ овог рада је да прикаже редак случај метастаза лобуларног карцинома дојке у штитасту жлезду.

Приказ болесника Код жене старе 33 године која је лечена због лобуларног карцинома десне дојке пре пет година, утврђено је да има два суспектна тумора у левој дојци као и у штитастој жлезди који је дијагностикован као метастаза карцинома дојке.

Закључак Болесници са променом у штитастој жлезди и историјом малигнитета имају већи ризик да је у питању метастаза и потребан је додатни опрез током дијагностике и лечења.

Кључне речи: метастазе у штитастој жлезди; карцином дојке; дијагностика; хистопатолошке анализе

INTRODUCTION

Although the thyroid gland is richly supplied with blood, the occurrence of a secondary malignancy of the thyroid gland is relatively rare. According the literature of clinical papers, the incidence of a secondary malignancy of the thyroid gland is low, representing 2%-3% of all malignant tumors of the thyroid [1]. However, the most common among metastasizing cancers related to this gland are melanoma, as well as kidney, breast, and lung cancer [2].

In autopsy series, the lung is the most common site of primary tumor metastatic to the thyroid, whereas in clinical series, renal cell carcinoma is the most frequent, followed by breast and gastrointestinal neoplasms [3]. According to Nixon et al., the high oxygen and iodine environment may impair the ability of metastatic cells to settle and develop in the thyroid. Additionally, the fast blood flow could make adhesion and implantation of tumor cells difficult [4].

The aim of this paper was to present a rare case of breast carcinoma metastatic to the bilateral thyroid lobes. The thyroid metastasis appeared five years after the initial diagnosis of breast carcinoma in the right breast and was confirmed by histopathological analysis. After the surgery, it was also found that this patient had two new lobular breast carcinoma in the left breast. The patient was not found to have any other distant metastases.

CASE REPORT

The patient, a 28-year-old female, underwent a nipple areola sparing mastectomy (NASM) and primary breast reconstruction for right breast carcinoma in 2011 at the Institute for Oncology and Radiology of Serbia.

On histopathological examination, it was diagnosed as lobular carcinoma of the breast. The primary tumor was 52x22x20 mm in size and nine axillary lymph nodes showed a tumor deposit (9/10). Immunohistochemically, the tumor was positive for estrogen receptors (ER) and progesterone receptors (PR). The Ki67 was 50% and negative for HER-2-neu. The patient then underwent adjuvant chemotherapy, endocrine therapy and radiotherapy, and was followed up on every six months. The disease was asymptomatic for five years. After this time, two tumors developed in the left breast were found to be suspicious after clinical examination and an MRI. An ultrasonography of the neck also showed a suspicious neoplastic lesion in the bilateral thyroid lobes.

According to subsequent testing, while the patient was euthyroid (serum TSH, fT4 and fT3 in a normal range), the thyroglobulin had a higher level 98.6 ng/ml (normal, 1.4-78 ng/ml). Serum Ca 15.3 elevated to a slightly higher level of 32.7 kU/L (normal, 0-25.0 kU/L). The patient was asymptomatic.

A histopathological examination of the left breast after surgery showed two lobular carcinoma of the breast, (12x10x9 mm and 18x8x6 mm in size, respectively), and negative sentinel lymph nodes (0/2). Both tumors also expressed positive receptors for ER, PR and negative for HER-2-neu, and had the same Ki67 of 40%. The total thyroidectomy revealed a metastatic lobular carcinoma of the breast in the bilateral thyroid lobes. Nine neck lymph nodes showed a tumor deposit (9/14) after the right modified radical neck dissection (MRND) and extirpation of the lymph nodes in the central region of the neck.

The tumor cells in the metastatic foci (Figure 1) also expressed positive for ER (Figure 2) and PR (Figure 3), but negative for HER-2-neu. They were, however, positive for mamoglobin (Figure 7), GCDFP-15 (Figure 8), confirming their origin from breast. Furthermore, the metastatic cells were negative for thyroglobulin (Figure 4), TTF-1 (Figure 5) and CK7 (Figure 6), they all were positive in the surrounding normal thyroid parenchyma, suggesting the neoplastic cells did not originate from the thyroid gland.

After the surgery, testing showed TG and Ca 15.3 to be in the normal range.

The metastasis to the thyroid gland occurred five years after the original diagnosis of the primary disease. The thyroid deposits were the only distant metastasis.

DISCUSSION

The thyroid gland is a rare site for metastatic disease to develop, and an infrequent location for metastatic lesions to appear [5-7]. Since it is a challenge to diagnose a thyroid gland metastasis in

breast cancer prior to the actual operation, the diagnosis itself is mainly based upon a pathological biopsy and immunohistochemical staining.

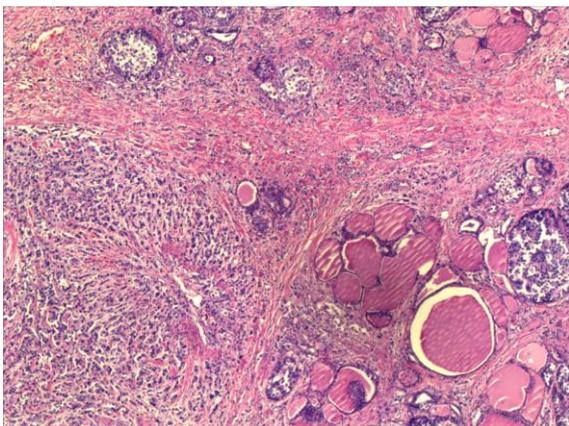


Figure 1. A histological section from the metastatic lesion of the thyroid originating from breast cancer (H&E, x10).

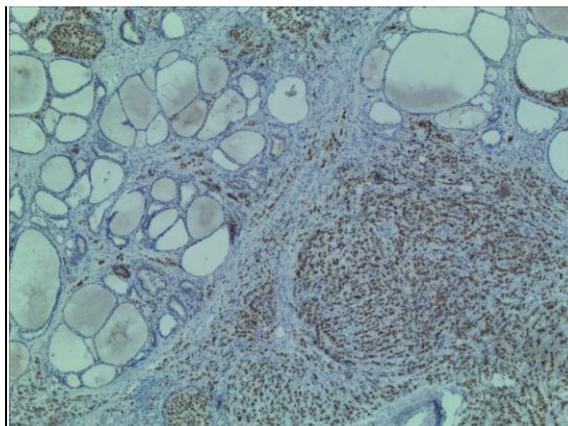


Figure 2. IHC staining for ER (20x) in the metastatic lesion of the thyroid originating from breast cancer. A positive reaction was observed in over 75% of the nuclei cells evaluated.

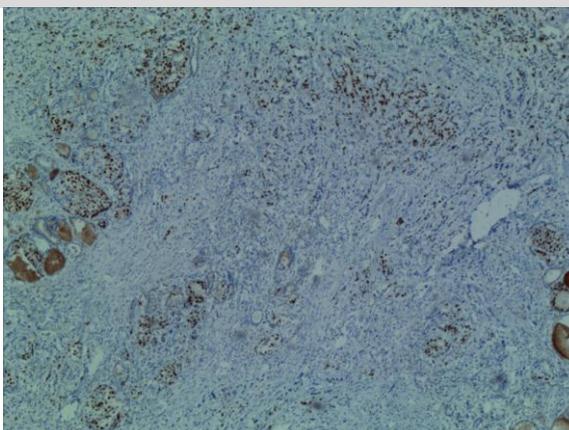


Figure 3. IHC staining for PR (20x) in the metastatic lesion of the thyroid originating from breast cancer. A positive reaction was observed in over 75% of the nuclei cells evaluated.

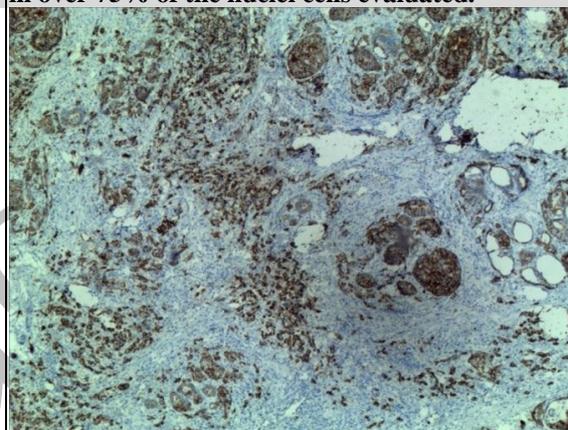


Figure 4. IHC staining for thyroglobulin (x20).

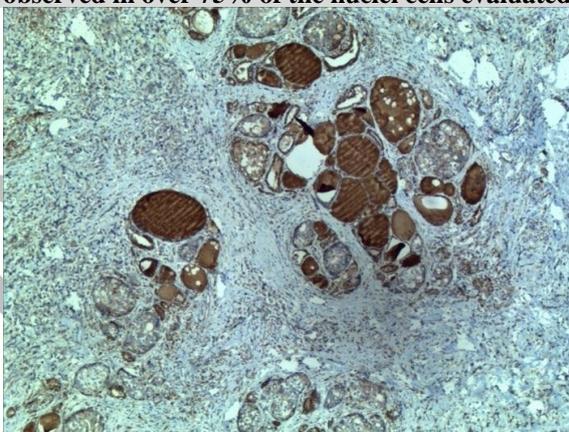


Figure 5. IHC staining for TTF1(x20).

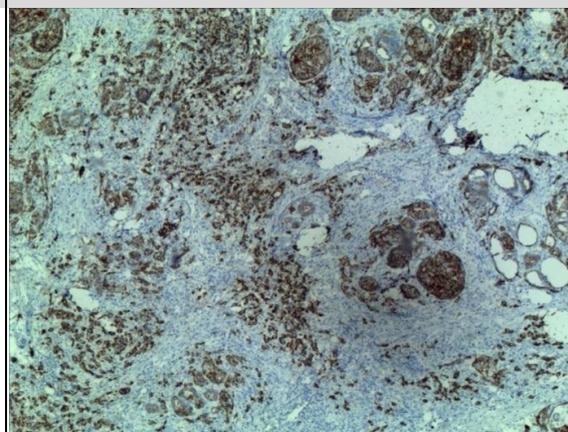


Figure 6. IHC staining for CK7 (x10)

According to the literature, the involvement of the thyroid generally becomes apparent either simultaneously or anywhere in a spectrum from a few months to 14 years after the original diagnosis of the primary tumor [1,8-15]. The long interval between the original primary tumor and subsequent

thyroid metastases presents a diagnostic problem. In this case, we made the diagnosis five years subsequent to the history of the primary tumor.

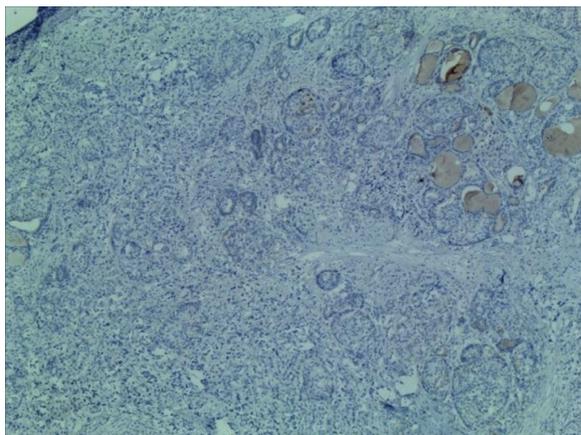


Figure 7. IHC staining for mammoglobin (x20).

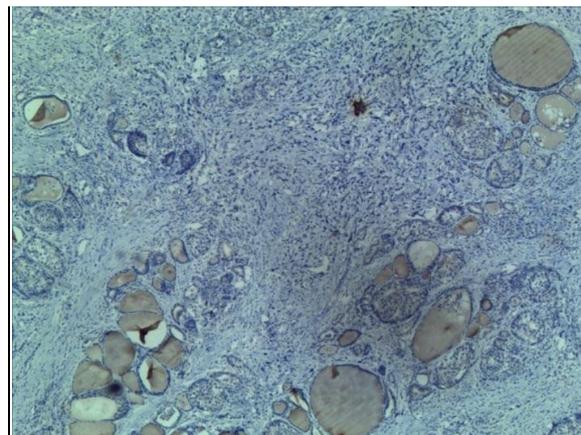


Figure 8. IHC staining for GCDFP-15(x20).

Metastatic disease involving the thyroid is generally observed in elderly individuals in their sixth and seventh decades of life [1]. However, the presently analyzed female patient was only 33 years old. Therein, it may be common for the clinical manifestation of metastatic disease to have no importance, such as in this case presented. In this regard, Ca 15.3 and ultrasonography of the neck played a major role in the diagnostic process.

Although thyroid metastases from breast cancer are uncommon, the routine use of fine needle aspiration may better assist in its more frequent detection due to its ready ability to confirm a clinical suspicion [6,14]. A total thyroidectomy is recommended for patients with metastatic cancer limited to the thyroid because of the multifocality of metastases to the thyroid gland [17]. Our patient therefore underwent total thyroidectomy and nine neck lymph nodes showed a tumor deposit (9/14).

In the reported case, the diagnosis of metastatic breast carcinoma to the thyroid was confirmed with the help of histopathology and immunohistochemistry. The latter was particularly helpful in differentiating the metastatic breast carcinoma from the primary thyroid malignancy. Thyroglobulin, TTF1 and CK7 are the tumor markers that are positive in those of the thyroid follicular epithelial cells. In the case being presented, all of these markers were found to be negative in the tumor cells, but strongly positive in the surrounding normal thyroid parenchyma. Furthermore, the tumor cells tested strongly positive for mamoglobin and GCDFP-15 confirming their origin from a breast lesion [18,19]. The hormonal status (ER and PR) were found to be positive and HER-2-neu was negative in the metastatic tumor, similar to the expression pattern of the primary breast carcinoma.

It may be concluded that a patient with a thyroid lesion and a history of malignancy is at a higher risk for metastasis. Such a patient therefore requires additional caution during their diagnosis and treatment. One method of screening is for clinicians to pay specific attention to the elevated Ca 15.3 levels after surgery of the primary breast carcinoma. It is also, therefore, advisable to do a fine needle aspiration which may help detect metastasis in future cases.

REFERENCES

1. Cichoń S, Anielski R, Konturek A, Barczyński M, Cichoń W. Metastases to the thyroid gland: seventeen cases operated on in a single clinical center. *Langenbecks Arch Surg.* 2006; 391(6): 581–7.
2. Shimaoka K, Sokal JE, Pickren JW. Metastatic neoplasms in the thyroid gland. Pathological and clinical findings. *Cancer.* 1962; 15 (3): 557–65.
3. Nixon IJ, Coca-Pelaz A, Kaleva AI, Triantafyllou A, Angelos P, Owen RP, et al. Metastasis to the Thyroid Gland: A Critical Review. *Ann Surg Oncol.* 2017; 24: 1533–9.
4. Nixon IJ, Witcher M, Glick J, Palmer FL, Shaha AR, Shah JP, et al. Surgical Management of Metastases to the Thyroid Gland. *Ann Surg Oncol.* 2011; 18: 800–4.
5. Chen H, Nicol TL, Udelsman R. Clinically significant, isolated metastatic disease to the thyroid gland. *World J Surg.* 1999; 23 (2): 177–80.
6. Willis RA. Metastatic Tumours in the Thyroid Gland. *Am J Pathol.* 1931; 7(3): 187–208.
7. Yang M, Wang W, Zhang C. Thyroid gland metastasis arising from breast cancer: A case report. *Oncol Lett.* 2013; 5(6): 1836–8.
8. Gerges AS, Shehata SR, Gouda IA. Metastasis to the thyroid gland: unusual site of metastasis. *J Egypt Natl Canc Inst.* 2006; 18(1): 67–72.
9. Jiménez-Heffernan JA, Perez F, Hornedo J, Perna C. Massive thyroid tumoral embolism from a breast carcinoma presenting as acute thyroiditis. *Arch Pathol Lab Med.* 2004; 128(7): 804–6.
10. Tütüncü NB, Akçer N, Arican A, Bascil N, Güvener N, et al. Unusual case of metastatic thyroid nodule: nonpalpable breast mass as origin. *Endocr Pract.* 2001; 7(5): 379–82.
11. Leboeuf R, Bénard F, Langlois MF. Thyroid cancer presenting as a PET incidentaloma in a patient with concomitant breast cancer metastases to the thyroid. *Clin Nucl Med.* 2006; 31(7): 382–5.
12. Loo CK, Burchett IJ. Fine needle aspiration biopsy of neuroendocrine breast carcinoma metastatic to the thyroid. A case report. *Acta Cytol.* 2003; 47(1): 83–7.
13. Owens CL, Basaria S, Nicol TL. Metastatic breast carcinoma involving the thyroid gland diagnosed by fine-needle aspiration: a case report. *Diagn Cytopathol.* 2005; 33: 110–5.
14. Gong Y, Jalali M, Staerkel G. Fine needle aspiration cytology of a thyroid metastasis of metaplastic breast carcinoma: a case report. *Acta Cytol.* 2005; 49(3): 327–30.
15. Kim TY, Kim WB, Gong G, Hong SJ, Shong YK. Metastasis to the thyroid diagnosed by fine-needle aspiration biopsy. *Clin Endocrinol (Oxf).* 2005; 62(2): 236–41.
16. Yu J, Seethala RR, Walls A, Cai G. Fine-needle aspiration of breast carcinoma metastatic to follicular variant of papillary thyroid carcinoma. *Diagn Cytopathol.* 2009; 37(9): 665–6.
17. Calzolari F, Sartori PV, Talarico C, Parmeggiani D, Beretta E, Pezzullo L, et al. Surgical treatment of intrathyroid metastases: preliminary results of a multicentric study. *Anticancer Res.* 2008; 28(5B): 2885–8.
18. Mazoujian G, Bodian C, Haagensen DE Jr, Cushman HD. Expression of GCDFP-15 in breast carcinomas. Relationship to pathologic and clinical factors. *Cancer.* 1989; 63(11): 2156–61.
19. Wang Z, Spaulding B, Sienko A, Liang Y, Li H, Nielsen G, et al. Mammaglobin, a Valuable Diagnostic Marker for Metastatic Breast Carcinoma. *Int J Clin Exp Pathol.* 2009; 2(4): 384–9.