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Uncommon metastatic journey: unusual breast metastases of medullary thyroid carcinoma: a case report

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Abstract

Medullary thyroid carcinoma is a neuroendocrine tumor derived from thyroid C-cells. It is a rare aggressive tumor, known to metastasize to lymph nodes, liver, bones, and lungs. We report a case of a young patient with a family history of breast cancer, who developed breast metastases six months post-treatment for medullary thyroid carcinoma. The breast lesion was initially considered benign in ultrasound. Unlike the high prevalence of primary mammary malignancies, metastases to the breast are uncommon, and account for only 0.2–2.7% of all malignancies affecting this organ. This case emphasizes the need for thorough and continuous monitoring of patients with Medullary thyroid carcinoma, even in unusual locations, to ensure early detection and appropriate management. New lesions on imaging should be interpreted with caution to avoid underdiagnosing metastasis. Immunohistochemical analysis confirmed the metastatic origin, underscoring the challenges in distinguishing between primary and secondary breast tumors. This case contributes to the limited literature on MTC breast metastases and advocates for heightened clinical awareness regarding atypical metastatic sites in thyroid cancer patients.

Keywords Medullary carcinoma, Thyroid, Breast, Metastasis, Surgery

Introduction

Medullary thyroid cancer is a rare tumor originating from thyroid c-cells accounting for less than 5% of thyroid cancers. With a hereditary component in 25% of cases, it often presents as Multiple Endocrine Neoplasia type 2 (MEN 2) [1]. While slow-growing, known to metastasize to lymph nodes, liver, bones, and lungs, it may manifest breast metastases, posing diagnostic challenges due to a lack of clinical and radiological specificity [2]. Carcinoma originating in the thyroid and spreading to the breast is exceptionally uncommon. Such metastatic tumors in the breast comprise only 0.8 to 6.6% of all breast malignancies [3].

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Case report

The case concerns a 28-year-old Tunisian woman who reported a family history of breast cancer. She was diagnosed in June 2020 with medullary thyroid carcinoma without family history of hereditary Multiple Endocrine Neoplasia.

The patient underwent total thyroidectomy with bilateral cervical lymph node dissection. The pathological diagnosis was multifocal mixed medullary-follicular carcinoma in the left lobe. Sixteen of the forty isolated cervical lymph nodes were involved by carcinoma. The patient underwent adjuvant radiotherapy.

Six months after treatment, a body scan revealed a lump in the right breast. Ultrasound showed a hypoechoic, well-circumscribed 10 mm lump in the right breast, classified as ACR 3 (Fig. 1). Follow-up breast imaging performed three months later revealed two bilateral masses: one located in the right upper-outer quadrant and the other in the left lower-inner quadrant. Both masses displayed a homogeneous hypoechoic oval shape, were micro-lobulated, and had long axes oriented parallel to the skin. They measured 15 mm on the right and 10 mm on the left side and were classified as ACR 4b. Calcitonin levels were raised to 270pg/ml. Breast biopsy revealed atypical cells exhibiting nuclei with a coarse chromatin pattern and granular cytoplasm, situated within a fibrous stroma that contains amorphous eosinophilic deposits, along with the presence of vascular emboli. (Fig. 2). Immunohistochemistry revealed positivity for calcitonin, TTF1 and chromogranin A (Fig. 3). The findings were in favor of secondary medullary carcinoma in the breast.

Discussion

Thyroid medullary carcinoma originates from thyroid c-cells, which produce the calcitonin hormone. These tumors are uncommon, constituting 1–2% of all thyroid cancers [4].

Notably, 25% of medullary thyroid cancers are hereditary, manifesting in a familial form identified as MEN 2, with peak incidence occurring in younger patients during the second or third decade, while sporadic forms have a peak incidence around the fifth or sixth decade of life [1].

Medullary thyroid carcinoma is typically a slow-growing tumor, generally exhibiting locoregional progression. Metastasis often occurs late in the disease, and is generally localized in the liver, bone, central nervous system and adrenal glands [5–9]. Metastatic thyroid carcinoma to the breast is extremely rare, with about 40 reported cases in the literature [10]. In our institute, this case is the second case of medullary thyroid carcinoma metastatic to the breast; the first one was reported in 2017 by El Bez et al. [11].

These metastases can occur either unilaterally or bilaterally and are most frequently observed in women with an average age of 42 at diagnosis. The time interval between thyroidectomy and identification of breast metastasis varies significantly—from a few months to 28 years, averaging about 6 years [3, 6, 12, 13].

Secondary tumors of the breast lack clinical or radiological specificities, complicating diagnosis significantly [2]. The pathological similarity between tumor cells from a primary breast tumor with neuroendocrine differentiation and secondary thyroid medullary carcinoma poses major diagnostic problem, making knowledge of the patient's history an important guide to this distinction. Amorphous eosinophilic material in tissue can indicate the presence of amyloid, particularly in the context of medullary thyroid carcinoma. Immunohistochemistry aids diagnosis: TTF1 positivity points to thyroid origin, chromogranin A positivity to endocrine origin, and calcitonin positivity to medullary thyroid carcinoma origin [2, 6]. Diagnosis becomes more challenging when differentiating between primary and secondary breast endocrine tumors. The expression of GATA3 is indicative of primary breast carcinoma [14].

For treatment options regarding these metastases, there has been no consensus; some patients underwent surgery while others received systemic treatment [2].

Conclusion

This case of unusual breast metastases from medullary thyroid carcinoma underscores the need for heightened vigilance in monitoring patients' post-treatment. Despite the rarity of such occurrences, this report illustrates that breast metastases can arise even months after conventional therapies. The diagnostic challenges posed by the clinical and radiological non-specificity of these lesions necessitate a proactive approach to evaluation, including histological verification for any new breast findings. As demonstrated in this case, clinical history, multiplicity of breast lesions and elevated calcitonin levels can provide essential clues for diagnosis. This highlights the importance of a multidisciplinary approach in managing patients with medullary thyroid carcinoma, ensuring that both oncologists and radiologists remain alert to the potential for distant metastasis in atypical locations.

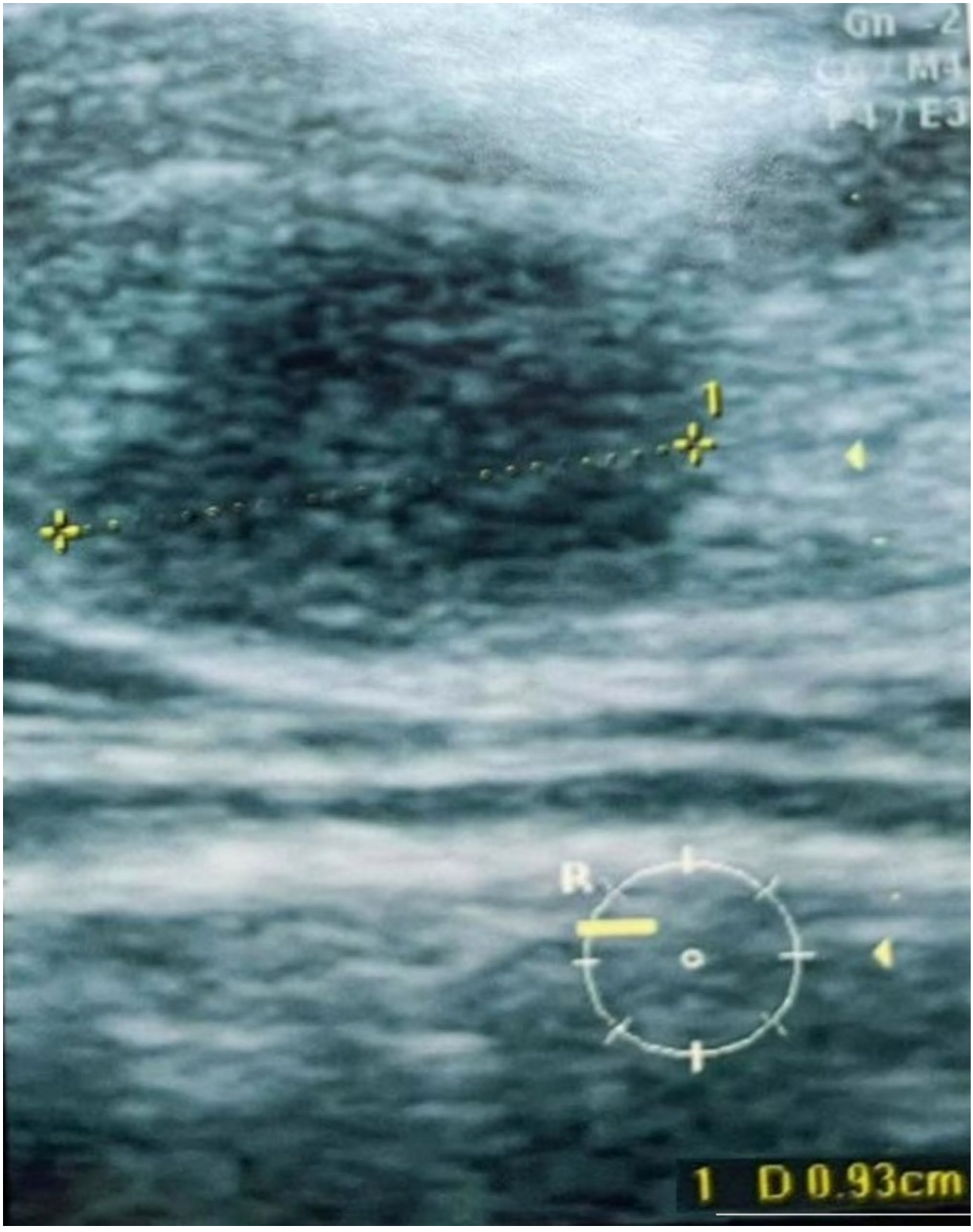

Fig. 1 Ultrasound image of the right breast showing a hypoechoic, well-circumscribed 10 mm lump

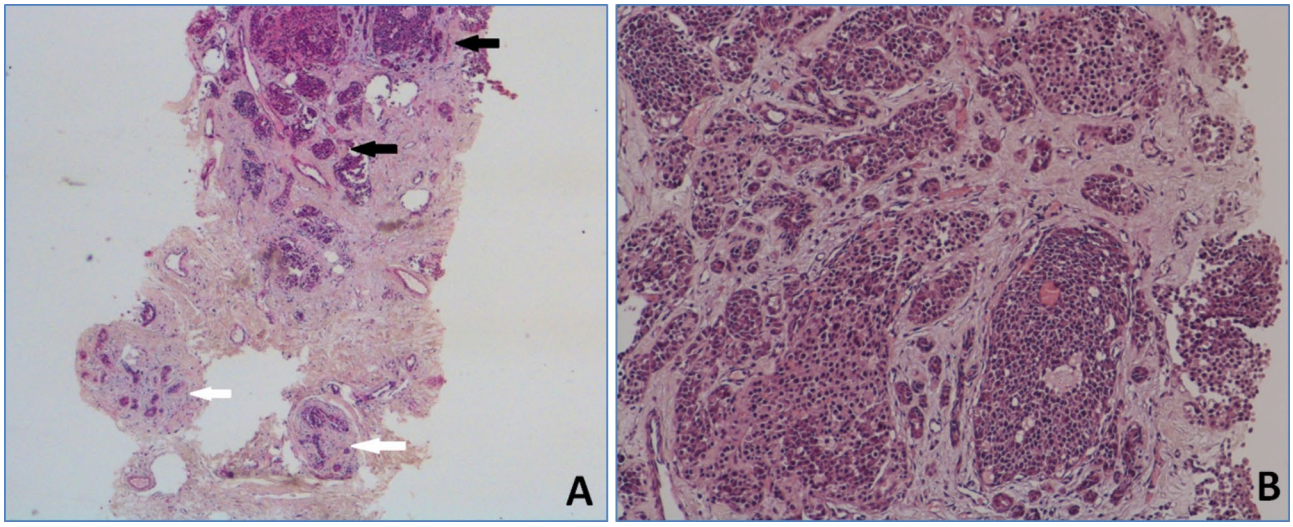

Fig. 2 (A) Histological section at low magnification showing the carcinomatous proliferation (black arrow) invading the non-neoplastic mammary stroma (white arrow) (H&E x40). (B) Histological section showing the carcinomatous proliferation arranged in islands and clusters of monomorphic cells (H&E x100)

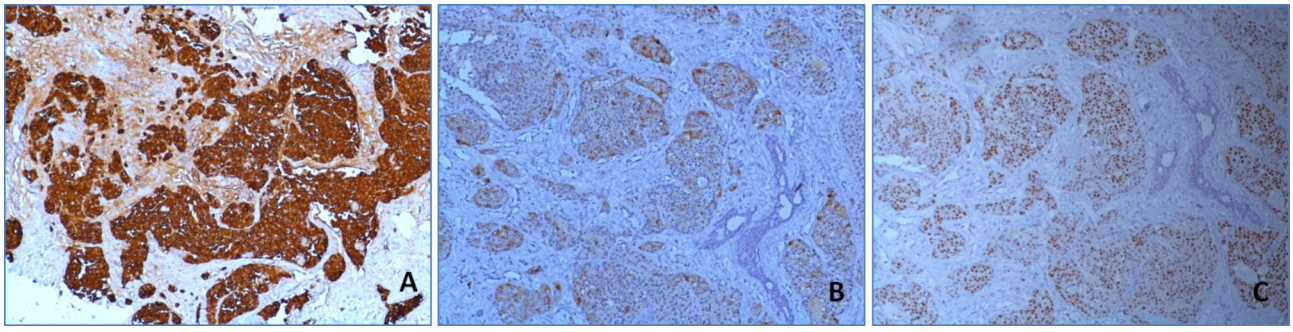

Fig. 3 (A) Positive cytoplasmic staining for chromogranin (IHC x100). (B) Focal positive cytoplasmic staining for calcitonin (IHC x100). (C) Positive nuclear staining for TTF1 (IHC x100)

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12905-025-03564-y.

Supplementary Material 1

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Author contributions
FS, IZ, and SK collected the data and drafted the manuscript. MC, YH and SJ collected the data and reviewed the literature. MD, and TD drafted the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The authors declare no conflicts of interest, and that this work was done with all due respect to the code of ethics under the supervision of the medical and ethics committee of the Salah Azaiez Institute.

Consent for publication
Written informed consent was obtained from the patients to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare no competing interests.

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References

1. Hu J, Yuan IJ, Mirshahidi S, Simental A, Lee SC, Yuan X. Thyroid carcinoma: phenotypic features, underlying Biology and potential relevance for Targeting Therapy. Int J Mol Sci. 2021;22(4):1950. https://doi.org/10.3390/ijms22041950. PMID: 33669363; PMCID: PMC7920269.
2. Gardair C, Drabent P, Charveriat P, Bertheau P, Cahen-Doidy L, de Roquancourt A. Métastase mammaire d'un carcinome médullaire thyroïdien: un

challenge diagnostique [A misleading breast metastasis of medullary thyroid carcinoma]. Ann Pathol. 2019;39(1):9–13. https://doi.org/10.1016/j.annpat.2018.07.004. French. doi:.
3. Hassan A, Siddiqui M, Jahangir S. A rare case of medullary carcinoma thyroid metastasizing to bilateral breast parenchyma. Nucl Med Rev Cent East Eur. 2016;19(B):17–9.
4. Somnay YR, Schneider D, Mazeh H, Thyroid. Medullary carcinoma. Atlas Genet Cytogenet Oncol Haematol. 2013;17(4):291–6. https://doi.org/10.4267/2042/48876. PMID: 28111594; PMCID: PMC5242095.
5. Martins SN, Giannotti MA, Siqueira SAC. Medullary carcinoma of the thyroid metastatic to the breast: a case report and literature review. Autopsy Case Rep 31 mars. 2014;4(1):53–7.
6. Gavilán I, Astorga R, Sasián S, Acosta D, Aguilar M, Leal A, Escobar L, Córdoba JA, Girón JA. Carcinoma medular de tiroides. Factores pronósticos [Medullary carcinoma of the thyroid gland. Prognostic Factors] Rev Clin Esp. 1996;196(2):92–8. Spanish. PMID: 8685495.
7. Pelizzo MR, Boschin IM, Bernante P, Toniato A, Piotto A, Pagetta C, et al. Natural history, diagnosis, treatment and outcome of medullary thyroid cancer: 37 years experience on 157 patients. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol Mai. 2007;33(4):493–7.
8. Nofech-Mozes S, Mackenzie R, Kahn HJ, Ehrlich L, Raphael SJ. Breast metastasis by medullary thyroid carcinoma detected by FDG Positron emission tomography. Ann Diagn Pathol 1 févr. 2008;12(1):67–71.
9. Vaughan A, Dietz JR, Moley JF, DeBenedetti MK, Aft RL, Gillanders WE, et al. Metastatic disease to the breast: the Washington University experience. World J Surg Oncol 5 Juill. 2007;5(1):74.
10. Kazakou G, Simeakis M, Alevizaki, Saltiki K. MedullaryThyroid Carcinoma (MTC): unusual metastatic sites. Endocrinol Diabetes Metabolism Case Rep. 2021;2021:21–0063.
11. El Bez I, Mimita W, Mhiri A, Slim I, Ben Slimene MF. Métastase Exceptionnelle D'un carcinome médullaire de la thyroïde [Exceptional metastasis of medullary thyroid carcinoma]. Ann Endocrinol 1 sept. 2017;78(4):394–5.
12. Delair D, Corben A, Catalano J, Vallejo C, Brogi E, Tan L. Non-mammary metastases to the breast and axilla: a study of 85 cases. Mod Pathol off J U S Can Acad Pathol Inc 23 nov 2012;26.
13. Mandanas S, Margaritidou E, Christoforidou V, Karoglou E, Geranou C, Chrisoulidou A, et al. Breast metastasis from medullary thyroid carcinoma in a male patient: Case Report and Review of the literature. Rare Tumors 21 mai. 2015;7(2):60–3.
14. Özdirik B, Kayser A, Ullrich A, Savic LJ, Reiss M, Tacke F, Wiedenmann B, Jann H, Roderburg C. Primary neuroendocrine neoplasms of the breast: Case Series and Literature Review. Cancers (Basel). 2020;12(3):733. https://doi.org/10.3390/cancers12030733. PMID: 32244940; PMCID: PMC7140078.

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