

Metastases to the breast. A clinical series from a single institution experience with review of the literature



Ann. Ital. Chir., 2021 92, 2: 141-148
pii: S0003469X21034618

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INTRODUCTION: Breast metastases although rare are challenging for diagnostic difficulties and management. Treatment differs according to morphological, immunophenotypic and biologic features of the primary tumor and their general behaviour is extremely different compared to primary breast cancer. The most frequent primary tumors include melanoma, lymphomas, gynecological, pulmonary, head and neck, gastroenteric and urinary tract cancers. Patient's prognosis is poor being generally associated to disseminated systemic disease with limited survival despite the effects of systemic treatment. **PATIENTS AND METHODS:** We report the analysis of the diagnostic and therapeutic approach on the institutional experience of four cases of breast metastases originating from melanoma, pulmonary adenocarcinoma and differentiated thyroid carcinomas.

CONCLUSIONS: The management of breast secondarisms requires focused diagnosis and evaluation in order to provide an adequate treatment with a multidisciplinary approach especially when the primary tumor is unknown.

KEY WORDS: Breast metastases, Melanoma, Pulmonary, Thyroid

Introduction

Breast metastases originating from solid malignancies of extra mammary site are rare, counting for about 0.2-1.3% of all breast cancers, although post-mortem studies observed higher frequency around 2-7%¹. The first observation of this rare entity was described in 1903². Correct identification of metastatic breast malignancy is

of great significance since the clinical presentation may be confused with primary benign or malignant breast disease. Despite their rarity, breast secondary tumors represent a relevant clinical problem since their treatment differs according to the morphological, immunophenotypic and biologic features of the primary tumor and their general behaviour is extremely different compared to primary breast cancer. Breast metastases usually originate from lymphomas, especially large B-cell type, from skin melanoma, gynecological, pulmonary, head and neck, gastroenteric and urinary tract cancers³⁻⁴. In pediatric patients, cases of metastases to breast from rhabdomyosarcoma were described whereas in male patients almost all cases are referred to metastatic prostatic cancer⁵⁻⁶. Patient's prognosis in case of breast metastases is poor being generally associated to disseminated systemic disease⁷ and survival is usually limited to one year since diagnosis despite cases of improved survival due to the

Pervenuto in Redazione Agosto 2020. Accettato per la pubblicazione Agosto 2020

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effects of systemic treatment^{2,7,8}. The detection of breast lesions in patients affected by primary malignancies of extramammary origin or in those with occult primary tumor requires focused diagnosis and evaluation in order to provide an adequate multidisciplinary approach. We report our institutional experience with review of the literature.

Cases Experience

We retrospectively examined the clinical records of patients admitted to our Institution, Breast Unit of Santa Maria University Hospital, Terni, Italy over a period of 5 years (2014-2019). Among 8900 cases investigated for symptomatic breast lumps or for suspicious radiological imaging requiring a biopsy, we selected four cases of secondary breast tumors diagnosed and treated in our institution. All patients included in the present series gave their informed consent for the participation in this clinical report.

CASE N. 1 - MELANOMA

A 57-year-old woman, underwent screening mammography (Mx) revealing, in her right breast a 13 mm round shaped image without microcalcifications, not detected in the previous control. The personal history revealed a previous surgery for a Breslow 4, T3N0 melanoma in her left gluteus three years before. The patients had been treated with wide local excision and groin sentinel node biopsy followed by immunotherapy. In our unit she underwent breast ultrasound (US) and a core needle biopsy (CNB). Histology showed infiltration by metastatic melanoma without any sign of breast primary cancer. After discussion in the multidisciplinary meeting (MDM) indication to metastatectomy was given. After US dermographic marker at the level of the lower right external quadrant a breast lumpectomy was carried out. Final histology confirmed the diagnosis of melanoma metastasis (Fig. 1). The post-operative course was

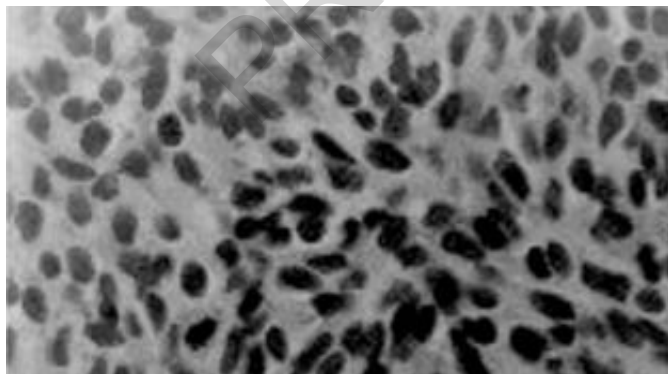


Fig. 1: Histology confirming the diagnosis of melanoma metastasis.

uneventful for 3 years when in the contralateral gluteus a subcutaneous 10 mm nodule was detected and excised with confirmed diagnosis of recurrent melanoma. The patient was referred to oncological evaluation for further medical treatment. She is still alive at the follow-up control.

CASE N. 2 - PULMONARY ADENOCARCINOMA

A 43-year-old woman was referred to our institution for bilateral palpable breast lumps, back pain and weight loss. Mx and US showed bilateral breast nodules with a 2 cm large more suspicious lump in the external left quadrant associated to skin thickening and hyperaemia suggesting inflammatory carcinoma and a 3 cm large lump in the ipsilateral supraclavicular fossa and ipsilateral enlarged axillary lymph nodes. Patient's anamnesis was negative for breast cancer history. A total body CT scan showed a pulmonary spiculated 17x12 mm large nodule in the upper right lobe (Fig. 2) with concomi-



Fig. 2: CT scan showing a pulmonary spiculated 17x12 mm large nodule in the upper right lobe.



Fig. 3: CT scan showing bilateral breast nodules.

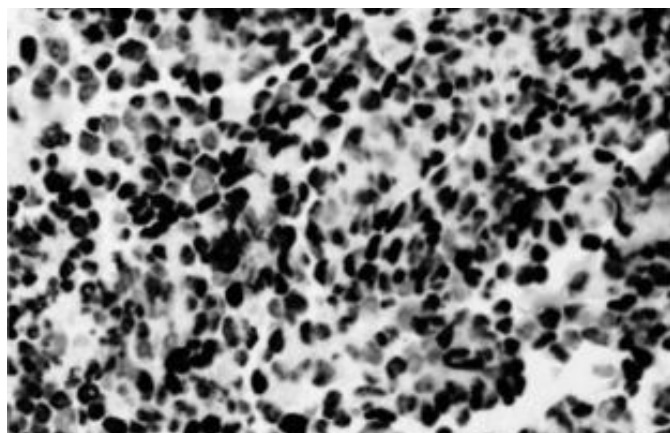


Fig. 4: Histology with positive immunostaining for TTF-1 suggesting a pulmonary origin.

tant bilateral breast nodules (Fig. 3), axillary left enlarged lymph nodes, adrenal bilateral masses of 70x25 mm on the right and of 40x35 mm on the left, suggestive for metastases, multiple mediastinal and retroperitoneal pathological lymph nodes and multiple vertebral, costal and pelvic bone osteolytic lesions. CNB of the left breast nodule showed adenocarcinoma with positive immunostaining for TTF-1 (FLEX Monoclonal Mouse Anti-Thyroid Transcription Factor, TTF-1, IR056, Dako, Denmark) suggesting a pulmonary origin (Fig. 4). After discussion in the MDM the patient was referred to the oncological department for further evaluation and treatment but died five months after the start of chemotherapy.

CASE N. 3 - FOLLICULAR THYROID CARCINOMA

A 63-year-old woman was referred to our unit for a superficial palpable nodule in her right breast. Concomitant uninodular goiter was observed at clinical examination. Ordinary Mx and US were carried out with evidence of a 12 mm ovoidal nodule without microcalcifications in the superior external quadrant with negative axillary lymph nodes and mixed hypo-anechoic features. Neck US documented a taller than wide, hypoechoic, 2 cm nodule in the right thyroid lobe with negative cervical nodes. A CNB and a fine needle aspiration (FNA) were carried out respectively on the breast lesion and on the thyroid nodule. The breast lesion histological sections showed grouped cells with a clearly follicular pattern containing colloid. Thyroglobulin positivity (Polyclonal Rabbit Anti-Human Thyroglobulin, A0251, Dako, Denmark) suggested the diagnosis of metastases from thyroid follicular carcinoma (Fig. 5). A compatible follicular neoplasm C5 was as well documented in the thyroid cytology. After MDM discussion a combined approach was carried out with total thyroidectomy and lumpectomy of the right breast. Final post-operative histology confirmed a breast metastatic fol-

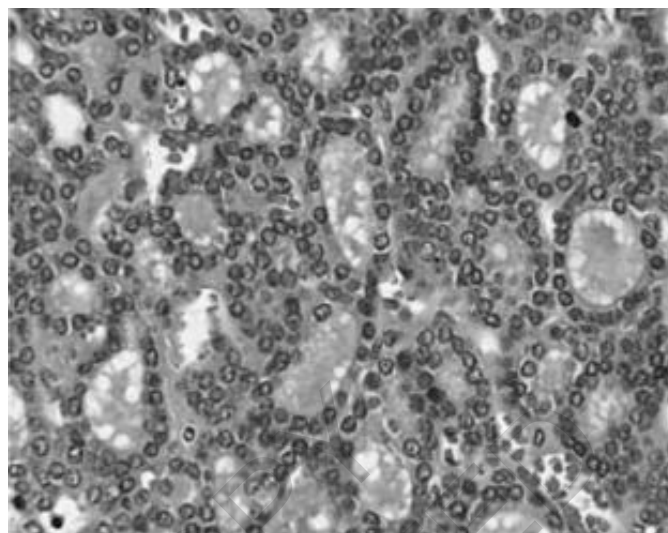


Fig. 5: Metastasis of follicular thyroid carcinoma E/E 100X, positive immunohistochemistry for thyroglobulin.

licular thyroid carcinoma. The patient underwent post-operative radioiodine treatment and the current follow-up, is uneventful with the patient doing well.

CASE N. 4 - PAPILLARY THYROID CARCINOMA

A 39-year-old woman was referred to our institution for a palpable lump in her left breast. US showed a 2 cm large hypoechoic nodule with regular shape which was further investigated with Mx with no evidence of microcalcifications. CNB was carried out showing papillary features with atypia. A wide lumpectomy was carried out and histology revealed metastasis of papillary thyroid carcinoma with positive immunohistochemistry for thyroglobulin tested as in the above reported case. A neck US showed a 14 mm irregular hypoechoic hypervascular nodule in the right thyroid lobe with associated pathological nodes in the ipsilateral laterocervical levels. Positive thyroglobulin in the cervical node aspiration was documented. The patient therefore underwent total thyroidectomy and modified radical right lateral cervical lymphadenectomy. A papillary thyroid carcinoma with metastatic cervical nodes and a breast metastasis was evident at the pathological examination. The patients was referred to radioiodine treatment and at three year follow-up she is doing well.

Discussion

Breast metastases of solid extramammary tumors are rare entities whose incidence varies between 0.5% and 2% of all breast malignancies and follow in frequency the metastatic carcinomas originating in the contralateral breast ⁹.

In a large series of 85 cases from Memorial Sloan-Kettering Cancer Center¹⁰ a wide range of non-mammary metastases of the breast was reported. Most patients present with metastatic disease at the time of tumor diagnosis, but in a relevant percentage of cases, the breast or axillary lesion is the first presentation of an occult primary tumor. These two different scenarios are present respectively in case 2 and in case 3-4 of our reported series. The median patient age reported was 54 years with a prevalence of females¹⁰. Breast only involvement was present in 2/3 of cases and a simultaneous axillary disease in 14%¹⁰. In the present series only case 1 showed concomitant pathologic nodes in the axilla within a wide spread disease. Breast metastases were mostly unilateral and solitary. In the above study carcinoma was the most common tumor reported (58%), followed by melanoma (21%) and sarcoma (21%), with usually a long interval between the primary diagnosis and the onset of the metastatic disease. Among carcinomas the most common primary site was the gynecologic tract (39%), with prevalence of the ovary as most frequent primary source, the lung (22%) and the gastrointestinal tract (13%)¹⁰. Other primary sites included the genitourinary tract (10%), head and neck (8%), and rarely the skin¹⁰. In occult primary malignancy the main diagnostic point is the identification of the breast lesion as potential secondary tumor in order to avoid a too extensive breast demolition especially if a multifocal disease is present¹¹. More often a concomitant or previous already well known tumor is reported in the patient's history and this must be considered when examining breast lump with atypical features as occurred in reported case 1.

Radiological aspect of breast metastases is strictly related to the path of dissemination since more often the haematogenous route leads to circumscribed tumors with calcifications and cystic areas mimicking benign lesions, whereas the lymphatic dissemination is associated to wider breast involvement with trabecular thickening, skin thickening and oedema mimicking mastitis or even inflammatory carcinoma¹² as we could observe in case 2.

Usually Mx shows high density, round and circumscribed lesions with microlobulated or indistinct margins and microcalcifications whereas desmoplastic reaction is seldom observed. Metastases at US detection usually present as a round or oval shape lesions still with circumscribed, indistinct or microlobulated margins. Axillary lymph nodes are seldom affected compared to what observed in primary breast cancers. In selected locally advanced cases or more often in patients with known primary tumor at the time of systemic staging or in the follow-up study the use of magnetic resonance (MRI) or positron emission computed tomography (PET/CT) might be adopted to define diagnosis and show respectively lesions with intermediate signal on T2 weighted sequences and low signal on T1 weighted sequences associated to a fast and homogeneous enhancement and lesions with increased metabolism¹³⁻¹⁴.

Variable time may occur between diagnosis of the primary neoplasm and the following breast secondarism and it may result in misdiagnosis of the metastases versus a primary breast carcinoma.

Furthermore since the majority of cases presents with a firm freely mobile lump without microcalcifications mimicking benign disease, the risk of underestimation is possible especially in young patients¹⁵⁻¹⁸.

Immunohistochemical analysis is always associated to ordinary histology to complete diagnosis in primary as in secondary breast tumors. A combination of antibody is used to confirm or to rule out the different hypothesis in the differential diagnosis process. The combination of cytokeratin 7 and cytokeratin 20 is useful in categorising carcinomas and breast cancer, including the special types, typically positive cytokeratin 7 and negative cytokeratin 20 are observed. Almost all breast cancers stain with the cytokeratin antibody CAM5.2 and are positive for epithelial membrane antigen. S100 is expressed in 50% and carcinoembryonic antigen in 30% of mammary carcinomas. Oestrogen and progesterone receptor are highly expressed in luminal subtypes of mammary carcinomas up to respectively 80% and 60% of cases. Similar staining is observed in endometrium and ovary cancers whereas rarely metastatic tumours from other origin express weak and focal oestrogen receptor positivity¹⁹. As in the presented series, approximately 20% of malignant melanomas become metastatic during the follow-up. Malignant melanoma is the most common cancer to metastasize to the breast and therefore a secondarism should be always considered in the differential diagnosis²⁰. According to a quite large series presented by Arora and Robinson melanoma breast metastases may present a long interval between the first diagnosis and the detection of the breast lesion up to several years²¹. In breast metastatic melanoma of the upper limb, back or upper abdomen the axillary involvement is not uncommon¹². In the reported case 1 no lymph node enlargement was observed. The immunohistochemistry of metastatic melanoma of the breast is negative for estrogen and progesterone receptors, as well as for E-cadherin and HER-2.

This helps in excluding most of the primary breast lesions. Differently staining can be positive for protein S-100 and vimentin, therefore leading to a correct differential diagnosis. In melanomas, S100 is present in the nucleus and cytoplasm and has a sensitivity of 97-100% but the specificity is limited. HMB-45 a marker of the cytoplasmic premelanosomal glycoprotein gp100, was one of the first melanoma specific markers discovered and it is not as sensitive as S100 but its expression seems to be highly specific for the diagnosis of melanoma since the expression is maximal in primary melanoma specimens (77-100%) although less in metastases (58-83%). Ki-67 is commonly used as an adjunct in distinguishing benign nevi from melanoma which is frequently high in metastatic melanoma detection²². Some cases of

occult melanoma breast metastases were reported and in these patient primary differential diagnosis is difficult with possible lack of primary tumor localization despite extended dermatologic investigation after metastases excision²⁰⁻²³. The 5-year overall survival for patients with metastatic melanoma is about 20%, with the median survival time ranging from 6 to 9 months; the prognosis is worse when a bilateral metastatic disease is present²¹.

Stage IV lung cancer is associated to a very poor prognosis. Approximately one fifth, of newly diagnosed lung adenocarcinomas, present with distant metastases. The most common sites of metastases are brain, bone, liver, and adrenal glands, in decreasing order. However autopsy series have demonstrated that lung cancer may spread to virtually any organ. There is no real prognostic benefit after removal of breast lesion in patients presenting synchronous metastatic lung cancer, however for patients with metachronously presenting lung cancer metastasizing to the breast only, metastasectomy could have a rationale. In the presented case 2 the spread systemic metastatic disease contraindicated a surgical approach to the breast lesion²⁴. In breast metastatic lung cancer secondarisms usually present as irregular lesions, in most cases synchronous, more rarely metachronous and lymphatic involvement mimicking inflammatory features is not uncommon²⁴.

The membranous staining for CD56 is present in 95% of cases and other neuroendocrine markers, such as synaptophysin and chromogranin A, are less frequently seen. Also positivity for CAM5.2 is frequently observed. Thyroid transcription factor-1 (TTF-1) is highly expressed in pulmonary small cell carcinomas and in adenocarcinoma. Although TTF-1 is not specific for the pulmonary origin, apart from thyroid carcinomas, it is rarely expressed in carcinomas of other origin including primary mammary neoplasms thus supporting the differential diagnosis in such cases (21). Our reported case showed a clear TTF-1 positivity at immunohistochemistry (Fig. 4). The treatment of breast metastases requires a multidisciplinary approach with discussion in the MDM finalized to the identification or reevaluation of the primary disease with specific oncologic management in the relative MDM and to the management of the metastatic lesions usually requiring a limited local radical excision. The most of breast carcinomas are cytokeratin 7 positive and cytokeratin 20 negative, and therefore a different pattern of cytokeratin expression would make breast origin less likely²⁵.

Advanced head and neck carcinomas primarily involve loco-regional lymph nodes while the detection of distant metastases is limited around 15%-20% of cases. Those cases report of patients with an average age at presentation of 47 years and with in an overall survival of approximately 10 months²¹. Differentiated thyroid carcinoma (DTC), are mainly metastatic only to neck lymph nodes. Distant metastases occurring in advanced

disease are rare and show prevalence in lungs and skeleton. Few cases of thyroid metastases to the breast are also reported²⁶⁻²⁹. A case of metastatic follicular carcinoma was previously observed and reported from our institution but it was not included in this more recent series³⁰.

Based on high sensitivity and specificity, post-therapeutic ¹⁻³¹I-whole body scintigraphy (WBS) and ¹⁻³¹I-PET/CT represent effective tools in the management of DTC patients. ¹⁻³¹I-SPECT/CT is of incremental value over ¹⁻³¹I-WBS at increasing diagnostic accuracy and in multimodal therapeutic approach. Since incremental use of ¹⁻³¹I-SPECT/CT imaging techniques, metastases of DTC once occasional is nowadays becoming a more frequent incidental finding³¹.

The histologic picture of metastases of thyroid papillary cancer shows arranged follicles separated by delicate vascularised septae. The follicles usually small to medium sized are lined by cells with grot thyroid transcription factor 1 (TTF-1), cytokeratin 19 and anti-thyroglobulin antibodies²⁶ which can be used to confirm diagnosis as in case 3 and 4.

Immunohistochemistry has a fundamental role in the detection of the primary tumor, in addition to ruling out a breast component. Cytokeratins are effective markers for epithelial differentiation and are highly expressed in tumors of carcinomatous nature.

DTC in advanced stage with lymph nodes and distant metastases is associated to poorer prognosis compared to localized disease, nevertheless also metastatic patients treated by radioiodine treatment can benefit of prolonged survival and adequate disease control as in our reported series³².

After exploring in detail the patient's clinical history, an appropriate radiologic evaluation is extremely important in the initial evaluation of any breast lesion and also helps in identifying any occult malignancy. Evaluation of biopsy material by precise histologic and immunohistochemical studies is always the gold standard to establish a definitive diagnosis of primary versus metastatic tumor of breast and, thus provides guidance to the surgeons and oncologists to determine the appropriate further management options.

Surgical treatment can be modulated from limited lumpectomy to partial or radical mastectomy if multiple and wide lesions are present and lymphadenectomy can be associated as reported. The use of primary or complementary radiotherapy is also described³³.

Conclusions

Our institution experience although limited confirms that the management of breast secondarisms requires focused diagnosis and with a multidisciplinary approach in order to provide an adequate treatment especially when the primary tumor is unknown.

Riassunto

Le metastasi mammarie sebbene rare sono caratterizzate da notevole complessità nella fase diagnostica e nella gestione clinica. Il trattamento delle metastasi mammarie si differenzia in relazione alle caratteristiche morfologiche, immunofenotipiche e biologiche del tumore primitivo e il loro comportamento è estremamente diverso rispetto a quello dei tumori mammari primitivi. I tumori primitivi più frequentemente associati a metastasi mammarie sono il melanoma, i linfomi, i tumori ginecologici, polmonari, del tratto testa-collo, i tumori gastroenterici e dell'apparato urinario. La prognosi è generalmente infausta ed è spesso associata a malattia sistemica al momento della diagnosi, con limitata sopravvivenza nonostante gli effetti del trattamento sistemico. Presentiamo la nostra esperienza di metastasi mammarie relativa a quattro casi con origine rispettivamente da melanoma, da adenocarcinoma polmonare e da due carcinomi differenziati della tiroide con l'analisi del percorso diagnostico-terapeutico. La gestione delle metastasi mammarie necessita di valutazione multidisciplinare e diagnosi mirata soprattutto in presenza di tumori primari occulti o non noti in anamnesi.

Acknowledgements

Fondazione Cassa di Risparmio di Terni e Narni for grants.

References

1. McFarlane ME: *Metastasis to the breast: A rare site for secondary malignancy*. Int J Surg, 2006; 4:4:204-05.
2. McIntosh IH, Hooper AA, Millis RR: *Metastatic carcinoma within the breast*. Clin Oncol, 1976; 2:4:393-401.
3. Cohen PL, Brooks JJ: *Lymphomas of the breast. A clinicopathologic and immunohistochemical study of primary and secondary cases*. Cancer, 1991; 67:5:1359-369.
4. Topalovski M, Crisan D, Mattson JC: *Lymphoma of the breast. A clinicopathologic study of primary and secondary cases*. Arch Pathol Lab Med, 1999; 123:12:1208-218.
5. Toombs BD, Kalisher L: *Metastatic disease to the breast: Clinical, pathologic, and radiographic features*. Am J Roentgenol, 1977; 129:4:673-76.
6. Vizcaino I, Torregrosa A, Higuera V, et al.: *Metastasis to the breast from extramammary malignancies: A report of four cases and a review of literature*. Eur Radiol, 2001; 11:9:1659-665.
7. Chaignaud B, Hall TJ, Powers C, Subramony C, Scott-Conner CE: *Diagnosis and natural history of extramammary tumors metastatic to the breast*. J Am Coll Surg, 1994; 179:1:49-53.
8. Hajdu SI, Urban JA: *Cancers metastatic to the breast*. Cancer, 1972; 29:6:1691-696.
9. Georgiannos SN, Chin J, Goode AW, Sheaff M: *Secondary neoplasms of the breast: A survey of the 20th century*. Cancer, 2001; 92:9:2259-266.
10. Delair DF, Corben AD, Catalano JP, Vallejo CE, Brogi E, Tan LK: *Non-mammary metastases to the breast and axilla: A study of 85 cases*. Mod Pathol, 2012; 26:3:343-49.
11. Sanguinetti A, Polistena A, D'Ermo G, et al.: *Axillary metastases from occult breast cancer. Our experience*. Ann Ital Chir, 2014; 85:S2239253X14022129.
12. Bitencourt AGV, Gama RRM, Graziano L, et al.: *Breast metastases from extramammary malignancies: multimodality imaging aspects*. Br J Radiol, 2017; 90:1077:20170197.
13. Surov A, Fiedler E, Holzhausen HJ, Ruschke K, Schmoll HJ, Spielmann RP: *Metastases to the breast from non-mammary malignancies: Primary tumors, prevalence, clinical signs, and radiological features*. Acad Radiol, 2011; 18:5:565-74.
14. Benveniste AP, Marom EM, Benveniste MF, Mawlawi OR, Miranda RN, Yang W: *Metastases to the breast from extramammary malignancies-PET/CT findings*. Eur J Radiol, 2014; 83:7:1106-112.
15. Saritas AG, Atar C, Gul MO, Teke Z, Ulku A, Sahin B: *Bilateral breast lesions mimicking metastases of hepatocellular carcinoma in a male patient*. Ann Ital Chir, 2020; 9:S2239253X2003279X.
16. De Cesare A, Fiori E, Burza A, et al.: *Malignant fibrous histiocytoma of the breast. Report of two cases and review of the literature*. Anticancer Research, 2005; 25:1B:505-08.
17. Paliotta A, Sapienza P, D'Ermo G, et al.: *Epidermal inclusion cyst of the breast: A literature review*. Oncology Letters, 2016; 11:1:657-60.
18. Bernardi G, Cavallaro G, Indinnimeo M et al.: *Usefulness of ultrasounds in the management of breast phyllodes tumors*. G Chir, 2012; 33:3:81-85.
19. Lee AHS, Hodi Z, Soomro I, et al.: *Histological clues to the diagnosis of metastasis to the breast from extramammary malignancies. Revised version*. Histopathology, 2020; 10.1111/his.14141. doi: 10.1111/his.14141.
20. Nacchiero E, Stucci S, Annoscia P, Vestita M, Elia R, Marannino PC: *A large metastatic intramammary lesion of an occult melanoma*. Ann Ital Chir, 2017; 88:553-56.
21. Arora R, Robinson WA: *Breast metastases from malignant melanoma*. J Surg Oncol, 1992; 50:1:27-29.
22. Ohsie SJ, Sarantopoulos GP, Cochran AJ, Binder SW: *Immunohistochemical characteristics of melanoma*. J Cutan Pathol, 2008; 35:5:433-44.
23. El-Tani Z, Duc C, Gluecker T, Cottier O: *Intramammary metastatic melanoma of unknown primary origin in a 58-year old patient: A case report*. J Med Case Rep, 2016; 10:1:363.
24. Mirrieles JA, Kapur JH, Szalkucki LM et al.: *Metastasis of primary lung carcinoma to the breast: A systematic review of the literature*. J Surg Res, 2014; 188:2:419-31.
25. Tot T: *Cytokeratin 20 and 7 as biomarkers: Usefulness in discriminating primary from metastatic adenocarcinoma*. Eur J Cancer, 2002; 38:6:758-63.
26. Nusrath S, Mahajan M, Rao TS, Raju KV, Murthy SS: *Follicular variant of papillary thyroid cancer with breast metastasis*. Indian J Surg Oncol, 2016; 7:3:356-58.

27. Chisholm RC, Chung EB, Tuckson W, Khan T, White JE: *Follicular carcinoma of the thyroid with metastasis, to the breast.* J Natl Med Assoc, 1980; 72:11:1101-104.
28. Tan PK, Chua CL, Poo WT: *Thyroid papillary carcinoma with unusual breast metastasis.* Ann Acad Med Singapore, 1991; 20:6:801-02.
29. Loureiro MM, Leite VH, Boavida JM et al.: *An unusual case of papillary carcinoma of the thyroid with cutaneous and breast metastases only.* Eur J Endocrinol, 1997; 137:3:267-69.
30. Cristallini EG, Ascani S, Nati S, Liberati F, Farabi R: *Breast metastasis of thyroid follicular carcinoma.* Acta Oncol, 1994; 33:1:71-73.
31. Song HJ, Xue YL, Xu YH, Qiu ZL, Luo QY: *Rare metastases of differentiated thyroid carcinoma: Pictorial review.* Endocr Relat Cancer, 2011; 18:5:R165-174.
32. Elisei R, Molinaro E, Agate L, et al.: *Are the clinical and pathological features of differentiated thyroid carcinoma really changed over the last 35 years? Study on 4187 patients from a single italian institution to answer this question.* Journal of Clinical Endocrinology and Metabolism, 2010; 95, 4:1516-527.
33. Shah P, Mustafa F, Aiman A, et al: *Metastases to breast. A 29 year experience in a tertiary care hospital.* Gulf J Oncolog, 2014; 1:16 1:40-45.

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