A unique case of total metastatic lobular breast carcinoma, originating from diffused microcalcifications, presented in a postmenopausal woman, without clinical manifestations

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**A R T I C L E  I N F O**

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**A B S T R A C T**

**INTRODUCTION:** Lobular breast carcinoma includes lobular carcinoma in situ (LCIS) and invasive lobular carcinoma (ILC). The association of LCIS with total metastatic lobular breast cancer is very rare.

**PRESENTATION OF CASE:** We present a case of a totally metastatic lobular breast cancer in an asymptomatic 64-year-old postmenopausal woman, with no suspicious microcalcifications in mammography. A total hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy, infracolic omentectomy and appendectomy was performed along with a quadrantectomy of the upper outer quadrant of left breast, and systematic lateral lymphadenectomy of the left axilla.

**DISCUSSION:** LCIS is usually undetectable because it isn’t associated with clinical abnormalities in clinical examination and is presented in mammography as microcalcifications or focal asymmetric densities. ILC histopathologic features are responsible for the high false-negative rates on mammography, leading to moderate detection sensitivity.

**CONCLUSION:** Our case is a very rare condition. No ‘similar’ case have been described in the literature so far.

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1. Introduction

Lobular breast carcinoma is a subtype of breast cancer, including lobular carcinoma in situ (LCIS) and invasive lobular carcinoma. There is still no general agreement whether LCIS is just a marker of an increased risk of invasive carcinoma or represents a direct precursor of invasive breast cancer [1]. While mammographic calcifications have not been commonly considered a typical presentation of LCIS, more recent studies correlate grouped amorphous calcifications and LCIS [2]. The sensitivity of mammography for the detection of ILC ranges between 57 and 81%, while microcalcifications seems to be presented in less than 3% of cases and often not typically malignant-looking [3]. Reported false negative rates for ILC on mammography vary widely (e.g. 19%, 66%) [4]. The main purpose of this report is to present an extremely rare case of a 64-year-old postmenopausal woman with foci microcalcifications in the mammography as the only radiological finding, without clinical manifestations, and a total metastatic lobular breast cancer. This work has been reported according to the SCARE criteria [5].

2. Case presentation

A 64-year-old woman, gravida 1, para 1, in good physical condition, postmenopausal since 55yo, presented to our unit for investigation and evaluation of diagnostic imaging performed in a private base for urine problems (amber of honey urine color). Her medical history included hypertension treated medically and no other pathology or allergies. She was nonsmoker and consumes alcohol only in social occasions. She had undergone total arthroplasty of her left hip 6 years ago due to degenerative arthropathy. Her mother died from pancreatic cancer and her sister received bone marrow transplant 7 years ago due to leukemia. The donor was our patient. Her body mass index (BMI) was 26 kg/m\(^2\).

On admission, the gynecological examination revealed that the vagina and cervix were presented with normal epithelium, uterus contiguous to mobile pelvic tumor estimated at 15–20 cm, no parametrium involvement and no tenderness in the pouch.
of Douglas, but with possible palpated nodules. Her laboratory workup was all normal, except neoplasia marker CA-125 which was increased (917.0U/mL). She had a temperature of 36.3°C, her blood pressure was 120/65 mmHg, and her pulse rate was 60 beats/min. Abdominopelvic CT scan showed a massive cystic lesion with dimensions of 13 × 10 × 16 cm originating from the right ovary, multiple osteoblastic lesions in the displayed bones and a sole enlarged lymph node 1.3 cm in the lesser curvature of stomach and a cystic lesion of 2.6 cm in the 4A segment of the liver [Fig. 1]. The thorax CT scan also revealed multiple osteoblastic lesions in the displayed bones and a sole enlarged lymph node in the frond mediastinum. Digital mammography revealed 3 clusters of grouped punctate microcalcifications and a few diffused ones, on the upper outer quadrant of left breast with a distance of 7–10 cm from the nipple (ACR BI-RADS classification 2) [Fig. 2]. The breast ultrasonography revealed only a sole lymph node 24 × 20 mm with normal vascularization, in the left axillary cavity.

Based on the results of the CT scan and laboratory findings, a total hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy, infracolic omentectomy and appendectomy was performed by a gynecologist specialized in gynaecological oncology, under general anesthesia. Postoperatively the patient was followed up in a simple ward. She was administered intravenous antibiotics, fluids and painkillers.

After a hospitalization of 6 days, she was discharged on the 7th postoperative day, in good condition. She was prescribed postoperatively tinzaparin (u) for 8 days and cefuroxime (u) peros for 7 days. The patient was compliant with the therapeutic program which was well tolerated with no significant side effects. Histological examination of surgical specimens revealed a mucinous cystadenoma of the left ovary and invasion of its cortex from malignant neoplasia, diffuse deployed and interlaced as individual cells. The cortex of fallopian tubes was invaded from the above neoplasia. Similarly, metastases to the omentum, appendix, excised lymph nodes, cervix and myometrium were revealed [Fig. 3]. Morphologic and immunophenotypic characteristics of the tumor suggested metastatic invasion from breast carcinoma with differentiation of a lobular subtype. Thus, the patient readmitted for a complete breast workup investigation. In order to exclude multifocal and multi-centric lesions, Contrast-Enhanced Spectral Mammography (CESM) was performed (opposite to Breast MRI, due to our Breast Unit Protocol) along with clinical evaluation, breast ultrasound, bone scanning with Tc99m MDP and suggested surgical screening.

The ultrasonic examination of the breast described only a single lymph node with dimensions of 22 × 10.6 mm, with normal vascularization in the left axillary cavity. CESM revealed scattered regions with confluent microcalcifications on the left breast and no abnormal areas of enhancement in either breast after the iv injection of iodinated contrast material or visual masses suspected for neoplastic proliferation [Fig. 2]. Bone scanning revealed areas of increased radionuclide uptake along the vertebral column, sternum, pelvis, sacrum, occipital bone and vertebrosternal ribs; findings compatible with metastatic disease [Fig. 4].

Given the diagnostic findings and the fact that the patient should be treated with the correct chemothrapy protocol for the metastatic disease, we performed surgical investigation to reveal the origin of the primary lesion. The patient underwent a quadrantectomy of the upper outer quadrant of left breast, excision of 3 lymph node blocks and level 1–2 systematic isolated lymphadenectomy of the left axilla by a gynecologist specialized in breast and 5 year experienced in breast surgical procedures under general anesthesia. Postoperatively the patient was followed up

Fig. 1. Abdominopelvic CT scan; a–c. Massive cystic lesion originating from the right ovary and multiple osteoblastic lesions in the displayed bones; d. Enlarged lymph node in the lesser curvature of stomach.
in a simple ward. She was administered intravenous antibiotics, fluids and painkillers. She was hospitalized for 11 days and was discharged on the 12th postoperative day, in good condition, without postoperative complications [Fig. 5]. Histologic examination of surgical specimens identified that the mammary gland was totally invaded from lobular carcinoma grade 2, with co-existing in situ lobular carcinoma outspread to ducts with necrosis and calcifications [Fig. 3]. Also, invasion of all the excised lymph nodes from the lobular carcinoma, equally of the breast fat tissue and the outer coat of vessels. Immunohistochemistry analysis in cellular level showed ER (clone 6F11) stain positive (moderate to intense) in 90% of tumor cells and Ki-67 (clone M1B1) stain positive in 4% of tumor cells. The margins of the resected surgical specimen were negative for cancer cells, so we didn’t proceed to a more radical surgery such as radical mastectomy. Soon after, the patient started first line chemotherapy for metastatic breast cancer (aromatase inhibitors).

3. Discussion

LCIS was initially first described by Foote and Stewart in 1941 [1]. It occurs most frequently in premenopausal women aged 40–50 years, despite the fact that the incidence in post-menopausal women augments [1]. Usually incidentally identified as a microscopic finding in breast biopsy performed for other reasons, LCIS has no macroscopic features to guide tissue sampling [6].

Although the incidence of ILC occurring with LCIS is notably greater than without, there is a suggestion in latest literature that LCIS is not a true precursor lesion [1]. LCIS is usually undetectable;

**Fig. 3.** a. Massive infiltration by non-cohesive neoplastic cells in the endo-myometrium (H-EX100); b. Immunohistochemical stain for Estrogen Receptors (ER) positive in neoplastic cells in the appendix (X100); c. Breast biopsy revealed diffuse infiltration by lobular type carcinoma with typical features and adjacent intraepithelial (in situ) lobular cancer (H-EX100).
most (but not all) LCIS are not associated with clinical abnormalities such as a palpable lump in clinical examination [6]. Generally it is uncommon for LCIS to be presented as a radiographic mass substantially less usual than other mammographic findings, such as microcalcifications, architectural distortions or focal asymmetric densities [7]. Thus, ultrasonography and mammography do not appear to have a role to diagnose LCIS prospectively [6].

According to the eight edition of the AJCC staging system for the breast cancer, LCIS is treated as a benign entity with an associated risk for a future developing carcinoma and not as a potentially metastasizing malignant mass [8]. There is a small subset of LCIS that has high-grade nuclear features and may exhibit central necrosis [2]. This subset has been referred as pleomorphic LCIS with a strong positive predictive value for malignancy invasion [2]. When classic LCIS is found on breast biopsy preoperatively, a more conservative follow up seems to play the pivotal role for its treatment; radiological (mammography, ultrasonography) and clinical follow-up is a way for avoidance the surgery [2,6].

Invasive or infiltrating lobular carcinoma (ILC) represents 5–10% of invasive breast cancer [4]. It is characterized by malignant behavior monomorphic cells which form linear invasive columns, loosely dispersed (referred as ‘Indian-Filing’) and as they often encircle the ducts, they preserve their architecture [4,3]. These histopathologic features are responsible for the high false-negative rate of 4–19% of these lesions on mammography, thus, the detection sensitivity of ILC have been accounted between 57 and 81% [4,3].

Normal or benign mammographic findings are more frequently reported with ILC (8%–16% of cases) than with other invasive breast cancers [3]. Mammographic abnormalities associated with ILC can be subtle, including spiculated mass ranging from 44% to 65% (often representing a coexisting malignancy such as IDC), asymmetrical and focal densities (3–25%), opacities or architectural distortions (10–25%) and microcalcifications in less than 10% of cases (which are far less frequently associated with ILC than with the usual type IDC) [4,3]. Because of the limitations of mammography in detecting ILC, ultrasonography and breast MR imaging are being used in evaluating suspicious findings of disease, providing
4. Conclusion

Overall, according to the literature, we did not manage to find a similar case report presenting a totally metastatic lobular breast cancer in an asymptomatic patient with no suspicious microcalciﬁcations in mammography. Left ovary metastases, fallopian tubes metastases, omental metastases, appendix metastases, cervical metastases, myometrial metastases, bone metastases to vertebral column, sternum, pelvis, sacrum, occipital bone and vertebral sternal ribs, following a ‘not suspicious’ mammography and a negative for malignancy CESM, depict this ﬁrst presenting very rare phenomenon.

Conflicts of interest

NA.

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Ethical approval

IRB/Ethics Committee ruled that approval was not required for this study.

Consent

Written informed consent was obtained from the patient, and this has been stated in the manuscript per the submission instructions.

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