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Case Report
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Extensive, diffusely invasive lobular carcinoma of the breast mistakenly presumed to be posttraumatic scarring

Abstract

Background: The imaging biomarker, extensive, non-calcified architectural distortion on the mammogram, is characteristic for only a few differential diagnostic options. The benign diagnostic options are traumatic fat necrosis, radial scar and granulomatous mastitis; the malignant diseases are either breast cancer originating in the hybrid stem cells of the mesenchyme (aka invasive lobular carcinoma) or non-calcified neoductgenesis, an invasive breast cancer originating in the major lactiferous ducts. Thorough clinical breast examination followed by multimodality breast imaging and microscopic examination of the larger-bore specimen can lead to the correct diagnosis.

Case presentation: The two deceptive cases presented here illustrate important teaching points. Their common features were a history of considerable trauma to the chest and each patient's insistence upon the benign nature of the palpable findings. These factors misled the breast imagers and caused a delayed diagnosis.

Conclusion: The main teaching point for the breast imager is that a palpable thickening at clinical breast examination associated with non-calcified architectural distortion on the mammogram should always be considered a malignant process, despite any misleading information about a history of trauma to the breast. The diagnosis should be based on the microscopic examination of a sufficient amount of tissue removed from the palpable lesion, using a larger bore needle biopsy or surgical biopsy. Fine needle aspiration biopsy may lead to underdiagnosis.

Key words: breast cancer, traumatic fat necrosis, invasive lobular carcinoma, BCMO (breast cancer of mesenchymal pluripotent hybrid stem cell origin

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Abbreviations: AI, artificial intelligence; ILC, invasive lobular carcinoma; BCMO, breast cancer of mesenchymal pluripotent hybrid stem cell origin; MLO, mediolateral oblique projection; CC, craniocaudal projection; IHC, immunohistochemical; ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2; Ki67, proliferation index; LVI, lymph vessel invasion; GATA3, glutamyl aminotransferase subunit A; CAM 5.2, anti-cytokeratin

Introduction

The detection of architectural distortion on the mammogram remains a difficult perception problem for breast imagers and artificial intelligence (AI) algorithms alike. It is difficult to detect even when extensive, in fatty replaced breasts and especially in dense fibroglandular tissue.[1–3] In the classic form of invasive lobular carcinoma the malignancy stimulates increased collagen production, until the haphazard growth of fibrosis combined with cancer cells becomes evident as architectural distortion, often at the size of several centimetres.[1,4] The pathologic lesion does not initially distort the concave border of fibroglandular tissue with the adipose tissue, since it fails to form a tumour mass.

Cell culture studies have provided evidence showing that the classic form of invasive lobular carcinoma arises from the pluripotent hybrid stem cells of the extralobular mesenchyme and not, as its name implies, from the acinar epithelium of the lobule. The authors have proposed the term breast cancer of mesenchymal stem cell origin, BCMO, to more adequately describe this poorly understood malignancy.[5] The transformed stem cells mimic epithelial cells; successive layers of thin sheets of tumour cells spread through the mesenchymal interstitium, where they are interlaced with ever-thickening sheets of collagen and fibroblasts.

Architectural distortion caused by traumatic fat necrosis is more readily detected and easily related to the external trauma or surgical procedures. The imaging biomarker, architectural distortion, is formed within a few months, and tends to remain unchanged thereafter. Ultrasound can reveal multiple encapsulated inclusions of necrotic matter more reliably than mammography. Other benign differential diagnostic options are granulomatous mastitis, often causing tumour-imitating mass lesions requiring percutaneous biopsy to rule out malignancy. An additional benign lesion producing architectural distortion is the radial scar, having a low-opacity radiating structure called a "black star."[6]

Architectural distortion can also be caused by neoductgenesis, a duct forming invasive carcinoma, where the components of the imaging findings consist of distended, disorderly duct-like structures. The corresponding, most frequent histopathologic finding is extensive fluid-producing micropapillary and/or cribriform cancer of ductal origin (DAB). The characteristic skipping-stone-like calcifications develop late; making the detection of the non-calcified architectural distortion difficult before it achieves a size of several centimetres.[7] Differentiating non-calcified neoductgenesis from BCMO requires histopathological proof.

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Case presentation

Case 1

A 69-year-old woman presented with a self-detected firm, extensive thickening in the lower half of her right breast. She had had an automobile accident several years earlier and since then she had noted a palpable lesion in the lower half of her right breast, which she considered to be a consequence of her trauma. A series of mammograms illustrate the gradually increasing architectural distortion and shrinkage of the right breast, more pronounced in the MLO projections (Figures 1-4). The patient insisted at each follow-up examination that the palpable lesion had been present in her right breast since the time of her car accident. She skilfully persuaded several of the examining breast imagers that this lesion had developed soon after the car accident and that "it was nothing to worry about." Eventually the right breast became deformed to the extent that a comprehensive examination was performed. The microscopic examination of the 14G core biopsy specimen uncovered the true nature of the disease and the reason for the architectural distortion: an invasive breast malignancy instead of scar tissue.

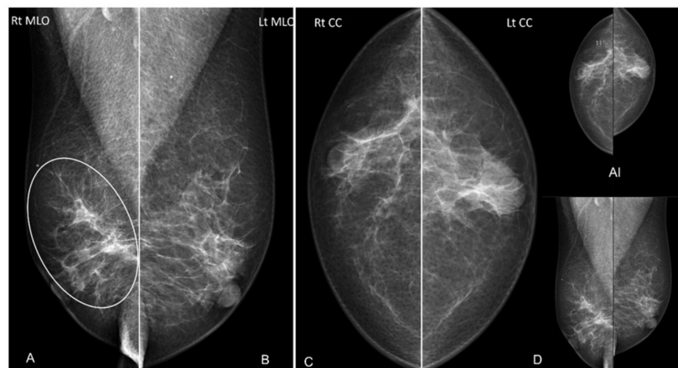


Figure 1 MLO (A,B) and CC (C,D) projections. Already at this examination, 72 months before diagnosis and surgery, non-calcified architectural distortion can be observed in the right MLO projection (encircled). The AI algorithm did not react to the presence of extensive architectural distortion.

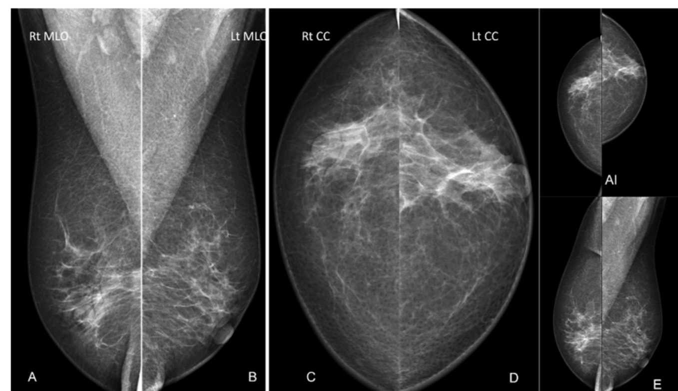


Figure 2 Twenty-one months later the architectural distortion was more obvious in the right MLO projection and the central fibroglandular tissue began to shrink on the CC projection as well. The AI algorithm did not react to the presence of extensive architectural distortion.

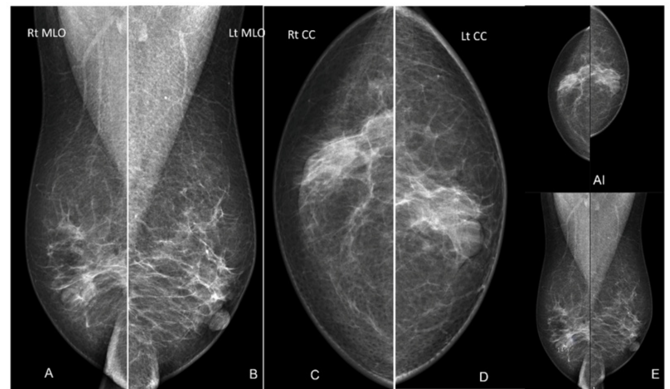
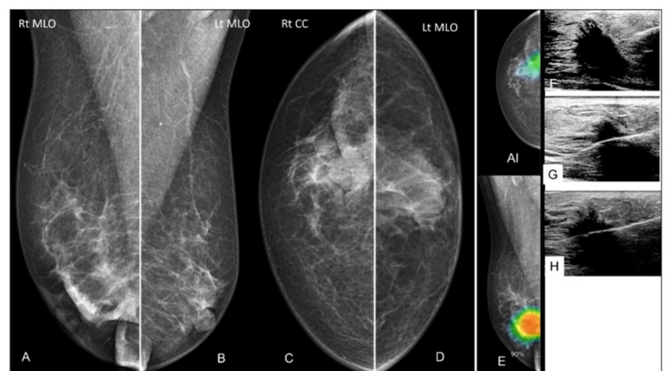
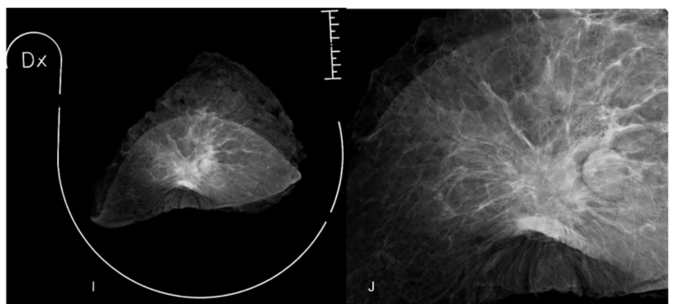
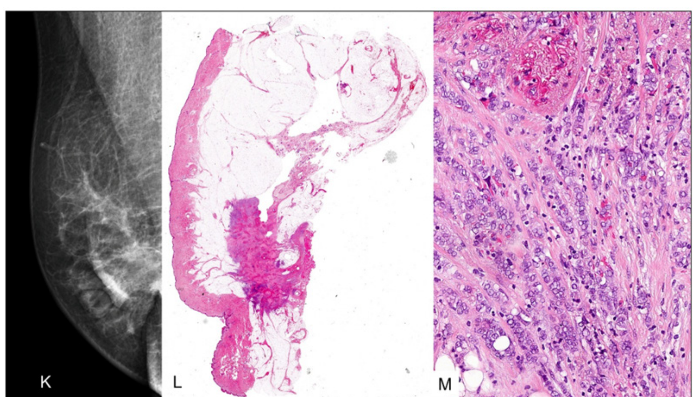


Figure 3 An additional 24 months later positioning of the right MLO projection became difficult due to the presence of the slightly increasing architectural distortion. The AI algorithm did not react to the presence of extensive architectural distortion.







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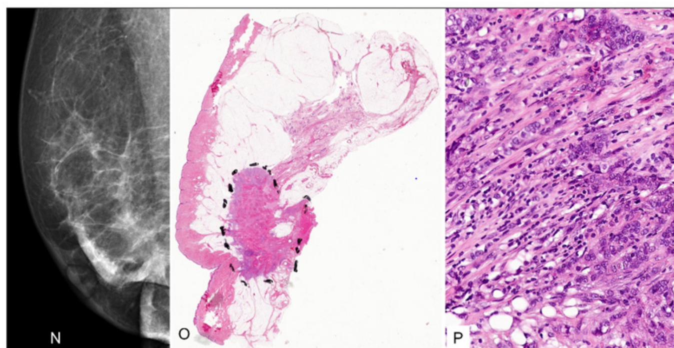


Figure 4 An additional 24 months later there was a gross deformation of the entire right breast, retraction of the skin and nipple-areola complex (A,C). The patient still insisted that the palpable thickening in the lower-central portion of her right breast was the consequence of the trauma she had undergone from the automobile accident. The AI algorithm marked the presence of an extensive abnormality in the right breast (E). Hand-held ultrasound examination (F) showed a mass lesion with acoustic shadowing. US-guided 14G core biopsy (G,H) confirmed the presence of a malignancy containing a massive amount of fibrous tissue, characteristic for BCMO. Microscopic examination of the core biopsy specimen revealed invasive BCMO (aka classic invasive lobular carcinoma). Mastectomy specimen radiography (I) and microfocus magnification of the portion of the specimen containing the architectural distortion (J). Mammographic (K,N), large format thin section histopathologic (L,O) and higher power histopathologic image (M,P) correlation.

Histopathology report of the mastectomy specimen: 24x13 mm moderately differentiated breast cancer of mesenchymal stem cell origin (BCMO) (aka as classic ILC) combined with foci of the solid form of invasive lobular carcinoma. IHC biomarkers: ER/PR positive, HER2 negative, Ki67 12%, E-cadherin negative. No LVI.

Follow-up: Eight years and four months after diagnosis and treatment the patient is well with no signs of recurrence.

Case 2

An 82-year-old woman felt a firm thickening occupying the central and upper portion of her left breast. Clinical breast examination confirmed a grossly deformed breast, skin thickening, palpable abnormal axillary nodes and retraction of the nipple-areola complex. The patient reported trauma five years previously, when she fell upon a heavy silver statue, causing a large hematoma in her left breast. At each subsequent mammography examination, she insisted that the palpable thickening was scar tissue from that trauma. During the following years the palpable lesion in her left breast gradually increased in size (Figures 5-8). Microscopic examination of the 14G core biopsy specimen showed diffuse invasive lobular carcinoma (Figures 8,9). She also had core biopsy proven left axillary metastases. The patient refused surgery. Histologically proven ILC metastases developed on her skin. Six years and ten months after diagnosis the patient died from disseminating BCMO (aka ILC).

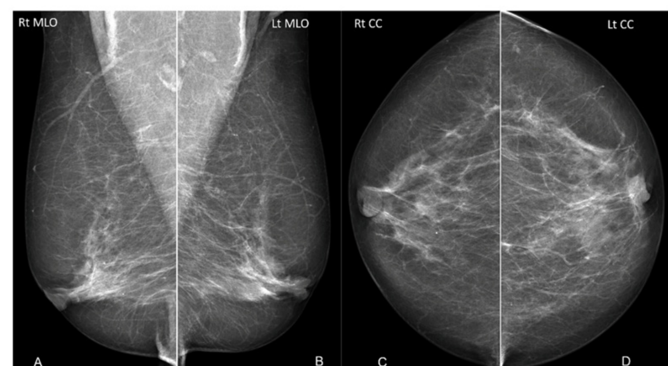


Figure 5 Mammograms taken prior to the patient's breast trauma. No mammographic abnormality can be detected on the MLO (A,B) and CC (C,D) projections.

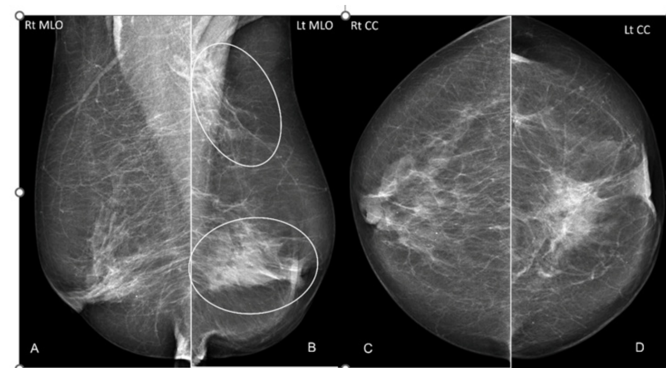
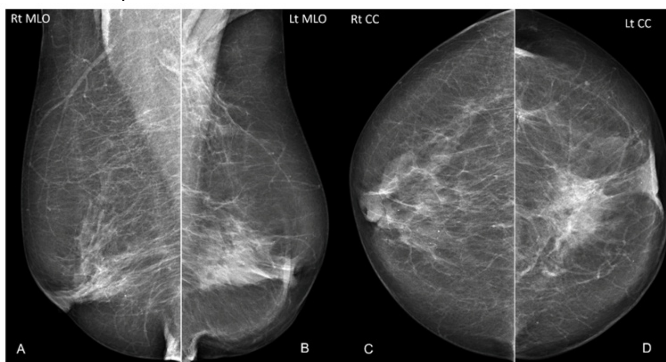


Figure 6 Three years and three months later *de novo* architectural distortion was seen in the left axillary tail (B) and centrally localized architectural distortion (B,C) also developed. The patient insisted that these findings were the result of previous trauma to her breast.



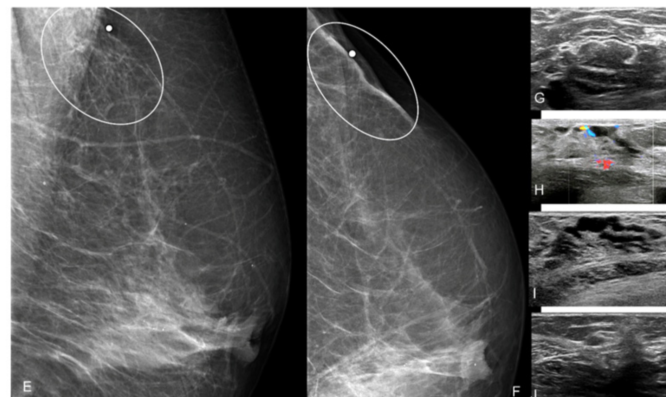
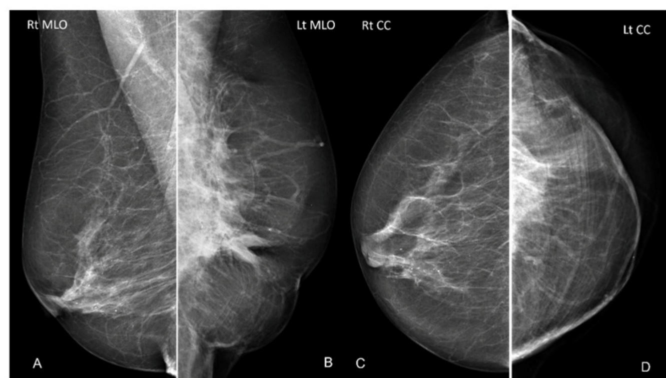


Figure 7 Sixteen months later the architectural distortion in the left axilla became palpable.



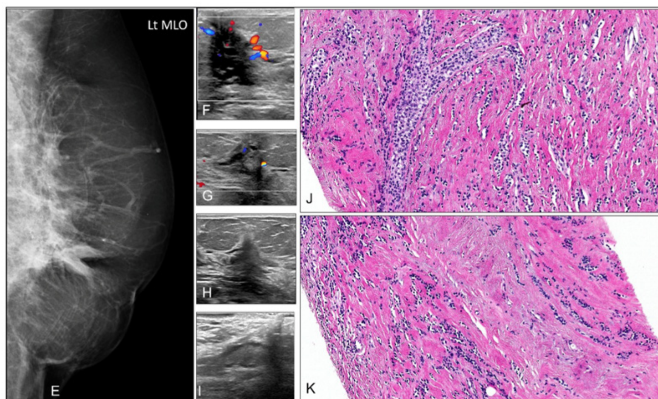


Figure 8 MLO (A,B) and CC (C,D) projections 48 months later show the gross deformation of the entire breast due to the extensive, diffusely infiltrating malignancy. Hand-held ultrasound images (F-I) demonstrate several malignant tumour foci. Histopathology of the 14G core biopsy sample (J,K): Invasive breast cancer of mesenchymal stem cell origin, (BCMO), aka ILC).

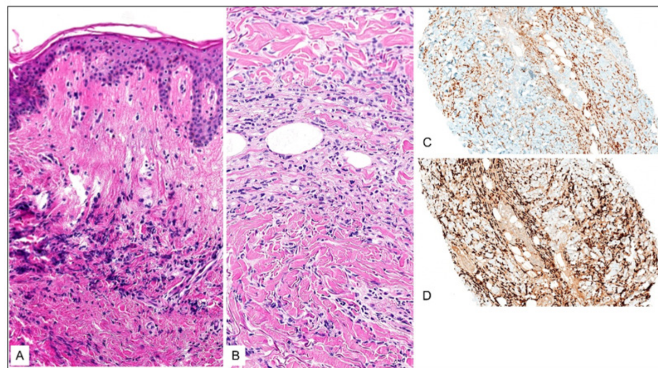


Figure 9 Intermediate-power histopathology images (A,B) of the skin metastases of this BCMO. ER (C) and GATA3 (D) positivity confirmed the breast cancer origin.

Histopathologic diagnosis: 14G core biopsy was performed, diagnosed as classic invasive lobular carcinoma (according to our suggested terminology: breast cancer of mesenchymal pluripotent hybrid stem cell carcinoma, BCMO). The patient agreed to meet a surgeon for consultation only and refused surgery. The extensive tumour was not removed from the breast.

One month after diagnosis 14G core biopsy was performed on her skin metastases. CAM 5.2 and GATA3 positivity proved that the origin of skin metastases was breast cancer.

Outcome: Five years and nine months after diagnosis the patient died from disseminating BCMO.

Conclusion

These two cases carry important teaching points. When clinical breast examination reveals extensive thickening and the mammograms show large regions of architectural distortion, diffuse malignancy should be the overriding diagnosis. Use of a multimodality imaging approach combined with larger bore needle biopsy should be sufficient to rule out or confirm malignancy. Patients with a history of trauma to the breast may persuasively insist that the palpatory findings are caused by the trauma, possibly leading to a delay in diagnosis, as in the second of these two cases. Fine needle biopsy has a poor sensitivity for cases with architectural distortion due to the predominance of fibrous tissue. AI algorithms also have poor sensitivity in cases with architectural distortion due to the lack of a tumour mass and calcifications.

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Conflict of interest

The authors declare that they have no competing interests.

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