Radiology Case Reports 19 (2024) 483–488

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Case Report

Calcified axillary lymph nodes in a case of de novo metastatic breast cancer ☆

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ARTICLE INFO

Article history:
Received 16 February 2023
Revised 25 October 2023
Accepted 26 October 2023
Available online 17 November 2023

Keywords:
Breast cancer
Metastatic breast cancer
Calcified axillary lymph nodes

ABSTRACT

At the time of a mammogram, calcifications may be seen in axillary lymph nodes. Metastatic breast cancer is the most common malignant cause of calcifications in the axillary lymph nodes. Benign causes may include but are not limited to granulomatous disease, fat necrosis, gold deposits in rheumatoid arthritis patients, pigmentation from tattoos, and sarcoidosis. We present a case of a 37-year-old female with axillary lymph node calcifications due to metastatic breast cancer. Calcification morphology seen in the primary breast tumor and the axillary lymph nodes are nearly identical on mammogram, which is seldom seen. The similar morphology almost guarantees metastatic breast cancer, underscoring the importance of identifying the etiology of any calcifications present in axillary lymph nodes on mammography.

Clinical case

A 37-year-old female presented to her primary care physician (PCP) with physical changes to the left breast for the past 3 months. She first noticed slight inversion of the left nipple as well as contour changes and progressive discomfort of the left breast. Eventually, the patient felt a lump in the lateral left breast which prompted a PCP visit. She denied nipple discharge and skin changes. Family history was significant for 2 maternal aunts with breast cancer diagnosed in their 50s. She denied any previous medical history. Her surgical history consisted of 2 C-sections and a cholecystectomy. Reproductive history included menarche at 11, Gravida 2, Para 2, abortions 0, with first live birth at age 18, and her last menstrual period was 3 weeks before PCP visit. She denied oral contraceptives and hormone replacement therapy. Her left breast exam demonstrated nipple inversion, mild pain, and palpable masses in the lateral left breast and right upper outer quadrant. Her physical exam and review of systems were otherwise within normal limits. Notably, there were no palpable axillary lymph nodes during physical exam. Her vital signs were normal. She specifically denied any cough or shortness of breath. Her body mass index (BMI) was 32.7 based on her height of 165.8 cm and weight of 89.9 kg. Given physical exam findings, bilateral mammography and ultrasound were performed. LEFT breast digital mammogram with tomosynthesis revealed a 3.5 cm high-density mass at 2:00 5 centimeters

☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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https://doi.org/10.1016/j.radcr.2023.10.067

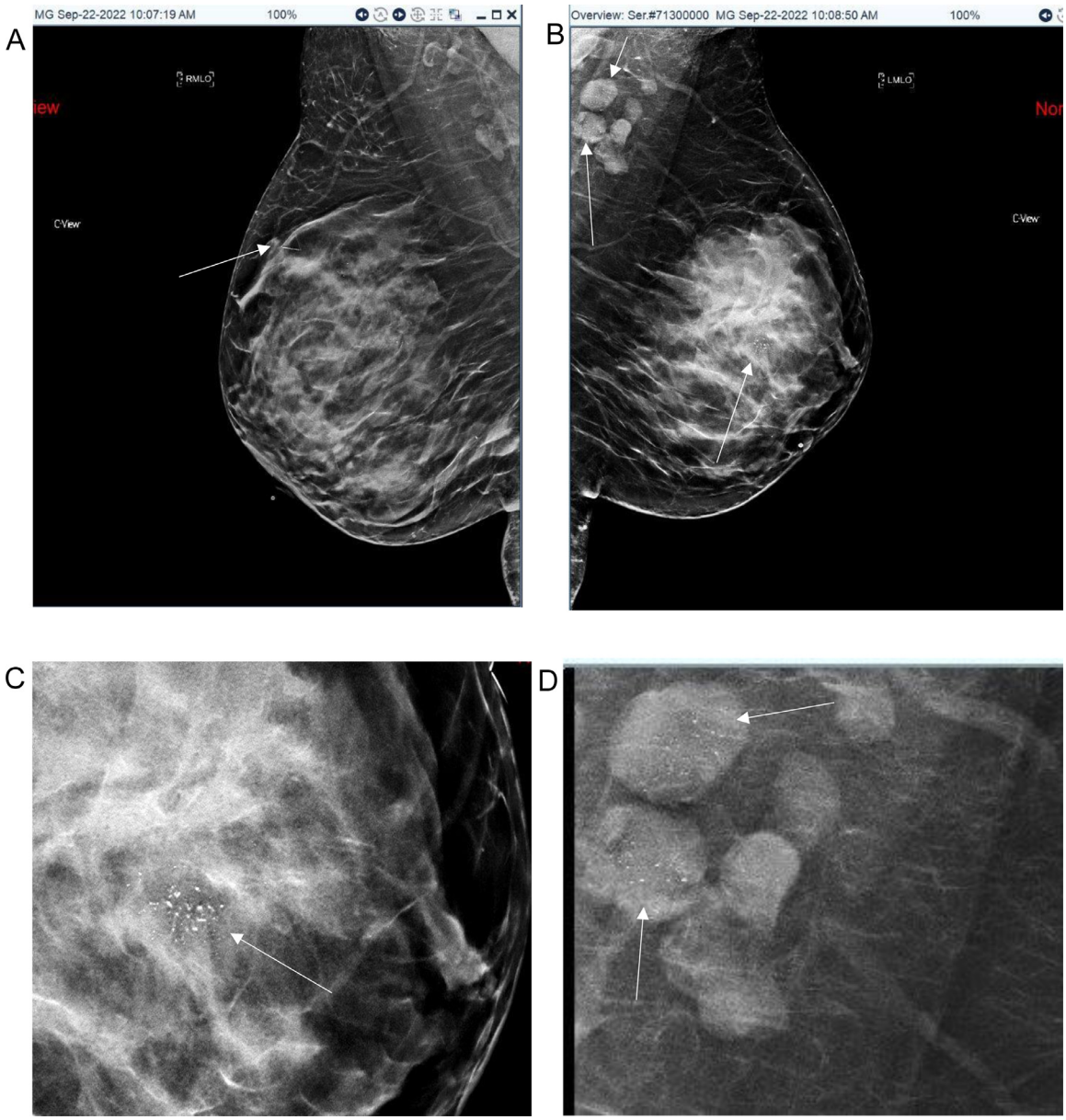

Fig. 1 – (A) Right MLO mammogram with palpable marker UOQ (white arrow). (B) Left MLO Mammogram showing calcifications in breast mass and axillary lymph nodes (white arrows). (C) Left MLO magnification of 2:00 5CMFN pleomorphic calcifications (white arrow) (D) Left MLO magnification of axillary lymph node calcifications (white arrows).

from nipple (CMFN) with associated architectural distortion, trabecular thickening, and pleomorphic calcifications as well as multiple LEFT axillary lymph nodes containing pleomorphic calcifications. RIGHT breast mammogram revealed subtle architectural distortion visible on tomosynthesis (Fig. 1A and B; magnification of calcifications in the left breast and left axillary lymph nodes shown in Fig. 1C and D). High-frequency US demonstrated an irregular hypoechoic heterogeneous mass in the left breast at 2:00 5CMFN location measuring 2.5 × 2.1 × 1.9 cm, as well as enlarged left axillary lymph nodes containing multiple echogenic foci and loss of normal morphology (Figs. 2A and B). US of the RIGHT breast palpable area at 10:00 9CMFN revealed a hypoechoic 2.2 cm mass. US-guided core biopsy of all three findings were performed. Pathology from the RIGHT breast 10:00 palpable area 14-gauge (14G) US core biopsy was benign breast parenchyma with fibroadenomatoid change and focal stroma fibrosis. Pathology from the LEFT breast 2:00 5CMFN breast mass 14G US core biopsy demonstrated invasive ductal carcinoma (IDC) with associated calcifications, shown in the hematoxylin and eosin (H and E) stained section (Fig. 6A). Pathology from the LEFT axillary lymph node 16G US-guided core biopsy also demonstrated invasive ductal carcinoma with necrosis and associated coarse calcifications morphologically similar to the calcifications found in the left breast, shown in the H and E stained section (Fig. 6B). Staging breast MRI confirmed the above find-

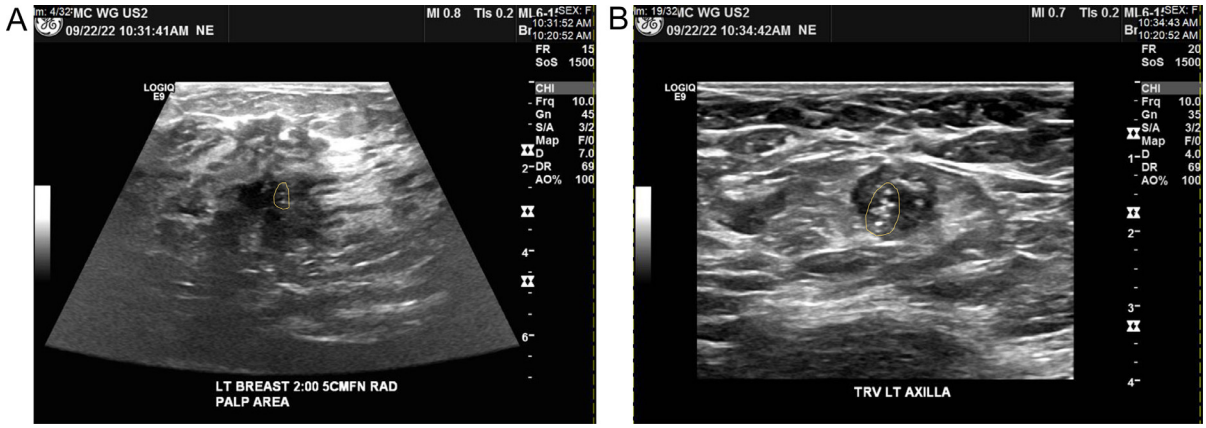

Fig. 2 – (A) Left 2:00 5CMFN hypoechoic mass with echogenic foci consistent with calcifications (circled in yellow) seen on mammogram. (B) Left axillary ultrasound demonstrates a lymph node with abnormal round morphology, no visible hilum & multiple echogenic foci consistent with calcifications (circled in yellow).

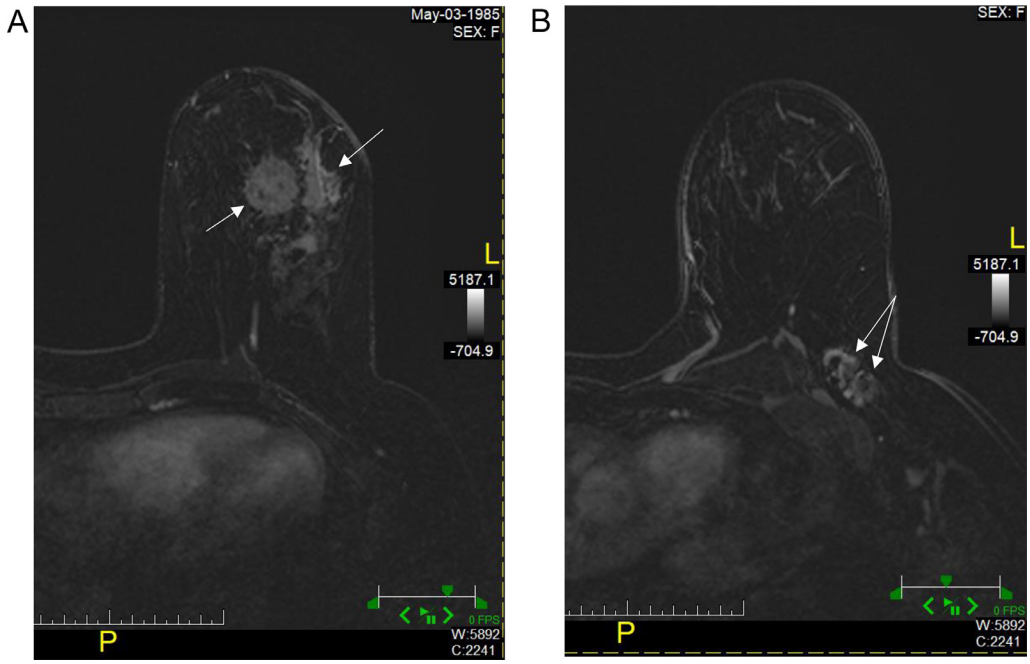

Fig. 3 – (A) T1 postcontrast subtracted axial dynamic series MRI demonstrates multiple enhancing masses (white arrows) in the left breast associated with skin thickening and enhancement. (B)T1 postcontrast subtracted axial dynamic series MRI demonstrates multiple enhancing left axillary lymph nodes (white arrows).

ings, along with multiple additional LEFT breast masses and nonmass enhancement (NME) and skin thickening of the LEFT breast consistent with multicentric LEFT breast IDC (Fig. 3A and B). Additionally, subtle T2 intense nodules were visualized in the anterior aspects of bilateral lungs (Fig. 4). PET/CT showed multiple bilateral pulmonary nodules with mediastinal and hilar lymphadenopathy (Fig. 5). SUV Max values within a right medial upper lobe pulmonary nodule and subcarinal nodal station were 12.9 and 8.1, respectively. Right lung core biopsy demonstrated adenocarcinoma, consistent with metastasis from breast, shown in the H and E stained section (Fig. 6C).

Discussion

In the differential diagnosis of women presenting with axillary lymph node calcifications, benign and malignant causes both need to be considered. The most common cause of malignant calcifications in the axillary lymph nodes is metastatic breast cancer [1]. Benign causes may include but are not limited to granulomatous disease, fat necrosis, gold deposits in rheumatoid arthritis patients, pigmentation from tattoos, and sarcoidosis [2–5]. In cases without a known cause, a complete work-up to find the etiology should be performed. Axil-

Fig. 4 – Breast MRI axial T2 STIR demonstrates a 10 mm T2 intense nodule in RIGHT anterior lung (white arrow).

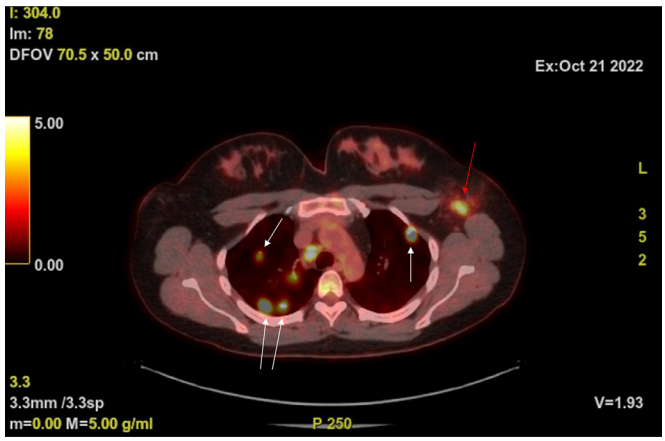

Fig. 5 – Axial FDG-18 PET/CT demonstrates multiple hypermetabolic lung masses (white arrows) and mediastinal/ LEFT axillary lymphadenopathy (red arrow).

lary lymph node calcification morphology, which can be dystrophic, punctate, amorphous, or coarse, can help elucidate the etiology [6].

MLO view mammography may or may not demonstrate abnormal axillary adenopathy. In cases of clinically detected abnormal axillary lymph nodes, negative mammograms are typically followed by US imaging of the axilla [6]. A normal lymph node has a thin (<3 mm) hypoechoic smooth cortex and an iso-to-hyperechoic hilum, with an oval, reniform-like shape. Abnormal lymph nodes can appear more rounded with thickened cortices over 3 mm, and obliteration of the hilum is associated with malignancy [6,7]. Hyperechoic foci seen within the cortex of lymph nodes, as in this case, warrant a biopsy if there is no known benign cause. Calcifications are not typically seen within the normal architecture of lymph nodes.

The radiologist should always be concerned when calcifications within axillary lymph nodes are found on imaging. This case not only underscores the importance of determining the etiology of calcifications but should also prompt the radiologist to investigate further when the axillary calcifications have similar morphology to known breast cancer, as this finding implies an advanced breast cancer. Calcification presentation in breast malignancy can be variable, with the presence of fine linear branching, pleomorphic or coarse heterogenous calcifications implying a more aggressive cancer. When calcifications are seen by the radiologist in tandem with a suspicious mass or architectural distortion, this should also trigger magnification views for better characterization and to help guide further testing and predict the likelihood of invasive disease. The positive predictive value of invasive cancer is as high as 70% in cases with suspicious morphologies (coarse heterogenous, fine pleomorphic and fine linear branching) with an associated mass or focus of architectural distortion [8]. There are multiple causes of benign axillary calcifications including systemic diseases such as sarcoidosis and rheumatoid arthritis, granulomatous reactions such as tuberculosis, and even pigment deposition from tattooing [9–11]. In these benign entities, the calcifications typically have a different morphology. In a case report by Oktay et al. [12], breast calcifications in a patient with lupus mimicking a breast mass were more diffuse, coarse, and curvilinear in shape, most consistent with fat necrosis. Furthermore, axillary calcifications seen with gran-

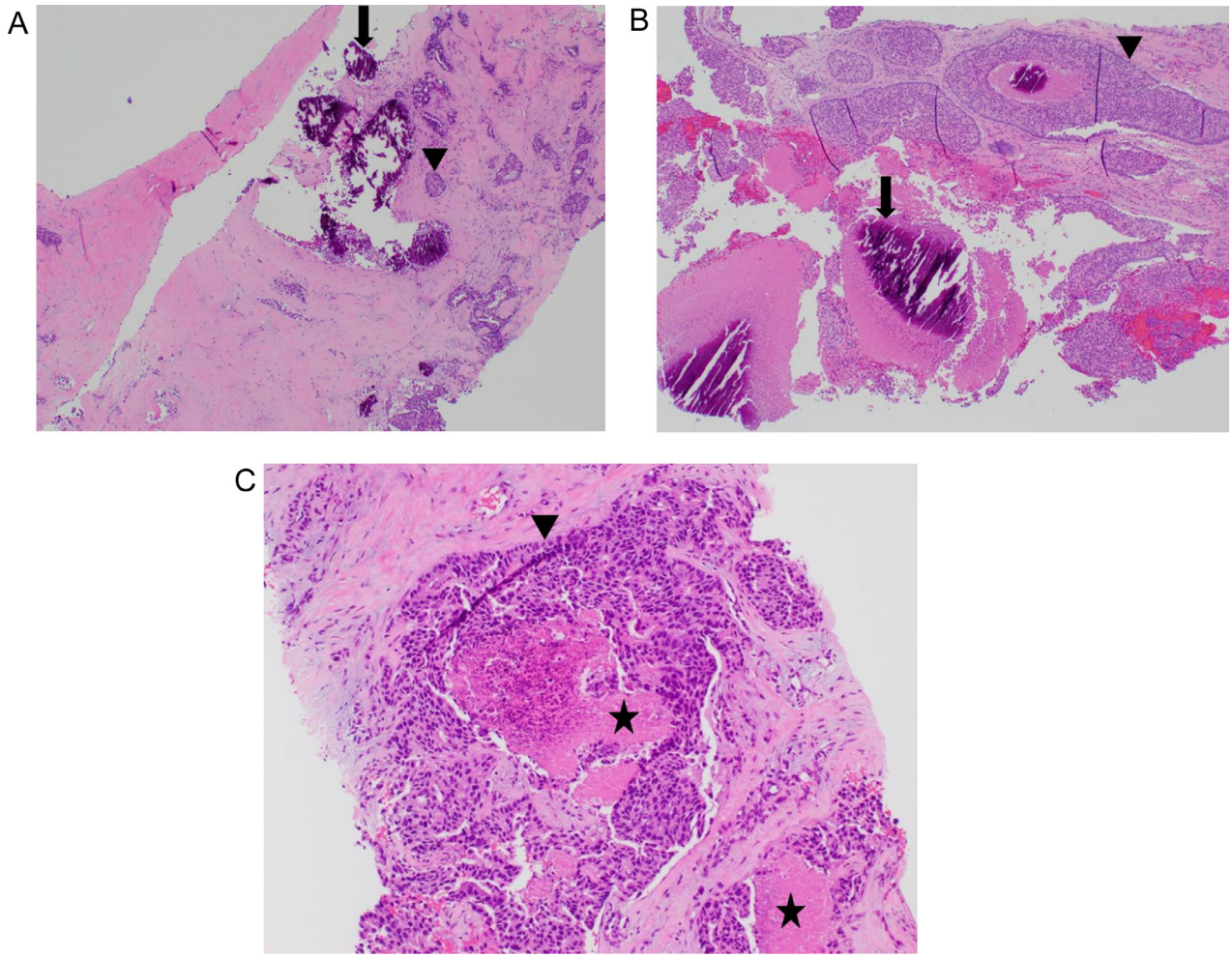

Fig. 6 – (A) H and E stained section from the breast showing invasive carcinoma (arrowhead) with calcifications (arrow) (4X magnification) (B) H and E stained section from the lymph node showing metastatic carcinoma (arrowhead) with necrosis and calcifications (arrow) (4X magnification) (C) H and E stained section from the lung showing metastatic carcinoma (arrowhead) with necrosis (stars) (10X magnification).

ulomatous disease are also less suspicious in morphology. These are typically also coarse and large [13]. A less common cause of benign axillary calcifications results from pigment deposition related to prior tattooing [14]. A review of a case series performed by Lane et al. demonstrates that these calcifications are more punctate or grouped amorphous in morphology, rather than the most suspicious morphologies as described in primary breast cancers above.

It is imperative that the radiologist clearly states the similar morphology in both the breast and axilla in the impression of the report. Thus, when similar calcifications in the axilla and breast are reported, and especially when they are of suspicious morphology, this should heighten the awareness of the clinician of the potential of advanced metastatic disease. The clinician should evaluate the patient and their history to see if the calcifications can be attributed to a benign etiology, and if not, prompt them to order further imaging or consider a biopsy to obtain a definitive answer.

Furthermore, when advanced disease is found within the axilla, this should also prompt further evaluation, which may include imaging such as PETCT and/or Breast MRI. These modalities can help to give a full picture of the patient's disease extent. Additionally, although breast MRI can be suboptimal for pulmonary metastasis evaluation, this case demonstrates the importance of not overlooking the lungs on breast MRI when staging advanced breast cancers. Ultimately, CT of the thorax and abdomen/pelvis with contrast is preferred for metastatic evaluation. PET/CT is not a routine part of staging advanced breast cancer, but can be indicated in this clinical situation.

Conclusion

The differential diagnosis for axillary lymph node calcifications is extensive, including both benign and more serious etiologies. There are many causes of benign axillary lymph node calcifications, including systemic causes including autoimmune disease and granulomatous reactions. Less commonly,

axillary microcalcifications can be due to pigment deposition from tattooing. Benign calcifications often appear coarse, dystrophic, and/or rounded. In the setting of a suspicious breast mass which contains calcifications, any calcifications found in the axilla become more suspicious and warrant a biopsy. The radiologist must scrutinize these axillary calcifications carefully. If they have similar morphology to those associated with the primary breast mass or architectural distortion, this almost guarantees malignant involvement. Furthermore, extensive calcifications in the axilla can suggest an *advanced* malignancy, and additional screening for distant metastatic disease is warranted. In conclusion, it is imperative to consider the diagnosis of malignancy in the setting of calcifications within axillary lymph nodes seen on mammography. Clear radiologic description of axillary calcifications can assist clinicians with differential diagnosis of benign and malignant etiologies.

Patient consent

Informed consent was obtained both for experimentation with human subjects and to publish the case report.

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