Traumatic neuroma in mastectomy scar
Two case reports and review of the literature

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Abstract
Rationale: Traumatic neuroma is a reparative proliferative response of the nerve after trauma or surgery, which rarely occurs in the breast. However, it must be distinguished from tumor recurrence.1–12

Patient concerns: A 78-year-old woman underwent left-sided modified radical mastectomy for invasive carcinoma, 7 years before this case. Two painless nodules near the mastectomy scar were discovered in regular follow-up physical examination. A 62-year-old woman had received right-sided modified radical mastectomy for intraductal carcinoma, 4 years before this case. An asymptomatic nodule near the mastectomy scar was detected during follow-up ultrasound (US) examination.

Diagnosis: The lesions in both patients were diagnosed as traumatic neuroma.

Interventions: The first patient underwent excisional biopsy. The second patient underwent US guided core-needle aspiration, followed by conservative therapy.

Outcomes: Neither patient complained of any discomfort, nor both exhibited normal physical and US findings during follow-up examinations.

Lessons: Newly discovered nodules with the benign imaging features near the mastectomy site of a patient, especially with the tail sign, traumatic neuromas should be taken into consideration. Routine US examination is important for follow-up of breast cancer patients who have undergone mastectomy.

Abbreviations: CDI = color Doppler flow imaging, MRI = magnetic resonance imaging, US = ultrasound.

Keywords: imaging, mastectomy, traumatic neuroma

1. Introduction

Traumatic neuroma is a chronic reparative proliferative response of the nerve after trauma or surgery, which is composed of disorganized nerve fiber bundles with fibrous stroma, Schwann cells, perineurial cells, axons, and endoneurial fibroblasts; importantly, neuroma does not constitute tumor recurrence.1–12 However, traumatic neuroma mimics tumor recurrence in mastectomy sites; thus far, it has been infrequently reported.1–12 However, it is crucial to distinguish between neuroma and tumor recurrence to provide the appropriate patient prognosis.13 Some reports have described a “tail sign” (focal thickening of adjacent nerve, similar to the dural tail sign) in ultrasound (US) images, which can be used to distinguish traumatic neuroma.7,10 Nonetheless, it is difficult to identify this uncommon lesion based on its atypical appearance. Here, we report 2 cases of traumatic neuroma discovered during follow-up US examination near the mastectomy scar in 2 postmenopausal patients who had previously undergone mastectomy for breast cancer. Additionally, we reviewed the literature regarding the imaging features of traumatic neuroma in the breast. The West China Hospital of Sichuan University Research Ethics Committee approved this retrospective report and waived the requirement for written informed consent.

2. Case 1

A 71-year-old postmenopausal woman was diagnosed with invasive lobular and ductal carcinoma with a clinical stage of T2N0M0 in 2011. Left-sided modified radical mastectomy was subsequently performed. Additionally, anastrozole-based endocrine therapy was administered to the patient for 5 years. During routine follow-up, a lymph node—measuring 6 × 6 mm and exhibiting an abnormal structure—was discovered in the left supraclavicular area in 2015 (Fig. 1). US-guided fine-needle aspiration was performed as a conservative strategy. Lymph node reactive hyperplasia was confirmed by histology and the lymph node remained stable in follow-up US examinations. In 2018, 2 painless nodules near the mastectomy scar were discovered during regular follow-up physical examination. US examination revealed 2 oval, well-circumscribed, parallel subcutaneous nodules with homogenous hypoecho near the mastectomy scar in the upper-outer quadrant of the left breast (Fig. 1). The nodules...
were approximately $6 \times 2 \times 4$ mm and $4 \times 2 \times 3$ mm in size; neither exhibited any blood flow signals in color Doppler flow imaging (CDFI) or posterior acoustic features in routine US. Considering the high possibility of malignancy, excision biopsy of the nodule was performed. During the operation, 2 defined, regular nodules with intact capsule were detected near the mastectomy scar in the upper-outer quadrant of the left breast; these were movable and demonstrated no adhesion to the surrounding tissue. White homogenous tissue was present on the cut surface. Histopathology showed disorganized proliferation of nerve fiber bundles, which is a typical characteristic of traumatic neuroma (Fig. 2). No abnormalities were found in 10 months of subsequent follow-up US examination.

3. Case 2

A 58-year-old postmenopausal woman was diagnosed with intraductal carcinoma (stage TisN0M0) in the right breast and underwent right-sided modified radical mastectomy in 2013. She subsequently received anastrozole-based endocrine therapy. Annual follow-up ultrasonography examination showed no abnormality in the operative site or axilla for 3 years. In 2017, a de novo nodule in the pectoral muscle layer near the mastectomy scar in the upper-outer quadrant of the right breast was revealed by US examination. The lesion was oval, well-circumscribed, homogenous hypoechoic, and measured $10 \times 4 \times 8$ mm in size (Fig. 3). No blood flow signal was detected in CDFI and no posterior features were detected in routine US. The patient showed no symptoms and no abnormalities were observed in physical examination. In order to differentiate the lesion from recurrent tumor, US-guided core-needle aspiration was performed. Traumatic neuroma was confirmed by pathology (Fig. 4). The nodule was stable during 1 year of follow-up US examination.

4. Discussion

Traumatic neuroma is the result of neural fiber regeneration and excessive disorganized proliferation after nerve injury, which frequently occurs in the lower extremities after surgical amputation, as well as after surgery in the head and neck.\[11]
We reviewed the English-language literature and found 11 publications regarding the imaging features of traumatic neuroma in the breast.[2–12] Table 1 summarizes the clinical findings and imaging features of these 11 reported cases, as well as our present report. Finally, 34 lesions in 26 patients were included for further analysis. Overall, the incidence of traumatic neuromas in breast is approximately 0.09%.[7] The age of the included patients ranged from 31 to 78 years. Neuromas occurred at 2 to 22 years after breast surgery, and were typically located in subcutaneous or pectoral muscle layer near the mastectomy scar. The size of the neuroma ranged from 0.2 to 1.6 cm. Patients were either asymptomatic or complained of pain, tenderness, or extreme pain during aspiration.[7,11] The mechanisms of neuroma-associated pain are not fully understood. Some research has indicated that increasing levels of nerve growth factor, alpha-smooth muscle actin, cannabinoid CB2 receptor, and unmyelinated fiber, as well as changes in peripheral and central sensitization, may be related to neuroma-associated pain.[14] In previous reports, patients typically underwent surgical excision or core needle biopsy. Therapy was generally considered unnecessary for patients who were asymptomatic. In contrast, patients with pain were administered conservative therapy, such as physical therapy, local injection of long-acting local anesthetics, steroid, or surgical excision.[14]

The majority of the reports described US findings of traumatic neuromas after breast surgery. In US, most lesions comprised oval, well-circumscribed, parallel, and avascular nodules that were homogenously hypoechoic,[4–10] which were consistent with our report. However, 4 lesions exhibited indistinct margin and irregular shape,[3,10] 2 lesions in 1 patient demonstrated inner vascularity,[10] and one 0.2-cm lesion was unremarkable in a surgical scar after breast-conserving surgery.[11] The tail sign was described in 2 reports with an incidence of 33.3% to 50%.[7,10] Nonetheless, this sign was absent in our cases. This might have been because the nerve was extremely thin and thus prevented detection, or the operator had not reached the appropriate section. Strain elastography was reported for the examination of 7 lesions in 2 papers.[7,10] All lesions in the first paper showed benign elasticity scores and benign fat-to-lesion ratios. In the second report, there were more lesions with low elasticity than with high elasticity. Traumatic neuromas were firm oval nodules in macroscopy,[1] which contradicted the findings of the first report. Notably, further confirmatory research is needed.

There have been a few reports of other imaging techniques for evaluation of traumatic neuromas after breast surgery. Six lesions were investigated by mammography.[7,8,11,12] However, 3 of these 6 nodules were not detected after breast-conserving surgery. Among the 3 remaining lesions, 1 demonstrated clustered
| Reference     | Patients | Age, yr | Neuromas, n | Locations | Size, cm | Time after surgery, yr | Palpable Pain | Pain | US | Imaging findings | CT | MNR | PET | Treatment |
|---------------|----------|---------|-------------|-----------|----------|-----------------------|---------------|------|----|------------------|----|-----|-----|-----------|
| Haj et al. 2004 [12] | 1        | 47      | 1           | lower inner quadrant | 10       | No                     | Yes           | N/A  | N/A | clustered heterogeneous calcification | N/A | N/A | N/A | core needle biopsy |
| Baltalarli et al. 2004 [2] | 1       | 54      | 1           | Subcutaneous, mastectomy scar | 2        | Yes                    | No            | well-circumscribed, homogenous, hypodense, clustered heterogeneous calcification | N/A | triangular, not mentioned |
| Wang et al. 2007 [3] | 64–66    | 31–61   | 8           | Subcutaneous, near mastectomy scar (2), axillary (2), not mentioned (3) | 1.0–1.2   | 14                     | No            | Yes   | No | well-circumscribed, homogenous, hypodense, clustered heterogeneous calcification | N/A | N/A | N/A | surgical excision |
| Kim et al. 2011 [4] | 1        | 47      | 1           | pectoralis muscle layer, 9 o'clock position | 0.7–1.0  | 3                     | No            | No    |否 | oval, well-defined, homogenously hypoechoic | N/A | N/A | N/A | ultrasound-guided core biopsy |
| Li et al. 2012 [5] | 1        | 45      | 1           | Subcutaneous, near mastectomy scar (2), subclavian (2), axillary (1), not mentioned (3) | 0.3–0.5   | 2                     | No            | No    |否 | oval, well-defined, homogenously hypoechoic | N/A | N/A | N/A | surgical excision |
| Ashkar et al. 2013 [6] | 1        | 63      | 1           | pectoralis muscle layer, upper outer aspect | 0.7      | 3                     | No            | No    |否 | oval, well-defined, homogenously hypoechoic | N/A | N/A | N/A | ultrasound-guided core biopsy |
| AlSharif et al. 2018 [7] | 64–68    | 48–71   | Mean:56     | upper outer quadrants (4), lateral aspect (1), supraclavicular aspect (2) | 0.2–0.9   | 2                     | No            | No    |否 | parallel, avascular, hypoechoic | N/A | N/A | N/A | ultrasound-guided core biopsy |
| Fitzpatrick et al. 2018 [8] | 1        | 73      | 1           | lateral aspect | 0.7–1.6  | 16                    | No            | No    |否 | oval, well-defined, homogenously hypoechoic | N/A | N/A | N/A | ultrasound-guided core needle biopsy |
| Messinger et al. 2018 [9] | 1        | 74      | 2           | Subcutaneous, lateral, axillary in deep of axillary dissection scar | 0.6–1.6   | N/A                    | N/A           | No    |否 | oval, well-defined, homogenously hypoechoic | N/A | N/A | N/A | ultrasound-guided core biopsy |
| Sung et al. 2017 [10] | 5        | 36–63   | Mean:44     | pectoralis muscle layer, near the mastectomy scar | 0.39–0.55 | 1.9                     | No            | No    |否 | oval, parallel, circum-scribed, avascular, hypoechoic | N/A | N/A | N/A | ultrasound-guided core biopsy |
| Salemis et al. 2018 [11] | 1        | 65      | 1           | area of surgical scar | 0.6       | 2                     | Yes           | No    |否 | oval, parallel, circum-scribed, avascular, hypoechoic | N/A | N/A | N/A | surgical excision |
| Present case   | 2        | 62.78   | 3           | Subcutaneous, pectoralis muscle layer | 0.6–0.4  | 4                     | Yes (2), No (1) | No    |否 | oval, parallel, circum-scribed, avascular, hypoechoic | N/A | N/A | N/A | surgical excision |

(n1/n2)=n1: number of the lesions with specific performance; n2: number of lesions assessed by specific examination technique, CT=computed tomography, FDG=fluorodeoxyglucose, PET=positron emission tomography, SE=Strain elastography.
heterogeneous calcification in the surgical site after nodule resection surgery; 1 showed clustered microcalcifications with architectural distortion after breast-conserving surgery; and the other comprised a small, oval, well-circumscribed, equal-density nodule in the mastectomy site. Baltalarli et al[3] reported 1 neuroma that presented as a triangular, muscle-dense nodule in computed tomography. AlSharif et al[7] investigated 5 lesions by magnetic resonance imaging (MRI); 2 of the 3 nodules were occult, while the remaining 3 were isointense foci on T1-weighted images with benign type 1 enhancement in time/signal intensity curves. Furthermore, 1 lesion was hyperintense on T2-weighted images. Finally, in positron emission tomography computed tomography, 3 neuromas showed no focal fluorodeoxyglucose uptake.[4,10]

The locoregional recurrence rate after mastectomy of breast cancer is approximately 5.3% to 8.95%. The incidence of tumor recurrence is much higher than that of traumatic neuromas or other benign lesions. Therefore, a nodule discovered in a mastectomy site is suspected to be recurrent tumor. Early diagnosis of tumor recurrence, as well as appropriate and rapid therapy, is critical for optimal patient prognosis. Most recurrent cancers in mastectomy sites appear as hypoechoic lesions on US.[13] They are similar to some benign lesions, such as traumatic neuromas or granulomas. Additionally, some traumatic neuromas demonstrate indistinct margin and irregular shape with internal vascularity on US,[10] which resembles tumor recurrence. Therefore, misdiagnosis may occur based on US images. Some reports have described greater specificity on MRI, as most recurrent tumors demonstrated type 3 enhancement curves on MRI, whereas benign lesions always demonstrated type 1 enhancement curves.[17] These findings indicate that, when difficulties arise in differentiating recurrent tumor from traumatic neuroma on US, MRI examination may aid in distinguishing benign and malignant lesions. However, biopsy remains the most robust modality for definite diagnosis.

US, mammography, and MRI are the primary tools for use in follow-up of breast cancer patients after mastectomy. Some lesions in mastectomy sites may be enigmatic in mammography or MRI,[17] whereas nearly all lesions in mastectomy sites can be detected by US. US is an economic and widely available tool in most medical institutions. Additionally, US has few contraindications, whereas MRI should not be performed in patients with cardiac pacemakers or other metal implants. Breast US is important in early detection of abnormalities in breast cancer patients who have undergone mastectomy. In Salemis et al[11] report, a single lesion with diameter of 0.2 cm could not be detected in surgical sites by US after breast-conserving surgery, which maybe owing to the presence of operative scar and small nodule diameter. However, it could be identified as cluttered microcalcifications with architectural distortion in mammography. Therefore, it is better to combine US with mammography or MRI for follow-up in breast cancer patients who have undergone breast-conserving surgery. According to previous reports, most traumatic neuromas appear as benign features. So, a nodule with benign features near the mastectomy site after breast cancer surgery, especially with the tail sign, is suggestive of traumatic neuroma.

Author contributions

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