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Caught in the middle: case study of a brachial (sentry) lymph node recurrence after resection and locoregional breast radiotherapy

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ABSTRACT

To reduce local recurrence, adjuvant locoregional radiotherapy is given routinely for post-mastectomy breast patients with 4 or more positive lymph nodes. Most institutions adopt a 3- or 4-field radiotherapy technique, in which the field and shielding placements are informed by bony anatomic landmarks viewed on digitally reconstructed radiographs.

Here, we report on a 40-year-old woman who underwent a lumpectomy with axillary node dissection, followed by chemotherapy, completion mastectomy, and adjuvant locoregional radiotherapy (50 Gy in 25 fractions) for a multicentric pT1cN2aM0 invasive ductal carcinoma of the right breast. At 9 months after radiotherapy, she presented with a palpable brachial lymph node, a major draining node of the upper extremity, in the axilla, abutting the previous anterior supraclavicular and axillary radiation fields. This occurrence highlights the potential superolateral border of the level I axillary nodal chain and its relationship to the upper extremity lymphatics via the brachial ("sentry") node. Adapting the delineated nodal target volume in locoregional radiotherapy of the breast for disease with extensive nodal involvement or other high-risk pathologic indications may be warranted in certain situations. Careful imaging and an informed discussion with the patient is needed before deciding to treat the sentry node and including the acromial–clavicular joints, balanced with the potential increased risk of lymphedema.

KEY WORDS

Breast cancer, lymph node, regional recurrence, radiation field, regional radiotherapy

1. INTRODUCTION

In breast cancer, axillary lymph node status is one of the most powerful prognostic factors. In post-mastectomy breast cancer patients with 4 or more positive lymph nodes, adjuvant radiotherapy to the breast or chest wall and regional lymph nodes is a standard treatment [1,2]. To reduce local recurrence, basic oncologic principles dictate the inclusion of all potentially involved lymph nodes in the radiotherapy treatment fields. In locoregional breast treatment, conventional techniques for beam placement rely on anatomic landmarks seen on the digitally reconstructed radiograph. Here, we report a case of sentry lymph node recurrence, illustrating the potential benefit of customized radiotherapy fields tailored to axillary (AX) lymph node contours.

2. CASE PRESENTATION

A 40-year-old premenopausal woman presented with a several-month history of pain in the right axilla descending down her arm, and subsequently, a self-detected discrete mass in the right breast. The physical examination at the time described this mobile mass to be approximately 1.0×2.0 cm in size, with no palpable lymph nodes. No nipple dimpling or associated skin retraction was noted. This nulliparous woman had been on oral contraceptive pills for 15 years before her breast cancer diagnosis. She had no family history of cancer.

A bilateral mammogram showed her breasts to be heterogeneously dense, with a suspicious irregular mass in the right breast that corresponded to an ultrasonography-detected hypoechoic lesion at the 12 o'clock position 2 cm from the nipple. On biopsy this mass proved to be invasive breast carcinoma. An AX lymph node that was fine-needle aspirated proved to be positive for adenocarcinoma. A further magnetic resonance imaging (MRI) investigation revealed a 1.6×2.2-cm spiculated mass with multiple smaller nodular densities in the retroareolar region, near the chest wall and in the upper outer aspect of the right breast.

The patient underwent breast-conserving surgery with AX lymph node dissection. The pathology report showed a 1.7-cm high-grade invasive ductal

carcinoma with lymphovascular invasion that was estrogen receptor–positive, progesterone receptor–negative, and HER2 negative, with the closest resection margin being 1 mm in the anterior inferior aspect. Of 20 nodes removed, 4 were positive for metastatic disease, with no extracapsular extension; the largest node was 2.0 cm in size.

The patient's staging workup included a bone scan, chest radiography, and abdominal ultrasonography; all were negative for distant metastases. She recovered well from the surgery and, within 6 weeks, was started on the FEC 100 (5-fluorouracil–epirubicin–cyclophosphamide) chemotherapy regimen. After the start of chemotherapy, MRI imaging revealed two other suspicious areas of enhancement, one of 0.9 cm immediately behind the nipple, and the other of 2.0 cm in the upper outer quadrant. A subsequent ultrasound-guided biopsy and fine-needle aspiration demonstrated the presence of invasive ductal carcinoma in both areas. In light of this potential disease progression on chemotherapy, FEC 100 was stopped after 5 cycles. Docetaxel was given for 4 cycles before an eventual completion mastectomy, which showed 3 residual foci of poorly differentiated adenocarcinoma, the largest measuring 1 cm in the retroareolar region. Given the patient's positive estrogen receptor status, she was started on tamoxifen.

At 8 weeks post mastectomy, an adjuvant course of radiotherapy was given to the patient's right chest wall and the supraclavicular and AX lymph nodes. The nodal irradiation consisted of 50 Gy in 25 daily fractions delivered using parallel-opposed anterior 6-MV and posterior 18-MV beams, with dose prescribed to midplane. The treatment fields adhered to the department's standard 4-field asymmetric technique. After radiotherapy, mild lymphedema and arm discomfort persisted.

At 9 months post radiotherapy, the patient presented with a 2.0-cm mobile nodule in her right axilla overlying the humeral head. A PET scan revealed a mild focus in the right axilla [maximum standardized uptake value (SUVmax): 2.6] that closely resembled the palpable abnormality, another discrete focus above the right shoulder joint (SUVmax: 3.2), and an additional positive uptake in the right internal mammary node chain (SUVmax: 6.8). The suspicious AX node was then biopsied and confirmed for metastatic adenocarcinoma. Subsequent chest computed tomography (CT) revealed an additional 1.0-cm abnormal lymph node in the internal mammary chain. Bone scan and abdominal ultrasonography showed no evidence of distant metastasis.

The patient's endocrine therapy was reassessed, and she was managed using anastrozole and goserelin acetate. Within 2 months, the internal mammary lymph node had shown regression on CT, and 4 months later, the AX lymph node was no longer detected on MRI. However, 3 months after that response, the AX lymph node was again of palpable size (0.5 cm), and 3 months later, the node was clinically 1.5×2.0 cm. Endocrine therapy was changed to exemestane. Despite initial shrinkage of the nodule, the enlarged—and now tender—4.0×4.0-cm node was associated with nerve pain in the neck and lower arm 4 months later.

A re-evaluation of the patient's treatment options considered re-irradiation, but this approach was not recommended because of a likely overlap of treatment fields, given that the recurrent node was in close proximity to the previous treatment area. She ultimately underwent a local excision for the node. She recovered well, with near-normal movement of the shoulder 2 weeks post surgery; no lymphedema was observed.

3. DISCUSSION

The incidence of AX recurrence in patients with an adequate AX lymph node dissection has been reported to be low, approximately 1% [3,4], and this risk can further be reduced with AX irradiation [5]. However, when they do occur, these recurrences are generally associated with the development of distant metastasis and poor overall prognosis.

In this case, the recurrent lymph node was located near the AX inner surface of the upper arm (Figure 1). Anatomically, this location corresponds to a node described by Suami *et al.* [6,7] as the "sentry" node (brachial lymph node), which plays a key role in lymphatic drainage of the upper limb and upper torso. This sentry node is thought to drain most of the lymph vessels of the upper limb, directing them into the AX region [6] and covering a wide range of lymphatic drainage in the anterior upper torso [7].

When the three-dimensional topography of this sentry lymph node was delineated on the planning CT, with the arm abducted in treatment position (>90 degrees), the node's position coincided with the lateral extent of the level I AX lymph node boundaries described by Dijkema *et al.* [8] in a study of the nodal clinical target volumes for breast radiotherapy (Figure 2). Guidelines set out by those authors suggest that cranially, the level of the AX level I target volumes should fall caudal to the tendon of the latissimus dorsi muscle. Had we followed those guidelines for this patient, the resulting treatment volume would likely have included the sentry node within the treatment field and thereby reduced the chance of local recurrence in that area. However, routinely adhering to that target volume guideline in all patients undergoing AX lymph node irradiation would require extension of the treatment borders superiorly beyond the acromion process and proximally beyond the surgical neck of the humerus, resulting in an increase in the irradiated volume. Wang *et al.* [9], in their study looking at optimal treatment techniques for level I AX lymph nodes, limited the AX contours to the region just lateral to the pectoralis minor, extending posteriorly

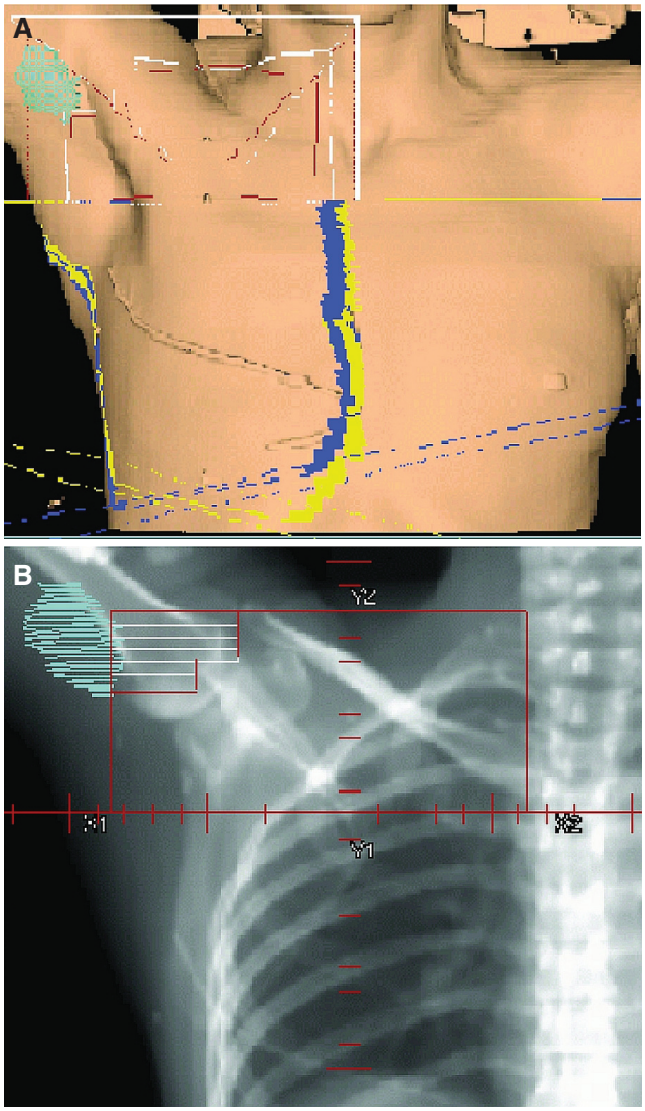

FIGURE 1 (A) Skin rendering of previous radiation treatment fields with new recurrent node (aqua). (B) Digitally reconstructed radiograph of previous anterior treatment field with new recurrent node (aqua).

to the latissimus dorsi. In a study examining variability in treatment depths during supraclavicular fossa (SCF) and AX nodal radiation, Bentel *et al.* [10] defined the border of the AX lymph nodes to be at the axial CT images approximately 2–3 cm caudal to the inferior aspect of the humeral head. The location of the AX lymph nodes was estimated according to the AX vessels, the surgical scar, or surgical clips within the CT scan.

At our institute, the standard SCF and AX treatment fields are placed with respect to the patient's anatomy as viewed on the axial CT slices and the digitally reconstructed radiograph. The lateral border of the field is at the proximal humeral head. Superiorly, the field is 3.0 cm above the mid-clavicle and would encompass the entire clavicle. Inferiorly, it lies at the inferior border of the head of clavicle. The medial border falls

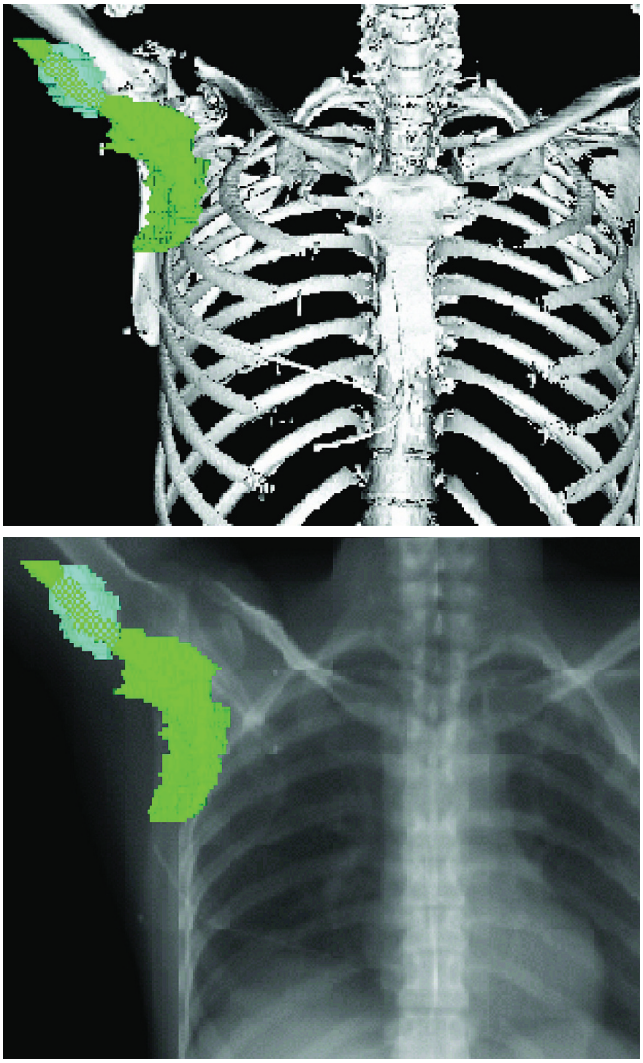

FIGURE 2 Level I axillary nodes (green) with new recurrent node (aqua).

at the lateral aspect of the pedicle. Shielding is placed to block dose to the acromioclavicular joint and half the humeral head. A survey in Australia and New Zealand showed that the radiation oncologists plan the supraclavicular fossa in a similar fashion, most of them based on bony landmarks identified on the digitally reconstructed radiograph [11]. The radiation oncologists placed the superior border at the lateral end of the clavicle, medially between the facet joints and the medial head of clavicle, laterally to include the coracoid process, and inferiorly determined either by the superior border of the tangential field or otherwise not specified. Of the 123 radiation oncologists who completed the survey, 93 (76%) marked the fields on the digitally reconstructed radiograph based on bony anatomy; 21 (17%) contoured only the SCF; and 10 (8%) used both techniques. Not all radiation oncologists routinely delineate the AX and SCF nodal regions as target volumes, but considering it on a regular basis for regional nodal treatment is prudent.

However, other factors must be taken into account to ensure the accuracy and safety of SCF and AX nodal treatment plans with dose optimization around the delineated nodal volumes.

Computed tomography is an important imaging modality that aids in radiotherapy treatment volume delineation for many cancer sites. The CT used in radiotherapy planning has known limitations with respect to lymph node identification and delineation. When added to preoperative diagnostic CT, complementary imaging modalities such as MRI and MRI with novel lymphotrophic contrast agents such as ultrasmall particles of iron oxide may help to ensure more accurate staging and nodal volume delineation [12]. However, both of the latter modalities are limited, because the positioning of the patient during the scans is different from that used for radiotherapy treatment. Furthermore, the AX nodal area is often located in close proximity to the end of the breast coil used in MRI, resulting in poor visualization of the area. In the present case, all of the diagnostic imaging completed before the patient's radiotherapy treatment was reviewed to determine the presence or absence of sentry node involvement. The node was neither seen on the diagnostic imaging nor reported by the radiologist.

Further compounding the situation is the current limitation in detecting occult micrometastatic disease in lymph node regions at risk. In both the normal and abnormal state, a number of lymph nodes comprising the AX and internal mammary chains may, while harbouring metastases, remain below the threshold of detection for CT and MRI. In women who have locoregional nodal disease in the absence of distant metastases, the ability to accurately delineate the target volumes at risk will help to further the probability of a cure. Ideally, with improved imaging techniques and review of the AX nodal regions, accurate target delineation of the AX and SCF region can be assured.

It has been shown that approximately 10% of patients undergoing AX dissection will develop lymphedema; regional nodal radiation can further increase that risk to more than 30% [13]. Hayes *et al.* [14] reported similarly increased lymphedema risks of 31% and 23% when radiation was given, respectively, to the AX plus SCF and to the SCF only. Although the severity of lymphedema was not significantly different between the groups, the study found that the risk of lymphedema increased significantly when AX boost treatment was added in the group of women with 4 or more positive nodes. In a study by Graham *et al.* [15], who examined 91 women after AX dissection followed by SCF irradiation, the medial border of the SCF field was located at the lateral border of the pedicles, and the lateral border was limited by the coracoid process for the 13 patients who received treatment only to the SCF. The remaining patients were all treated with fields extending laterally to the coracoid process to include the AX lymph nodes in part or in full. The study concluded that the severity of lymphedema was greatly increased when the radiotherapy fields were extended past the coracoid process and that the lateral border of the SCF radiotherapy field should be limited by the coracoid process to reduce the risk of lymphedema. In our case, the patient underwent locoregional radiotherapy involving both the SCF and AX fields according to departmental guideline for post-mastectomy patients with 4 or more positive lymph nodes. Were we to contour the AX level I nodes as recommended by Djikema *et al.* [8], the lateral field border would extend more than 2 cm beyond the humeral head to cover the sentry node within the planning target volume, likely increasing the risk of lymphedema.

To our knowledge, this is the first reported case of a sentry lymph node recurrence, and it highlights several important treatment considerations. Because of the location of the node, detailed diagnostic imaging assessments are problematic. Despite the appropriate use of diagnostic imaging to assess for any suspicious nodal involvement, this nodal area remains a challenge for inclusion in the treatment volume. Achieving an adequate radiation dose in the superiorly located level I AX node also presents complications, because the SCF and AX treatment borders would extend superiorly and laterally beyond the coracoid process. The resultant radiotherapy fields would increase the probability of subsequent lymphedema. Furthermore, the sentry node connects most of the lymph vessels of the upper extremities proximally with other lymph nodes situated in the axilla, and disruption of the sentry node, whether by malignancy or surgery, may also carry increased risk of lymphedema. Some posterior forearm vessels, observed to bypass the sentry node by reaching other smaller nodes into the axilla, have been reported [6]. Although such vessels may help to reduce the risk of surgery-induced lymphedema, the accessory pathways may still fall within or may abut the irradiated volume. Close follow-up and surveillance for lymphedema is warranted for these patients.

4. CONCLUSIONS

The adjuvant locoregional radiotherapy treatment for breast cancer with a high nodal burden should include delineation of nodal regions as target volumes. To standardize that process, guidelines for nodal delineation are currently being developed within our department. The decision to treat the superior aspects of level I AX lymph node must be weighed against the potential risk of increased lymphedema.

5. CONFLICT OF INTEREST DISCLOSURES

The authors have no known financial conflicts of interest to declare.

6. REFERENCES

1. Truong PT, Olivotto IA, Whelan TJ, Levine M on behalf of the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Clinical practice guidelines for the care and treatment of breast cancer: 16. Locoregional post-mastectomy radiotherapy. *CMAJ* 2004;170:1263–73.
2. Recht A, Edge SB, Solin LJ, *et al.* Postmastectomy radiotherapy: clinical practice guidelines of the American Society of Clinical Oncology. *J Clin Oncol* 2001;19:1539–69.
3. Voogd AC, Cranenbroek S, de Boer R, Roumen RM, Rutten HJ, van der Sangen MJ. Long-term prognosis of patients with axillary recurrence after axillary dissection for invasive breast cancer. *Eur J Surg Oncol* 2005;3:485–9.
4. Newman LA, Hunt KK, Buchholz T, *et al.* Presentation, management and outcome of axillary recurrence from breast cancer. *Am J Surg* 2000;180:252–6.
5. Voogd AC, de Boer R, van der Sangen MJ, Roumen RM, Rutten HJ, Coebergh JW. Determinants of axillary recurrence after axillary lymph node dissection for invasive breast cancer. *Eur J Surg Oncol* 2001;27:250–5.
6. Suami H, Taylor GI, Pan WR. The lymphatic territories of the upper limb: anatomical study and clinical implications. *Plast Reconstr Surg* 2007;119:1813–22.
7. Suami H, O'Neill JK, Pan WR, Taylor GI. Superficial lymphatic system of the upper torso: preliminary radiographic results in human cadavers. *Plast Reconstr Surg* 2008;121:1231–9.
8. Dijkema IM, Hofman P, Raaijmakers CP, Lagendijk JJ, Battermann JJ, Hillen B. Loco-regional conformal radiotherapy of the breast: delineation of the regional lymph node clinical target volumes in treatment position. *Radiother Oncol* 2004;71:287–95.
9. Wang X, Yu TK, Salehpour M, Zhang SX, Sun TL, Buchholz TA. Breast cancer regional radiation fields for supraclavicular and axillary lymph node treatment: is a posterior axillary boost field technique optimal? *Int J Radiat Oncol Biol Phys* 2009;74:86–91.
10. Bentel GC, Marks LB, Hardenbergh PH, Prosnitz LR. Variability of the depth of supraclavicular and axillary lymph nodes in patients with breast cancer: is a posterior axillary boost field necessary? *Int J Radiat Oncol Biol Phys* 2000;47:755–8.
11. Morgia M, Lamoury G, Morgan G. Survey of radiotherapy planning and treatment of the supraclavicular fossa in breast cancer. *J Med Imaging Radiat Oncol* 2009;53:207–11.
12. Kimura K, Tanigawa N, Matsuki M, *et al.* High-resolution MR lymphography using ultrasmall superparamagnetic iron oxide (USPIO) in the evaluation of axillary lymph nodes in patients with early stage breast cancer: preliminary results. *Breast Cancer* 2010;17:241–6.
13. Chua B, Ung O, Boyages J. Competing considerations in regional nodal treatment for early breast cancer. *Breast J* 2002;8:15–22.
14. Hayes SB, Freedman GM, Li T, Anderson PR, Ross E. Does axillary boost increase lymphedema compared with supraclavicular radiation alone after breast conservation? *Int J Radiat Oncol Biol Phys* 2008;72:1449–55.
15. Graham P, Jagavkar R, Browne L, Millar E. Supraclavicular radiotherapy must be limited laterally by the coracoid to avoid significant adjuvant breast nodal radiotherapy lymphoedema risk. *Australas Radiol* 2006;50:578–82.

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