Sonographic Evaluation of Isolated Abnormal Axillary Lymph Nodes Identified on Mammograms

Mahesh K. Shetty MD, FRCR, Wendy S. Carpenter, MD

Objective. To evaluate the role of sonography in evaluation of abnormal axillary lymph nodes identified in patients with otherwise negative or benign findings on mammography. Methods. For 3 years 2 months, we retrospectively reviewed 30 consecutive cases that had undergone sonographic evaluation for abnormal axillary lymph nodes identified in patients whose mammograms had an American College of Radiology Breast Imaging Reporting and Data System final assessment of 1 or 2. Mammographic and sonographic features of the lymph nodes were analyzed and correlated with the histologic diagnosis in patients undergoing biopsy. Patients who did not undergo biopsy had clinical or imaging follow-up. Results. Twenty of the 30 patients studied had an abnormal sonographic appearance. Biopsy was recommended in 17 of the 20 patients on the basis of an abnormal sonographic appearance. In the remaining 3 patients, there was an underlying cause for lymphadenopathy, and these patients underwent clinical and sonographic follow-up. Eighteen patients underwent biopsy, including 1 patient with normal findings on sonography. Ten of these patients had malignant histologic findings: 6 were metastatic adenocarcinoma; 1, poorly differentiated sarcoma, and 3, lymphoma. The remaining 8 patients had benign histologic findings. The nonbiopsy group had clinical and or imaging follow-up (mean, 17.6 months; range, 6–25 months). The sensitivity (true-positive/true-positive + false-negative) of sonography for assessment of suspected abnormal lymph nodes in the patients studied was 100% (10 of 10); specificity (true-negative/true-negative + false-positive), 50% (10 of 20); positive predictive value (true-positive/true-positive + false-positive + false-negative) for malignancy based on the presence of 2 or more abnormal sonographic features, 50% (10 of 20); and negative predictive value, 100%. Conclusions. Sonography is useful in further characterization of isolated abnormal axillary lymph nodes identified on mammography. Sonographic evaluation helps improve the specificity of imaging evaluation in assessment of these lymph nodes. Key words: axillary lymph nodes; breast; sonography.

Identification of abnormal axillary lymph nodes on mammography without an associated mammographic abnormality in the breast is uncommon. There are no clear guidelines for reporting and treatment of abnormal axillary lymph nodes identified on mammography in the absence of an abnormality in the breast. In the American College of Radiology Breast Imaging Reporting and Data System lexicon, reference is made to axillary adenopathy under “associated findings.” It states: “enlarged, non-fatty, replaced axillary lymph nodes may be commented on. Mammographic assessment of these nodes is unreliable.”1 In addition, the criteria in the radiology literature for classifying a lymph node as abnormal...
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are not consistent. Some of the proposed criteria for malignant lymph nodes have included size greater than 2 cm, round or irregular shape, absence of a fatty hilum, and increased density.

Several investigators have studied the role of imaging to stage axillary lymph nodes in patients with breast cancer.⁵⁻¹⁰ There have been few studies in the radiology literature, however, that have addressed the problem of patients in whom abnormal axillary lymph nodes are identified as isolated findings. Two such studies reported malignancy rates of 52.3% (11 of 21) and 45.4% (10 of 22).¹¹,¹² In a series of 24 patients with unilaterally enlarged nodes, 2 of the 7 patients undergoing biopsy had malignancy; both patients had a known history of malignancy.¹³

To our knowledge, no previous studies have examined the role of sonography in patients with abnormal axillary lymph nodes identified on mammography. Therefore, we undertook this retrospective study to determine whether sonography helps in the further management of patients in whom abnormal axillary lymph nodes are identified on mammography. We present our findings in 30 patients who underwent sonographic evaluation. Eighteen of the patients underwent biopsy.

Materials and Methods

The study group included consecutive patients who had suspected abnormal lymph nodes identified on screening or diagnostic mammography with an American College of Radiology Breast Imaging Reporting and Data System final assessment category of 1 or 2 and who underwent sonographic imaging of the abnormal lymph nodes. The principal author (M.K.S.) reviewed the mammographic features of the lymph nodes that had prompted imaging with sonography. Abnormal mammographic findings included size greater than 20 mm, absence of a fatty hilum, increased density, and a round shape. Any case with abnormal lymph nodes detected on mammography that fulfilled at least 2 of the above criteria or fulfilled 1 of the above criteria plus had substantial interval enlargement or was palpable was included in this retrospective study. An increase in long axis measurement of greater than 100% was considered substantial interval enlargement. Sonographic images were reviewed. Abnormal sonographic findings of the axillary lymph nodes were as follows: size greater than 20 mm, absence of a fatty hilum, abnormal sonographic appearance of the cortex, which included diffuse or focal thickening of the cortex or abnormal echo texture, and round shape. The longitudinal measurement was used for determining the size of the lymph node. The patients’ clinical records were examined to note the physical examination findings and to identify any history of associated malignancies.

Mammographic examinations were performed with a Mammoplus system (International Med Systems, Riverside, CA), a Senographe DMR system (GE Medical Systems, Milwaukee, WI), a Performa system (Instrumentarium Corp, Tuusula, Finland), or a Contour Mammography system (Bennett Trex Medical, Copiague, NY). Sonographic examinations were performed with a 10- or 12-MHz transducer and a LOGIQ 9 or LOGIQ 700MR system (GE Medical Systems) or an Acuson 128XP system (Siemens Medical Solutions, Mountain View, CA).

Results

There were 33 cases identified that had undergone additional sonographic evaluation between September 1999 and November 2002 for abnormal axillary lymph nodes identified on mammography. During the study period, 93,698 mammographic examinations and 10,427 breast sonographic examinations were performed. Three of these 33 patients were excluded from this study: 1 was lost to follow-up, and in 2, axillary lymph nodes identified on mammography did not fulfill the criteria of showing at least 2 abnormal features.

The series included 30 patients. Patients ranged in age from 30 to 65 years (mean, 53.2 years). Abnormal lymph nodes were located on the right in 12 patients and on the left in 17 patients. There were more than 1 abnormal lymph node in 3 patients, and in 1 patient, bilaterally enlarged multiple nodes were present. Screening mammography was performed in 16 patients, and diagnostic mammography was performed in 14. Patients who underwent diagnostic mammography had palpable lymph nodes. In this group, 2 patients had an additional palpable abnormality in the ipsilateral breast. One of the 2 patients had a cyst corresponding to the palpable abnormality. The other patient had negative mammographic and sonographic findings at the site of the palpable abnormality; biopsy of the abnor-
mal lymph node and the palpable breast lump was performed despite negative mammographic and sono-
graphic findings. None of the patients had a personal history of breast cancer or other malignancy at the time of either mammographic or sono-
graphic evaluation.

The lymph nodes were palpable in 9 of the 10 patients with a malignant diagnosis (Figures 1 and 2). In 5 of the 20 patients with a benign out-
come, the lymph nodes were palpable. In 15 cases there were 3 abnormal mammographic features; in 12 cases there were 2 abnormal mammographic features; and in 2 cases the lymph node had 1 abnormal feature and was either palpable (n = 1) or was palpable and had undergone an interval change (n = 1). In 1 case the axillary lymph node had 4 abnormal mammographic features. The mean long axis length of lymph nodes with a benign outcome was 2 cm (range, 0.9–3.5 cm), and in patients with a malignant outcome, it was 3.72 cm (range, 1.2–9 cm). The positive predictive value for malignancy when combinations of any 2 abnormal features (increased size, absence of a hilum, round shape, and increased density) were present was 35.7%, and specificity was 10% (2 of 20). When 3 abnormal mammographic features were present, the positive predictive value for malignancy was 31.2%, and specificity was 45% (9 of 20).

Two or more abnormal sonographic features were seen in 20 patients. In 3 of these 20 patients, there was an underlying cause for the abnormality; hence short-interval imaging follow-up was recommended, with resolution noted at 3-month follow-up sonographic examinations (n = 2) and at 1- and 2-year follow-up examinations (n = 1). One of these 3 patients was postpartum and had mastitis associated with a tender enlarged palpable abnormality in the left axilla. Mammographically the palpable finding corresponded to an enlarged lymph node without a fatty hilum. The second patient had an associated chest wall skin infection resulting from a spider bite. The third patient had an inflamed cyst.

In 17 patients biopsy was recommended on the basis of the presence of at least 2 abnormal sonographic features. An additional patient underwent sonographically guided core biopsy for a palpable lymph node despite absence of any abnormal sono-
graphic finding. Table 1 lists the histologic diagnoses and physical examina-
tion findings for the 18 patients undergoing biopsy. Of the 18 patients undergoing biopsy, 1 patient underwent fine-needle aspiration (FNA) biopsy in the surgeon’s office with benign results; 4 underwent sonographically guided core biopsy; and 13 underwent excisional biopsy, of whom 2 had FNA biopsy before excisional biopsy. In 1 of these 2 cases, FNA biopsy results were false-negative, showing reactive changes. At excisional biopsy, metastatic adenocarcinoma was diagnosed in this patient. Ten of the 18 cases had malignant histologic diagnoses: 5 were metastatic adenocarcinoma with a presumed occult primary malignancy in the breast (Figures 1 and 3); 3 were lymphoma; 1 was a poorly differentiated sarcoma; and 1 was a poorly differentiated carcinoma with an unknown primary malignancy. There were 5 patients with a suspected occult primary malignancy in the breast; in 1 patient a mammographically and sonographically occult 7-mm focus of invasive ductal and invasive lobular carcinoma was identified on excisional biopsy of a palpable area in the axillary tail of the ipsilateral breast. Two patients underwent mastectomy, but a primary focus was not evident in the mastectomy specimen; the remaining 2 patients underwent axillary dissection without mastectomy and postoperative radiation therapy.

Eight of the 18 cases undergoing biopsy had benign diagnoses (Figures 2 and 4), including the 1 patient who underwent percutaneous biopsy despite the absence of abnormal sono-
graphic features. When 2 abnormal sonographic features were present, sensitivity was 100% (10 of 10); specificity was 50% (10 of 20); and the positive predictive value for malignancy was 50% (10 of 20). When at least 3 abnormal features were present on sonography, sensitivity was 100%; specificity was 70% (14 of 20); and the positive predictive value for malignancy was 62.5% (10 of 16). The single most predictive sonographic feature for malignancy was a round shape, with sensitivity of 71% and specificity of 78.2%.

In 9 patients who had 1 (n = 6) or no (n = 3) abnormal sonographic feature, biopsy was not performed. Five of these patients had follow up mammograms at a mean interval of 18.2 months (range, 6–25 months), with no interval changes; the remaining 4 patients had clinical follow-up at a mean interval of 16.5 months (range, 6–24 months), with interval resolution.
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Discussion

On mammography, normal axillary lymph nodes are smaller than 2 cm and have a hilar notch or a lucent center. It is not possible to differentiate benign lymphadenopathy from metastatic lymphadenopathy or lymphoma on mammography.\textsuperscript{14} On standard projections only the lower part of the axilla can be seen, and during mammography positioning, axillary nodes may be pushed out of the field of the mammographic image. Mammography is not considered a reliable method for axillary lymph node imaging.\textsuperscript{15} However, for axillary lymphadenopathy seen on mammography, there are no consistent criteria for classifying a lymph node as abnormal.

Figure 1. Palpable abnormality in the left axillary region in a 59-year-old woman. A and B, Mediolateral oblique (A) and cranio-caudal (B) mammograms with focal spot compression showing an abnormally enlarged high-density lymph node (arrows) in the left axilla. C and D, Transverse (C) and long axis (D) sonograms of the left axillary region showing an enlarged round lymph node (D, arrow) with a central echogenic fatty hilum. An excisional biopsy specimen (not shown) of this lymph node revealed metastatic adenocarcinoma.
Several authors have used a combination of abnormal features to classify a lymph node as abnormal, including increased size, round shape, increased density, absence of a fatty hilum, irregular or spiculated margins, and intranodal calcifications. It is generally accepted that a lymph node larger than 2 cm is abnormally enlarged when not fatty replaced. Imaging evaluation of axillary lymph nodes in patients with known breast cancer has been studied extensively. However, there have been few studies of patients with isolated abnormal lymph nodes detected on mammography.

The presence of abnormal lymph nodes with otherwise negative mammographic findings is an uncommon finding. The incidence of axillary adenopathy detected by screening mammography in patients without additional mammographic abnormalities was reported to be 0.02% (21 per 95,806) in one series. Lee et al reported an incidence of 0.2% (24 per 14,833) for interval enlargement of unilateral axillary or intramammary lymph nodes in diagnostic mammograms obtained over 5 years. We studied patients who had undergone sonographic evaluation for isolated abnormal axillary lymph nodes identified on screening mammography (n = 16) or diagnostic mammography (n = 4). The mammographic criteria that had prompted additional sonographic evaluation for abnormal lymph nodes were similar to those reported previously in patients with isolated axillary lymphadenopathy. The mammographic criteria that we used in our study were size greater than 2 cm, round shape, high density, and absence of a fatty hilum. We used the long axis measurement of the lymph nodes, as used by other investigators.

Walsh et al studied 76 patients with abnormal axillary lymphadenopathy detected on mammography. They analyzed the length, margins, density, and shape of the lymph nodes and the

Table 1. Histologic Diagnosis in 18 Women Undergoing Biopsy of Abnormal Axillary Lymph Nodes

<table>
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<tr>
<th>Diagnosis</th>
<th>Palpable (n = 14)</th>
<th>Nonpalpable (n = 4)</th>
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<tr>
<td>Malignant</td>
<td>9</td>
<td>1</td>
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<tr>
<td>Metastatic adenocarcinoma</td>
<td>7</td>
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<td>Lymphoma</td>
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presence of intranodal calcifications. In that series, when a lymph node length of greater than 33 mm was used as a predictor of malignancy, specificity was 97% and sensitivity was 31%. For a combination of 2 abnormal mammographic features that we used in our study (size >2 cm, absence of a hilum, round shape, and increased density), we found mammographic specificity to be low (10% [2 of 20]). We therefore wanted to assess the value of sonographic imaging of nodes that were mammographically abnormal.

Sonography has been shown to be useful in assessing axillary lymph nodes for metastatic involvement in patients with breast cancer. An in vitro study that examined the sonographic criteria that are helpful for distinguishing metastatic and nonmetastatic nodes in 84 histologically characterized lymph nodes reported that the best single feature was a circular shape (sensitivity, 65%; specificity, 73%). In that study the best combination of sensitivity (85%) and specificity (73%) was obtained when at least 3 positive features were present. Similar to that study, we found that a circular shape was the single best predictor of malignancy on sonography, with sensitivity of 71% and specificity of 78.2%. When at least 3 abnormal features were present on sonography, sensitivity was 100%, and specificity was 70% (14 of 20), clearly showing the value of sonographic evaluation of abnormal axillary lymph nodes. The high sensitivity that we had in our series for sonographic evaluation was in patients with mammographically abnormal lymph nodes. The sensitivity for sonographic assessment would not be expected to be as high in women with breast cancer and mammographically normal-appearing lymph nodes.

In our series there were 4 patients with axillary metastasis from an occult primary tumor in the breast. Two of the patients underwent mastectomy in addition to axillary clearance, without evidence of breast carcinoma in the mastectomy specimens. The remaining 2 patients did not undergo mastectomy. All 4 of these patients were alive at a mean of 28 months (range, 19–32 months) after diagnosis. Axillary metastasis from an occult primary breast tumor is a rare but difficult problem. It has been reported that patients with occult breast carcinoma have a poor outcome. In 1 series all 8 patients with axillary metastasis from an occult primary breast tumor died of breast cancer at a mean of 42

Figure 3. Palpable abnormality in the right axilla in a 47-year-old woman. A, Mediolateral oblique mammogram showing an abnormally enlarged lymph node (arrow) with internal microcalcifications in the right axilla. B and C, Transverse (B) and long axis (C) sonograms of the same area showing an enlarged lymph node (arrows) with an abnormal cortex. An excisional biopsy specimen (not shown) of this mass revealed benign reactive hyperplasia.
months (range, 2–91 months). Several investigators have used magnetic resonance imaging (MRI) in patients with metastatic lymph nodes and mammographically and clinically occult breast cancer. Morris et al reported that MRI showed areas of abnormal enhancement.

Figure 4. Palpable abnormality in the left axilla in a 47-year-old woman. A and B, Mediolateral oblique (A) and craniocaudal (B) mammograms showing an abnormally enlarged palpable lymph node (arrows) without a fatty hilum in the left axilla. C and D, Transverse (C) and long axis (D) sonograms of the palpable abnormality showing an enlarged lymph node with a nearly anechoic cortex and a small fatty hilum. An excisional biopsy specimen (not shown) of this mass revealed a lymph node abscess.
that were proven to be breast carcinoma by sonographically guided FNA cytologic analysis in 9 of 12 patients. There was 1 MRI examination with false-positive findings. In another series of 4 patients, MRI was able to show breast cancer that was proven by sonographically guided FNA in all 4. Obdeijn et al reported that MRI revealed occult breast cancer in 8 of 20 patients with metastatic axillary nodes without a history of breast cancer and in 3 of 11 patients with previous or simultaneous breast cancer.

Our study had several limitations. There was a selection bias because only cases that had undergone sonographic evaluation were included; not all patients with mammographically abnormal axillary nodes had undergone sonographic examination. The true incidence of isolated abnormal nodes detected on mammography could not be determined. Our series included patients with both palpable and nonpalpable lymph nodes undergoing both screening and diagnostic mammography. This retrospective analysis was also limited by the small sample size. A large prospective study is needed to examine the true incidence of abnormal axillary lymph nodes identified as isolated findings on mammography and to analyze the role of sonography in the additional evaluation of those lymph nodes so that more definitive guidelines can be established for treatment of patients with isolated abnormal axillary lymph nodes identified on mammography.

We conclude that axillary lymph nodes identified on mammography that have at least 2 abnormal features and either are palpable or have undergone substantial interval enlargement may need further evaluation if there is no underlying clinical explanation for axillary adenopathy. Additional sonographic evaluation is helpful for improving the low specificity of mammographic evaluation of abnormal axillary lymph nodes. The rate of malignancy in our series that had at least 2 abnormal sonographic features was 50%, justifying the use of additional imaging with sonography. We were able to show in our small series that sonography is efficacious in identifying malignancies in patients with axillary lymphadenopathy identified on mammography.

References


