Reactive Spindle Cell Nodules of the Breast After Core Biopsy or Fine-Needle Aspiration

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Key Words: Spindle cell nodules; Breast fine-needle aspiration; Post–core needle biopsy changes; Complex sclerosing lesion; Papilloma; Inflammatory pseudotumor

Abstract

Reactive spindle cell nodules (RSCNs) arising postoperatively or after fine-needle aspiration (FNA) have been reported previously in the genitourinary tract and thyroid. We describe 18 cases of similar lesions in breast, associated with a history of core needle biopsy or FNA. The majority of the RSCNs (15 cases) were associated with papillary lesions or complex sclerosing lesions. The RSCNs were nonencapsulated and relatively nodular, measuring 1.5 to 9 mm. They were composed of spindle cells with mild to moderate nuclear pleomorphism and a low mitotic count. A network of small blood vessels, macrophages, and lymphocytes was present in all cases. Immunohistochemically, the spindle cells expressed smooth and specific muscle actins, supporting a myofibroblastic origin. The association of RSCNs with needle trauma to fibrosclerotic lesions, such as complex sclerosing lesions and papillary lesions that regularly have myofibroblasts, suggests an exuberant reparative cause. Recognition of this reactive process will avoid overdiagnosis of mammary spindle cell malignant neoplasm.

Postoperative spindle cell nodules were first described by Proppe et al1 in the genitourinary tract. More recently, Baloch et al2 described similar reactive spindle cell nodules after fine-needle aspiration (FNA) of the thyroid gland. Those lesions show exuberant proliferation of spindle cells with frequent mitoses and neovessels and can be misinterpreted as malignant neoplasms. FNA and core needle biopsies have been used extensively in the management of breast diseases.3-12 Complications related to these procedures have been studied thoroughly and are considered uncommon events of minor clinical implications. A variety of tissue changes have been described after FNA13,14 and core needle biopsy of the breast.15-17 The more common changes include hemorrhage, hemosiderin deposits, and infarction, and the less common include epidermoid inclusion cysts, pseudoaneurysm formation, and epithelial implantation.5,13,15-20 Fresh hemorrhage and destruction of lesions with hematoma formation also may be seen after FNA,13,14 and fibroblastic and vascular proliferation have been reported in the FNA or core needle biopsy site.14 However, proliferation of spindle cells to yield a tumor-like appearance, such as the reactive spindle cell nodules (RSCNs) developing after needle aspiration or surgery, has not been recognized in the breast to our knowledge. Most benign spindle cell lesions described in breast, including inflammatory pseudotumor,21-24 nodular fasciitis,25 fibromatosis,26,27 and myofibroblastoma28 develop spontaneously. We describe uncommon reactive spindle cell proliferations of the breast associated with previous needle biopsy trauma to lesions with fibrous stroma as an intrinsic element, such as papillomas and complex sclerosing lesions (CSLs). Our emphasis is on the histologic features and differential diagnosis of such cases.
Materials and Methods

The files of the Breast Pathology Consultation Service at Vanderbilt University Medical Center, Nashville, TN, for the years 1994 through 1998 were reviewed. All cases with a diagnosis of reactive changes after FNA or stereotactic core needle biopsy, benign spindle cell lesions, and low-grade spindle cell metaplastic carcinomas were retrieved. The slides were reviewed and, after assignment to recognizable or accepted neoplastic categories, 18 cases interpreted as reactive spindle cell proliferation were selected for study. The clinical history of trauma and FNA or core needle biopsy was obtained from referring pathologists or physicians responsible for patient care. Histologic evaluation was performed using H&E-stained sections, and the associated underlying breast lesions were noted using published diagnostic criteria.29-32

The following histologic features were analyzed: size of the spindle cell lesion, growth pattern, cellularity, nuclear atypia, and mitotic rate. The microscopic growth pattern was classified as nodular with relatively smooth borders or partially infiltrative. The overall cellularity was evaluated considering the area occupied by spindle cells compared with the area occupied by fibrous tissue. Nuclear pleomorphism was graded on a scale of 1 to 3, with 1 indicating nuclei that were uniform and small and 3 indicating larger nuclei showing variation in shape and size. Areas of maximum mitotic activity were identified, and the number of mitoses was expressed per 10 high-power fields. The diameter of the high-power field was 0.49 mm (area, 0.20 mm²). The presence of the following other features was evaluated: glands entrapped in the needle tract, squamous metaplasia, inflammatory cells, foamy cells, hemosiderin-laden macrophages, edema, and acute hemorrhage associated with the spindle cell proliferation.

Immunohistochemical stains Table 1 were performed in 7 cases using a Ventana ES automated immunostainer (Ventana, Tucson, AZ) and the streptavidin-biotin-peroxidase method.

Results

Clinical History and Underlying Lesions

Results are summarized in Table 2. All patients were women, and the average age at diagnosis was 55.1 years (range, 30-76 years). All 18 patients had a history of a needle biopsy procedure, including core needle biopsy (10 cases), FNA (6 cases), or both (2 cases). The interval between the needle trauma and the subsequent excisional biopsy was available for 12 cases and ranged from 6 to 38 days (average, 16.4 days). Patients were treated with excisional biopsy (12 cases), wide excision (5 cases), and partial mastectomy (1 case).

In 11 (61%) of 18 cases, the underlying diagnoses were papillary lesions including papilloma (6 cases) Image II, multiple micropapillomas (3 cases), and encysted noninvasive papillary carcinomas (2 cases). In 2 cases (11%), the underlying lesions were CSLs Image 2I, and 2 cases (11%) showed CSLs and papillary lesions. The other underlying diagnoses included fibroadenoma (1 case), nodular adenosis (1 case), and ductal carcinoma in situ (1 case). Four lesions were partially infarcted, and 2 papillary lesions were partially sclerosed.

Microscopic Features of the RSCNs

The number of slides reviewed in each case ranged from 1 to 10 slides (average, 3 slides). All 18 RSCNs included in the present study showed a tumor-like appearance; the average size of the spindle cell proliferation was 3.9 mm (range, 1.5-9 mm). A needle tract was identified, usually in the central part of the preexisting breast lesions, in the majority of cases.

The RSCNs associated with a previous core biopsy generally were larger than those arising after FNA. All lesions were nonencapsulated; 4 lesions were well-demarcated and nodular, and 14 lesions were partially nodular with areas of infiltrative growth pattern.

The RSCNs were composed of intersecting fascicles of generally plump spindle cells, focally suggesting a storiform pattern, intermixed with thin-walled vessels and various amounts of delicate collagen fibers, ranging from less cellular lesions to exuberant spindle cell proliferations. The spindle cells had abundant cytoplasm, oval to elongated nuclei, vesicular chromatin, and 1 or 2 nucleoli (Image 1) and Image 3I. The majority of cases showed mild to moderate nuclear pleomorphism. Mitotic figures were encountered rarely; 15 cases (83%) showed 0 to 1 mitosis per 10 high-power fields, and no atypical mitotic figures were seen.

All cases showed a mixed inflammatory infiltrate consisting mainly of macrophages, lymphocytes, and plasma cells Image 4I. Hemosiderin-laden macrophages, foamy macrophages, and rare giant cells were present in most cases. Areas of slight edema and small foci of acute hemorrhage were present in 12 cases, primarily the cases with short time intervals between trauma and the subsequent excision. Entrapment of glands or artifactual displacement of tumoral cells was seen in 10 cases, with some glands showing degenerative changes Image 5I. Lymphatic emboli were identified in one case. Small epithelialized cysts, lined by reactive squamous epithelium, were found in 2 cases in which a gradual transition from
the squamous or glandular epithelia to the spindle cells was seen (Image 4) and Image 6.

Immunohistochemical results (Table 1) showed that the spindle cells were positive for smooth muscle actin Image 7, muscle-specific actin, and vimentin and were negative for AE1/AE3 and high-molecular-weight keratin, supporting a myofibroblastic origin. The surrounding breast epithelium and entrapped glands stained for cytokeratins and were used as internal controls. The macrophages marked with CD68.

### Discussion

We describe 18 cases of exuberant reactive spindle cell proliferations arising in the breast after needle biopsy procedures. Most of the spindle cell proliferations (15 cases [83%]) arose within or in the vicinity of papillary lesions and CSLs, giving rise to distinct nodules or masses. The RSCNs likely are related to trauma in specially predisposed breast lesions, such as papillomas and CSLs that have a stromal component containing myofibroblasts as a fundamental part of the lesion. Therefore, the stromal component may determine the nature of the response enhancing the proliferation of myofibroblasts after trauma, and RSCNs probably represent an exuberant tissue response in these settings.

In our series, reactive spindle cell proliferation was seen in continuity with the radial cores of CSLs. Radial scars and CSLs are fibroelastic lesions mimicking invasive malignant neoplasms because of the presence of fibrous tissue proliferation in a radiating manner with entrapped glandular elements. The term radial scar often has been used for lesions that are smaller than 10 mm, with CSL being reserved for those that are larger.29

**Table 1**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Source</th>
<th>Clone</th>
<th>Dilution</th>
<th>No. of Cases Positive/No. of Cases Tested</th>
</tr>
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<tr>
<td>Vimentin</td>
<td>Boehringer-Mannheim, IN</td>
<td>V-9</td>
<td>1:300</td>
<td>7/7</td>
</tr>
<tr>
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<td>Enzo Diagnostics, Syosset, NY</td>
<td>HHF-35</td>
<td>Prediluted</td>
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<td>Smooth muscle actin</td>
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<td>1A-4</td>
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<tr>
<td>CD68</td>
<td>Dako, Carpinteria, CA</td>
<td>KP-1</td>
<td>1:1,200</td>
<td>0/5</td>
</tr>
<tr>
<td>AE1/AE3</td>
<td>Boehringer-Mannheim</td>
<td>AE1/AE3</td>
<td>1:200</td>
<td>0/6</td>
</tr>
<tr>
<td>High-molecular-weight cytokeratin</td>
<td>Dako</td>
<td>34 beta-E12</td>
<td>1:50</td>
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**Table 2**

<table>
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<tr>
<th>Case</th>
<th>Age (y)</th>
<th>Clinical History</th>
<th>Underlying Lesion</th>
<th>Size* (mm)</th>
<th>Nuclear Atypia</th>
<th>Mitosis per 10 HPF</th>
<th>Entrapped Glands</th>
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<tr>
<td>1</td>
<td>55</td>
<td>Core</td>
<td>Papilloma</td>
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<td>2</td>
<td>62</td>
<td>FNA/Core</td>
<td>Infarcted encysted papillary carcinoma</td>
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<td>2</td>
<td>4</td>
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<tr>
<td>3</td>
<td>61</td>
<td>Core</td>
<td>Multiple micropapillomas</td>
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<td>1</td>
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<tr>
<td>4</td>
<td>49</td>
<td>FNA/Core</td>
<td>Ductal carcinoma in situ</td>
<td>4</td>
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<td>Yes</td>
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<tr>
<td>5</td>
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<td>Core</td>
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<td>0</td>
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<td>52</td>
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<td>Complex sclerosing lesion</td>
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<tr>
<td>7</td>
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<td>FNA</td>
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<td>FNA</td>
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<td>64</td>
<td>FNA</td>
<td>Papilloma with ductal carcinoma in situ</td>
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<td>0</td>
<td>Yes</td>
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<td>2</td>
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<td>2</td>
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<tr>
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<td>Multiple micropapillomas with ductal carcinoma in situ</td>
<td>9</td>
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<tr>
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<td>76</td>
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<td>Infarcted fibroadenoma</td>
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<td>2</td>
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<tr>
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<td>30</td>
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<td>Nodular adenosis</td>
<td>3</td>
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<td>0</td>
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<td>17</td>
<td>42</td>
<td>FNA</td>
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<td>1</td>
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<td>Yes</td>
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<td>18</td>
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<td>Core</td>
<td>Complex sclerosing lesion</td>
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</tbody>
</table>

Core, stereotactic core needle biopsy; FNA, fine-needle aspiration biopsy; HPF, high-power field.

* Average size of the reactive spindle cell nodules, 3.9 mm.
Radial scars and CSLs in the early stages show abundant spindle cells of myofibroblastic origin around the central radiating parenchymal components.\textsuperscript{33,34} Vascular abnormalities, including traumatic arterial damage and extravascular spindle cell proliferation, have been described after FNA of CSLs.\textsuperscript{14} However, to our knowledge no published reports describe breast lesions comparable to the amount of the proliferative stroma or tumor-like appearance and nodule formation such as those present in RSCNs.

Hemorrhagic infarction often is present focally in papillomas and, in the late stages of the ischemic injury, produces an appearance similar to carcinoma with epithelium compressed and distorted into isolated clumps.\textsuperscript{30,35} Since hemorrhage and both regressive and reactive changes occur spontaneously in fibro sclerotic breast lesions,\textsuperscript{29-31,35} it is difficult to distinguish the extent of changes related to needle trauma. One case reviewed but not included in our series showed histologic features similar to RSCNs in a papilloma after breast trauma sustained by the patient.

Squamous metaplasia also may be seen in papillomas and sometimes may be extensive, particularly in larger encysted lesions.\textsuperscript{30,36} In 2 cases in our series, we observed...
islands of squamous metaplasia and small epithelialized cysts. In support of this, Davies et al\textsuperscript{16} described “epidermoid inclusion cysts” in the site of large core needle biopsies of the breast.

Normal epithelial elements or entrapment of glands intermixed with the proliferating spindle cells, such as those described in 10 cases of our series, can be misinterpreted as low-grade metaplastic carcinomas. Bland spindle cell proliferation associated with glandular or squamous elements has been considered a defining feature of low-grade spindle cell metaplastic carcinomas,\textsuperscript{37} metaplastic tumors with a dominant fibromatosis-like phenotype,\textsuperscript{38} and adenosquamous carcinomas.\textsuperscript{39}

RSCNs of the breast have histologic features similar to the reactive spindle cell nodules described after surgery of the genitourinary tract\textsuperscript{1} and after FNA of the thyroid gland.\textsuperscript{2} Florid myofibroblastic proliferation around hemorrhagic infarction, mimicking Kaposi sarcoma, also has been reported after FNA in lymph nodes.\textsuperscript{30} The main histologic features of breast RSCNs are the relatively small size and the exuberant proliferation of active spindle cells intermixed with inflammatory cells, histiocytes, foam cells, and hemosiderin, focally resembling granulation tissue. The spindle cells are likely to be myofibroblasts, which is supported by morphologic features of the cells and the immunohistochemical findings also described in other reactive spindle cell proliferations, such as spindle cell nodules of genitourinary tract and thyroid gland,\textsuperscript{1,2,41} inflammatory pseudotumors,\textsuperscript{42,43} nodular fasciitis, and desmoid tumors.\textsuperscript{44} The differential diagnosis of RSCNs considers other neoplastic and nonneoplastic spindle cell lesions of the breast. These include inflammatory myofibroblastic tumor or inflammatory pseudotumor,\textsuperscript{21-23,42} nodular fasciitis,\textsuperscript{25,45,46} myofibroblastoma,\textsuperscript{28} fibromatosis,\textsuperscript{26,27} low-grade spindle cell metaplastic carcinomas,\textsuperscript{37,38} and low-grade sarcomas.\textsuperscript{47-50} While RSCNs have many overlapping histologic and immunohistochemical features seen in those spindle cell lesions of the breast, history of previous needle procedure, identification of needle tract, and the presence of hemosiderin, foam cells, and low mitotic counts favor the diagnosis of RSCNs.

The RSCNs described in this series probably represent a reactive process occurring in the breast after needle biopsy.
procedures in association with papillary lesions and CSLs. RSCNs are likely myofibroblastic in origin and must be distinguished from other neoplastic and nonneoplastic spindle cell lesions of the breast. Awareness and recognition of this reactive process will avoid overdiagnosis of mammary spindle cell malignant neoplasms.

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References


