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H. James Williams, MD

The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see http://journals.sagepub.com/doi/10.1177/2374289517715040.

Keywords
pathology competencies, organ system pathology, disease mechanisms, breast, neoplasia, fibroadenoma, palpable breast lesion, mammographic findings, phyllodes tumor

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Primary Objective

Objective BR2.1: Fibroadenoma and Phyllodes Tumor. Compare and contrast fibroadenoma and phyllodes tumor in terms of clinical features, morphologic findings, and prognosis.

Competency 2: Organ System Pathology; Topic BR: Breast; Learning Goal 2: Molecular Basis of Breast Neoplasms.

Secondary Objective

Objective N3.1: Morphologic Features of Neoplasia. Describe the essential morphologic features of neoplasms and indicate how these can be used to diagnose, classify, and predict biological behavior of cancers.

Competency 1: Disease Mechanisms and Processes; Topic N: Neoplasia; Learning Goal 3: Characteristics of Neoplasia.

Patient Presentation

A 37-year-old woman presents to her physician with concern about a left breast nodule she recently discovered on self-examination. The patient states that the nodule is approximately 2 cm in size, close to her left axilla, and feels firm. She is concerned because her mother, age 54, was recently diagnosed with breast cancer.

Questions/Discussion Points, Part 1

What Pertinent Questions Should be Asked as Part of the Detailed History Prior to Physical Examination?

How long has the nodule been there? If the lesion developed very recently, one could choose to follow the lesion for a short time to see if it persists.

Has it changed in size over time? Change in size could include decreasing, increasing, or fluctuating lesions. Fluctuation in size would be suggestive of menstrual effect or fibrocystic change. A decrease in size might indicate a cyst getting smaller. An increase in size would be more worrisome for a more serious lesion.

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Is the nodule painful? Malignancies are not typically painful; however, inflammatory lesions can be painful as could benign lesions.

Has there been nipple discharge and if so, is it bloody? Bloody nipple discharge may be associated with an intraductal papilloma or, more rarely, cancer. A finding of nipple discharge would need to be investigated more carefully.

Does anyone in your family have or have had breast cancer? If there is a family history of breast cancer, what is the relationship of the family member with the patient (ie, is it the patient’s mother, sister, or daughter)? Also, what was the age at time of diagnosis of the family member? Younger age of breast cancer would be much more concerning for a possible familiar component of a breast cancer than breast cancer in an older first-degree relative. This question is addressing the associated increased risk of malignancy and/or hereditary disease in close relatives, especially if they developed breast cancer at a young age.

On physical examination of the patient’s left breast, what findings would favor either a benign or malignant diagnosis? Physical examination can be helpful, as some features are more common with benign or malignant lesions. Features of benign neoplasms include the following: multiple indistinct nodules (lumpy breast) that favor fibrocystic changes and lesions beneath the nipple which may suggest an intraductal papilloma.

However, a fixed, irregular, and firm mass is suspicious for malignancy as is dimpling of the overlying skin. Another important factor is location of the lesion within the breast, as 50% of breast cancers arise in the upper outer quadrant; thus, lesions in this area would be more suspicious for malignancy.

Figure 1. Mammogram of left breast nodule. The lesion is homogeneous and is sharply demarcated from the normal breast tissue.

Figure 2. Microscopic image of left breast nodule at low power, H&E 2×. On low power, the lesion is seen to be sharply demarcated from the adjacent normal breast tissue.

Figure 3. Microscopic image of left breast nodule at high power, H&E 20×. The stroma of the lesion has low cellularity with no mitoses or cytologic atypia. The epithelial component shows bland cytologic features with associated myoepithelial cells.

Diagnostic Findings, Part 2
The patient undergoes mammography of the left breast nodule. The mammography is shown in Figure 1.

Questions/Discussion Points, Part 2
What Radiographic Findings in Figure 1 Are Seen, and Do They Favor a Benign or Malignant Diagnosis?
Similar to physical examination, radiologic examination is important in working up breast lesions. Several factors are more suggestive of benign versus malignant lesions. The following findings favor a benign process when they
are present: sharp distinct borders, homogenous texture, and ovoid shape. The following factors favor malignant when they are present: stellate infiltrative borders, heterogeneous texture, round shape, and presence of coarse calcifications.

In the mammographic image for the patient, a round homogenous lesion is seen. This would favor a benign process. Confirmation of the imaging impression requires histologic examination of the lesion either by biopsy of the lesion or by conservative excision.

**Diagnostic Findings, Part 3**
The breast nodule is excised and sent for pathologic examination (see Figures 2 and 3).

**Questions/Discussion Points, Part 3**

*What are the Pertinent Histologic Findings Seen in Figures 2 and 3?*

On low-power image of the breast biopsy, as seen in Figure 2, the lesion is seen to be sharply demarcated from the adjacent normal breast tissue. This is suggestive of a benign process. When looking at higher power in Figure 3, there is a predominance of stromal tissue with compression of the epithelial component. The stroma is of low cellularity with no mitoses or cytologic atypia seen. In addition, the epithelial component shows bland cytologic features with associated myoepithelial cells.

*What Is Your Diagnosis?*

Fibroadenoma of the breast.

*Discuss the Clinical Features and Pathophysiology of Fibroadenomas and What Is the Prognosis and Management for This Lesion?*

Fibroadenomas are the most common benign breast neoplasms and typically present in women 20 to 35 years old.\(^1\) The tumors are usually solitary but may be multiple (20%). Clinically, they may be detected by the patient or the physician on breast examination as a well-demarcated, freely mobile, firm mass that is usually \(<3\) cm in diameter. The fibroadenoma is a neoplasm of the specialized lobular stroma with typically low cellularity, no cytologic atypia, and mitotic figures absent or rare. The associated benign epithelium has associated myoepithelial cells and may have an intracanalicular or pericanalicular pattern.\(^2\) The radiographic appearance of fibroadenoma characteristically shows an ovoid homogenous mass with sharp distinct borders.

Patients with fibroadenomas are associated with a slight increased risk of breast cancer, particularly when there are proliferative fibrocystic changes involving the tumor. As would be anticipated, fibroadenomas are hormonally responsive (may enlarge during pregnancy and reduce in size in postmenopause).

As the fibroadenoma is a benign tumor, in the appropriate clinicoradiographic setting, once the tumor is diagnosed by fine-needle aspiration or needle core biopsy, it may be safely followed. If the tumor is a cosmetic problem or if preferred by the patient, conservative excision can be performed.\(^3\)

*Discuss a Common Tumor in the Differential Diagnosis of a Fibroadenoma*

The histologic differential diagnosis includes the phyllodes tumor in which there is increased cellularity of the stroma, and the epithelial component demonstrates a “leaf-like” architectural pattern.\(^1\) Low-grade phyllodes tumors have these features with mild cytologic atypia and occasional mitoses. High-grade phyllodes tumors in addition to the increased stromal cellularity have marked cytologic atypia and increased mitoses, some of which may be atypical. Because of the higher risk of recurrences, wide excision is indicated for phyllodes tumors. In addition to the risk of recurrences, the high-grade phyllodes tumor has the potential to metastasize.

**Teaching Points**

- Benign features include the following: Multiple indistinct nodules (lumpy breast) favors fibrocystic changes, and lesions beneath the nipple may suggest a papilloma.
- A fixed irregular firm mass on physical examination is suspicious for malignancy, as is dimpling of the overlying skin.
- On radiography, a benign process tends to have sharp distinct borders, homogenous texture, and ovoid shape.
- Fibroadenomas are the most common benign breast neoplasms and typically present in women 20 to 35 years old.
- The fibroadenoma is a neoplasm of the specialized lobular stroma with typically low cellularity, no cytologic atypia, and mitotic figures absent or rare. The associated benign epithelium has associated myoepithelial cells and may have an intracanalicular or pericanalicular pattern.
- The phyllodes tumor has increased cellularity of the stroma, and the epithelial component demonstrates a “leaf-like” architectural pattern. Low-grade phyllodes tumors may have mild cytologic atypia and occasional mitoses. High-grade phyllodes tumors, in addition to the increased stromal cellularity, have marked cytologic atypia and increased mitoses, some of which may be atypical.

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