# Fibroadenoma

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## 8.1 Clinical, Radiological, and Epidemiological Findings

Fibroadenoma is the most common benign breast neoplasm that usually occurs in young women of childbearing age, though it can occur at any age. It often presents as a localized tumor which can be clinically palpable as a mobile rounded and rubbery lump, but asymptomatic lesions have been detected by mammography as well-defined masses. On ultrasound examination, the fibroadenoma appears as a solid, round, or oval mass with distinct margins (Fig. 8.1). Calcifications may be observed in fibroadenomas from older women (Mendoza et al. 2011).

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**Fig. 8.1** Ultrasound image demonstrates an oval, circumscribed, hypoechoic mass

## 8.2 Cytologic Findings

Diagnosis of fibroadenoma on FNAC is highly accurate with a 79.3% predictive value in one series of 362 cases (López-Ferrer et al. 1999). Aspirates from the fibroadenoma are usually cellular with antler- or staghorn-shaped epithelial clusters and honeycomb monolayered sheets, set within a clean background with many naked bipolar nuclei, giving an appearance of "sesame seeds strewn among epithelial fragments" (Fig. 8.2a–g). Branching epithelial sheets are commoner in aspirates from fibroadenomas with an intracanalicular growth pattern (Mendoza et al. 2011). The bimorphic or bimodal epithelial clusters feature ductal epithelial cells with generally bland and banal vesicular nuclei with smooth nuclear contours, often accompanied by a second population of myoepithelial cells with their angular small dark nuclei interspersed among the ductal epithelial cells or inconspicuously punctuating the periphery of epithelial sheets (Fig. 8.3). Presence of usual ductal hyperplasia within the fibroadenoma can lead to the presence of larger branched proliferative epithelial aggregates in the aspirates (Fig. 8.4a, b). Apart from bipolar nuclei in the background, there are scattered stromal clumps which can be associated with myxoid material. These fibromyxoid stromal clumps are usually paucicellular with a few spindled nuclei and sometimes occur in proximity to the epithelial clusters (Fig. 8.5).

FNAC of the cellular and juvenile fibroadenoma shows similar cytological features as the conventional fibroadenoma, with the possibility of an increased population of stromal cells (Fig. 8.6). The fibroadenoma is the most common cause of a false-positive diagnosis in FNAC of breast lesions. The reasons for this include the frequent presence of occasional isolated intact cells with dissociation, epithelial nuclear atypia, and high cellularity. Apocrine metaplasia, multinucleation, and paucicellularity in hyalinized fibroadenomas are additional pitfalls (Kollur and El Hag 2006). Pregnancy and lactation, infarction, and prominent myxoid stroma in a fibroad-

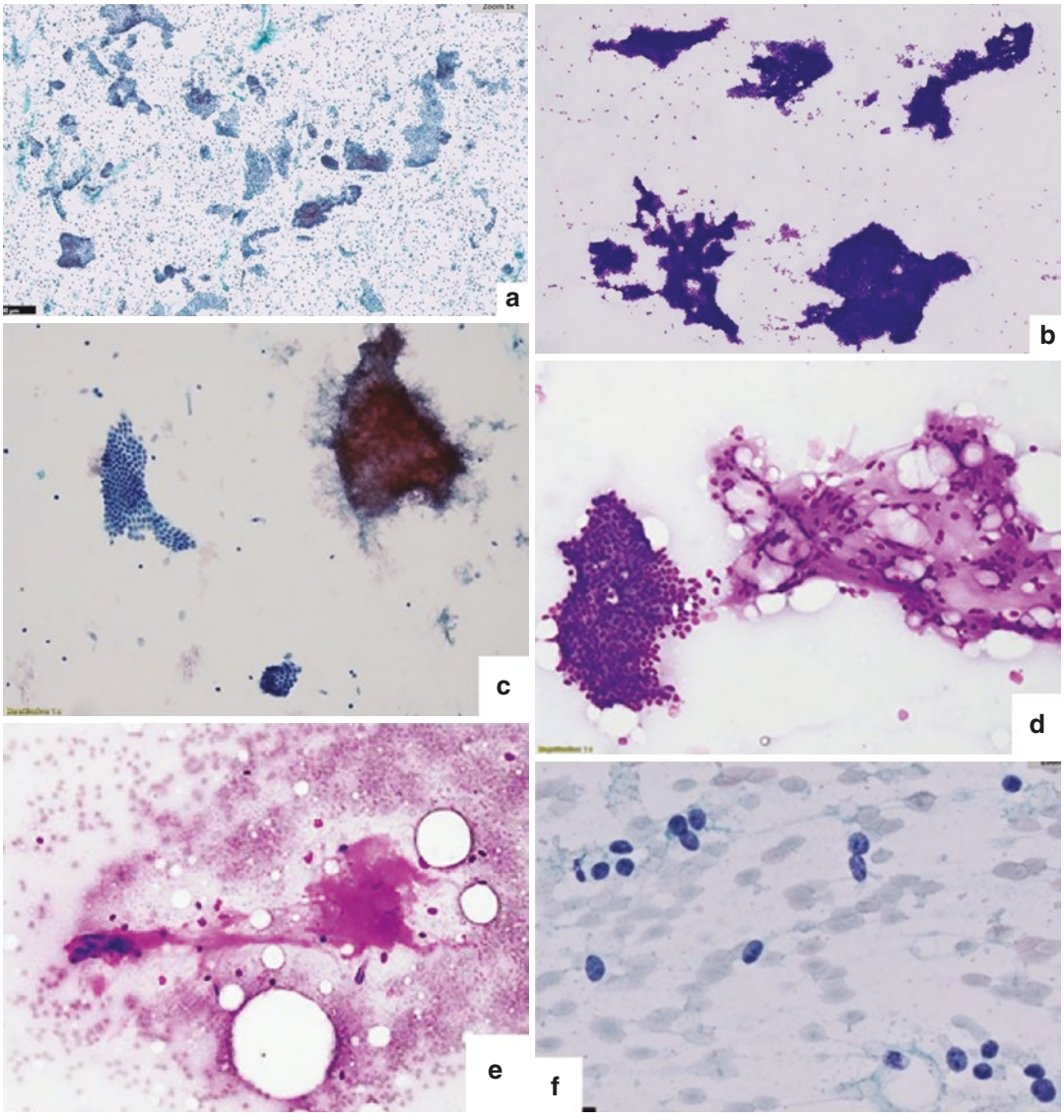


**Fig. 8.2** (**A**) Flat cohesive branching sheets of ductal epithelial cells interspersed with bare nuclei, PAP (**A**) and MGG (**B**). (**C**, **D**) Fibrillary stromal material admixed with cohesive sheets of ductal cells and bare nuclei PAP (**C**) and MGG (**D**). (**E**) Metachromatic stromal material (MGG). (**F**) Kissing pairs of small bare nuclei (PAP). (**G**) H & E stain of a core biopsy from a typical fibroadenoma

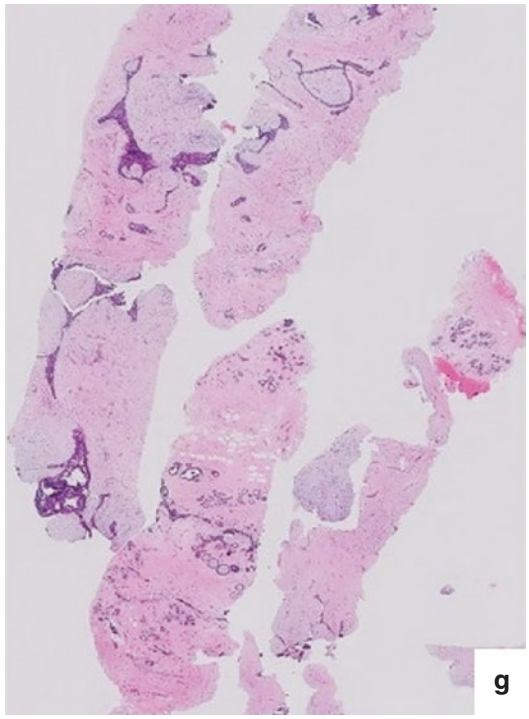


**Fig. 8.2** (continued)

enoma can aggravate worrisome cytological findings. Pregnancy or lactational atypia when superimposed on the cellularity of fibroadenoma aspirates can lead to a troublesome cytologic appearance with a potential false-positive result (Fig. 8.7) (Novotny et al. 1991). It has been observed that the majority of aspirates with cytologic features suggesting fibroadenomas but harboring atypia are often correlated with benign fibroadenomas on histology (Simsir et al. 2001). FNAC of fibroadenomas accounted for the majority of benign lesions in proliferative breast lesions with and without atypia (Zhao et al. 2009). Nevertheless, caution must be exercised in this equivocal or atypical category as there are also cancers that can mimic fibroadenomas on cytology, leading to false-negative diagnoses. If significant nuclear atypia is seen in a what otherwise appears to be a typical fibroadenoma aspirate, a diagnosis of fibroadenoma with atypia should be rendered, as low-grade DCIS/ LCIS or invasive tumor within or adjacent to a fibroadenoma can occur (Field et al. 2020). The role of the triple approach cannot be overemphasized.

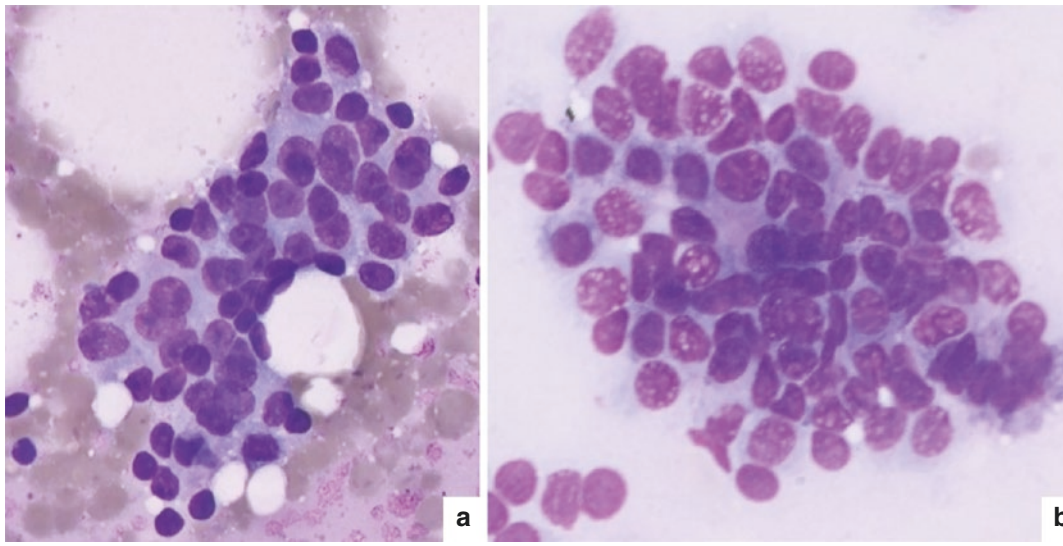


**Fig. 8.3** Fibroadenoma. A closer view of the bimodal epithelial aggregate with small dark nuclei of myoepithelial cells at the periphery of the cluster (**A**), as well as intermixed among the ductal epithelial cells (**B**), (MGG)

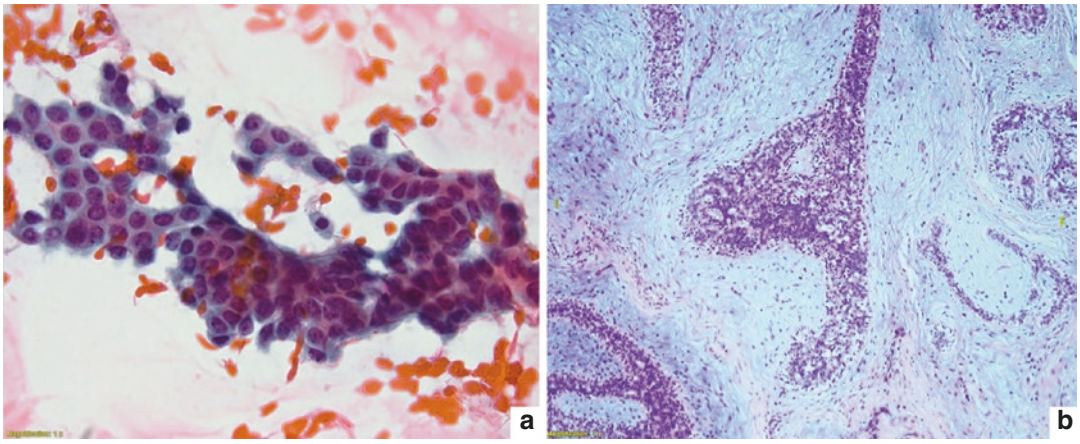


**Fig. 8.4** Fibroadenoma with usual ductal hyperplasia. (**a**) Large and branched cohesive epithelial sheet with admixed myoepithelial cells. There is a degree of nuclear atypia and some nuclear overlapping (**b**) Corresponding histology shows a fibroadenoma with the epithelial component demonstrating usual ductal hyperplasia

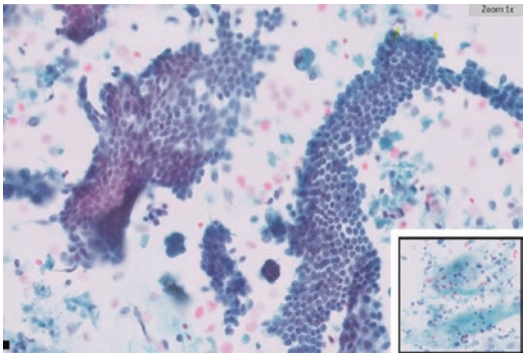

**Fig. 8.5** Fibroadenoma with usual ductal hyperplasia. Large bimodal epithelial aggregate shows ductal epithelial cells admixed with darker nuclei of myoepithelial cells. A loose myxoid stromal clump with elongated nuclei is noted (inset)

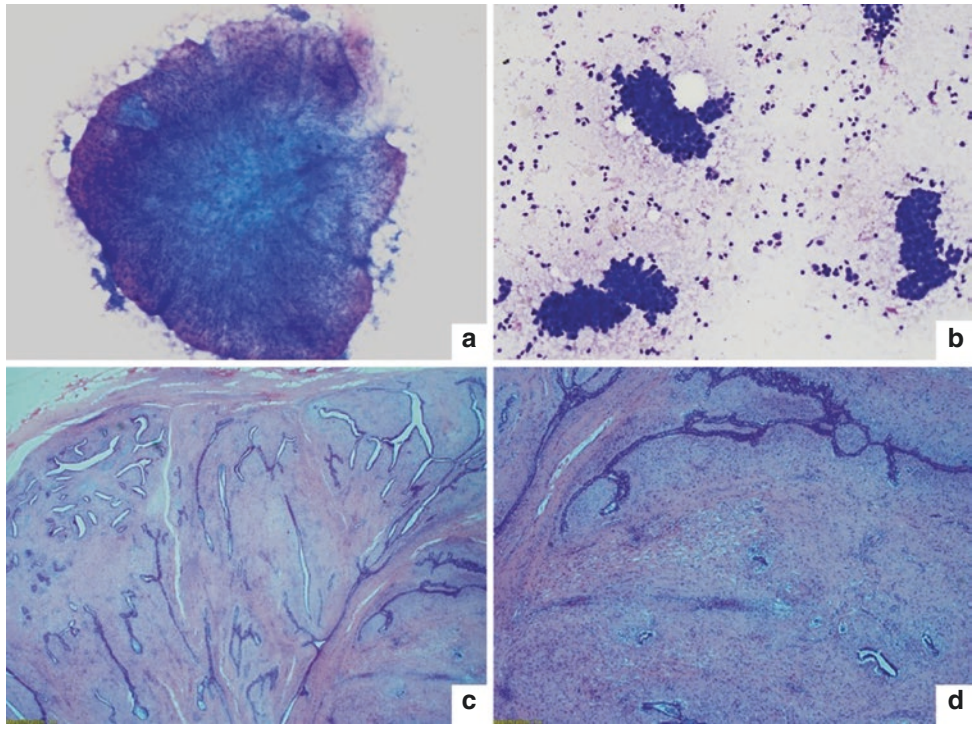


**Fig. 8.6** Cellular fibroadenoma. Diff-Quik smear shows cohesive epithelial clusters (**b**) accompanied by more cellular myxoid stromal clumps (**a**). H&E sections show a cellular fibroadenoma with a pronounced intracanalicular growth pattern and a mildly cellular intervening stroma (**c**, **d**)

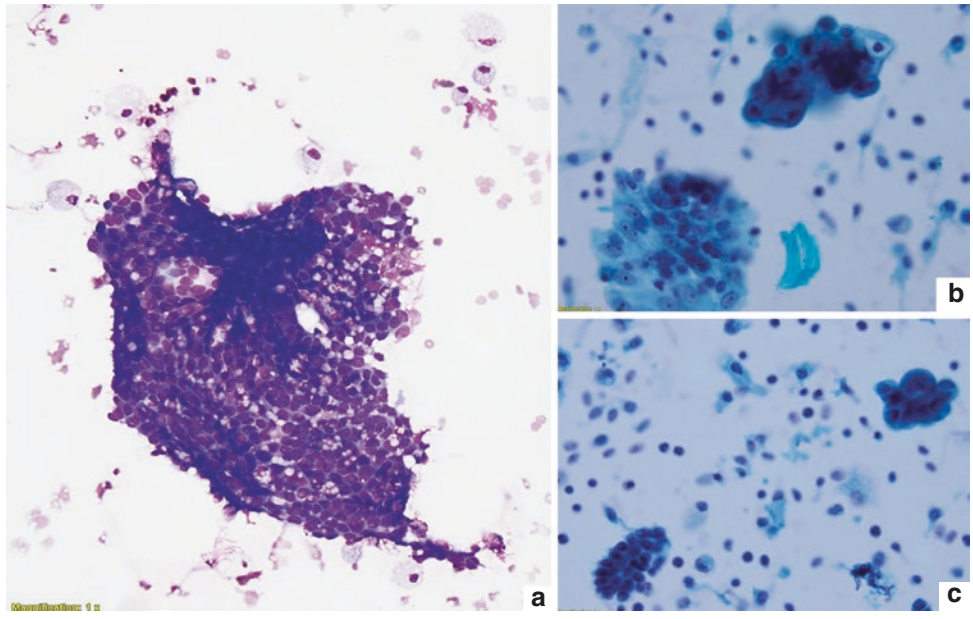


**Fig. 8.7** Fibroadenoma with lactational change. (**a**) Flat cohesive sheet of ductal epithelial cells with vacuolated cytoplasm and foamy histiocytes in the background; MGG. (**b**, **c**) A hyperchromatic cluster of ductal cells with vacuolated and foamy cytoplasm, containing nuclei with prominent nucleoli, admixed with many bare nuclei in the background (PAP); features seen in pregnancy and lactation. (**d**) H&E from the core biopsy showed a fibroadenoma and background lactational change

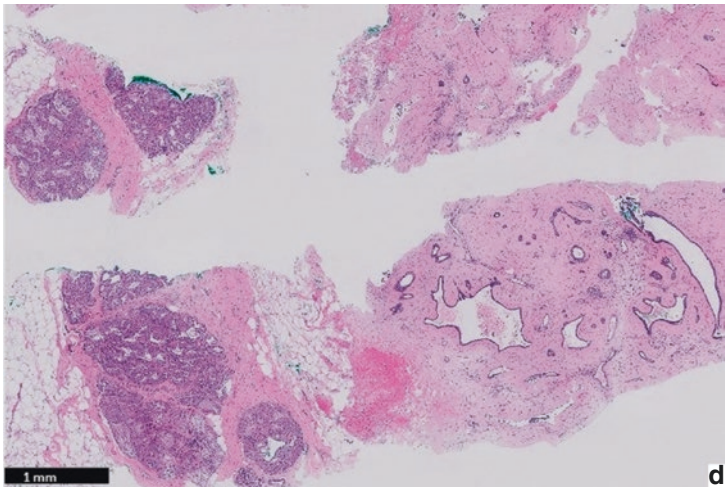


**Fig. 8.7** (continued)

## 8.3 Differential Diagnosis

### 8.3.1 Fibrocystic Changes

While fibrocystic change can usually be readily distinguished from fibroadenoma by the lower cellularity and presence of foam and apocrine cells, occasional aspirate yields from fibroadenoma can show similar appearances (Fig. 8.8). Presence of fibromyxoid stroma, staghorn-shaped epithelial clusters, and higher cellularity are considered key cytologic criteria to separate fibroadenoma from fibrocystic change (Bottles et al. 1988).

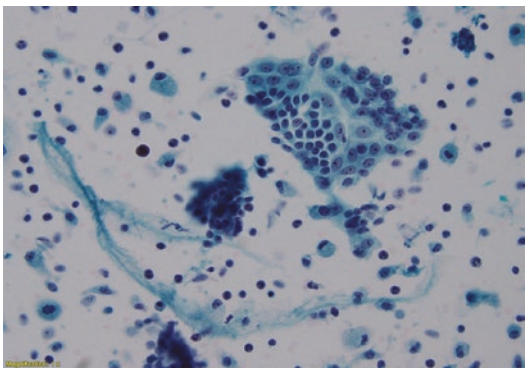

**Fig. 8.8** Fibroadenoma with cystic change shows cohesive clusters of ductal cells, some with apocrine features, many bare nuclei, cyst macrophages, and a wispy stromal fragment (PAP)

### 8.3.2 Pseudoangiomatous Stromal Hyperplasia (PASH)

PASH is often encountered incidentally in breast biopsies for other conditions, but it may also present as a breast mass in some women. FNAC of PASH can be moderately cellular with clusters of bland epithelial cells that can be branched and staghorn-like, in a background of single naked nuclei as well as spindle cells. Loose hypocellular stromal fragments can be identified, and these cytologic features are similar to those found in fibroadenoma (Ng et al. 2003).

### 8.3.3 Mucocele-Like Lesions

Aspirates from a myxoid fibroadenoma can mimic a mucocele-like lesion due to the presence of mucoid material in the background of the smears (Fig. 8.9). The myxoid fibroadenoma demonstrates greater cellularity than the benign mucocele-like lesion, and it is reported that the mucoid material of myxoid fibroadenoma shows a brighter pink coloration than the magenta hue of the mucocele-like lesion (Yeoh et al. 1999).

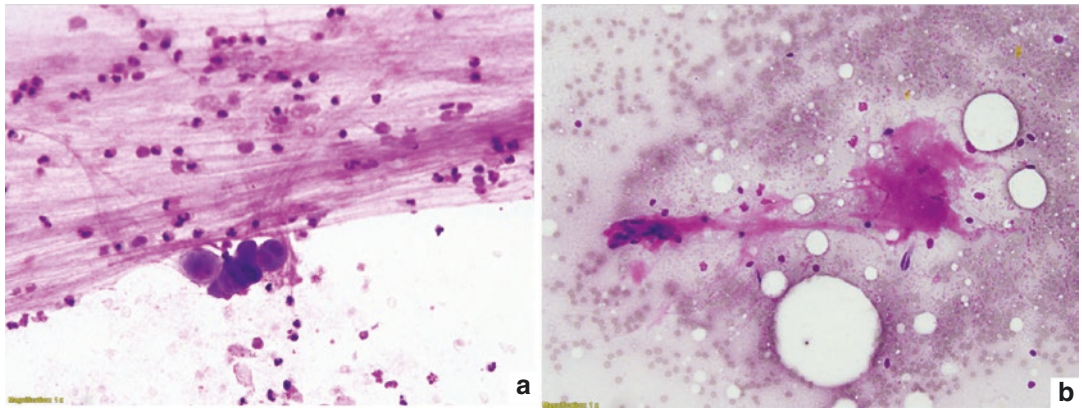


**Fig. 8.9** Background fluid mucin with magenta hue from an aspirate of a mucinous carcinoma (**a**) in contrast to brighter pink fibrillary stromal material in a myxoid fibroadenoma (**b**); MGG

### 8.3.4 Phyllodes Tumors

Phyllodes tumor is a fibroepithelial neoplasm that is closely related to fibroadenoma. Cytological distinction can be particularly problematic since both lesions possess overlapping characteristics. In particular, aspirates from cellular fibroadenomas are both cytologically and histologically difficult to distinguish from the benign phyllodes tumor. Fibromyxoid stromal clumps that are cellular and contain spindled nuclei (Fig. 8.10), fibroblastic pavements (El Hag et al. 2010), reduced epithelial–stromal ratio (Tse et al. 2002), larger epithelial clusters with wavy or folded shapes (Shimizu and Korematsu 2002), and stromal cytologic atypia (Scolyer et al. 2001) favor phyllodes tumor. One study has advocated that recognition of long spindled nuclei in more than 30% of the dispersed stromal cell population is the most reliable feature to favor phyllodes tumor over fibroadenoma (Krishnamurthy et al. 2000). While multinucleated giant cells have been described in fibroadenomas as well, it has been reported that these cells are found more frequently in phyllodes tumors (Tse et al. 2002; Simi et al. 1988).

### 8.3.5 Hamartoma

As compared with the fibroadenoma, aspirate of the breast hamartoma is less cellular and shows cytologically intact lobular units with lack of stromal elements (Herbert et al. 2006). Distinction is often possible radiologically.

### 8.3.6 Tubular Adenoma

Cytological features of tubular adenoma resemble the fibroadenoma. More specific appearances of tubular adenoma are three-dimensional cohesive epithelial balls and tubular aggregates in a cellular background, with a relative lack of stag-horn epithelial clusters (Kumar et al. 1998). Epithelial cells are uniform. Intracytoplasmic magenta granules (observed in Giemsa smears), straight tubules, and closely placed acini have been described as findings that are not seen in aspirates from fibroadenomas (Shet and Rege 1998).

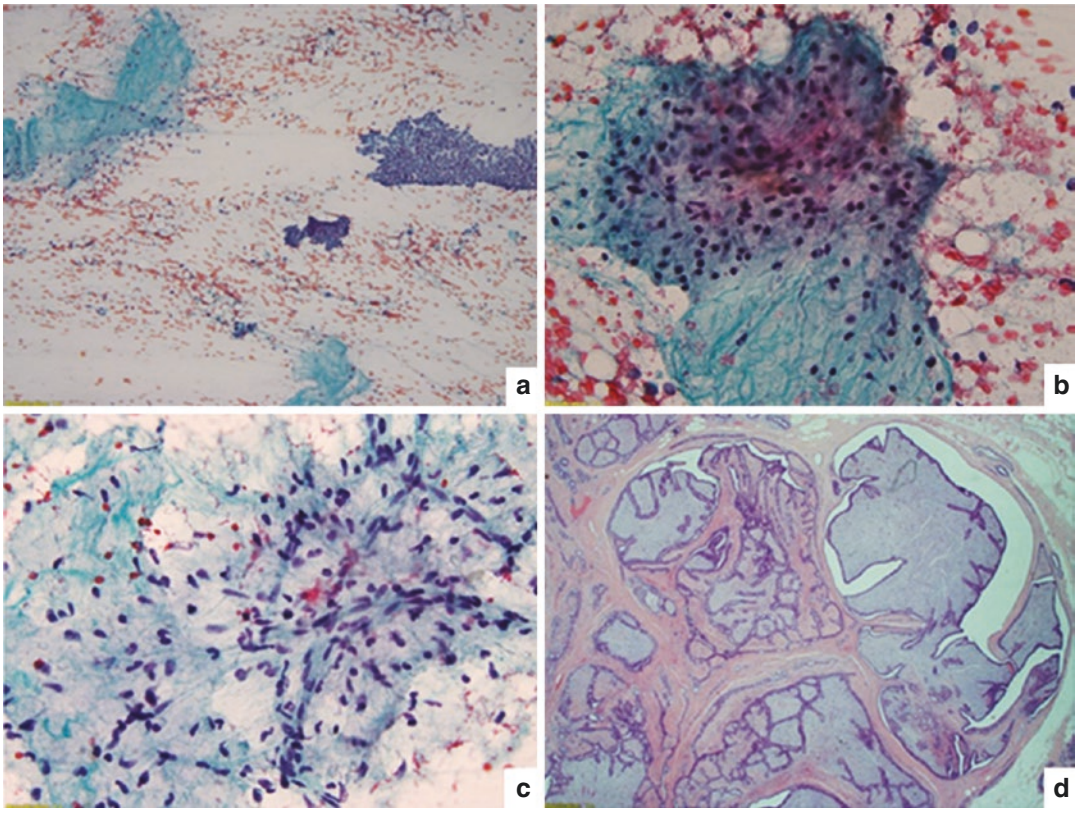


**Fig. 8.10** Benign phyllodes tumor with increased stromal fragments (**a**) PAP. Increased stromal cells within the stromal fragments (**b** and **c**) PAP. H&E sections from a benign phyllodes tumor with fronded architecture and well-circumscribed borders (**d**)

### 8.3.7 Adenomyoepithelioma

The adenomyoepithelioma of the breast is a neoplasm that consists of a biphasic proliferation of both ductal epithelial and myoepithelial components. FNAC of this lesion is often moderate to highly cellular with clusters of both epithelial and myoepithelial cells. Myoepithelial cells are also seen as naked bipolar nuclei. Intranuclear and intracytoplasmic vacuoles have been described in the myoepithelial cell population (Iyengar et al. 2006). Cytologic recognition of adenomyoepithelioma is difficult, and the lesion may be initially diagnosed as fibroadenoma or other lesions including cancer. Differences from fibroadenoma include the higher volume of dispersed myoepithelial cells as well as epithelioid myoepithelial cells with discernible nucleoli (Iyengar et al. 2006; Loh et al. 2004).

### 8.3.8 Pleomorphic Adenoma

Pleomorphic adenoma is a very rare neoplasm in the breast, sharing similarities to the adenomyoepithelioma. Cytological features of this tumor are difficult to recognize and may resemble the fibroadenoma (Iyengar et al. 2005). Myxoid and squamous material may be present.

### 8.3.9 Papillary Lesions

FNAC of papillary lesions can mimic the fibroadenoma (Simsir et al. 2003; Michael and

Buschmann 2002). The intraduct papilloma is characterized by epithelial aggregates with broad ruffled branching and scalloped contours, smaller tongue-like projections, and columnar cells (Fig. 8.11). Fibrovascular cores when identified are helpful in corroborating a papillary lesion along with associated foam cells. Myoepithelial cells tend to be fewer than in the fibroadenoma (Michael and Buschmann 2002). Central papillomas are usually solitary and seen subareolarly.

### 8.3.10 Carcinoma

Some breast cancers can be underdiagnosed as fibroadenomas on FNAC. These may occur in young women where there often is a hesitation to make an outright diagnosis of cancer on aspirate smears unless cytologic changes are overt, and in pregnant and lactating women where presence of atypia can be erroneously attributed to physiological alterations (Fig. 8.12). It is prudent to recommend histological confirmation when cytologic atypia is discovered, in order not to overlook cancer (Maygarden et al. 1991).

Carcinomas with osteoclastic giant cells can mimic fibroadenoma on cytology (Jogai et al. 2004). Mucinous carcinoma with the background mucinous material can be difficult to distinguish from myxoid fibroadenoma. Tubular cancer can also be mistaken for fibroadenoma with its low-grade features and presence of angular epithelial groups. Careful scrutiny of isolated or dispersed

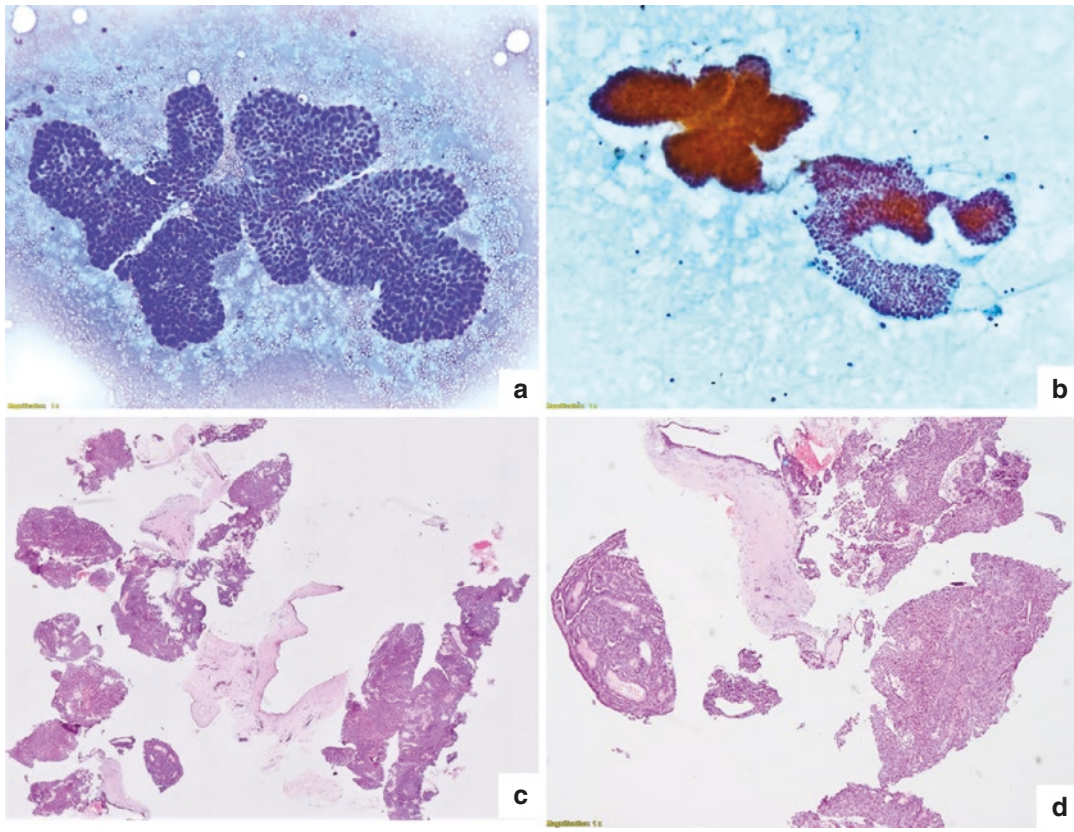


**Fig. 8.11** Papilloma with three-dimensional papillary clusters of ductal cells in a background of blood and macrophages (**a**. MGG; **b**. PAP). H&E stained section showing fragments of a distended duct with freelying fragments of a papilloma (**c, d**)

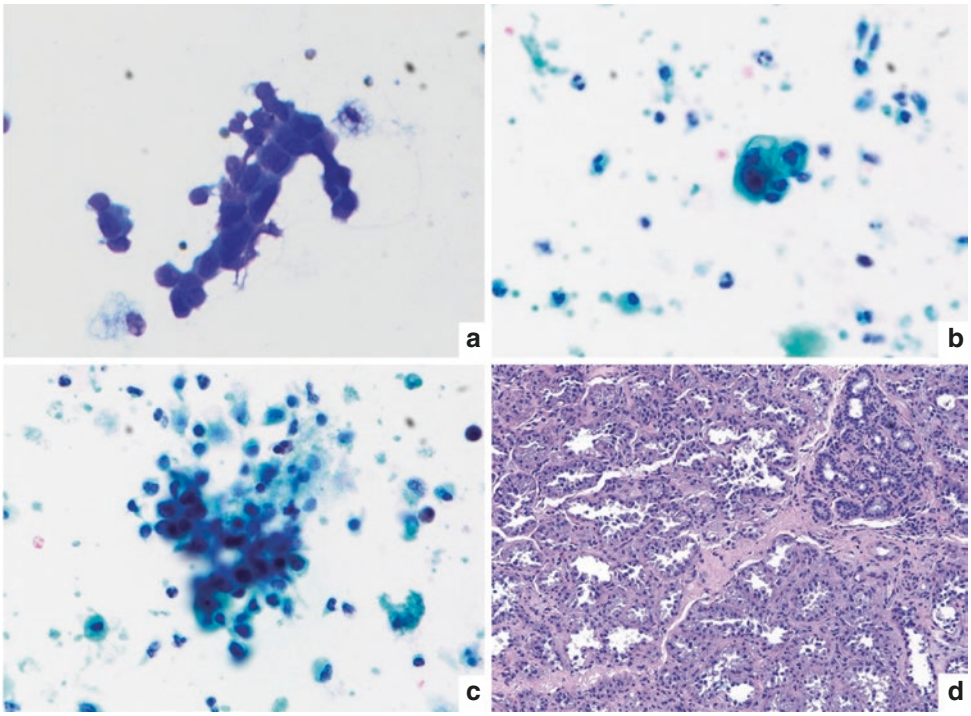


**Fig. 8.12** Lactational adenoma (**a**). A loosely cohesive cluster of enlarged ductal cells with moderate amounts of pale cytoplasm; MGG. (**b**). A three-dimensional cluster of ductal cells with hyperchromatic nuclei, vacuolated cytoplasm, and background cystic proteinaceous debris PAP. (**c**). A loosely cohesive cluster of enlarged ductal cells with moderate amounts of pale cytoplasm and background proteinaceous cystic debris; PAP. (**d**). H&E stain showing a lactational adenoma/change

cells in an aspirate can assist in correct classification of malignant disease (Benoit et al. 1992), in conjunction with the triple approach.

Presence of carcinoma within a fibroadenoma (Fig. 8.13) can lead to potentially confusing cytological appearances, with pleomorphic abnormal cells of the malignant component superimposed on a background population of bland epithelial cells derived from the fibroadenoma (Psarianos et al. 1998).

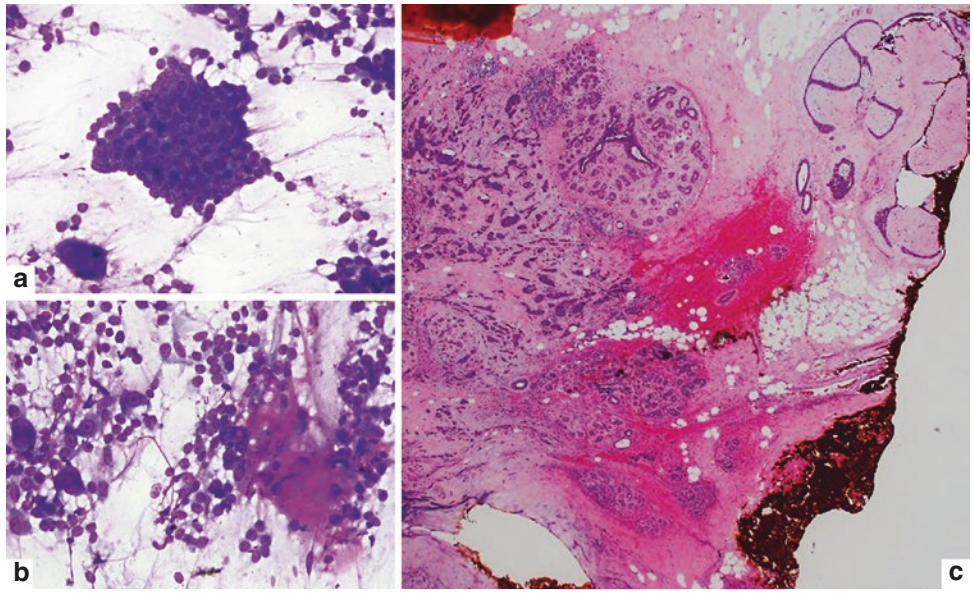


**Fig. 8.13** (**a**, **b**) MGG. Fibroadenoma infiltrated by invasive ductal carcinoma. (**a**). Flat cohesive sheet of ductal cells surrounded by bare nuclei. (**b**). Stromal fragment from the fibroadenoma surrounded by dispersed atypical cells including pleomorphic forms from a carcinoma. (**c**). H&E stain showing an invasive ductal carcinoma infiltrating into a fibroadenoma

## 8.4 Histologic Correlations

Macroscopically circumscribed, encapsulated, and lobulated, the fibroadenoma shows two main histological patterns of intracanalicular and pericanalicular growth which are without clinical significance, apart from the more frequent association of intracanalicular fibroadenomas with MED12 gene mutations which have been discovered to be an early step in the pathogenesis of fibroepithelial neoplasms. The admixture of epithelial and stromal elements gives rise to the cytological appearances of epithelial aggregates within the background of scattered naked nuclei of bipolar myoepithelial and stromal cells. Presence of usual ductal hyperplasia and fibrocystic changes within the fibroadenoma leads to more complex and branched epithelial fragments, histiocytes, columnar cells, and apocrine cells on cytology.

Histological variants include the cellular fibroadenoma which discloses increased stromal cells (Fig. 8.14); the juvenile fibroadenoma which is usually diagnosed in adolescents and are characterized by increased stromal cellularity with usual epithelial hyperplasia and a pericanalicular growth pattern; and the complex fibroadenoma that contains cysts larger than 3 mm, sclerosing adenosis, epithelial calcifications, or papillary apocrine hyperplasia.

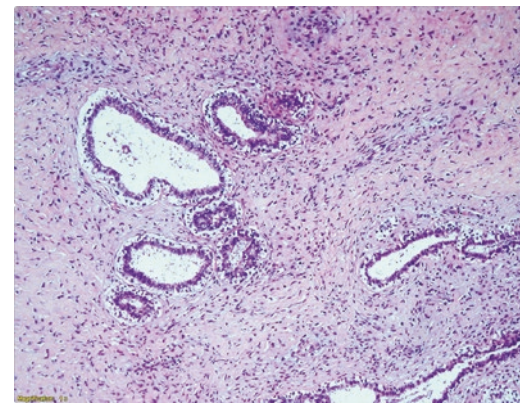

**Fig. 8.14** Cellular fibroadenoma. Cellular stromal component intermixed with epithelial elements

## 8.5 Management

A definitive FNAC diagnosis of fibroadenoma, when concordant with clinicoradiological features, can be observed nonoperatively. In the presence of any doubt or discordance, histological confirmation must be pursued. For some institutions, a large lesional size despite a benign fibroadenomatous cytological conclusion will prompt excision through surgical or mammotome approaches in view of inherent sampling issues and possibility of phyllodes tumor for larger masses. When atypia is observed in an aspirate that is otherwise in keeping with a fibroadenoma, there ought to be a discussion to determine if close surveillance or excision is required. In certain situations when both clinical and radiological opinions are benign and the cytologic atypia is mild and focal, the option for follow-up and later review may be acceptable. However, if atypia is more worrisome or if there is clinicoradiological concern, excision is advised.

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