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Can True Papillary Neoplasms of Breast and Their Mimickers Be Accurately Classified by Cytology?

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BACKGROUND. The cytologic accuracy in assessing malignancy in papillary breast neoplasms (PBNs) is controversial. This is further complicated by overlapping features observed in other breast lesions that produce papillary-like tissue fragments.

METHODS. The authors reviewed 22 fine-needle aspirates (FNAs) from histologically proven papillary neoplasms: papillary carcinoma (PCA; 10 aspirates) and intraductal papilloma (IDP; 12 aspirates). They also reviewed 8 FNAs in which a papillary neoplasm was suggested by cytology but not confirmed by follow-up biopsy: fibroadenoma (6), mucinous carcinoma (1), and cribriform ductal carcinoma in situ (1).

RESULTS. Papillary carcinoma can be distinguished from IDP by the higher cellularity, more complex papillae with thin disorganized fronds, mild to moderate nuclear atypia, and prominent dissociation with many single papillae. Fibrovascular cores (FVCs) were more common in PCA than IDP in which detached fibrous tissue fragments were frequently seen. Atypical IDP exhibited features intermediate between PCA and IDP. Apocrine metaplasia was variably present in IDP, atypical IDP, and fibroadenoma but absent in all carcinomas. Intraductal papilloma can be distinguished from fibroadenoma by their broad ruffled branches, scalloped borders, and tiny tongue-like projections. True papillae were commonly covered by tall columnar cells. Myoepithelial cells were few in IDP but were numerous in fibroadenoma. The epithelial fragments in nonpapillary lesions presented as cellular spheres and/or complex sheets with finger-like projections but lacked FVCs and columnar cells.

CONCLUSIONS. Papillary breast neoplasms can be accurately classified by cytology. Closer evaluation of the tissue fragments architecture and the background can help in separating PBN from their mimics. ***Cancer (Cancer Cytopathol)* 2002;96:92–100.** © *2002 American Cancer Society.*

KEYWORDS: papillary carcinoma, intraductal papilloma, ThinPrep, breast neoplasms.

A papillary neoplasm is defined histologically as one that exhibits an arborescent epithelial proliferation with fibrovascular cores (FVCs) and is attached by a stalk to the wall of a dilated duct. These FVCs vary in thickness and may be very delicate at times. As described in the literature,[1,2] these papillary neoplasms produce thick vascular tissue fragments with finger-like smoothly contoured projections when aspirated. The branching pattern can be either simple or complex. Single detached fronds appear as either irregular cylindrical structures or tightly cohesive cell balls. Despite the distinct cytomorphologic features of papillary breast neoplasms (PBNs) that have been described, the literature suggests that papillary carcinoma (PCA) cannot be separated reliably from intraductal papilloma (IDP) by cytol-

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TABLE 1
Fine-Needle Aspiration Diagnosis of Papillary Carcinoma (10 Cases)

Patient no.	Age (yrs)	Cytologic diagnosis	Histologic diagnosis
1	46	Ductal carcinoma	Noninvasive papillary carcinoma
2	75	Ductal carcinoma	Noninvasive papillary carcinoma
3	90	Suspicious for carcinoma	Noninvasive papillary carcinoma
4	60	Suspicious for carcinoma	Invasive papillary carcinoma
5	69	Papillary neoplasm	Invasive papillary carcinoma
6	68	Proliferative breast disease	Noninvasive papillary carcinoma
7	68	Atypical	Noninvasive papillary carcinoma
8	68	Atypical	Noninvasive papillary carcinoma
9	69	Papillary carcinoma	Invasive papillary carcinoma
10	75	Papillary carcinoma	Invasive papillary carcinoma

ogy.[2] In addition, several other breast lesions such as fibroadenoma may have similar features and may mimic a true PBN, when the above description is applied.[1,3,4]

The purpose of this study is twofold: first, identification of the cytologic features that distinguish PCA from IDP, and second, identification of features that may separate true papillary lesions from their mimickers.

MATERIALS AND METHODS

Patient Selection

We retrospectively reviewed slides from 30 fine-needle aspirates (FNAs) of the breast pooled from the files of the University of Michigan and the University of South Alabama. Histologic follow-up was reviewed in all cases. Twenty-two FNAs were from histologically proven papillary neoplasms: invasive PCA (4), intraductal PCA (6), and IDP (12). We also reviewed 8 FNAs in which a papillary neoplasm was suggested by cytology but not confirmed by follow-up biopsy: fibroadenoma (6), mucinous carcinoma (1), and cribriform ductal carcinoma in situ (1). A summary of the original cytologic diagnoses and the histologic follow-up is presented in Tables 1–3.

Histologic Criteria for Papillary Neoplasms

PCA

The epithelial proliferation usually involves the circumference of the duct wall and is predominantly frond-forming. The papillae characteristically have central FVCs, although they may be inconspicuous, have secondary and tertiary branches, and may exhibit variable patterns such as micropapillary, filiform, cribriform, trabecular, and solid. The epithelial cells are arranged in a disorderly pattern and are crowded. Their nuclei are hyperchromatic and may have a high nuclear to cytoplasmic ratio. Myoepithelial cells are absent. There is multilayering of the epithelium on the papillary fronds and merger of adjacent fronds. Invasive PCA is characterized by extension of the carcinoma into the adjacent stroma.[5,6]

TABLE 2
Fine-Needle Aspiration Diagnosis in Papilloma with and without Atypia (12 Cases)

Patient no.	Age (yrs)	Cytologic diagnosis	Histologic diagnosis
1	63	Fibrocystic changes	Papilloma
2	58	Benign mammary epithelium	Papilloma
3	46	Fibrocystic changes	Papilloma
4	58	Benign mammary epithelium	Papilloma
5	76	Papillary neoplasm, favor papilloma	Papilloma
6	55	Papillary neoplasm, favor papilloma	Papilloma
7	31	Suspicious for papillary carcinoma	Papilloma
8	36	Fibroadenoma	Papilloma
9	52	Fibrocystic changes	Papilloma
10	46	Fibroadenoma	Papilloma
11	79	Suspicious for carcinoma	Papilloma with atypia
12	75	Suspicious for carcinoma	Papilloma with atypia

TABLE 3
Histologic Diagnosis in Needle Aspirates Misclassified as Papillary (8 Cases)

Patient no.	Age (yrs)	Cytologic diagnosis	Histologic diagnosis
1	79	Papillary neoplasm	Mucinous carcinoma
2	54	Papillary neoplasm	Ductal carcinoma in situ
3	24	Papillary neoplasm, favor papilloma	Fibroadenoma
4	41	Papillary neoplasm with atypia	Fibroadenoma with lactational changes
5	34	Papillary neoplasm, favor papilloma	Fibroadenoma
6	17	Papillary neoplasm, favor papilloma	Juvenile fibroadenoma
7	41	Papillary neoplasm, favor papilloma	Fibroadenoma
8	29	Papillary neoplasm, favor papilloma	Fibroadenoma

IDP

The papillary intraductal proliferation consists of orderly epithelial fronds around well defined FVCs. There is little cellular pleomorphism or nuclear hyperchromasia and minimal evidence of multilayering of the epithelium. Myoepithelial cells are readily seen. Apocrine metaplasia is present and sometimes constitutes a major portion of the lesion. The papillary proliferation usually is attached to the wall through a distinct stalk or several stalks; however, the remaining epithelial lining of the duct lacks any proliferative

TABLE 4
Features Evaluated in Cytologic Smears

Primary feature	Secondary feature
Background	Blood
	Calcifications
	Single scattered columnar cells
	Hemosiderin-laden macrophages
	Myoepithelial cells
Cellular features	Cellularity
	Dissociation
	Nuclear atypia
	Nuclear pseudoinclusions
	Cell morphology, e.g., apocrine, columnar
Tissue fragments	Long finger-like branching fragments
	Complex vs. simple branching
	Presence of fibrovascular cores
	Complex fragments, other than papillary
	Cellular balls
	Single detached papillae
	Tiny tongue-like projections

activity, thereby contrasting with the circumferential involvement by PCA. The surrounding breast tissue usually exhibits fibrocystic changes.

IDP with atypia

These are papillary lesions that contain any of the following atypical features in an otherwise benign appearing papilloma: a papillary proliferation that involves a major portion of the duct circumference with some evidence of epithelial multilayering or merger of fronds, focal areas of atypical ductal hyperplasia or severe cytologic atypia, focal areas of carcinoma in situ.[5–7]

FNA

All aspirates were obtained using a 23- or 25-gauge needle attached to a 10-mL plastic syringe. A droplet was deposited on one slide, and smears were prepared by the two-slide pull technique. In all cases, ethanol-fixed and Papanicolaou-stained smears were available; four cases had additional air-dried and Diff-Quik (Baxter Scientific Products, McGraw Park, IL) stained slides (two PCAs, one IDP, and one IDP with atypia [IDPA]).

Smears were evaluated for the following features: background, cellularity, and papillary fragments. Details of the evaluated features are presented in Table 4. Each of these features was given an approximate quantitative value: +3 when present in abundance, +2 when present in moderate amount, and +1 when present in small amount and only detected after search.

RESULTS

Papillary Carcinoma (n = 10)

The average age of the patients was 69 years with a range of 46–90 years (Table 1). The original cytologic diagnosis correctly identified four cases as carcinoma, two as suspicious for carcinoma, and two as atypical. One case was diagnosed as papillary neoplasm without further qualification. One case was completely misinterpreted as benign proliferation (false-negative). On second review, it was noted that the misinterpreted case lacked obvious papillae or cellular atypia. Of all 10 cases, only 3 were recognized originally as papillary in nature. Six patients had intraductal PCA, and three had an additional component of invasive carcinoma (4, 5, 9, and 10). Table 5 summarizes the most significant cytologic features evaluated in these cases. Low-power examination revealed highly cellular smears with significant discohesion. The background was considerably bloody in nine cases. The cellular proliferation was composed of branching papillary fragments, numerous scattered single fronds, few cell balls, and a background of numerous columnar cells singly scattered and in short cords. Frequently the single fronds were close to each other and loosely interconnected by individual single cells. The papillary fragments were generally complex in architecture and variable in shape; some appeared as irregular "geographic sheets," consisting of small aggregated clusters, whereas others were branching fragments with thin filiform fronds and bulbous ends or feather-like fragments with numerous thin branches (Fig. 1A–E). Regardless of their shape, these branching fronds were numerous, crowded, and thin.

The papillae were covered by tall columnar cells that were crowded, arranged disorderly, and exhibited mild to moderate cytologic atypia in the form of high nuclear to cytoplasmic ratio and hyperchromasia. Frequently tiny tongue-like projections with smooth contours and no FVCs were protruding from the papillary fragments. Fibrovascular cores were easily detectable in six cases and were easier to recognize by Diff-Quik stain. These cores were at times obscured by the numerous hanging thin fronds flowing in different directions. Although papillae with thick cores were occasionally present, the overlaying epithelium retained the characteristic complex architecture. A few tight cell balls and oval clusters with smooth well defined borders were also present. Histiocytes were present in nine cases and hemosiderin-laden macrophages (HLMs) were seen in eight of them. Calcifications were detected in only two cases. Myoepithelial cells, apocrine metaplastic cells, and intranuclear cytoplasmic inclusions were absent in all cases. There was no cy-

TABLE 5
Summary of Cytologic Features Evaluated in Papillary Carcinomas

Case no.	Cellularity	Papillae	Complex sheets	Cell balls	Single papillae	Discohesion	Columnar cells	HLM
1	+3	+2	+3	+2	+3	+3	+3	+2
2	+3	+3	+1	+1	+3	+3	+3	+2
3	+3	+1	+3	+1	+4	+4	+1	0
4	+1	+1	0	+1	+2	+2	+2	0
5	+3	+3	+3	+1	+3	+3	+3	+1
6	+3	+1	+2	+1	+3	+2	+3	+1
7	+2	0	+1	+2	+2	+2	+3	+1
8	+3	+1	0	+1	+3	+3	+3	+2
9	+3	+3	+3	+1	+3	+3	+3	+2
10	+3	+2	+3	+1	+3	+3	+3	+1

HLM: hemosiderin-laden macrophages; 0, absent; +1, only detectable after search; +2, present in moderate quantity; +3, present in abundance.

tologic difference between the intraductal and the invasive cases.

Intraductal Papilloma without Atypia ($n = 10$)

The average age of patients was 51 years with a range of 31–76 years (Table 2). The original cytologic diagnosis correctly identified 9 of 10 cases as benign (papilloma, 2 cases; fibrocystic changes, 5 cases, and fibroadenoma, 2 cases). One case was falsely diagnosed as suspicious for carcinoma. Review of this case revealed cytologic atypia and some cellular dissociation within the apocrine population accounting for the suspicious diagnosis. Table 6 summarizes the most significant cytologic features evaluated in this group. By low-power examination cellularity was widely variable among this group. Generally these patients had low to moderate cellularity. Histiocytes were present in nine cases; however, HLM were detected in only two cases. Seven cases had a very bloody background. The epithelial proliferation consisted primarily of broad and complex branching sheets. Within these sheets, the epithelium appeared as separate compartments flowing in different directions and formed tiny tongue-like projections at the periphery. The branches were thick and frequently much broader toward their periphery than their branching point with ruffled and scalloped borders (Fig. 2 A,B). Fibrovascular cores were easily detected in only three cases in which they appeared as thick portions of fibrous tissue situated at the periphery of the branching sheets and only transected few tissue fragments. Separate fragments of detached fibrous tissue, sometimes with evidence of branching and interrupted covering epithelium were seen in the background of nine cases (Fig. 2C). The columnar cells were obvious in only five cases and were mainly confined to the complex sheets with few single cells in the background. There was a low number of myoepithelial cells in eight cases and a moderate number of myoepithelial cells in two cases. Apocrine cells were present in moderate to high numbers in four FNAs and low numbers in one FNA. Mild discohesion was present in four cases. When closely examined, the discohesive cells were found to be of apocrine metaplastic origin in three cases. Atypia was only detected in five cases and were confined to apocrine metaplastic cells in four. Two of the patients had predominantly apocrine IDP and presented with a moderate amount of cytologic atypia and discohesion. Frequently, these highly atypical apocrine cells were contained within completely normal apocrine sheets. Cell balls were present in low to moderate numbers in 10 cases. There were very few single detached thin fronds. Calcifications were present in three cases. Intranuclear inclusions were absent.

Intraductal Papilloma with Atypia ($n = 2$)

The average age of patients was 77 years with a range of 75–79 years (Table 2). Both of these cases originally were diagnosed as suspicious for carcinoma. Table 6 includes a summary of the most significant cytologic features detected in this group. Low-power examination revealed highly cellular smears with low to moderate discohesion. The epithelial proliferation was composed of branching papillary fragments with features overlapping with those of IDP and PCA. Both feather-like tissue fragments with readily detected FVCs and large complex fragments with thick branches were present. Detached fibrous tissue was also seen in the background. Although the feather-like fragments were superficially similar in appearance to those of PCA at low magnification, they had some dissimilarity when closely examined. In IDPA, these

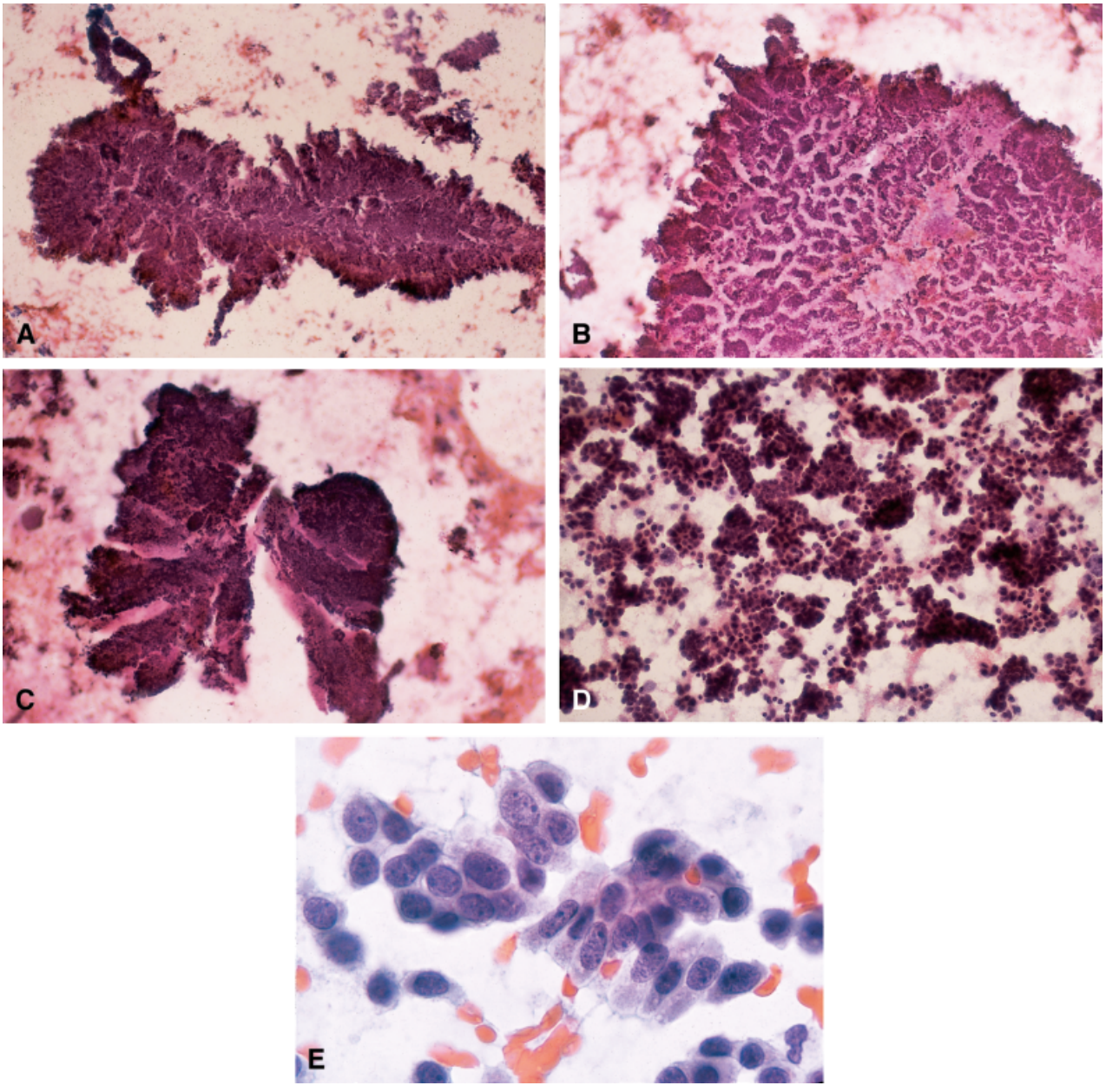

FIGURE 1. (A) Papillary carcinoma. Feather-like papilla with numerous thin haphazardly arranged fronds and a delicate fibrovascular core. Papanicolaou stain, original magnification ×100. (B) Papillary carcinoma. A highly complex papilla consisting of numerous small clusters aggregated around a well defined fibrovascular core. Papanicolaou stain, original magnification ×100. (C) Papillary carcinoma. Filiform fronds with bulbous ends in a complex papilla. Papanicolaou stain, original magnification ×100. (D) Papillary carcinoma. Numerous detached single fronds in a bloody background. Papanicolaou stain, original magnification ×100. (E) Papillary carcinoma. Cellular discohesion and columnar cells with mild cytologic atypia. Papanicolaou test, original magnification ×400.

fragments were simpler in configuration with thicker and more rigid branches (Fig. 3). The covering epithelium was tall columnar and orderly in arrangement with no cytologic atypia. Tiny tongue-like projections were also seen in this group. A moderate number of single detached fronds and tall columnar cells singly scattered or forming short cords were present in the background. Apocrine metaplastic cells were present in large numbers in one (Case 11) and in low numbers in the other (Case 12). Histiocytes were present in both cases, but HLMs were seen in only one. Calcifications were present in one case (Case 12) only. Myoepithelial cells were very difficult to find and intranuclear inclusions were absent.

TABLE 6
Cytologic Features Evaluated in Intraductal Papilloma

Case no.	Cellularity	Papillae	Complex sheets	Cell balls	Single papillae	Discohesion	Columnar cells	HLM
1	+3	+2	+1	+1	+1	0	+1	+1
2	+1	+1	+1	+1	0	0	0	+1
3	+2	+1	0	+1	+1	0	0	0
4	+1	0	0	+1	0	0	0	0
5	+3	+2	+3	+1	+1	+1	+2	0
6	+3	0	+3	+2	0	0	0	0
7	+3	+1	+3	0	0	0	+3	0
8	+2	0	+2	0	+1	0	0	0
9	+2	+2	+2	+1	0	0	+1	0
10	+3	+1	+3	0	+1	+1	+3	0
11[a]	+3	+3	+3	+3	+2	+1	+3	0
12[a]	+3	+2	+1	+2	+2	+2	+2	+1

HLM: hemosiderin-laden macrophage; 0, absent; +1, only detectable after search; +2, present in moderate quantity; +3, present in abundance.
[a] Papilloma with atypia.

Fibroadenoma ($n = 6$)

The average age of patients was 33 years, with a range of 17–41 years. The cellularity was high in half the cases and moderate in the other half. Bloody background was moderate in one and low in five cases. The epithelial component was composed of large monolayer and folded sheets intermixed with branching sheets (Fig. 4). The branches were wide with rounded and smoothly contoured ends (mitten-like) or long cylindrical finger-like projections (staghorns) and lacked FVCs. Cell balls were numerous in one case. Tiny tongue-like projections similar to those seen in papillary neoplasms were present in very few clusters of one highly cellular fibroadenoma. Apocrine metaplasia was prominent in one case, low in one case, and absent in four cases. Columnar cells, histiocytes, cellular discohesion, and cytoplasmic vacuoles were seen from a single postpartum patient with associated lactational changes. Myoepithelial cells were numerous in two cases and moderate in three cases. In the case with lactational changes, the myoepithelial cells were indistinguishable from the stripped nuclei in the background. Calcifications and histiocytes were present in one case each.

Ductal carcinoma in situ ($n = 1$)

The patient was 54 years old. The smears were highly cellular and bloody. The epithelial component was composed of geographic sheets with a nonspecific appearance. Some sheets presented as branching fragments mimicking papillary fragments but lacked FVCs. The branches appeared as curved arches crossing each other (Fig. 5). On histologic correlation, these fragments corresponded to ductal centers involved with cribriform carcinoma in situ. Cell balls were absent. Cellular discohesion was moderate, and few singly scattered cells with intact cytoplasm and nuclear atypia were present in the background among few myoepithelial cells. Apocrine metaplasia, histiocytes, and intranuclear inclusions were absent.

Mucinous carcinoma ($n = 1$)

The patient was 79 years old. The smears were moderate in cellularity and consisted predominantly of cell balls with slightly irregular contours and minimal cytologic atypia. The background mucin was indistinct by the Papanicolaou stain and initially was misinterpreted as hemolyzed blood. Except for few histiocytes, all other features examined were absent.

DISCUSSION

Benign and malignant papillary neoplasms of the breast are characterized by their arborescent pattern of growth. The extent of circumferential involvement by the epithelial proliferation and the degree of branching and complexity of their papillae, along with the thickness of the FVCs within their fronds, help to distinguish an IDP from PCA in histologic sections. Several investigators previously have described the cytologic features of these neoplasms. The presence of branching fragments with columnar cell lining is characteristic. Although nuclear inclusions and psammoma bodies are particularly helpful in diagnosing PCA of the thyroid, they have no significance in the diagnosis of PBN. All previous reports agree that PCA yields highly cellular smears with abundant single cells and papillary clusters with or without FVCs.[1–4,7–11] However, opinions differ on the degree of nuclear atypia.

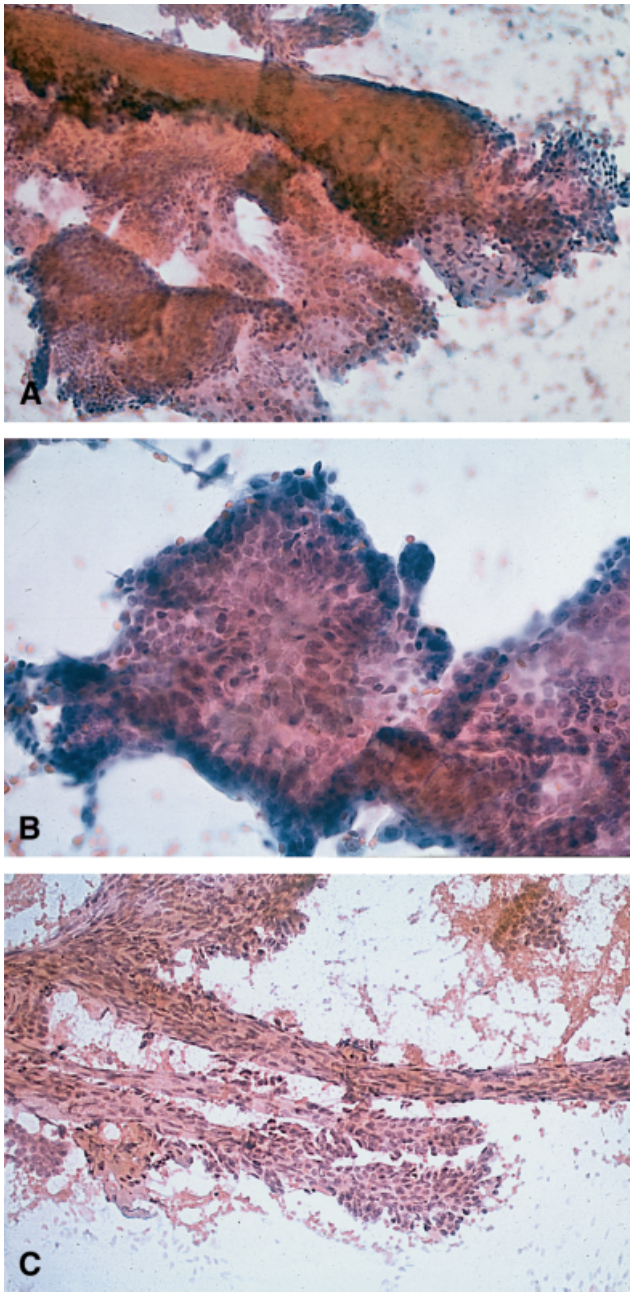

FIGURE 2. (A) Intraductal papilloma. Large branching tissue fragment. Notice the broad ruffled fronds thrown in different directions. Papanicolaou stain, original magnification ×200. (B) Intraductal papilloma. Small tongue-like projections extending from the surface of a papillary fragment. Papanicolaou stain, original magnification ×200. (C) Intraductal papilloma. Fibrous tissue fragments with interrupted covering epithelium, probably representing detached portions of thick fibrovascular cores. Papanicolaou stain, original magnification ×200.

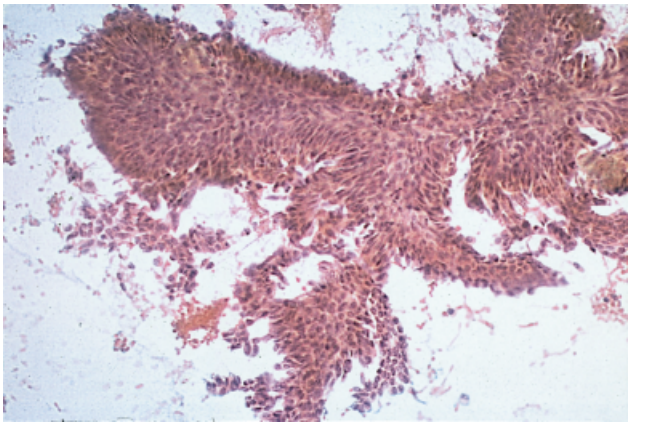

FIGURE 3. Intraductal papilloma with atypia. Feather-like papilla with thick rigid branches contrary to those seen in Figure 1A. Papanicolaou stain, original magnification ×200.

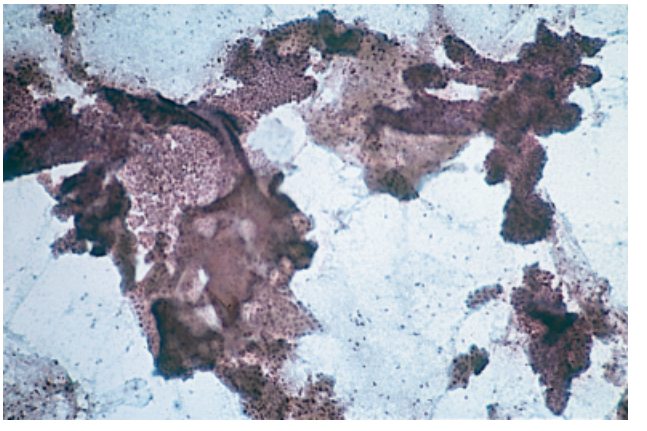

FIGURE 4. Fibroadenoma. Large monolayer sheets and numerous cylindrical branches with rounded smooth borders (staghorns). Papanicolaou stain, original magnification ×100.

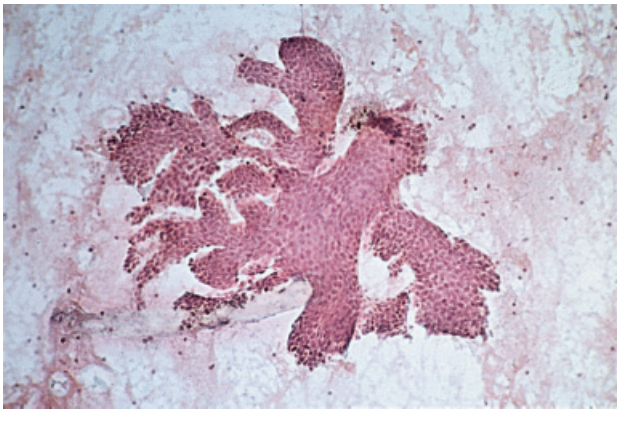

FIGURE 5. Cribriform carcinoma in situ. A complex tissue fragment superficially resembles branching papillae. Notice the difference in configuration with intercepting arches and lack of fibrovascular cores. Papanicolaou stain, original magnification ×200.

TABLE 7
Comparison of Different Breast Papillary Neoplasms

Criteria	IDP	IDPA	PCa
Cellularity	Low to moderate	Moderate to high	High
Cell population	Polymorphous	Polymorphous	Monomorphous
Papillary fragments	Thick branches broader at the periphery with ruffled and scalloped contours	Simple rigid branching, fronds are relatively longer and thinner than IDP	Very complex branching with numerous thin fronds
Discohesion	Minimal	Moderate	Marked
Columnar cells	Orderly arranged	Orderly arranged in most fragments	Crowded and disorderly arranged
Fibrovascular cores within epithelial fragments	Occasionally thick and eccentrically placed	Thin or thick centrally placed	Mostly thin and centrally placed
Detached fibrous tissue	Frequently present	Present	Rare
Single detached papillae	Absent	Moderate	Abundant
Nuclear chromatin	Vesicular	Variable	Mild to moderate hyperchromasia

IDP: intraductal papilloma; IDPA: intraductal papilloma with atypia; PCa: papillary carcinoma.

Although Kline and Kanna[3] reported nuclear irregularity only after diligent search, Naran et al.[4] found a moderate degree of anisonucleosis in their 11 cases and nuclear irregularity in one-third of them. Jeffrey and Ljung[2] reported slight nuclear atypia in five of their cases and moderate to severe atypia in the remaining two. Flow cytometric analysis of eight cases by Corkill et al. revealed aneuploidy in seven.[8]

Based on our findings, PCA and IDP with or without atypia can be accurately classified on FNAs provided that the sample is optimal. Criteria helpful in accurately classifying these PBNs are summarized in Table 7. Although smears of IDP were low to moderate in cellularity and frequently diluted with blood, those of PCA were highly cellular. Considerable discohesion, characterized by numerous detached fronds and single columnar cells, was only observed in PCA and IDPA. In addition, the papillary fragments in PCA were morphologically different from those of IDP. They exhibited a higher degree of complexity, numerous thin fronds flowing in different directions and a disordered arrangement of the lining epithelium. Slight to moderate nuclear atypia in the form of a high nuclear to cytoplasmic ratio and nuclear hyperchromasia was noted in all cases. However, irregularity of nuclear contour was seen only after a meticulous search.

The presence of FVCs and their appearance are significantly different in PCA and IDP. Because the FVCs are thicker in IDP, they tended to be incompletely aspirated and appeared either as a small thick fibrous portion at the periphery of the branching fragments (3 of 10) or separately detached (9 of 10). In contrast, 6 of 10 PCAs contained well defined thin FVCs transecting the branching fragments. Older age and the presence of HLM were two criteria that better correlated with PCA but did not seem reliable in separating it from IDP. Although the average age was 69 years for PCA versus 51 years for IDP, there was a significant overlap in the age range (46–90 vs. 31–76). Similarly, whereas the presence HLM was more common in PCA (8 of 11), they were also present in 2 of 12 IDPs.

Atypical IDP account for particular difficulty in differential diagnosis. Jeffrey and Ljung,[2] reported high cellularity, complex papillae, single columnar cells, and slight to moderate nuclear atypia in half of their cases, which resulted in their misinterpretation as carcinomas. Our two cases of IDPA presented with similar features; however, on close examination there were subtle differences and findings intermediate between IDP and PCA. Features that separate them from PCA included detached fibrous fragments that correspond to thick FVCs, simple branching papillae rather than the complex thin fronds, and a polymorphous cell population consisting of mammary epithelium and apocrine metaplasia. Cellular discohesion and numerous single detached fronds identify them as atypical.

Although fibroadenoma is histologically distinct from IDP, the two lesions can easily be confused on cytologic preparations because of several overlapping features. Both lesions produce cohesive cell balls and three-dimensional branching fragments with finger-like projections occupying multiple planes in the same field. Myoepithelial cells may be present in variable numbers in both lesions and cellular fibromyxoid fragments from fibroadenoma may be confused with the detached fibrous fragments of IDP. However, the branching fragments of fibroadenoma are morphologically different; they are either in the form of long slender cylinders that resemble staghorns or branches with smooth, rounded, and broad tips that resemble

dumbbells or mittens. Characteristically, these branches lack FVCs and columnar cells. The monolayer and folded sheets intermixed with the branching fragments and a background rich with myoepithelial cells are other clues for fibroadenoma. In contrast, the branching fronds of IDP are never in the form of long cylinders (staghorns). They tend to be much broader at their tips than their branching point and frequently have ruffled edges rather than those well defined rounded borders seen in fibroadenoma. Tiny tongue-like projections were only seen in rare fragments from one fibroadenoma but were noted in all our papillary neoplasms, a finding that potentially could help separating true papillary fragments from their mimics. Columnar cell lining was exclusively seen in PBNs and appeared highly sensitive but not as specific because it was only seen in 5 of 12 IDPs.

The presence of cell balls although highly suggestive are not specific for papillary lesions as they may be seen in other breast lesions such as fibroadenoma and mucinous carcinoma. Similarly, branching cell aggregates may be seen in a variety of breast lesions, and the diagnosis of a papillary neoplasm should be based on the characteristic complex branching fragments covered by columnar cells as described above.

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