Cytological Findings in Benign Phyllodes Tumors

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Keywords
Breast · Phyllodes tumor · Fibroadenoma · Cytology

Abstract

**Objective:** Phyllodes tumors are fibroepithelial breast lesions with many cytological and histopathological similarities to fibroadenomas. The aim of this study was to investigate cytological findings in benign phyllodes tumors.

**Study Design:** Seventy-six histologically proven cases of benign phyllodes tumors were selected from 1982 to 2017. Cytological criteria, including cellularity, the number and shape of epithelial clusters, the shape and number of stromal fragments, and the presence of atypia, were evaluated.

**Results:** Cytological slides were hypercellular and showed dimorphic populations of cells. The epithelial clusters were moderate in amount and had a bonsai-like configuration. The stromal fragments consisted of oval-to-spindle shaped cells with preservation of the cytoplasm. Some popcorn-like cells and intranuclear inclusions in stromal cells and deposition of pinkish and amorphous material at the border of the stromal fragments were also noted in the stromal cells.

**Conclusion:** Stromal hypercellularity and large amounts of stromal fragments, the presence of bonsai-like epithelial clusters, and deposition of amorphous pinkish material at the border of the stromal fragments, as well as newly observed findings including the presence of intranuclear inclusions and popcorn-like nuclei in the stromal cells, can aid in the diagnosis of phyllodes tumors.

Introduction

Phyllodes tumors are a variant of breast fibroepithelial lesions with the potential tendency toward recurrence or, rarely, metastasis. Differentiation from their closely related mimicker “fibroadenoma” (another benign breast fibroepithelial lesion) is very important, and thus it is crucial to correctly diagnose fibroepithelial lesions as the diagnosis will dictate further treatment [1–6]. Fine-needle aspiration cytology is a simple, safe, and accurate method for the evaluation of breast lesions. The cytologic criteria for differentiation of fibroadenomas from phyllodes tumors has been described previously, but some of them are subjective and overlap between the 2 groups. This cytologic confusion is greater in differential diagnosis of benign phyllodes tumors and fibroadenomas. In this study, we examined cytological slides of benign phyllodes tumor to establish useful cytologic criteria.

This study was presented at the 19th International Congress of Cytology in Tokyo, Japan, in 2016.
Materials and Methods

A retrospective search of our cytology wards affiliated with the Shiraz University of Medical Sciences (Shiraz, Iran) during 1982–2017 revealed 76 cases of benign phyllodes tumors proven on histopathology. Clinically, all of them were suspected to be fibroadenomas. Tumor sizes ranged from 3 to 12 cm and patient ages ranged from 12 to 36 years. Cytology slides studied using Wright-Giemsa, Papanicolaou, and H&E stains were reviewed for different cytological criteria, including cellularity, the number and shape of epithelial clusters, the shape and number of stromal fragments, and the presence of atypia.

Results

Cytological slides were hypercellular (72 cases, 94%), showing a dimorphic population of cells, i.e., epithelial and stromal fragments. The epithelial clusters were moderate in amount (2–5 clusters per slide) and had a bonsai-like configuration (Fig. 1). The stromal fragments consisted of cells with an oval-to-spindle shape (65 cases, 85%) with preservation of the cytoplasm in some of them (39 cases, 51%). Some popcorn-like cells (4 cases, 5%) and intranuclear inclusions (10 cases, 13%) were also noted in stromal cells (Fig. 2). An interesting finding was the deposition of pinkish and amorphous material at the border of stromal fragments (25 cases, 32%) (Fig. 3). None of the cases showed atypia. Mitoses, bipolar naked nuclei, foamy macrophages, and apocrine cells were rarely noticed. Table 1 summarizes the cytological findings in our cases, and Table 2 summarizes the cytological differences between phyllodes tumors, fibroadenomas, and breast carcinomas.

Discussion

Fibroepithelial lesions of the breast consist of a large heterogeneous group of breast tumors with different outcomes ranging from completely benign (fibroadenoma), treated by enucleation, to more aggressive lesions with a tendency toward local recurrence or metastasis (phyllodes tumor), which require wide excision. Fine-needle aspiration cytology can be regarded as a simple and accurate method for the primary evaluation of breast masses. In this study, we evaluated different cytology criteria that are useful for distinguishing between these 2 lesions.

We observed cellular smears composed of epithelial and stromal clusters. The epithelial clusters were moderate in amount. They formed large bonsai-like structures in contrast with the smaller, staghorn clusters of fibroadenomas. Although Shabalova et al. [7] showed that the epithelial clusters of phyllodes tumors have different patterns, including branched, staghorn-like, honeycomb arrangements, strips, and small groups, Mitra and Dey [8] stated that the epithelial component of phyllodes is broad and rounded; also, Giri [2] showed that the epithelial clusters of phyllodes tumors are elongated and wavy [2], but bonsai-like clusters have not been reported previously. According to previous studies, epithelial clusters are more abundant in fibroadenomas with a higher epithelial-to-stromal ratio [1–5].

In our study, in concordance with other studies [3, 5], the smears showed large stromal fragments composed of cells with an oval-to-spindle shape, most of which showed preservation of the cytoplasm in contrast to bipolar naked nuclei which are prominent in fibroadenomas. It has been stated that these fibroblast-like cells may form...
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**Table 1.** Frequency of different cytological findings in benign phyllodes tumors

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Finding</th>
<th>Frequency, n (%)</th>
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<tbody>
<tr>
<td>Background</td>
<td>Pinkish amorphous material</td>
<td>25 (32)</td>
</tr>
<tr>
<td>Epithelial</td>
<td>Bonsai-like cluster</td>
<td>60 (78)</td>
</tr>
<tr>
<td>architecture</td>
<td>Preserved</td>
<td>39 (51)</td>
</tr>
<tr>
<td>Stromal cell cytoplasm</td>
<td>Atypia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Stromal cell nuclei</td>
<td>Intranuclear inclusions</td>
<td>10 (13)</td>
</tr>
<tr>
<td></td>
<td>Popcorn-like nuclei</td>
<td>4 (5)</td>
</tr>
<tr>
<td></td>
<td>Spindle-to-oval shape</td>
<td>65 (85)</td>
</tr>
<tr>
<td>Cellularity</td>
<td>Scant</td>
<td>2 (6)</td>
</tr>
<tr>
<td></td>
<td>Moderate to hypercellular</td>
<td>74 (94)</td>
</tr>
</tbody>
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**Fig. 2.** a, b Stromal cells of a phyllodes tumor showing preservation of the cytoplasm. Papanicolaou stain. ×400. c Intranuclear inclusions in a stromal cell (popcorn-like cell). H&E. ×1,000.

**Fig. 3.** Epithelial cluster and stromal fragments showing amorphous material. Papanicolaou stain. ×400.
monolayer pavements [4, 7]. We also observed deposition of pinkish and amorphous material at the border of the stromal and epithelial fragments. Previous studies have demonstrated that the size and cellularity of stromal fragments as well as the presence of atypia in stromal cells is found more frequently in phyllodes tumors, showing well-defined borders compared to fibroadenomas [1–5]. It has been suggested that the degree of background cellularity, the composition of these cells, and the epithelium-to-stroma ratio may be useful features for differentiation [1].

Strands of myxoid material have been noted in some cases of phyllodes tumors [5–7]. Although some authors believe that hypocellular and myxoid stromal fragments are more prominent in fibroadenomas, others have stated that fibromyxoid and hyalinized stromal fragments are seen in both tumors [4].

Intranuclear pseudoinclusions have been observed in stromal cells of other breast lesions such as myofibroblastosomas and adenomyoepitheliomas, but their presence in the stromal cells of phyllodes tumors has not been reported previously [9, 10]. However, this finding has been reported in epithelial cells of proliferative breast disorders and some types of breast carcinoma [11]. We also observed popcorn-like nuclei in the stromal fragments of phyllodes tumors. This finding has been previously reported in the aforementioned cells, especially in histologic preparations [12].

**Conclusion**

Besides some previously mentioned cytological findings favoring phyllodes tumors including stromal hypercellularity and a large amount of stromal fragments, the presence of bonsai-like epithelial clusters, deposition of amorphous pinkish material at the border of stromal fragments, and new findings including the presence of intranuclear inclusions and popcorn-like nuclei in stromal cells can aid in the diagnosis of phyllodes tumors.

**Acknowledgement**

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**Disclosure Statement**

The authors have nothing to disclose.
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References


