Introduction

Papillary breast lesions present infrequent but important diagnostic challenges. This report summarizes our experience with certain unusual findings of papillary breast lesions that may present differential diagnostic difficulties.

Our experience with 12 papillary breast lesions included eight intraductal papillomas, three primary papillary carcinomas, and one metastatic papillary ovarian carcinoma. Five of the eight intraductal papillomas displayed diagnostic findings including tridimensional papillary fragments of ductal cells with distended cytoplasmic vacuoles and dense scalloped cytoplasm. Three intraductal papillomas displayed cohesive fragments containing epithelial cells surrounding metachromatic, globoid, and cylindrical structures that were bright red following Diff-Quik staining and pale blue following Papanicolaou staining. Such unusual findings may raise the differential diagnoses of adenoid cystic carcinoma and collagenous spherulosis. However, the metachromatic material of intraductal papilloma represents type-I collagen-rich stroma of hyalinized fibrovascular stalks, while the material of adenoid cystic carcinoma and collagenous spherulosis represents type-IV collagen. Two of the three primary papillary carcinomas displayed cytologic findings similar to those of intraductal papillomas except for increased anisonucleosis and cell dyshesion, while the third displayed innumerable psammoma bodies similar to the metastatic ovarian carcinoma.

Fine needle aspiration (FNA) cytology of benign and malignant papillary breast lesions has been widely recorded in the literature. Similarly, the difficulty in differentiating benign from malignant tumors as well as primary from metastatic papillary tumors, especially in the presence of associated unusual features, has also been noted. Some of the unusual features associated with such papillary lesions that we have encountered in our series of breast aspirates are presented.

Materials and Methods

We reviewed the FNA cytology of 12 papillary breast lesions (0.6% of breast aspirates) that were received during a six-year period at the Pathology Service at our center. All patients clinically presented with palpable breast masses. The mean age of these patients was 59.6 with a range of 37 to 74 years. The FNA biopsies were performed with a 21-gauge, 1-1/2-inch-long butterfly needle apparatus connected to a 20-cc syringe under vacuum. Papanicolaou stain on alcohol-fixed smears and Diff-Quik stain on air-dried smears were prepared from the aspirated material in all cases. Cytospins were prepared in those cases that yielded cyst fluid. Cell block material from three cases of intraductal papillomas (cases 2, 7, and 8) were stained with trichrome and reticulin cytochemical stains as well as immunocytochemical stains using the peroxidase-antiperoxidase technique with monoclonal antibodies against type-IV collagen, S-100, and muscle-specific antigen. One aspirate (case 9) was fixed in 2.5% gluteraldehyde and processed for ultrastructural evaluation.

The 12 cases included eight intraductal papillomas, three primary papillary carcinomas, and one metastatic papillary ovarian carcinoma. Nine cytologic diagnoses were confirmed on subsequent excisional biopsy or mastectomy at our institution.

Results

The clinical features, cytologic findings, and histologic findings of all cases are summarized in Table 1. The cytologic features of five of the eight intraductal papillomas were similar and included (1) three-dimensional papillary and tight cohesive fragments of uniform epithelial cells, occasionally with traversing fibrovascular stroma, (2) some fragments with scalloped...
outline, peripheral flattened nuclei, and distended cytoplasmic vacuoles, and (3) foam cells, hemosiderin-laden macrophages, apocrine cells, occasional spindle-shaped stromal cells, and dirty proteinaceous background (Figs 1A-B). Three cases of intraductal papilloma (cases 2, 7, and 8) were cellular and showed unusual cytologic features consisting of large, cohesive fragments of epithelial cells surrounding numerous metachromatic, globoid, and cylindrical structures. These structures were bright red after Diff-Quik staining and pale blue after Papanicolaou staining. They contained occasional stromal cells (Figs 2A-B).

Case 8 showed numerous isolated cells with a focal nuclear atypia, which is a potential pitfall in the diagnosis of intraductal papillomas. However, benign background cells such as apocrine cells and foam cells were present. All three cases were confirmed by subsequent histology. The results of cytochemical and immunocytochemical reactions for intraductal papillomas are summarized in Table 2.

The cytologic features of all three cases of primary papillary carcinoma (cases 9, 10, and 11) were similar to those of intraductal papilloma including three-dimensional papillary clusters. However, there was a distinct increase in cellularity with more frequent single and mild to moderately atypical epithelial cells (Figs 3A-B). Scattered tall, columnar cells and naked, enlarged atypical nuclei were also noted. These three cases showed no benign changes, eg, apocrine metaplasia. Case 10 displayed numerous psammoma bodies associated with atypical epithelial cells (Figs 4A-B). This unusual feature resembled a metastatic papillary serous adenocarcinoma of the ovary (case 12). In the latter case, cytology revealed numerous papillary fragments lined by cells that contained distended, clear cytoplasmic vacuoles and associated psammoma bodies (Figs 5A-B). Case 10, who also presented with a benign ovarian cyst, received ultrastructural confirmation for breast primary revealing cytoplasmic secretory granules (Fig 4C) and underwent mastectomy.
Discussion

The presence of metachromatic, globoid, and cylindrical structures surrounding epithelial cells in large cohesive fragments in intraductal papilloma (cases 2, 7, and 8) may raise the differential diagnoses of adenoid cystic carcinoma and collagenous spherulosis. Adenoid cystic carcinoma is a rare malignant tumor of the breast that accounts for less than 1% of all breast carcinomas. FNA cytology of this lesion reveals metachromatic, globoid, and cylindrical acellular material surrounded by neoplastic, uniform basaloid cells (Figs 6A–B). Collagenous spherulosis is a distinctive entity that usually encompasses or is adjacent to fibrocystic changes. Collagenous spherulosis is composed of hyperplastic lobules containing well-circumscribed, acellular eosinophilic spherules of 20 to 100 µm in diameter (Fig 7A). As for adenoid cystic carcinoma, the globoid structures of collagenous spherulosis represented type-IV collagen (Table 2) and reduplicated basal lamina. In addition, amorphous material with thick fibrils showing periodic banding was noted within the spherules of collagenous spherulosis (Fig 7B). These findings are consistent with several reports. In contrast, the metachromatic, globoid, and cylindrical structures of intraductal papilloma (cases 2, 7, and 8) represent type-I collagen-rich stroma of hyalinized fibrovascular stalks (Table 2). Clinical features also may be helpful in distinguishing these three lesions since collagenous spherulosis almost always is an incidental microscopic finding, while adenoid cystic carcinoma and intraductal papilloma may present as palpable masses.

Numerous psammoma bodies were unusually observed in one case of primary papillary carcinoma (case 10) resembling a metastatic ovarian carcinoma. To our knowledge, psammoma bodies have not been reported in the FNA cytology literature with either benign or malignant primary papillary breast tumors. The presence of numerous psammoma bodies should help to detect this lesion by mammography, as in our case.

Extramammary neoplasms metastatic to the breast are rare (0.4% to 2.0% of all breast carcinomas). Most of these cases do not cause diagnostic problems due to the presence of cytologic features unusual for breast primary and a previous history of metastatic disease. However, gross and microscopic features may be similar to both primary and metastatic papillary neoplasms, as in case 12 (Figs 4A-B and 5A-B), and clinical history and ultrastructural studies (when secretory milk granules are present) may be most contributory. Our patient, who developed a hard, well-circumscribed mass, had a known history of stage IV recurrent ovarian papillary serous adenocarcinoma.
Conclusions

Familiarity with associated unusual findings in papillary breast lesions along with the knowledge of clinical history, the judicious use of immunocytochemical tools, and the selective use of excisional biopsy are mandatory for the appropriate diagnosis and management of papillary breast lesions.

References