Cytodiagnosis of papillary carcinoma of the male breast: Report of a case with histological correlation

ABSTRACT
Papillary lesions of the breast pose great diagnostic challenges on fine needle aspiration cytology (FNAC) due to overlapping features between benign and malignant entities. Preoperative cytodiagnosis is difficult. We present a case of a 52-year-old male who presented with a progressively increasing firm swelling in the left breast for 3 years. The nipple was eroded with ulceration and bleeding. Ultrasonography (USG) revealed a mass measuring 2.9 cm × 1.5 cm in the left breast. FNAC smears were hypercellular with ductal cells arranged in papillae and glandular clusters. At places, the cells had irregular nuclear membrane, prominent nucleoli, fine chromatin, scanty-to-moderate cytoplasm, and high nuclear-cytoplasmic ratio with pleomorphism. Histopathology of the excised swelling was consistent with intracystic papillary carcinoma (IPC) supported with immunohistochemistry markers. The case is being presented due to its rarity.

Key words: Cytodiagnosis; intracystic; male breast; papillary carcinoma

Introduction
Breast carcinoma constitutes less than 1% of all male cancers.[1,2] Mammary papillary lesions pose diagnostic challenges on FNAC due to overlapping features of benign and malignant entities. Intracystic papillary carcinoma (IPC) is rare and characterized by a low-grade malignancy.

Case Report
A 52-year-old male presented with chief complaints of swelling in the left breast for 3 years. The swelling was sudden in onset and progressively increasing from the size of a peanut to its present size of a lemon. There was associated on and off pain and bloody discharge from it. No history of fever, loss of appetite, or drug allergy was given. There was no significant past history. On examination, there was a subareolar swelling measuring 3 cm in diameter, which was nontender. The nipple was ulcerated and bleeding. There was no lymphadenopathy or any systemic complaints. A provisional clinical diagnosis of the male breast carcinoma was made. Ultrasonography (USG) showed small ill-defined homogenous lesion measuring 2.9 cm × 1.5 cm.

FNAC from the swelling showed hypercellular smears with ductal epithelial cells arranged in papillae and glandular clusters [Figure 1a]. At many places, cells had irregular nuclear membrane, prominent nucleoli, fine chromatin, scanty-to-moderate cytoplasm and high nuclear-cytoplasmic ratio. Pleomorphism was evident. The background showed abundant foamy macrophages, few naked bipolar nuclei,

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and necrotic debris [Figure 1b]. A cytodiagnosis of atypical ductal cells with suspicion of malignancy was given. Complete excision of the mass was done. Histopathology of the excised tissue showed well-circumscribed tumor nodule beneath the ulcerated skin. The cells were arranged in a papillary pattern within a cystic space, with a central true fibrovascular core [Figure 1c]. The tumor cells showed multilayering, loss of polarity, mild pleomorphism, and nuclear hyperchromasia [Figure 1d]. Few mitotic figures were noted. Histopathology report was IPC of the left breast. Immunohistochemistry showed positivity for progesterone receptor (PR) and Her2neu; negativity for estrogen receptor (ER) and S-100 markers. Ki-67 showed a low proliferative index [Figure 2a-e]. Systemic examination, chest X-ray, ultrasound liver, and bone scans did not show any evidence of metastases.

Discussion

Male breast cancer is rare constituting <1% of all breast cancers. Papillary lesions account for <10% of benign and 0.5-2% of all malignant breast lesions.[1-3] IPC is usually seen in postmenopausal women aged 55-67 years with a higher median age at presentation in males.[4,5] Only a few cases of IPC are available in the literature.

Clinically, it presents as a painless, firm subareolar mass or with a bloody nipple discharge, and at times remains asymptomatic.[1-3] The average size is 3.5 cm. Grossly, it can be cystic or encapsulated with most lesions not demonstrating infiltrating margins.

Papillary lesions of the breast encompass a complete spectrum including benign lesions (papilloma) to noninvasive (intraductal papillary carcinoma) to invasive papillary carcinomas. Noninvasive papillary carcinomas have two subtypes: The papillary variant of ductal carcinoma-in-situ and IPC. It is postulated that IPC arise in large central ducts and as the tumor develops, its secretions lead to cystic dilatation.[3] IPC is surrounded by a fibrous capsule and is characterized by a thin fibrovascular stalk devoid of a myoepithelial cell layer along with the presence of neoplastic cells of low-grade ductal carcinoma-in-situ (DCIS) type. It can be present as an isolated lesion or associated with nonpapillary DCIS and/or invasive ductal carcinoma. Genetic alterations in the form of interstitial deletions and fusion of chromosome 16 and 1 (1;16) have been described.[6]

The important differentials in males include gynecomastia, fibroadenoma, ductal carcinoma, and micropapillary carcinoma. In gynecomastia, the smears may be hypercellular, with crowded but flattened epithelial and stromal fragments. Nuclear atypia may be present; but, single epithelial cells and three-dimensional (3D) clusters are almost absent, distinguishing it from a papillary lesion. Fibroadenomas are uncommon in males, and aspirates are hypercellular with flat branching sheets of benign ductal cells, stromal fragments, and bare nuclei. True fibrovascular cores are not present. Invasive ductal carcinomas with focal papillary areas usually show high cellularity with complex crowded epithelial cells displaying nuclear atypia and absence of bare nuclei. Micropapillary carcinoma lacks true fibrovascular core and shows angulated papillary and tubuloalveolar pattern of cellular aggregates with single atypical cells.[7] Smears from the IPC are highly cellular, composed predominantly of discohesive epithelial cells with minimal-to-mild cytological atypia. Malignant lesions lack foamy or hemosiderin-laden macrophages.
Histopathology is a must for detecting invasion in IPC. Variable pattern on immunohistochemistry for ER, PR, Her2neu, and Androgen receptors have been reported by different authors.[5-8] In the present case, positivity for PR and Her2neu and negativity for ER and S-100 was observed. Ki-67 showed a low proliferative index with the presence of in-situ component and pushing borders rather than infiltrative. Few authors have demonstrated positivity for Collagen IV, around the IPC, concluding that it is intraductal.[9] Some pathologists now prefer the term “encapsulated papillary carcinoma” to the more traditional “intracystic papillary carcinoma.”[7]

Cytodiagnosis of IPC may at times be difficult since the smears may show presence of fibrosis, hemorrhage, or chronic inflammatory cells in the background. Aspiration of cyst fluid may dilute the cellularity, leading to errors in diagnosis.[7] Due to its indolent behavior on clinical and radiological examinations, the diagnosis is most often delayed. USG reveals a hypoechoic area indicating the cyst with hyperechoes projecting from the cyst wall indicating the tumor part. Lesions tend to be well-defined on mammography.[2]

As per the recommendations of the World Health Organization (WHO) Working Group, treatment for IPC and DCIS is the same. Wide local excision without axillary dissection is the treatment of choice.[10] Role of radiotherapy is debatable. In general, due to the low malignant potential and slow proliferative activity, prognosis of pure IPC is well-defined.[2,9]

**Conclusion**

Cytological diagnosis of IPC is difficult due to overlapping with benign entities and other mimics. All lesions with papillary configuration FNAC should be excised in total to be classified accurately. Wide, local excision without axillary dissection is currently the treatment of choice. IPC breast is extremely rare in males and carries a favorable prognosis.

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**Conflicts of interest**

There are no conflicts of interest.

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