

Case Report

Limitations of Fine Needle Aspiration Cytology in Subtyping Breast Malignancies - A Report of Three Cases

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Abstract

Fine needle aspiration cytology (FNAC) is a very accurate and safe procedure for the diagnosis of breast malignancies. Although rare, the various malignant tumours like squamous cell carcinoma, metaplastic carcinoma and other types can be diagnosed by their cytomorphological characteristics. But there are certain limitations of FNAC which require final histopathological diagnosis for determining prognosis and therapy (particularly conservative) in patients of breast malignancies. The difficulties encountered, and limitations of FNAC in sub typing three cases of breast carcinoma are discussed.

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Key Words : FNAC, breast malignancy, subtyping.

Introduction

Fine needle aspiration cytology (FNAC) of the breast is becoming an increasingly popular investigation in the diagnosis of breast malignancies and their further subtyping. Today the surgeons want to know the grade and subtype because the options for conservative breast cancer treatment are slowly being made available to the patient. With a high degree of accuracy of FNAC of breast, it is possible to subtype breast malignancies in many cases. Despite this, some lesions do create problems at cytodiagnosis. We describe three cases where cytodiagnosis turned out to be of a different type on histopathology, indicating limitations of FNAC in subtyping breast malignancies.

Case Reports

Case 1

The first patient was a 65 years old female who presented with a painless swelling in the right breast since 2 years. Clinical examination revealed a stony hard mass in the right breast occupying the upper, middle and right quadrant measuring 8x6x6cm. The mass was fixed to the underlying structures. The skin over the mass was red and oedematous but the nipple was

not retracted. A single lymph node was palpable in the right axilla. A clinical diagnosis of carcinoma of the right breast was made. FNAC from the right breast mass revealed loosely cohesive clusters of round to polygonal pleomorphic cells with large hyperchromatic nuclei and moderate to scanty cytoplasm. An occasional keratin pearl and isolated dysplastic cells were seen along with mature squamous cells (Fig.1a). The background showed neutrophils. Cytological findings were suggestive of squamous cell carcinoma.

The patient underwent a radical mastectomy with axillary lymph node clearance. Histopathological examination of specimen revealed many sheets of pleomorphic squamous cells, at places surrounded by fibrous stroma. The cells were round to polygonal with large dense round nuclei showing coarsely clumped chromatin, and moderate amount of cytoplasm. Keratin formation was seen in most of the cells. Areas resembling infiltrating duct carcinoma were seen within the tumour. Few areas revealed spindle shaped cells showing nuclear pleomorphism, abruptly between the sheets of squamous cells (Fig.1b). Histopathological diagnosis of metaplastic carcinoma of the right breast of carcinosarcoma subtype was given.

Case 2

A 55 years old female came with a lump in the right breast since 1 year. Clinical examination revealed a large mass in the right breast, firm to hard in consistency measuring 6x5.5x5cm. The mass was fixed to the underlying structures. Skin over the mass was red and ulcerated destroying the nipple and areola. A clinical diagnosis of carcinoma of breast was made. FNAC of the mass

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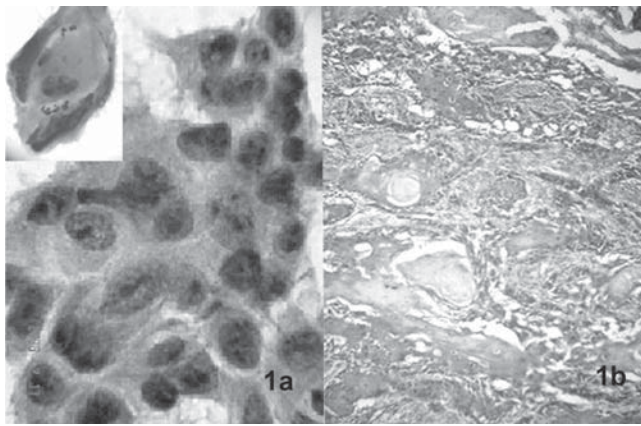


Fig. 1 (a) : FNAC smear showing loosely cohesive cluster of round to polygonal pleomorphic cells with hyperchromatic nuclei. Inset shows a keratin pearl (H&E, x 400). (b) : Histology section with sheets of malignant squamous cells surrounded by fibrous tissue and areas of infiltrating duct carcinoma (H&E, x 100).

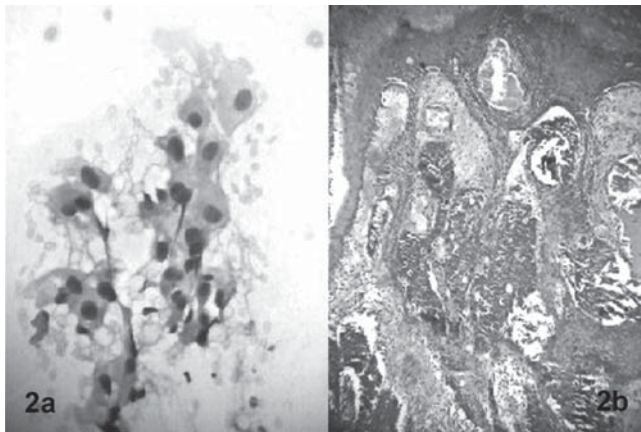


Fig. 2 (a) : Smears showing many loosely cohesive clusters of squamoid looking cells with round to oval hyperchromatic nuclei (H&E, x 100). (b): Histology sections showing foci of infiltrating duct carcinoma with involvement of the overlying skin (H&E, x 100).

revealed many loosely cohesive sheets and clusters of round to polygonal cells. The cells showed large hyperchromatic nuclei with coarse chromatin with or without nucleoli and moderate to scanty cytoplasm (Fig. 2a). Occasional multinucleated cells, bizarre large cells and keratinised cells were also seen. The cytological diagnosis of squamous cell carcinoma was made.

The patient underwent radical mastectomy. Histopathology revealed foci of infiltrating duct carcinoma in the deeper part of the tumour and squamous differentiation in the superficial part. At places the tumour cells were seen infiltrating into the epidermis (Fig. 2b). The cells were round to polygonal with moderate amount of cytoplasm and round to oval nuclei with prominent nucleoli. Histopathological diagnosis of infiltrating duct carcinoma with involvement of skin was kept.

Case 3

A 42 years old female reported in the surgical OPD with a lump in the left breast since 2 years. On examination a large lump in left breast, firm to hard in consistency, measuring 6x5.1x4.8cm was felt. The skin over the lump was ulcerated. A clinical diagnosis of carcinoma of the left breast involving skin was kept. FNAC of the

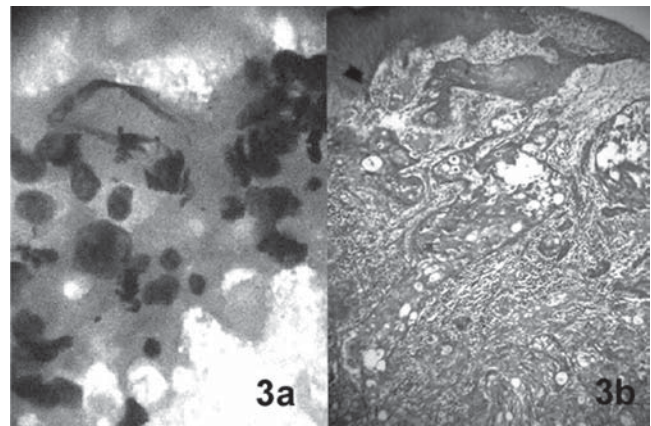


Fig. 3 (a) : Smears showing round to polygonal cells with large hyperchromatic nuclei with or without nucleoli and moderate amount of cytoplasm (H&E, x 400). (b) : Histology sections showing syncytial sheets of tumour cells with large nuclei, prominent nucleoli, and indistinct cell borders. They are separated by fibrous stroma with dense lymphoplasmacytic infiltrate (H&E, x 400).

mass revealed many loosely cohesive clusters and dispersed tumour cells with moderate to abundant amount of cytoplasm and round to oval or irregular hyperchromatic nuclei with coarsely clumped chromatin. Prominent nucleoli were seen in few cells (Fig. 3a). Cytological diagnosis of poorly differentiated epithelial malignancy was kept.

Radical mastectomy was done. Histopathology showed many syncytial sheets of tumour cells. The cells were large and pleomorphic with large nuclei and prominent nucleoli with indistinct cell borders. The syncytial sheets were separated by fibrous stroma with a dense lymphoplasmacytic infiltrate. The tumour cells were seen extending up to the overlying skin (Fig. 3b). Therefore the histopathological diagnosis of medullary carcinoma with involvement of skin was kept.

Discussion

Fine needle aspiration cytology of the breast has a wide range of accuracy in the diagnosis of malignancy and its subtyping. Many rare tumours of the breast like squamous cell carcinoma, metaplastic carcinoma, apocrine carcinoma can be diagnosed by their cytomorphological characteristics. Therefore accuracy of cytodiagnosis of malignant breast tumours is very important, to know the exact line of treatment preoperatively. Histologically 25-30% of epithelial malignancies fall into the specialized breast cancer groups like lobular, papillary, apocrine, tubular, cribriform, medullary, mixed and others. Both invasive ductal carcinoma (No specific type) and specialized types of breast carcinomas are best differentiated on the aspirates.

The sub typing of breast tumours on aspiration cytology is necessary, to know the exact type of treatment. If tumours are of low malignant potential, options for conservative breast cancer treatment are

slowly being made available to the patients.¹ But it is not always possible to label the exact subtype on aspiration cytology without correlating the clinical and histopathological findings. FNA has been successful in diagnosing epithelial lesions of the breast.² However breast lesions with squamous cells have to be interpreted carefully on FNA because they may be from pure squamous cell carcinoma of breast, metaplastic carcinoma, widespread metaplasia in infiltrating duct carcinoma or metastatic carcinoma.³ Sometimes apocrine metaplasia may be confused with squamous cells due to their polygonal appearance and dense eosinophilic cytoplasm. Malignant breast tumours are broadly divided into epithelial tumours arising from cells lining ducts and lobules, and non-epithelial tumours. Invasive duct carcinoma is the commonest pathological type amounting for 70% of invasive breast carcinoma. Infiltrating lobular, medullary, colloid carcinoma and other types constitute the remaining 30%.

Primary squamous cell carcinoma of the breast is rare and comprises < 0.11% of invasive cancers. Controversy exists whether a pure form of squamous-cell carcinoma exists or whether these cases actually represent extreme squamous metaplasia within an adenocarcinoma. Squamous metaplasia is seen in 36 out of 1000 cases and in 16% of typical medullary and 4% of non-medullary carcinomas. These variations range from minute areas of squamous differentiation in a predominant adenocarcinoma to pure squamous cell carcinoma where no glandular elements can be identified.⁴

Differentiation of breast carcinoma carries great prognostic significance as the squamous cell carcinoma behaves more aggressively as compared to other metaplastic carcinomas.⁴

In the first case FNA smears revealed malignant squamous cells with occasional keratin pearl formation. There was no evidence of malignant ductal cells, suggesting a cytological diagnosis of squamous cell carcinoma.³ The patient underwent radical mastectomy. Histopathology of received sample showed pleomorphic malignant squamous cells with areas of infiltrating duct carcinoma and few areas showing spindle shaped cells with nuclear pleomorphism suggesting a diagnosis of metaplastic carcinoma, carcinosarcoma type. In the FNA smears there was no evidence of malignant ductal cells or stromal cells. Only the malignant squamous cells were seen indicating their origin from one of the components of metaplastic carcinoma.⁵

In the second case, FNA smears from repeated aspirates revealed round to polygonal cells with large hyperchromatic nuclei, occasional multinucleated cells, bizarre large cells and keratinised cells. Classical features of ductal cell carcinoma like dispersed tumour cells, acinar pattern or three-dimensional clusters were not seen. Hence the cytological diagnosis of squamous cell carcinoma was given. Histopathology of the mastectomy specimen showed evidence of infiltrating duct carcinoma in the deeper portion of the tumour with squamous differentiation in the superficial part. This indicated extensive squamous metaplasia in the infiltrating duct carcinoma of breast, which was picked up on FNA and falsely diagnosed as squamous cell carcinoma.⁴

In the third case, cytology revealed loose clusters, scattered tumour cells with moderate to abundant cytoplasm and round to oval or irregular hyperchromatic nuclei. Prominent nucleoli were seen in few cells. The classical features of ductal carcinoma or squamous cell carcinoma was not seen. So the cytological diagnosis of poorly differentiated epithelial malignancy was kept. Subsequent histopathology of the resected specimen showed many syncytial sheets of round to polygonal cells with large nuclei and prominent nucleoli. The sheets of tumour cells were separated by thin fibrous tissue septae, infiltrated by many lymphocytes and plasma cells so the diagnosis of medullary carcinoma was given. On cytology typical features of medullary carcinoma of breast were not seen. There was no evidence of lymphocytes in the background hence medullary carcinoma could not be considered as the diagnosis, which is known to have a good prognosis. The squamoid looking epithelial cells could have come from metaplasia in medullary carcinoma.

Conclusion

Carcinoma of the breast is a leading cause of mortality in women in our country. There are malignancies like tubular carcinoma, medullary carcinoma, mucinous carcinoma, which have an excellent prognosis, and malignancies like squamous cell carcinoma, metaplastic carcinoma, which have a bad prognosis. Cytodiagnosis of these subtypes is required preoperatively. Therefore careful and accurate classification of these tumours is necessary in managing the patients. But there are certain limitations of FNA in subtyping. Squamous cells occur in FNA from a number of malignant breast lesions. Careful assessment of cytological features of squamous cells and the appearance of the background

is crucial for achieving a correct diagnosis.⁶ It is important to bear in mind the cytomorphology and the cytodiagnosis of rare malignant tumours of the breast in the analysis of breast FNA smears.

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