Case Report

Primary squamous cell carcinoma of the breast: A cytological and histological correlation

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ABSTRACT

Primary squamous cell carcinoma of the breast (PSCCB) is an extremely rare disease. Origin is controversial; it is thought to arise through the metaplasia of various benign and malignant breast lesions. It usually present with rapidly growing large mass, otherwise similar to that of ductal breast carcinoma. Fine needle aspiration cytology (FNAC) is an accurate and safe diagnostic procedure for breast malignancies. However, cytologists are still facing some difficulties in specific diagnosis of various subtypes of breast malignancy. Extensive squamous cells on cytology should be evaluated with the great caution. Ductal breast carcinoma with squamous metaplasia, squamous carcinoma of the breast skin, and metastasis from non-mammary tissues should be consider before the making the diagnosis of PSCCB. Specific management and prognosis of PSCCB is still debatable. We present a case of 52-year-old woman with a breast mass. FNAC revealed predominantly clusters and dispersed malignant squamous cells, without any ductal cells, suggest PSCCB; possibility of secondary or ductal breast carcinoma with squamous metaplasia should be ruled out. After modified radical mastectomy histology confirmed the diagnosis of PSCCB. Post-operative cisplatin and 5-fluouracil were administered. Patient is disease free at 12 months of follow-up.

Key words: Breast carcinoma, fine needle aspiration cytology, squamous cell carcinoma, squamous metaplasia

INTRODUCTION

Primary squamous cell carcinoma of the breast (PSCCB) is an uncommon disease, categorized under metaplastic breast carcinomas in the World Health Organization classification.[1-8] Origin is controversial.[1,7,9] Reported incidence of PSCCB is varying between 0.1% and lesser than 0.04% of all breast carcinomas.[1,3,6] PSCCB is frequently reaches large size with rapid growth.[4,5,7,9] Fine needle aspiration cytology (FNAC) of the breast is a valuable diagnostic tool for the detection of such rare type of breast carcinoma. Though, some cases create problems at cytodiagnosis.[9,10] Diagnosis is suspected when all of the malignant cells are of squamous type (>90% of cells).[1-3,6] In addition to the adequate sampling of tumor, exclusion of malignancies of the breast skin, metastasis of a squamous cell carcinoma somewhere else in the body and squamous metaplasia in ductal carcinoma of breast are the key for specific diagnosis and management.[1,4,6-8,10,11] The management and prognosis of PSCCB is still controversial.[2,4,5,7] We report a case of PSCCB in a 52-year-old woman, with discussion of cytology, and histology findings.

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CASE REPORT

A 52-year-old woman presented with a rapidly enlarging lump in the right breast since 6 months. Family history, medical history, and a history of oral contraceptives were not significant. Pap smear was negative for any squamous lesion. Physical examination revealed a firm to hard irregular, but well-circumscribed swelling in upper-outer quadrant of the right breast, which measured 5.0 cm × 4.8 cm. Overlying skin and nipple were unremarkable. The left breast, axilla, and supraclavicular lymph nodes were unremarkable. She had no history of any malignancy. The clinical diagnosis of breast carcinoma was made and FNAC was requested. Ultrasonographic examination of the right breast showed an irregular hypoechoic lesion of 5.0 cm × 4.5 cm size. Complete blood count, serum electrolytes, liver function tests, and creatinine were within normal limit.

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FNAC was performed by 22-gauge needle attached to 10 cc disposable syringe. Sampling was carried out from different sites. Hematoxylin and eosin (H and E) stained smears showed high cellularity, composed of clusters, syncytial groups and numerous dispersed malignant squamous cells admixed with numerous inflammatory cells and necrosis. Squamous cells showed moderate to markedly pleomorphic hyperchromatic nucleus and variable degree of orangeophilic keratinized cytoplasm. Few cells showed ted-pole shaped nucleus. Keratinous debris and atypical mitoses were also evident. On close scrutiny, ductal cells were not found [Figure 1]. A diagnosis of PSCCB was suspected; possibility of ductal breast carcinoma with squamous metaplasia or secondary squamous cell carcinoma should be ruled out. Computed tomography scan of the abdomen and thorax and bone scintigraphy were performed. However, these were not significant. Metastatic carcinoma from lung, pharynx, oral cavity, cervix, esophagus, stomach, and the skin were excluded.

A modified radical mastectomy with axillary lymph node dissection was performed. Histopathologically, entire tumor showed broad sheets and nests of squamous cells, with keratin pearl and intercellular bridges. There was no continuity with adjacent cutaneous structures. Squamous cells showed hyperchromatic irregular nuclei, occasional small distinct nucleoli and keratinized orangeophilic glassy cytoplasm. Frequent atypical mitoses were evident. Tumor was infiltrating into the breast stroma. Vascular or neural invasion was not identified. On multiple sampling components of obvious ductal carcinoma or metaplastic carcinoma, such as spindle cells or osseous or cartilaginous area were not found [Figure 2]. These findings suggested PSCCB. The axillary lymph nodes were negative for metastasis. The bloom Richardson score was 8 (high grade). The breast tumor cells were negative for estrogen receptors, progesterone receptors, and HER/neu (Human Epidermal Growth Factor Receptor 2) overexpression.

Post-operative course was uncomplicated. Post-operative adjuvant therapy based on 5-fluouracil and cisplatin were administered. Radiation therapy was not given. At present, she is asymptomatic and disease free at 12 months of follow-up.

DISCUSSION

Squamous cells are normally not found inside the breast, so a PSCCB is an exceptional phenomenon.[1-8] Until 2010, only 100 cases of PSCCB have been reported.[9] The World Health Organization categorized these tumor as a metaplasia carcinoma.[3,5,7] Exact subtyping of breast carcinoma carries great therapeutic and prognostic significance as the squamous cell carcinoma behaves more aggressively and is usually resistant to radio-chemotherapy as compared to usual ductal carcinoma.[2,4,6,9,10]

The etiopathogenesis of PSCCB is still unclear.[1,7,9] It has been reported to originate from epidermal or dermoid cysts of the breast, chronic abscesses, skin and complete metaplasia of glandular breast tissue.[3,4,7,9] Controversy exists whether a pure form of squamous cell carcinoma is exist or such cases are actually represent an extreme squamous metaplasia within an adenocarcinoma.[1,2,5,10] In our case, neither pre-existent chronic breast lesion nor

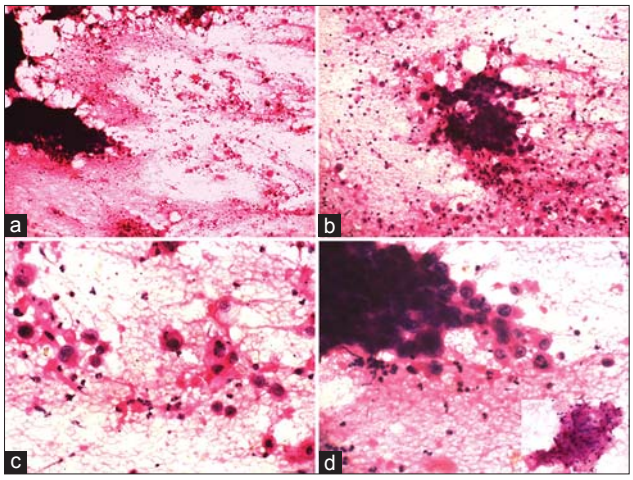

Figure 1: (a) High cellularity comprises of clusters and dispersed tumor cells (H and E stain, ×100). (b) Syncytial groups with many dispersed malignant squamous cells admix with numerous inflammatory cells and necrosis (H and E stain, ×200). (c) Cells are moderate to markedly pleomorphic and show hyperchromatic irregular nucleus and variable orangeophilic keratinized cytoplasm. Occasional ted-pole shaped nucleus is evident (H and E stain, ×400). (d) Atypical mitoses are evident. Inset figure shows keratinous material (H and E stain, ×400)

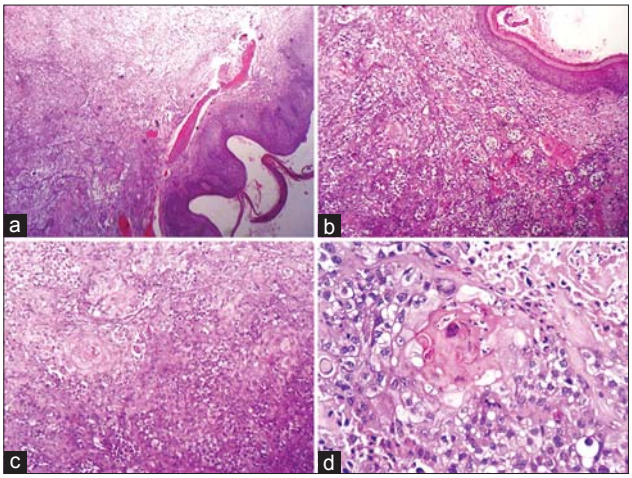

Figure 2: (a) Broad sheets and nests of tumor cells without any continuity with overlying skin (H and E stain, ×40). (b) Skin appears unremarkable with nests of malignant squamous cells and keratin pearls with few inflammatory cells (H and E stain, ×100). (c) Prominent component of tumor shows malignant squamous cells with keratin pearl and intercellular bridges (H and E stain, ×200). (d) Squamous cells show irregular hyperchromatic nuclei, occasional small distinct nucleoli and orangeophilic keratinized cytoplasm (H and E stain, ×400)

other component of ductal carcinoma was found, favors the *de novo* origin of pure PSCCB.

PSCCB is a tumor of an elderly age group.[3,4,9] It frequently reaches large volume (up to 5 cm) with rapid growth and cystic changes (in 50% of the cases), otherwise similar to that of usual breast carcinoma.[1,2,4-7,9] Few cases are associated with breast abscess, dermoid cysts, and adenofibromas.[1,3,4,6] Few cases have been reported during the pregnancy and lactation.[3] In the present case, the tumor was large and grew rapidly within few months. PSCCB does not have characteristic radiologic features like in our case.[2,3,6]

Although FNAC has a high accuracy (72-99%) in the diagnosis of breast malignancy, subtyping of rare lesions create problems at cytodiagnosis. The subtyping of breast malignancy on cytology is necessary, for management and prognosis purpose.[9,10] PSCCB is usually a high-grade tumor.[2] In most of the reported cases, the diagnosis of the PSCCB was based solely on histopathological findings.[6] The diagnosis of primary squamous cell carcinoma is established when the malignant cells are entirely of squamous type (>90% of cells).[1-3,6] Macia *et al.*, defined following criteria for the diagnosis of PSCCB: (1) no other neoplastic components, such as ductal or mesenchymal elements are present in the tumor, (2) the tumor origin must be independent from the overlying skin and nipple, (3) absence of an associated primary squamous cell carcinoma in a second site.[12] Our case satisfies all these criteria. Cytological findings showed predominantly malignant squamous cells without any obvious ductal carcinoma or other component such as spindle, osseous, and cartilage area, suggest PSCCB. Estrogen and progesterone receptors are negative in more than 90% of PSCCB cases like in our case. HER2/neu is also usually not over-expressed or amplified.[2,6,9] Menes *et al*. showed that squamous cell carcinoma of the breast was found to be associated with a lower rate of lymph node metastasis at presentation (22% vs. 40-60% for infiltrating ductal carcinoma) and a significant rate of distant metastasis without lymph node involvement.[13] Similarly lymph node was not involved in our case. Menes *et al*. proposed a more selective approach like sentinel node biopsy.[13] However, due to unpredictable lymph node dissemination, axillary lymph nodes dissection should always be performed for staging purposes similar to our case.[2]

Squamous cells on cytology of the breast lesions can be found in epidermoid cyst, subareolar abscess, fibroadenoma, infracted papillomas, phyllodes tumor, and pseudosarcoma.[7,10,14] These may sometimes mimic malignant squamous lesions.[7] Benign squamous cells are bland looking with good maturation pattern. Associated anucleated squames, absence of mitotic activity and abundant foamy macrophages in the background suggest a benign lesion.[14] Sometimes apocrine metaplasia may be confused with squamous cells due to their polygonal appearance and dense eosinophilic cytoplasm.[10] Malignant squamous cells are pleomorphic, bizarre-shaped, mitotically active, and dyskeratotic.[11] The differential diagnosis of malignant squamous cells on cytology of the breast include pure primary squamous cell carcinoma of breast, widespread squamous metaplasia in ductal carcinoma or metastatic squamous carcinoma.[1,4,6-8,10,11] Careful assessment of cytological features including the background appearance are critical for achieving correct diagnosis.[10,14]

Management of PSCCB is still unclear.[2,4,5] The treatment may involve surgery, chemotherapy, hormonal therapy and radiation therapy, similar to that of other malignant breast tumors.[5,6] Hormonal therapy is usually not indicated as tumor cells of PSCCB are negative for hormone receptors.[2,6,7] PSCCB is not sensitive to chemotherapeutic agents that are commonly used for ductal carcinomas. Some degree of success is achieved with 5-fluorouracil and cisplatin.[2,6] PSCCB is reported to be resistant to radiotherapy and locoregional relapse occurs frequently in irradiated field and hence radiotherapy was not given in our case.[2,6,7] Our case was treated with modified radical mastectomy with axillary clearance and post-operative adjuvant therapy of 5-fluorouracil and cisplatin. Such modality gave satisfactory results, without any recurrence or metastasis in our case.

Prognosis of PSCCB is uncertain.[4,7] The 5 years survival is 67% in a small retrospective series of 11 patients.[1] Many studies showed that it is an aggressive disease and behave like poorly differentiated breast carcinoma.[2,4,10] Prognosis is even worse in the gestational period even if diagnosed early and treated.[3] Some series revealed an indolent clinical course with relatively good prognosis.[4]

CONCLUSION

PSCCB is a rare disease of elderly women. Accurate cytological diagnosis is necessary for specific management and prognosis. The presence of abundant malignant squamous cells, without any ductal cells on cytology of the breast lesions may suggest PSCCB. For exact diagnosis, detailed work-up is necessary to exclude skin lesion, metastasis, and metaplastic changes in other breast malignancy. Squamous cells may be seen in many inflammatory, cystic and benign lesions. Its prognosis and appropriate management is still debated. Though, surgical therapy with 5-fluorouracil and cisplatin based chemotherapy gives good result.

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