

Invasive Solid Mucinous Papillary Carcinoma Breast with Neuroendocrine Differentiation: A Case Report with Immunohistochemical Study

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ABSTRACT

Solid papillary carcinoma of the breast (SPCB) is a distinctive form of papillary carcinoma that tends to occur in older women and usually has a favorable prognosis. We describe an invasive solid papillary carcinoma with extracellular and intracellular mucin and neuroendocrine differentiation in a 60-year old female. The cytological features have been also been highlighted with an insight on differentials that were helpful in its correct identification preoperatively.

Keywords: *Invasive Solid Papillary Carcinoma, Neuroendocrine, Extracellular, Intracellular Mucin, Immunohistochemistry*

Introduction

Solid papillary carcinoma (SPC) is considered a rare malignant breast tumor, with an incidence ranging from 1.1% to 1.7% of all malignant breast tumors [1,2]. Maluf and Koerner first reported this disease entity as a special type of ductal carcinoma in situ (DCIS) with several characteristic histopathological features, including low-grade cellular atypia, intracellular or extracellular mucin deposition, and solid papillary growth pattern, as well as neuroendocrine differentiation [3]. This tumor displays distinctive clinical and morphologic features and is believed to have good prognosis.

Case Report

A 60-year-old woman presented to the Department of Surgery of School of Medical Sciences & Research, Greater Noida with mass in right breast for one month. She gave the history of spontaneous nipple discharge from the same breast. There was 6cm. firm mass present below nipple and areola extending into upper quadrant of right breast. The nipple was retracted. There were no palpable lymph nodes. Fine needle aspiration cytology of the mass was performed which revealed cellular smears with abortive, papillary and occasional loose clusters. (Figure 1a,1b and 1c) Cells are present in three dimensional clusters, morules with scalloped angulated borders, few with neuroendocrine granules. The individual cells were small, uniform and ovoid with abundant finely granular cytoplasm. The

nuclei were round, without marked atypia and the nucleoli were inconspicuous. Both intracellular and extracellular mucin was evident. (Figure 1d) A diagnosis of malignant breast tumor with predominant micropapillary pattern and mucinous and neuroendocrine changes was made on cytological findings.

Subsequently mastectomy with axillary dissection was done and specimen was submitted in Pathology department. Specimen showed tumor measuring 6 X 5X 1.5cm.in upper outer quadrant below nipple and areola. Twenty-six lymph nodes were received and processed. Sections show multiple solid nests of neoplastic epithelial cells. The epithelial cells were supported by arborizing network of fibrovascular stroma. Focal areas show streaming appearance of cells. The individual cells are monotonous small round cells with salt and pepper chromatin and small inconspicuous nucleoli. (Figure 2a) Focal papillary areas with extracellular mucin seen. PAS and mucicarmine stain positive for mucin. (Figure 2b and 2c) Immunohistochemistry exhibited S100 and chromogranin negativity. However, NSE was positive in few cells. (Figure 2d) The final diagnosis of invasive solid mucinous papillary carcinoma breast with neuroendocrine differentiation was rendered. Twenty-six axillary lymph nodes showed reactive lymphoid hyperplasia and sinus histiocytosis. Postoperative chemotherapy was given, and the patient is on regular follow up for one year with uneventful period.

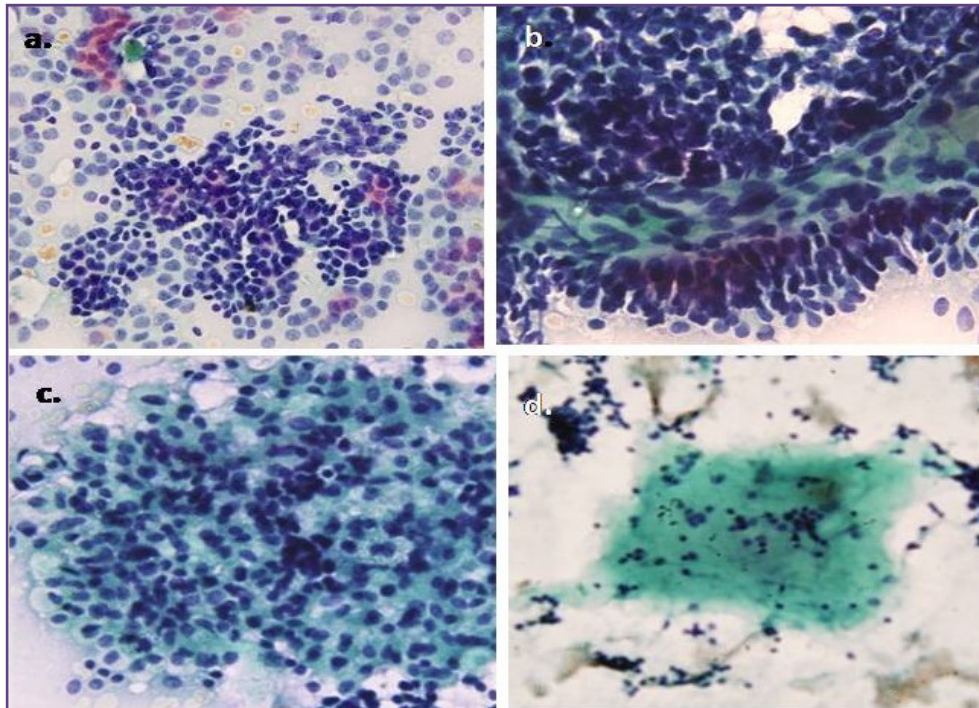


Fig. 1a: Smear showing loose clusters of tumour cells in fairly clean background. 1b. Cells lying in papillary clusters with round to oval nucleus and scant cytoplasm. 1c. Showing cells in acinar, abortive papillary and loose clusters. 1d. Areas of extracellular mucin. (PAP; 40X).

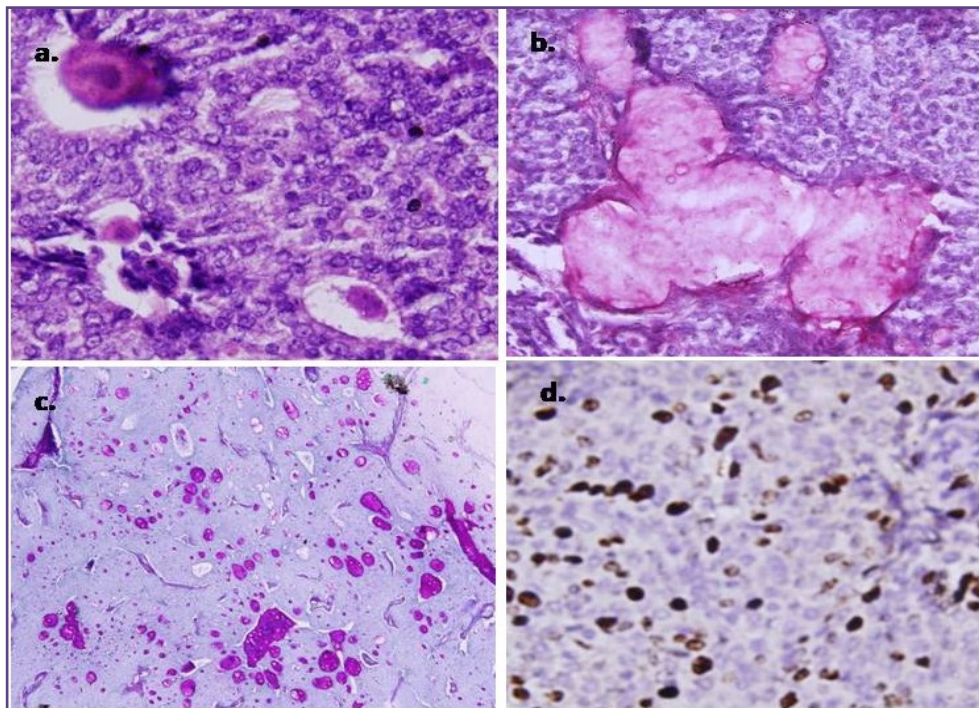


Fig. 2a: Section showing ducts filled with tumor cells. The individual tumor cells are monotonous round to oval with granular chromatin. Occasional psammoma bodies are seen (HE; 40X) 2bMucicarmine stain showing positivity for mucin. (Mucicarmine; 40X) 2c. PAS stain showing glycogen positivity (PAS; 40X) 2d. NSE positivity (NSE; 40X)

Discussion

SPC, a rare malignant breast tumor constitutes 1-2% of breast carcinomas in women. [4] It is most commonly seen in the postmenopausal women. [4,5] It is in concordance with our case who is 60 years old women. Approximately 50% of the papillary carcinomas develop from the central part of the breast; nipple discharge is observed in one-third of the patients. [6] Our patient also showed mass in the upper outer quadrant of right breast and history of bloody nipple discharge. [7, 8] Malignant cytological features include hypercellularity, highly discohesive clusters, numerous isolated cells and severe overcrowding. [9] Our tumor showed high cellularity, focal mucin, clean background with abortive papillary and acinar structures, predominantly dual pattern of cells, cells in three dimensional clusters, morules with scalloped angulated borders, few with neuroendocrine granules on cytology. [10]

The WHO Working Group provides recommendations to aid in categorization of solid papillary carcinoma as invasive disease if tumors composed of nests with irregular borders and a geographic jigsaw growth pattern and an absent myoepithelial cell layer. [11]

Many breast tumor that display varying degrees of neuroendocrine differentiation belong to recognized entities such as hypercellular mucinous carcinoma and solid papillary carcinoma of both in situ and invasive forms. [12]

Consistent with these histological findings, our tumor showed ducts filled with solid neoplastic proliferation supported by delicate fibrovascular stroma. Intra and extracellular mucin was present. It also has granular eosinophilic cytoplasm and fine nuclear chromatin consistent with neuroendocrine differentiation. The final diagnosis of invasive solid mucinous papillary carcinoma breast with neuroendocrine differentiation was rendered. Twenty-six axillary lymph nodes showed reactive lymphoid hyperplasia and sinus histiocytosis. It is important to distinguish SPC from encapsulated papillary carcinoma (EPC) and papillary DCIS. The Term EPC has been introduced to define papillary carcinomas that are typically circumscribed and encapsulated and often lacking myoepithelial cells at their periphery. SPCs on the other hand are typically solid, characterized by mucin production, neuroendocrine features, and multinodular architecture while papillary DCIS is typically surrounded by a peripheral layer of myoepithelial cells.

The differential diagnosis of SPC include both benign and malignant entities. Benign cases include florid ductal hyperplasia and lobular neoplasia. Malignant causes

include intracystic papillary carcinoma (IPC), ordinary low nuclear grade ductal carcinoma in situ (DCIS) and metastasis to breast. In florid ductal hyperplasia, there is no fibrovascular core, palisading of cells or mucin production and no mitotic activity. Lobular neoplasia, although can involve papillary lesions, is characterized by lack of discohesion and lack of papillary fronds. IPC like SPC, occurs in elderly, have papillary fronds, lack myoepithelial layer in periphery. However, the papillary fronds of IPC are lined by cuboidal cells and have high nuclear grade. DCIS, unlike SPC, does not have a monotonous morphology, mucin, fibrovascular stroma and ducts encompassed by fibrosis. Metastasis from a neuroendocrine tumor to breast is another differential. The presence of nuclear atypia or pleomorphism in a well-differentiated tumor favors a primary neuroendocrine tumor of breast.

Breast carcinomas showing neuroendocrine differentiation have a incidence of 2-5% while pure neuroendocrine carcinomas have a rarer incidence of 0.1% of all breast tumors. [13] SPC has a better prognosis than other breast cancers [6] and from pure neuroendocrine carcinoma which carries a poorer prognosis. [14] The morphological findings of nuclear palisading around fibrovascular core, solid papillary growth pattern, nuclear or cytoplasmic growth pattern or mucin production should prompt a diagnosis of solid papillary carcinoma.

Regarding neuroendocrine markers, the SPC cells were positive for neuron-specific enolase (NSE), chromogranin, and synaptophysin and negative for CD56 and S-100 antibodies. Our tumor expressed NSE positivity while chromogranin was negative. [15] Our tumor showed NSE positivity with chromogranin negativity. NSE being more sensitive marker than chromogranin was expressed in tumor

Conclusion

Solid papillary carcinoma of the breast is a rare entity with distinctive clinicopathological features and excellent prognosis. SPC's are commonly associated with mucin production and neuroendocrine differentiation. Neuroendocrine differentiation should be assessed carefully in the diagnosis of invasive SPC, the clinical implication of which remains unknown. It should be distinguished from conventional breast carcinoma to avoid over-treatment. Invasive SPC remains rare, and its biological and clinical behaviors are largely unknown. Therefore, further investigations, with molecular analysis and accumulation of clinical experience, are warranted.

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Competing Interests

Nil

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