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Case Report

Mucinous carcinoma of breast with neuroendocrine differentiation: a rare case report with review of literature

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ABSTRACT

Mucinous carcinoma of the breast is a relatively rare malignancy accounting for 2% of all breast cancers. Mucinous carcinoma of the breast has a favourable prognosis and is usually seen in postmenopausal women. Here, we report a 60 year old female patient presented with right breast lump was diagnosed on cytology as ductal carcinoma of the breast, on histopathology diagnosed as mucinous carcinoma with neuroendocrine differentiation, which was subsequently confirmed on IHC marker synaptophysin and chromogranin A positive.

Keywords: Breast, Mucinous breast carcinoma, Neuroendocrine differentiation

INTRODUCTION

Mucinous breast carcinoma (MBC), is a special type of breast carcinoma. Pure mucinous carcinoma of the breast is a rare histological type, which accounts for approximately 2% of all invasive breast cancers and is characterised by clusters of tumour cells floating in large amounts of extracellular mucin. Neuroendocrine carcinoma represents 2–5% of invasive breast cancers and displays morphological features similar to those of neuroendocrine neoplasm of other organs, including the gut.[1,2,3] Mucinous carcinoma of breast is histologically subtyped into mixed mucinous breast carcinoma (MMBC) containing a component of conventional invasive ductal carcinoma, and pure mucinous breast carcinoma (PMBC).[4] Here we report a case of mucinous carcinoma with neuroendocrine differentiation in a 60yr old female patient.

CASE REPORT

A 60 year old postmenopausal woman, who had no family history of breast cancer, history of reverse smoking since 35yrs presented with a mass in the right breast associated with pain and nipple bloody discharge. On clinical examination there is palpable lump which was observed as small swelling four years back and gradually progressed to this size (10 x 6 x 3 cm) involving whole right breast. The lump is attached to the overlying skin and underlying structure and soft to firm in consistency with irregular margins. On examination one enlarged axillary lymph node measuring 1x1cm was detected on right side. FNAC smears showed cellular smear showing pleomorphic cells with hyperchromatic nuclei in sheets and discretely in a red cell background, suggestive of duct cell carcinoma. FNAC from axillary lymph node shows features of reactive follicular hyperplasia. Other routine investigations were within normal limits. She underwent modified radical mastectomy. Post-operative period is uneventful.

On gross examination, the specimen measured 15 x 12 x 6cm with a skin flap measuring 13 x 10 cm. The nipple is retracted. The cut section showed a growth measuring11 x 6 cm, grey white, grey brown with foci of light blue areas extending up to the posterior margin, soft to firm in consistency with variegated appearance with solid, haemorrhagic and cystic areas (Fig 1). The cystic areas measuring 1 x 1 cm showed mucoid material. The specimen contained three lymph nodes, the largest being 2 x 1 cm cut section grey brown. Microscopy revealed tumour composed of small islands of malignant cells

suspended in contiguous pool of extra cellular mucinous material (Fig 2 & 3). Individual cells show round to oval shape with scanty cytoplasm and round nucleus showing strippled chromatin (Fig 4) with areas of palisading of tumor cells. There are occasional foci of in situ ductal carcinoma. Lymph nodes showed features of reactive follicular hyperplasia (Fig 5). Immuno-histochemical analysis (IHC) showed Synaptophysin and Chromogranin A positivity (Fig 6). Oestrogen receptors and Progesterone receptors are also positive. The patient is followed up to 6 months.

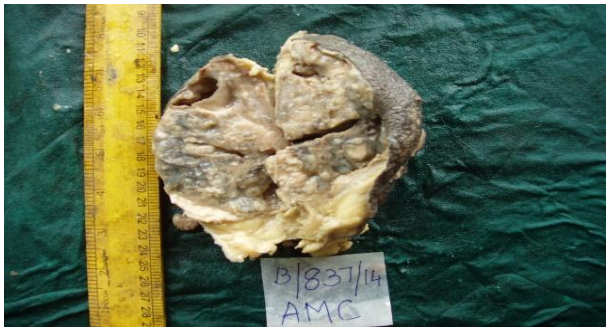

Figure 1: Cut section of gross specimen showing cysts filled with mucinous material.

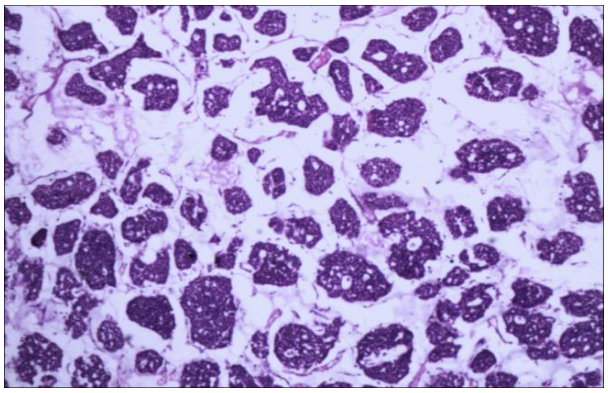

Figure 2: Photomicrograph showing sheets of tumor cells seperated by mucinous pools (H&E;40X).

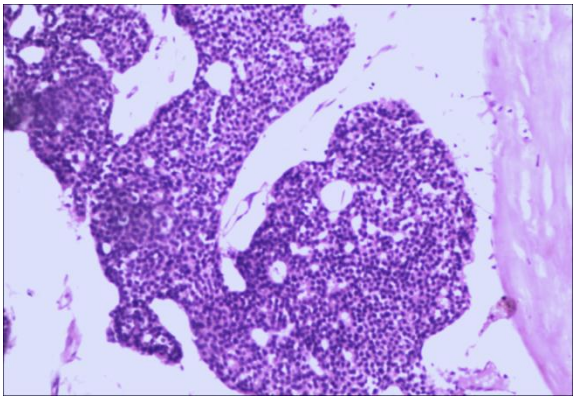

Figure 3: Photomicrograph showing neuroendocrine cells forming solid nests. Tumor cells are polarized around lumina. (H&E;100X).

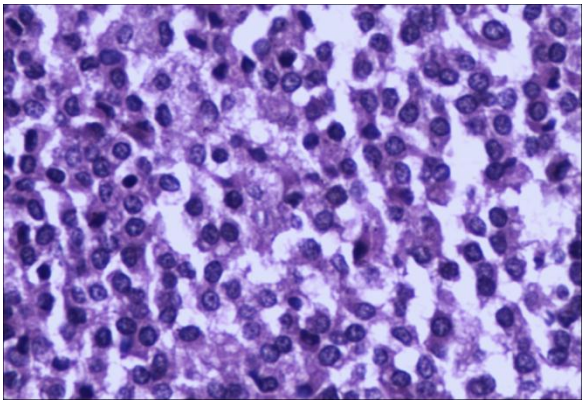

Figure 4: Photomicrograph showing individual tumor cells with mild Pleomorphism round to oval, scanty cytoplasm strippled chromatin & prominent nucleoli. (H&E;400X).

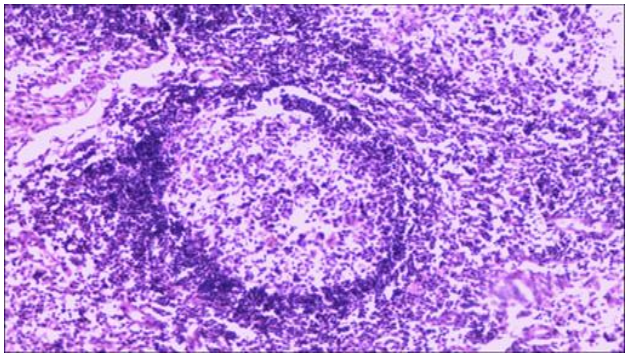

Figure 5: Photomicrograph of lymphnode showing features of Reactive Folicular Hyperplasia (H&E;40X).

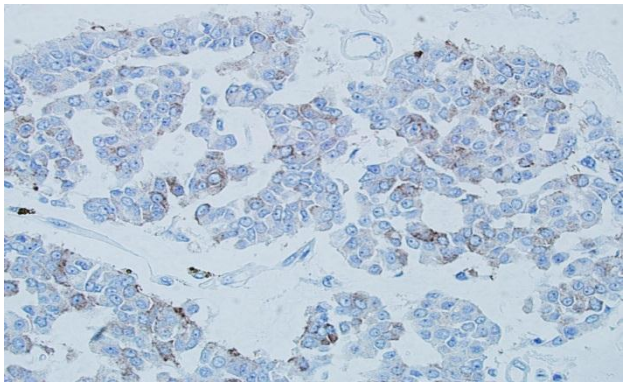

Figure 6: Photomicrograph showing immune-reactivity for synaptophysin positive.

DISCUSSION

Mucinous carcinoma is also called as colloid/gelatinous and mucoid carcinoma. It accounts 2-3% of all breast carcinoma. Most common in older women having good prognosis. Survival range is 85%to 95%.[2,3]

Morphologic characteristic has been subdivided mucinous carcinoma into 2 types. Type A tumour

characterized by trabeculae, ribbons and sheets of malignant cells with minimal intra-cytoplasmic mucin Type B characterized by sheets and clumps of tumour cells with little pleomorphism and often with abundant intra-cytoplasmic mucin are usually argyrophilic positivity. Special stain Alcain blue /PAS positive. IHC marker positive for Oestrogen & Progesterone.[5]

In 1977 the first eight cases of breast tumors were published, classified as neuro endocrine by the presence of argyrophilia and cytoplasmic dense core granules. NEBC (Neuro endocrine Breast Carcinoma) were not recognized as single breast cancer entities until the last WHO's classification of breast carcinomas in 2003.[6,7]

WHO's classification clearly establish that the immune-histochemical expression of neuroendocrine markers in more than 50% of the tumor cell population is the unique requisite for the diagnosis of primary pure neuroendocrine breast carcinomas (NEBC).[2]

The percentages of NEBC among breast cancers are variable. They were estimated in 2003 to represent 2-5% of breast carcinomas.[2] Lopez-Bonet et al found only 7 NEBC cases in 1368 breast cancers (0.5%), screening first for neuroendocrine histological features, then with IHC stains for proof. Recognition of the variable histological expressions and wide application of IHC could improve the diagnosis of NEBC.[8]

Focal neuroendocrine differentiation can be found in different histological types of breast carcinoma including in situ and invasive ductal, lobular, colloid or papillary breast cancer. Neuroendocrine differentiation in breast cancer has been found in ductal, lobular, mucinous, tubular and oat cell carcinomas.[9]

Majority of patients cited in literature concerning NEBC are women in the 6th and 7th decades of life.[2,10] But, Volger in 1947 indicated the existence of neuroendocrine cells in breast tissue including male breast. This has been verified by histochemical and immunological stains. Immuno-histochemical stains NSE (Neuron specific enolase), synaptophysin and chromogranin A is used to confirm the neuroendocrine differentiation.[11]

The presence of intracellular or extracellular mucin, or both, in tumor cells could also be features of mucinous NEBC. Mucin production is a common feature in NE breast tumor and the mucinous differentiation is an important indicator of low biological aggressiveness. Estrogen and progesterone expression is also correlated with a better prognosis.[7]

The unique requisite to diagnose a NEBC is the Immuno-histochemical expression of NE markers in >50% of the tumor cell population.[2]

Synaptophysin represents the major protein of the synaptic vesicle and is widely expressed in neurons but it is commonly present in other neuroendocrine tissues and in their corresponding tumors. Three histological characteristics that suggest endocrine differentiation in a breast carcinoma include low nuclear grade, palisading of nuclei at the periphery of tumor islands and dense sparsely cellular collagenous stroma surrounding it.[6]

Here we diagnosed a female patient with mucinous carcinoma with focal neuroendocrine differentiation with focal insitu duct cell carcinoma (No special type). Sapino et al. in one of the largest series of these tumors have described five subtypes; solid cohesive, alveolar, small cell, solid papillary and cellular mucinous. [7] In our case, the predominant pattern was solid.

Among composite tumors, the mucinous carcinoma is the type most commonly associated with neuroendocrine differentiation where 40% of the tumours shows neuroendocrine differentiation, with several distinctive features according to the NCCN (National Comprehensive Cancer Network) Clinical Practice Guidelines in Oncology.[12]

CONCLUSION

Mucinous carcinoma of breast with neuro endocrine differentiation is rare and its prognostic relevance is still a subject of debate. Therefore long term follow-up is essential in these rare variant of tumours.

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Ethical approval: Not required

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