

## **Primary Signet Ring Cell Carcinoma of the Breast: A Rare Pathologic Entity**

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**Primary signet ring cell carcinoma (SRCC) of the breast is a rare and aggressive variant of lobular carcinoma. We present a case of advanced stage primary SRCC of the breast in 71 year old female treated with palliative mastectomy and axillary lymph node dissection. Clinicopathologic features of this rare and aggressive tumor and its unique morphologic features are discussed.**

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Primary signet ring cell carcinoma (SRCC) of the breast is a rare morphologic type of breast cancer, which was first described in 1976<sup>1</sup>. It usually originates from lobular epithelium and it is considered a variant of lobular carcinoma<sup>2,3</sup>. However, there are suggestions that SRCC is a distinct clinicopathologic entity. It is a very aggressive morphologic type of breast cancer which usually presents as locally advanced with axillary lymph node and distant organ metastases. These tumors occasionally show an unusual metastatic pattern involving serosal surfaces of organs such as stomach, duodenum, endometrium, cervix and pelvic floor<sup>4-7</sup>.

The aim of this report is to present a case of pure SRCC of the breast in a female patient and a review of the literature.

### **The Case**

A seventy-one year old female presented with history of progressively enlarging right breast mass of one year duration and recent breast's skin erosion.

Examination revealed a large and firm mass occupying most of the right breast volume, measuring about 10 cm in diameter with peau d'orange, skin erosion, and nipple retraction, see figure 1. Right axillary lymphadenopathies were found. The left breast and axilla were normal. The rest of medical history and physical examination was unremarkable. Fine needle aspiration cytology of the right breast mass was positive for pleomorphic malignant cells with vacuolization and targetoid appearance. Computerized tomographic scan of chest

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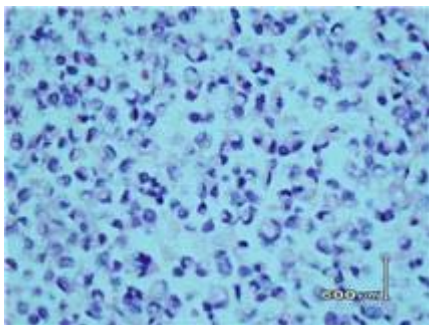
and abdomen revealed the right breast mass, axillary lymphadenopathy, one cm lymph node in the right internal mammary chain, and two small lesions in the liver measuring one cm and 0.6 cm in diameter. Bone scan was positive for multiple small metastases in the ribs. The patient underwent palliative right mastectomy and axillary lymph node dissection.



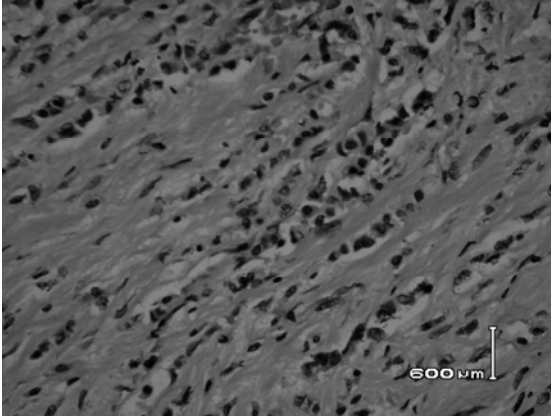
**Figure 1: Right Breast Occupied by Large Tumor with Peau d'orange, Skin Erosion and Nipple Retraction**

Pathologic examination of the surgical specimen showed 10 x 9 x 5 cm well demarcated fleshy mass with rubbery cut surface in the central part of the breast. Microscopically, the tumor showed pure signet ring cell morphology with focal Indian-file pattern, see figures 2 and 3. Tumor cells exhibited strong estrogen (ER) and progesterone (PR) receptor positivity by immunohistochemistry (IHC), see figures 4 and 5. E-Cadherin IHC was negative, see figure 6.

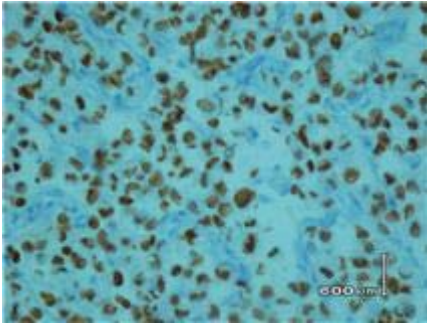
Twenty-one of 25 axillary lymph nodes were also involved with metastatic deposits. The patient had satisfactory postoperative course and was referred to oncology service for adjuvant therapy.



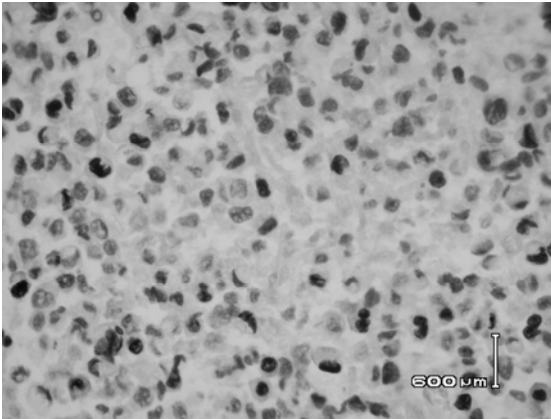
**Figure 2: Signet Ring Cell Morphology, H & E Stain**



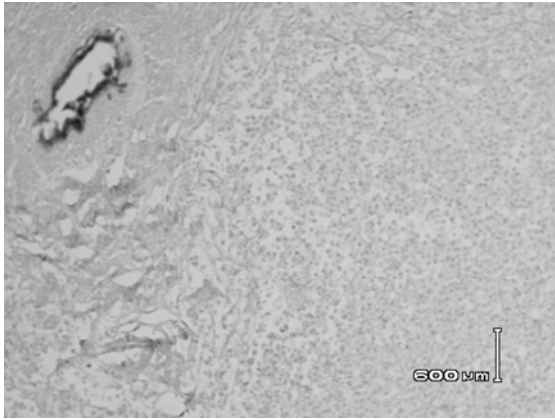
**Figure 3: Tumor Showing Indian-file Pattern, H & E Stain**



**Figure 4: ER IHC Showing Strong Positivity**



**Figure 5: PR IHC Showing Strong Positivity**



**Figure 6: E-Cadherin IHC Showing Complete Negative Staining. Note the Positive Internal Control in an Adjacent Normal Duct**

## **DISCUSSION**

Signet ring cell carcinomas in general are mucin producing epithelial malignancies (adenocarcinomas) that are poorly differentiated and are highly aggressive. They may arise from many different organs including stomach, colorectum, pancreas, lungs, prostate, bladder, ovaries, testes and breasts. In SRCCs, intra-cytoplasmic mucin production pushes the nucleus to the periphery of the cell producing the characteristic morphologic appearance of signet ring cells.

Mucins are high molecular weight glycoproteins produced by secretory epithelial cells; two types of mucin are recognized, secretory, and transmembrane. Secretory mucins act as physical defensive barriers protecting epithelial surfaces<sup>8</sup>.

Trans-membrane mucins may serve as ligands and modulators in cell signal transduction<sup>9</sup>. Mucins may protect cells from host immune response, decrease cell adhesion and protect from tumor invasion<sup>9-11</sup>. Paradoxically, in neoplastic transformation, mucins may assume new roles protecting the tumor from host immune response.

Primary SRCCs of the breast are quite rare and the exact incidence is unknown; however, it has been reported to be from 0.7% to 4.5% of all breast cancers. The five years mortality rate is 45.5% to 60%<sup>12</sup>.

Pure signet ring cell carcinoma is diagnosed in tumors when over 90% of the cells displaying this morphology<sup>2</sup>. The Indian file pattern and the negativity of E-Cadherin of our case support the fact that these tumors are variants of lobular carcinoma, which is similar to other studies<sup>2</sup>.

Pleomorphic lobular carcinoma in situ (LCIS) may occasionally contain signet ring cells; however, it is rare for an LCIS to be composed entirely of signet ring cells<sup>13</sup>.

Occasionally, the site of origin of SRCC tumor is obscure, and identification of its primary source is a challenging task. In this setting IHC played an important role in elucidating the site of the primary tumor<sup>14</sup>.

## CONCLUSION

**Primary signet ring cell carcinoma of the breast is a rare and aggressive variant of lobular breast carcinoma often presenting as locally advanced with axillary lymph node and systemic metastases.**

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## REFERENCES

1. Steinbrecher JS, Silverberg SG. Signet-ring Cell Carcinoma of the Breast. The Mucinous Variant of Infiltrating Lobular Carcinoma? *Cancer* 1976; 37(2): 828-40.
2. Tavassoli FA. *Pathology of the Breast*, Stanford Conn. Appleton and Lange: 1992; 454-9.
3. Raju U, Ma CK, Shaw A. Signet Ring Variant of Lobular Carcinoma of the Breast: A Clinicopathologic and Immunohistochemical Study. *Mod Pathol* 1993; 6(5): 516-20.
4. Kondo Y, Akita T, Sugano I, et al. Signet Ring Cell Carcinoma of the Breast. *Acta Pathol Jpn* 1984; 34(4): 875-80.
5. Sato T, Muto I, Hasegawa M, et al. Breast Signet-Ring Cell Carcinoma with Duodenal Obstruction and Acute Pancreatitis. *Asian J Surg* 2007; 30(3): 220-3.
6. Kennenbeck CH, Alagoz T. Signet Ring Breast Carcinoma Metastases Limited to the Endometrium and Cervix. *Gynecol Oncol* 1998; 71(3): 461-4.
7. Colak T, Akca T, Dirlik M, et al. Signet Ring Cell Carcinoma of the Breast as a Source of Pelvic Floor Metastatic Mass. A Case Report. *ActaChirBelg* 2005; 105: 224-6.
8. Gendler SJ. MUC 1, the Renaissance Molecule. *J Mammary Gland Biol Neoplasia* 2001; 6: 339-53.
9. Carraway K, Ramsauer V, Haq B, et al. Cell Signaling through Membrane Mucins. *Bio Essay* 2002; 25: 66-71.
10. Matsukita S, Nomoto M, Kitajima S, et al. Expression of Mucins (MUC1, MUC2, MUC5AC and MUC6) in Mucinous Carcinoma of the Breast: Comparison with Invasive Ductal Carcinoma. *Histopathology* 2003; 42(1): 26-6.
11. Wesseling J, van der Valk SW, Hilkens J. A Mechanism for Inhibition of E-cadherin-mediated Cell-cell Adhesion by Membrane-associated Mucinepsialin/MUC1. *MolBiol Cell* 1996; 7: 565-77.
12. Uroda N, Fujishima N, Ohara m, et al. Invasive Ductal Carcinoma of the Breast with Signet Ring Cell and Mucinous Carcinoma Components: Diagnostic Utility of Immunocytochemistry of Signet Ring-Cells in Aspiration Cytology Materials. *Diagn Cytopathol* 2007; 35(3): 171-3.
13. Fadare O. Pleomorphic Lobular Carcinoma in Situ of the Breast Composed Almost Entirely of Signet Ring Cells. *Pathol Int* 2006; 56(11): 683-7.
14. Peiguo G, Weiss LM. Immunohistochemical Characterization of Signet Ring Cell Carcinomas of the Stomach, Breast and Colon. *Am J Clin Pathol* 2004; 121: 884-92.