Primary Pure Signet Ring Cell Carcinoma Of The Breast – Case Report Of An Unusual Tumor With A Short Review Of Literature

S Sharma, V Monappa, G Krishnanand

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Abstract

Primary signet ring cell carcinoma (SRCC) of the breast are uncommon tumors with unique clinicopathologic features and aggressive nature. Histogenetically this tumor is distinct from both infiltrating ductal and lobular carcinomas. It is characterized by the presence of >20% signet ring cells (SRC). Pure SRCC breast is very rare and diagnosed when >90% of the tumor shows SRC. We report a case of primary pure SRCC breast in a 78 year old post menopausal woman with a short review of literature.

INTRODUCTION

Primary signet ring cell carcinoma (SRCC) of the breast was first described as a pathologically distinct entity in 1976 by Steinbrecher and Silverberg[1]. Recently, the 2003 World Health Organization (WHO) classification has placed this tumor as an independent entity under 'mucinous carcinomas and other tumors with abundant mucin'[2]. Primary SRCC can originate from both invasive lobular and ductal carcinoma, although it usually originates from the lobular epithelium[2].

SRCC breast is clinically distinct and usually presents as locally advanced tumor with axillary lymph node, distant organ metastases and occasionally with an unusual metastatic pattern involving serosal surfaces of organs such as stomach, duodenum, endometrium, cervix and pelvic floor[3]. Histologically, SRCC is defined by the presence of at least 20% of the malignant cells appearing as signet ring form in the tumor[1,2].

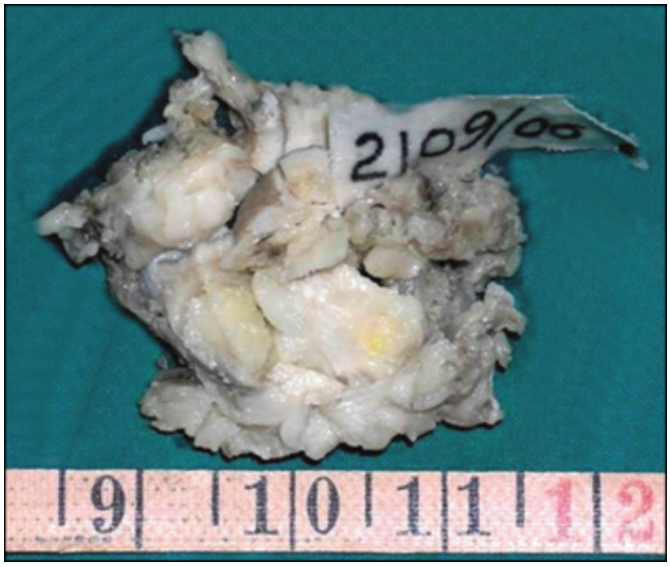
CASE REPORT

A 78 year old post menopausal woman presented with a history of painless lump in the left breast from 6 years with a gradual increase in size since 3 months. Patient also complained of neck and back pain since 2 months. She gave history of fracture right femur 5 years back. Local examination showed skin discoloration and 2 x2 cm lump in left upper outer quadrant. There was no discharge per nipple or enlarged lymph nodes. Chest X-ray, gastrointestinal endoscopy and ultrasound abdomen were normal. CA-125 was within normal limits.

Lumpectomy was done and sent for histopathological examination. Cut section of the lump showed an infiltrating grey white growth measuring 2x 1.5x 1 cms (Fig. 1).

Figure 1

Figure 1 Infiltrating grey-white growth



Microscopy showed a tumor composed of > 90% SRC with abundant vacuolated cytoplasm and peripherally pushed uniform round hyperchromatic nucleus, arranged in Indian file pattern along with focal glandular and alveolar patterns.(Fig 1 & Fig 2) Tumor cells showed cytoplasmic Periodic acid Schiff and mucicarmine positivity suggesting the presence of cytoplasmic mucin. (Fig 3 & 4). Surrounding

stroma was desmoplastic and showed elastosis.(Fig 5). Two of the margins were involved by tumor and showed areas of lobular carcinoma in situ (LCIS).

Figure 2

Figure 1 Indian-File pattern H & E X 100

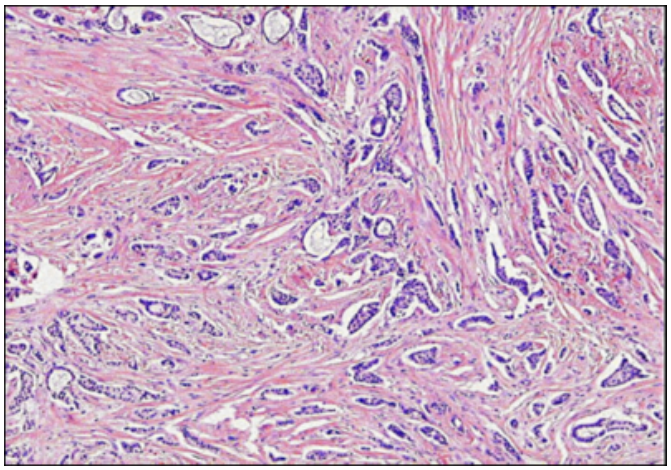


Figure 3

Figure 2 Glandular and Alveolar pattern H & E X200

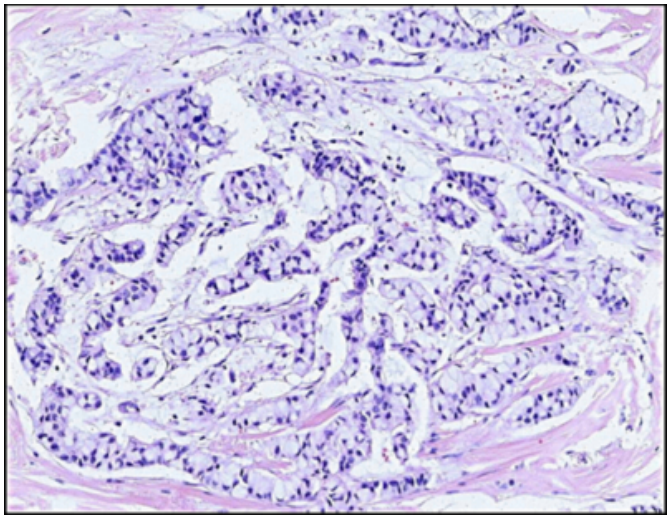


Figure 4

Figure 3 Periodic acid- Schiff +ve in tumor cells X 200

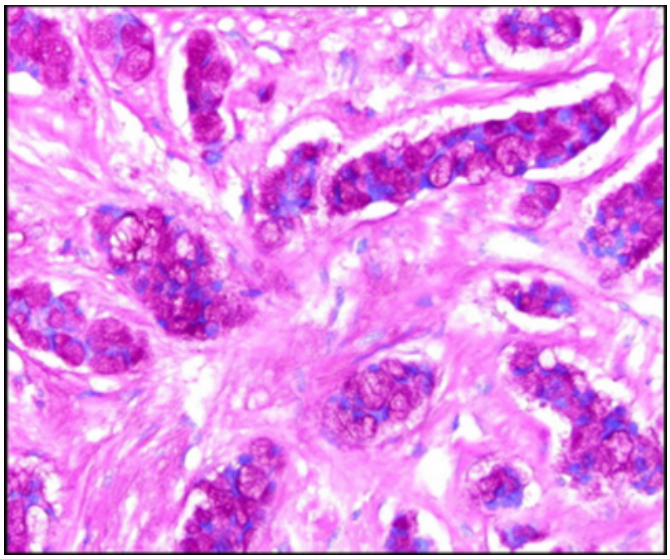


Figure 5

Figure 4 Mucicaramine +ve in tumor cells X 200

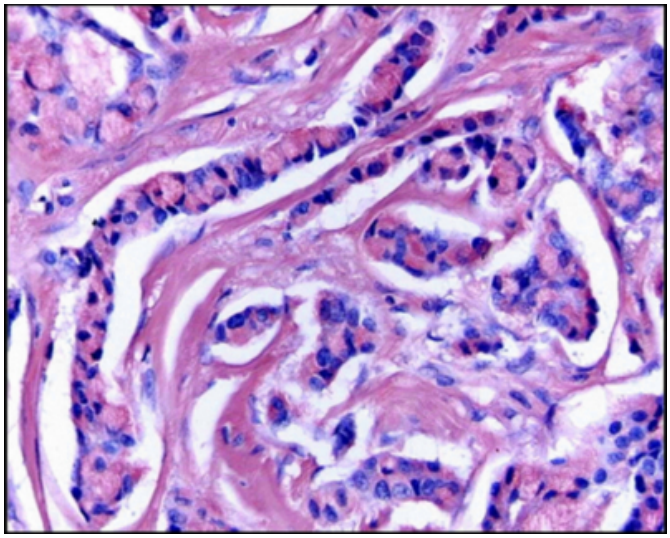
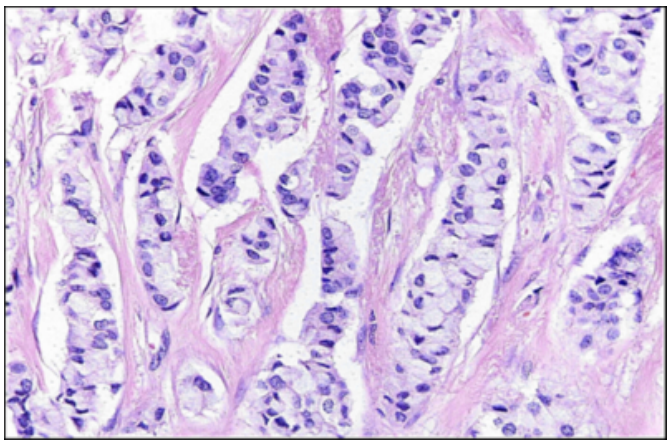


Figure 6

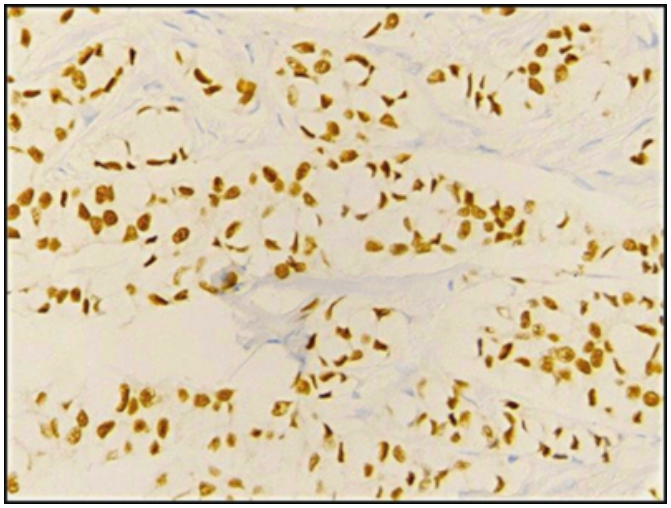
Figure 5 Surrounding stroma with desmoplasia and elastosis H & E X 400



The tumor cells showed strong nuclear positivity for estrogen receptor and were negative for progesterone receptor and Her 2 neu.(Figure 6) E-Cadherin was lost in the tumor cells

Figure 7

Figure 6 ER +ve in tumor cells X400



A diagnosis of pure SRCC breast was given after ruling out metastatic adenocarcinoma and other histologic mimickers. Bone scan done subsequently revealed multiple osteoblastic skeletal metastasis. Patient was started on palliative radiotherapy and was on regular follow up. After 2 years patient succumbed to the disease.

DISCUSSION

The earliest description of SRC in breast carcinoma was by Frantz in 1938, however it was Saphir in 1941 who grouped SRCC breast as a variant of mucinous (colloid) carcinomas[4].

In 1976, Steinbrecher and Silverberg reported SRCC breast as a distinct group with an aggressive clinical behavior and characterstic pathologic and clinical features[1].

Primary SRCC breast are rare and the exact incidence is difficult to evaluate as till recently WHO classification did not recognize it as a distinct entity[5]. However, its incidence was reported to vary from 0.7% to 4.5% of all breast cancers with the five years mortality rate of 45.5% to 60%[3]. Pure form of SRCC are very rare with few cases reported in literature[2].

SRCC breast was earlier considered to be related histogenetically to lobular carcinomas rather than duct lesions on basis of findings of mucin content, distribution and ultrastructure[1]. Later on, Hull et al[6] and Azzopardi[7] in their studies described a probability of ductal origin. Merino MJ et al[1] considered the possibility that SRC can be shed from ductal lesions and percentage of SRC in such tumors is less than 10%. This case showed evidence of lobular origin with foci of LCIS.

SRCC breast exhibits distinct clinical features. Average age of presentation is more than other breast carcinomas[1,4,8,9]. It is associated with an aggressive clinical course, most patients present in advanced stages of disease and have poorer prognosis[1]. Spread of disease past the regional lymph nodes presents as haematogenous metastasis to the lung, liver and bone. Other common sites of metastasis include the stomach, endometrium, cervix[5] and unusual sites like serosa, gastrointestinal tract, urinary tract and spleen[1].

Microscopically, SRCC are of two types, one related to lobular carcinoma with invasive component having targetoid pattern of classical lobular carcinoma, and the other similar to diffuse gastric carcinoma and associated with SRC variant of ductal carcinoma in situ. The characteristic histologic hallmark of SRCC is the signet ring cell (SRC) characterized by small, uniform cells with clear vacuolated cytoplasm (PAS and mucicarmine positive) and a compressed nucleus situated at the periphery[10]. According to Merino MJ et al SRC should comprise at least 20% of the tumor in SRCC breast[1,10]. Pure SRCC breast is diagnosed when > 90% of the tumor cells display this morphology[11].

The prognosis of SRCC breast is not discussed in detail in literature. This can possibly be attributed to the rarity of this tumor. Merino MJ et al[1] studied 24 cases of SRCC breast and reported a poor prognosis in 60% cases with almost all

patients being dead by 7 years. The present case had widespread bone metastasis and succumbed to the disease after 2 years of diagnosis.

It is thus important to recognize the presence of SRC in breast carcinomas because increased number of SRC have increased negative outcomes[10]. Frost et al in their study to determine the prognostic significance of SRC in infiltrating lobular carcinoma found that presence of at least 10% SRC represents a poor individual prognostic factor in stage I lobular carcinoma, but not in II, III or IV[2]. Bilateral involvement is associated with poor prognosis while positivity for hormonal receptors is a good prognostic factor[2].

SRCC breast must be differentiated from colloid (mucinous) carcinoma, lipid rich carcinoma, secretory carcinoma, squamous cell carcinoma with clear cell changes, glycogen rich carcinoma and metastatic clear cell adenocarcicnoma[1,2,4,11,12]. Mucinous carcinoma shows pools of extracellular mucin. Lipid rich carcinoma are composed of poorly differentiated masses of large cells with irregular nuclei and clear cytoplasm containing neutral lipids and are mucin stain negative. Secretory carcinoma is usually seen in children and adolescents and shows tubuloalveolar pattern. Primary / secondary squamous cell carcinoma with clear cell features usually shows foci of frank squamous cell carcinoma within the tumour. Glycogen rich carcinoma has cords, nests and papillary structures with cells having abundant clear cytoplasm containing glycogen and not mucin[10]. ER positivity in tumor cells, microscopic foci of LCIS, negative biochemical and radiological evidence of tumor elsewhere helped to exclude metastatic tumor in this case.

CONCLUSION

Pure SRCC breast are very rare tumors composed of > 90% vacuolated PAS positive, mucicarminophilic signet ring cells. They have unusual clinicopathological features distinct from infiltrating lobular and ductal carcinomas. Elderly age, advanced stage at presentaion and unusual sites of metastasis are some of its unique features. Histologically it must be distinguished from other clear cell and mucin-producing breast tumors and metastatic adenocarcinoma.

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Author Information

Swati Sharma
Department of Pathology, Center of Basic Sciences, Kasturba Medical College

Vidya Monappa
Department of Pathology, Center of Basic Sciences, Kasturba Medical College

Geetha Krishnanand
Department of Pathology, Center of Basic Sciences, Kasturba Medical College