Signet Ring Carcinoma of the Breast : An Uncommon Type of Breast Carcinoma

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Introduction

Signet ring cell carcinoma (SRCC) is a unique subtype of adenocarcinoma characterized by abundant intracellular mucin accumulation. SRCC of the breast, originally grouped as a variant of mucinous carcinoma, was later realized to be a pathologically distinct group [1]. We report a case of SRCC of the breast that is ductal in origin.

Case report

A 70-year old lady with a gradually increasing lump left breast of 16 years duration underwent a lumpectomy in a civil hospital – which was reported as infiltrating duct carcinoma (IDC) on histopathology. No chemotherapy / radiotherapy was taken. She presented to a service hospital a year later with a recurrence in the left breast. Clinically, the left nipple was retracted. The skin showed peau d'orange and was fixed to a lump in the Upper Inner Quadrant (UIQ) of the breast. She was staged clinically as stage IIIB ($T_4N_2M_0$) and a left radical mastectomy was performed. Grossly, a 5.5 X 3.0 X 2.0 cm grey-white tumour was seen just beneath the skin in the UIQ. Axillary dissection showed two metastatic masses and fourteen additional lymph nodes.

Fig. 1 : Sheets of signet ring cells separated by fibrous bands (HE x 100)

Microscopic examination showed an infiltrating carcinoma with individual signet ring cells (SRCs) comprising more than 90% of the tumour. The cells had abundant intracellular mucin and were seen in sheets (Fig 1). Numerous foci were seen which contained more than 50 SRCs / HPF (Fig 2). No areas of Ductal carcinoma in situ (DCIS) / Lobular carcinoma in situ (LCIS) / IDC / Infiltrating lobular carcinoma (ILC) were seen. Lymphatic tumour emboli were seen. The tumour cells were mucicarmine and PAS positive and Diastase resistant (DR). Axillary dissection showed metastasis of adenocarcinoma with IDC features. In addition, eight other lymph nodes showed metastasis.

Discussion

SRCC represents 2%-4.5% of all mammary carcinomas [2]. SRCC has been defined as a lesion with diffuse infiltration of the stroma by mucin containing signet ring cells. The mucin appears as a discrete, mucicarmineophilic, PAS⁺, DR cytoplasmic vacuole. The cells are small, uniform, dissociated, composed of a clear vacuolated cytoplasm and a compressed nucleus situated at the base of the cell. These SRCs should comprise at least 20% of the tumour mass, though the neoplastic

Fig. 2 : One HPF showing more than 50 signet ring cells (HE x 400)

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SRCs may make as much as 99% of the lesion [3]. The number of SRCs in the tumour to be 'significant' is used differently and varies from as less as 20% to more than 50%. The nature of the mucin is acid mucosubstances consisting mainly of sialomucin with minor quantities of sulphomucin.

SRCC is to be distinguished from mucinous or colloid carcinomas, which are duct-derived variants. Grossly, SRCC resemble IDC in that it is hard as it invokes an intense desmoplastic response and is infiltrating. Colloid carcinomas tend to be soft to firm, glistening on cut surface and well circumscribed. In SRCC, mucin is identified intracytoplasmically, whereas in mucinous / colloid carcinoma, the tumour is composed of small clusters of neoplastic cells disposed in large pools of mucin. This pattern must comprise at least 50% of the lesion. Distinguishing SRCC from mucinous carcinoma is clinically significant since SRCCs are associated with an aggressive clinical course and a poorer prognosis [3].

SRCs can occur in ILC and IDC. It is important to recognize the presence of these cells because studies have shown that patients who have tumours with an increased number of SRCs have increased negative outcomes [3,4]. Though several lines of evidence suggest that this neoplasm is related histogenetically to lobular carcinomas [5,6], the probability exists that a few are ductal in origin [4]. In our case there were no areas of DCIS / LCIS / IDC / ILC in the primary tumour with more than 90% of tumour cells exhibiting a signet ring cell morphology. However, the tumour showed a typical adenocarcinoma with IDC features in the axillary nodal metastasis. The appearance of IDC in the metastasis with the absence of ILC areas in the primary tumour suggests a ductal origin, which is unusual.

SRCC needs to be differentiated from a number of other neoplastic conditions. Lipid rich carcinomas do not show retraction of nipple on gross. Microscopically, lipid rich carcinomas show poorly differentiated masses of large cells with irregular nuclei and clear cytoplasm containing neutral lipids [7]. The cytoplasm stains positive for lipid stains and is mucin negative. Secretory carcinoma, squamous cell carcinoma, metastatic adenocarcinoma and glycogen rich carcinoma were ruled out in our case. Secretory carcinoma is usually seen in children and adolescents and shows tubulo-alveolar pattern [8]. Primary / secondary squamous cell carcinoma with clear cell features will usually show foci of frank squamous cell carcinoma within the tumour. Metastatic clear cell adenocarcinoma usually does not have such a high number of SRCs. Glycogen rich carcinoma has cords, nests or papillary structures and more than 90% of cells have abundant clear cytoplasm

containing glycogen and not mucin, which gives a positive, diastase labile reaction with the PAS stain.

Signet ring appearance in neoplastic cells in GIT, breast and ovarian cancers usually is linked to the presence of epithelial mucin; but it can also be seen in neoplasias like lymphoma, myeloma, liposarcoma, mesothelioma and squamous cell carcinoma in which the cytoplasmic material is not epithelial mucin. SRCs have also been reported in several non-neoplastic conditions (endometriosis, deciduas, prostate after TURP) and probably represent degenerative products. In none of these cases has an infiltrative pattern of mucin positive cells seen. In certain cases, muciphages can also be confused with signet ring cells, especially in the lymph nodes [9].

SRCC show a propensity to involve unusual metastatic sites – GIT, serosal and submucosal surfaces of the stomach, female genital tract, urinary tract and spleen [3,4,10]. SRCCs have a greater incidence and extent of axillary lymph node involvement [5]. In lymph nodes, metastases exhibit a 'sinus catarrh' pattern [1]. Clinically, the average age of patients with SRCC is somewhat older than that of patients with ordinary breast carcinoma. Patients of SRCC also present in advanced stage of disease [1]. The prognosis is generally poor. The histogenetic character of signet ring carcinoma of the breast remains controversial.

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