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Case Report

Secretory carcinoma of breast: No more a juvenile tumor

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ABSTRACT

Introduction: Secretory breast carcinoma (SBC) is one of the rare breast neoplasm with an incidence rate of < 0.15% of all breast cancers. Previously it was described as juvenile breast carcinoma. Young children and adolescent girls are most commonly affected. It is characterized by balanced translocation t (12;15), ETV6-NTRK3 gene fusion.

Case Presentation: A 45 -year-old female presented with palpable lump in left breast. FNAC was suggestive of mucinous carcinoma. The diagnosis of SBC was made through histopathology and Immunohistochemistry**.**

Discussion: Recent study report suggested that the disease may also occur at a later age group in contrast to the conventional thought of onset at juvenile age group. Long-term survival is good for these cases. In radiological studies of breast imaging it mimics a benign tumour Immuno-histochemistry and cytogenetic are of the tumour are the ancillary investigations for confirmation of diagnosis.

Conclusion: Although rare diagnosis of SBC can be confirmed by histopathological studies and IHC. It is slowly progressive but has a good prognosis.

1. Introduction

Secretory carcinoma of the breast (SBC) is an unusual breast tumour with overall incidence rate less than 0.15%. Mc Divitt and Stewart[1] described this tumour for the first time in 1966 and they named it as juvenile breast carcinoma. However it has been renamed as secretory carcinoma because of it's peculiar histopathological findings and occurrence in wide age range. Incidence of this tumour is equal in both males and females, but the median age of presentation is 25 years.[2]

Usually patients present at an early stage. Out of these 30% individuals have Lymph node metastasis but distant metastasis is infrequent.[3] Histologically SBC is quite characteristic and easily appreciable from invasive duct carcinoma. Three histological patterns, are seen primarily (i) microcystic, (ii) solid, and (iii) tubular with plentiful intra and extracellular secretory material. Minimal cellular atypia is seen.[4] Most frequently, they are triple negative {negative for estrogen receptor (ER), progesterone receptor (PR) and ERBB2 (HER2/neu)}. Therefore, SBCs often shows characteristics of triple-negative breast carcinoma (TNBC). They also positive for cytokeratin 5/6, 14, 17 and c-Kit (CD117), which are features of basal-like breast carcinomas (BLBC).[5] A very typical genetic translocation t (12;15) has been observed in this rare malignancy, leading to fusion between E26 transformation-specific translocation variant 6 (ETV6) and neurotrophic receptor tyrosine kinase

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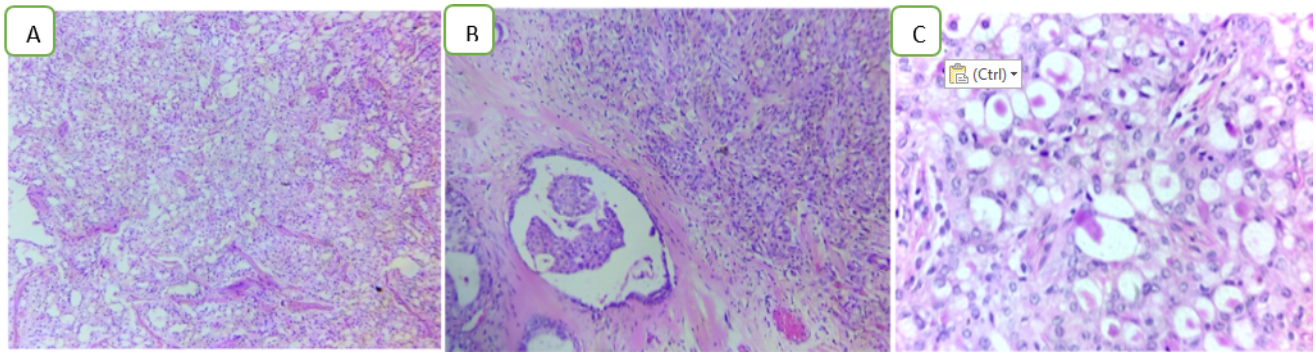

Fig. 1: A: Low power (10X x 10X) H&E Tumor cells arranged predominantly in micocystic and tubular pattern; **B:** Low Power (10X x 10X) H&E Shows Lymphovascular invasion; **C:** High Power (40X x 10X) H & E Shows glandular pattern with eosionphilic secretion.

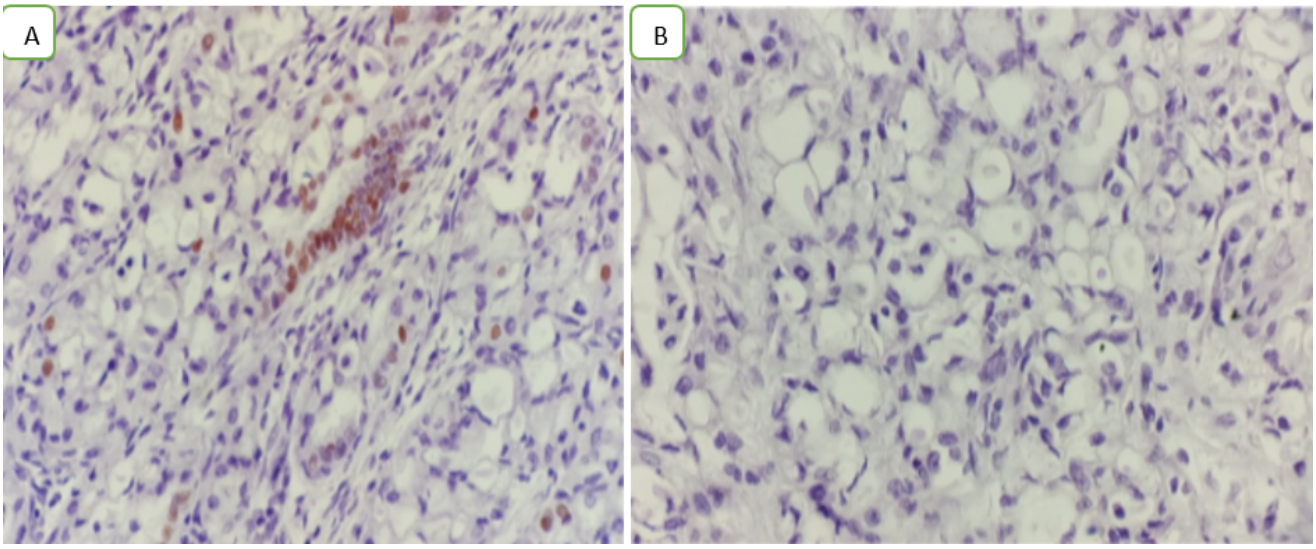

Fig. 2: A: High Power (40X x 10X) ER negative; **B:** High Power (40X x 10X) HER2 neu Negative.

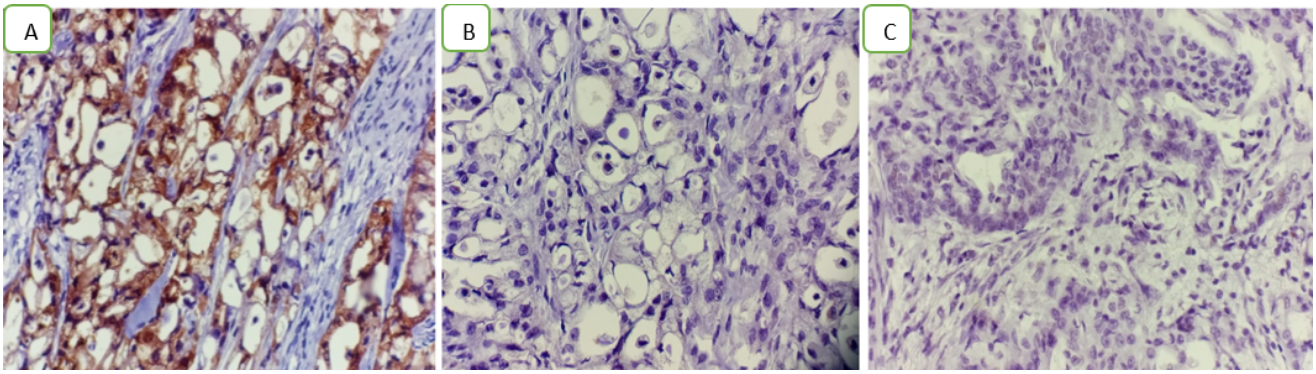

Fig. 3: A: High Power (40X x 10X) tumor cells are diffusely immunore active for S-100 protein; **B:** High Power (40X x 10X) p63; **C:** High Power (40X x 10X) Shows low Ki-67.

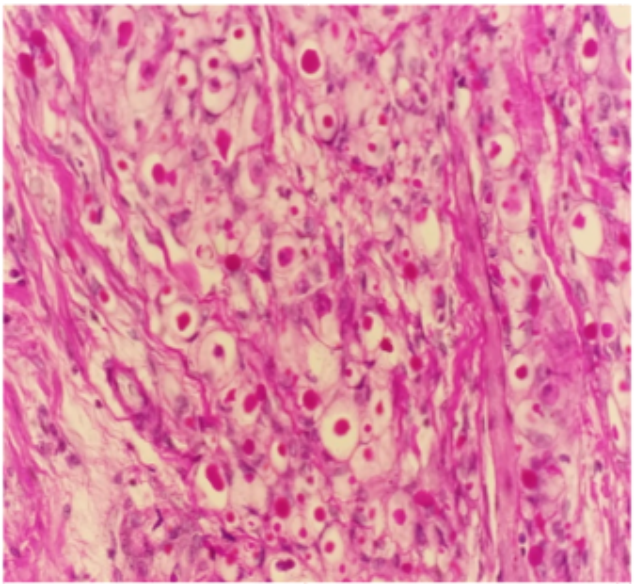

Fig. 4: High power (40X x 10X) Pink eosionphilic secretion intensely PAS positive.

3 (NTRK3) which gives rise to fusion protein ETV6-NTRK3, that triggers two oncogenic effector pathways.[6]

2. Case Presentation

A 45 year lady had a palpable lump in upper outer quadrant of left breast. The breast imaging was done (BIRADS -4b) and preoperative FNAC was suggestive of mucinous carcinoma of breast. Then the patient underwent a breast conservative surgery in SLN medical college Koraput, Odisha. The specimen was received in Pathology Department of SLN Medical college Koraput, Odisha. The histopathological and IHC slides with the blocks came to department of Pathology, PGIMER and Capital Hospital, Bhubaneswar, Odisha for review.

2.1. Gross and microscopic findings

The lumpectomy specimen well oriented with sutures, measured 2.3x2.2x2 cm. Histopathological study showed tumour cells arranged various patterns including microcysts, tubules and follicles. Tumour cells had low mitotic activity and minimal nuclear pleomorphism (Figure 1A,B,C). Hormone receptor status was assessed. The tumour cells are negative for ER (Figure 2A), PR and Her2neu (Figure 2B). In addition to that, IHC for S-100 protein showed diffuse cytoplasmic and membranous p (Figure 3A). P-63 was negative. (Figure 3B) Ki-67 index was low (Figure 3C) The microcysts were filled with copious, pink, eosinophilic secretions, which were bright Periodic acid Schiff (PAS) positive and diastase resistant.(Figure 4). Besides intracytoplasmic vacuolation and eosinophilic secretions were also observed in the tumour cells. All the resection margins were free of tumour (> 10 mm away). Hence, we gave a final diagnosis of secretory breast carcinoma.

3. Discussion

SBC is an uncommon breast malignancy with an overall incidence of less than 0.15. It was first named as juvenile breast carcinoma.[1] Later, it was observed that this tumour affects people of all age group with an no gender predisposition.[7] Jacob et al.[8] described the mean age of SBC to be 56 years. The tumour is very slow in progression. 5-year and 10-year cause-specific survival are observed to be 94.4% and 91.4%, respectively by Horowitz et al.[8,9] The location of the tumour is different for different age groups. In young patients the tumour is usually located in the subareolar region whereas in adult patients upper outer quadrant mass is the common presentation. In the present case, mass was located in upper outer quadrant of left breast.

SBC close mimicker a fibroadenoma in mammographic study of breast. In mammography it appears as a discrete, solitary lesion with a well-defined margin. This carcinoma is more common in young girls, in whom glandular elements of breast is dense causing diagnostic limitations of mammography. Ultrasonography of SBC also resembles a fibroadenoma. On ultrasound a well-circumscribed, hypo to isoechoic mass with micro lobulation is observed most times. Thus, radiological findings of SBC resemble other benign fibro-epithelial lesions of breast. In the present case, the mammography demonstrated a solitary, discrete lesion with well delineated margin.

The SBCs are usually negative for hormone receptor analysis (ER, PR, HER2/neu) with strong and diffuse cytoplasmic positivity for S-100. Therefore, SBC commonly behaves as TNBC. Strong and diffuse cytoplasmic positivity for S-100 is a unique finding of this tumour.[9] Perineural and lympho-vascular invasions are also quite rare.

The unique genetic translocation (ETV6- NTRK3) of SBCs leads to formation of a fusion gene encoding the chimeric protein. This fusion protein results in expression of mammary growth factor protein, key protein causing secretory changes in SBC.[10,11] The NTRK gene fusion involving NTRK1, NTRK2, or NTRK3 is observed in various tumours like congenital mesoblastic nephroma, infantile fibrosarcoma, mammary analogue secretory carcinoma and many other tumours of different organs making them susceptible to tyrosine kinase inhibitors (TKI).[12]

4. Conclusion

Secretory breast carcinoma is a rare triple-negative breast cancer with good prognosis. Radiologically, this tumour is a great mimicker of fibroadenoma and other benign

breast lesions. The morphology and genetic translocation of this tumour are very diagnostic. Due to the slow rate of progression of this tumour, most recurrences are observed within 10-20 years of initial presentation. Therefore, a long term follow-up is needed for all cases irrespective of their age.

5. Source of Funding

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6. Conflict of Interest

None.

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