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Metaplastic Carcinoma Breast with Chondroid Differentiation

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ABSTRACT

Metaplastic carcinoma of breast, previously called as carcinosarcoma, is one rare form of breast cancer. It accounts for less than 1% of all primary breast tumors. It consists of both glandular and nonglandular components admixed with epithelial and mesenchymal tissues. This type of breast cancer usually resembles invasive ductal carcinoma clinically and radiologically. This is a case of a 65-year-old female with painful lump in left breast for 2 months. Lumpectomy of the same showed features of metaplastic carcinoma of breast with chondroid differentiation, which is a rare form of metaplasia with better prognosis than other forms. Immunohistochemistry was helpful in confirming the diagnosis. Overall survival is less with this form of carcinoma as compared to intraductal carcinoma of breast.

Keywords: Metaplastic, epithelial and mesenchymal, breast carcinoma, prognosis

Metaplastic breast carcinoma (MBC) is a rare heterogeneous group of invasive breast carcinomas. Previously termed as carcinosarcoma, it is characterized by differentiation of neoplastic epithelial cells towards squamous and/or mesenchymal looking elements. It accounts for only about 1% of all invasive breast carcinomas.[1] This rare histopathological variant of breast malignancy is reported for its correct identification and appropriate management.

CASE DETAILS

A 65-year-old female presented with chief complaints of a lump in left breast for past 2 months. The swelling was insidious in onset and was progressive in nature and associated with pain. There was no nipple discharge. There was no history of fever or trauma or weight loss. Her past medical history was unremarkable with no comorbidities. She had no family history of breast or ovarian cancer.

General physical and systemic examination was unremarkable. On examination, left breast was showing fullness over lower inner quadrant. Skin over swelling was normal and pinchable with no dimpling or ulceration. Nipple areola complex was normal. On palpation, there was a 2 × 1 cm lump felt over lower inner quadrant, hard in consistency, nontender and was moving with breast tissue. Right breast was normal. No palpable lymph nodes were noted in left and right axilla. All baseline investigations were normal. True-cut biopsy was done and was reported as benign breast tissue. After a complete pre-surgery workup, wide local excision under general anesthesia was done.

Histological examination was suggestive of metaplastic carcinoma with heterogeneous mesenchymal differentiation (chondroid) (Fig. 1). The tumor showed <10% of areas with glandular or tubular formation and with marked nuclear pleomorphism, irregular nuclear membrane, vesicular nuclei and prominent nucleoli (Figs. 2 and 3). Mitosis was increased (16/10 hpf) with a Nottingham grade of three. The surgical margins were free of tumor. The tumor conferred to pT1c pNx. By immunohistochemistry, tumor cells were triple negative (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor 2 [HER2]) and

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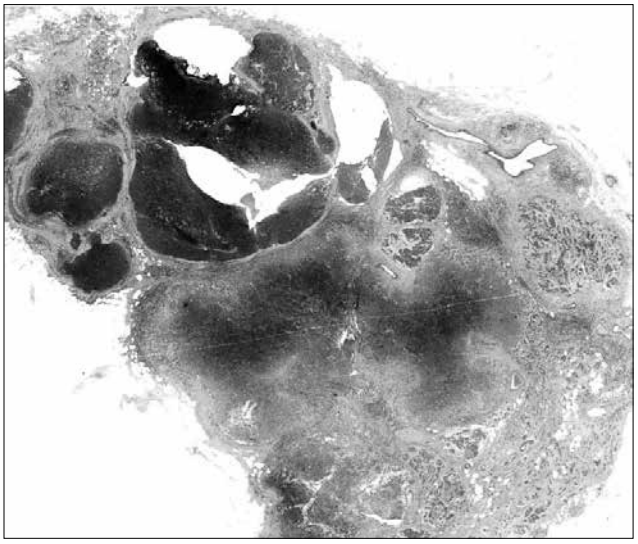

Figure 1. Breast tissue with multiple lobules of chondroid material (H&E x40).

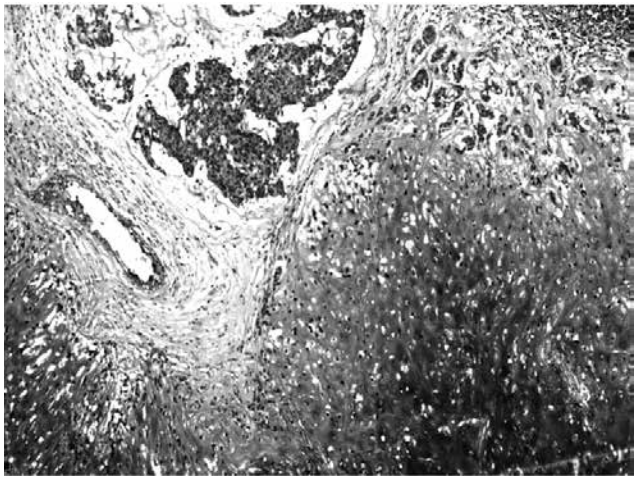

Figure 2. Invasive mammary carcinoma with <10% glandular formation and marked nuclear pleomorphism with chondroid differentiation (H&E x40).

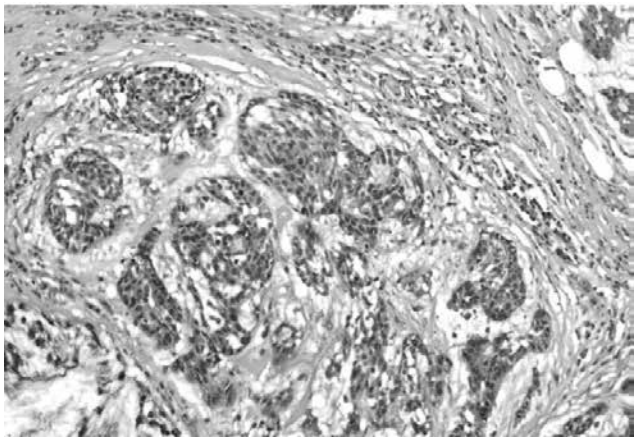

Figure 3. Higher magnification showing metaplastic carcinoma breast with chondroid differentiation (H&E x100).

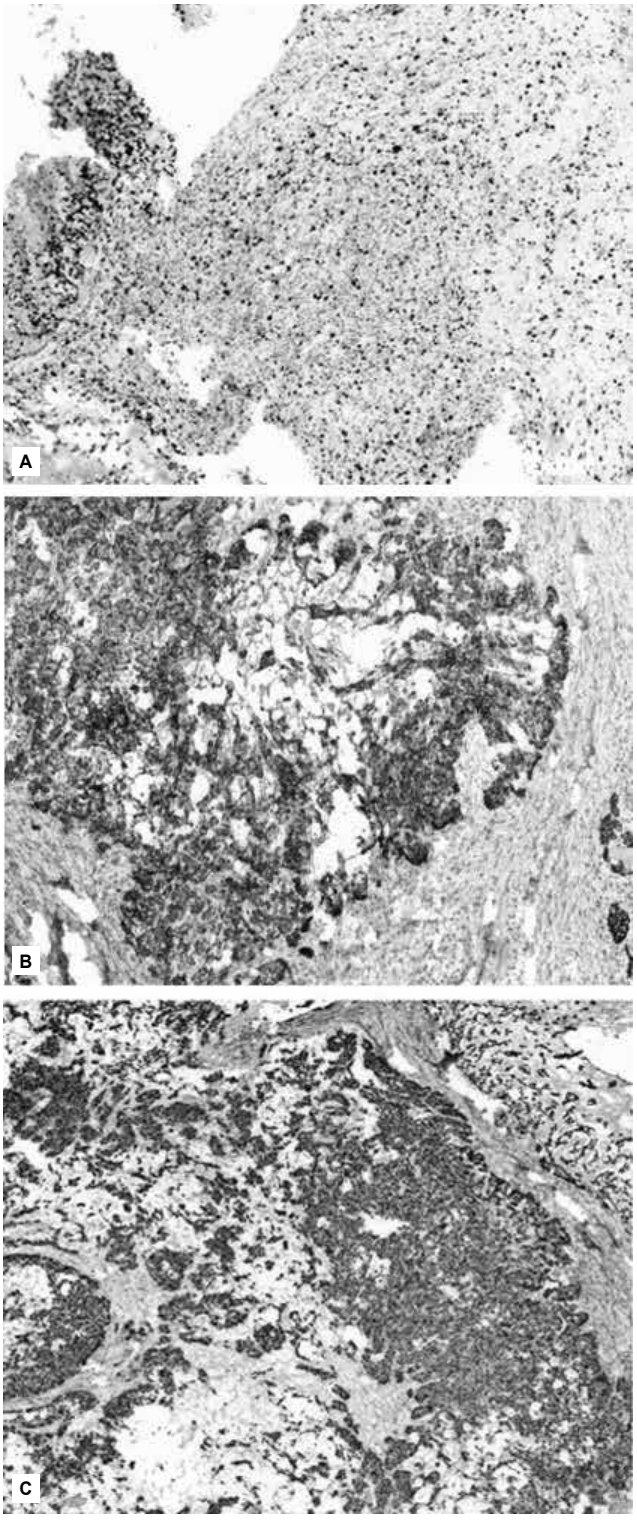

Figure 4. Immunohistochemistry showing Ki labeling index (**A**), CK positivity (**B**) and S-100 positivity (**C**).

p63 was negative. The tumor cells were strongly positive for S-100 and pan-cytokeratin (pan-CK). Ki-67 labeling index was 40% (Fig. 4). Postoperative period was uneventful.

DISCUSSION

Most of the benign and malignant tumors of breast originate from glandular epithelium.[1] In few instances, glandular epithelium differentiates into nonglandular mesenchymal tissue, known as metaplasia.[1] Metaplastic changes in breast include squamous cell, spindle cell and heterogeneous mesenchymal growth. Earlier it was known with different names like carcinosarcoma, sarcomatoid carcinoma, carcinoma with pseudosarcomatous metaplasia, carcinoma with pseudosarcomatous stroma, all of which are not recommended; rather it is known as metaplastic carcinoma not otherwise specified.

Metaplastic breast carcinoma is a rare, aggressive high-grade breast cancer. It accounts for <1% of all breast malignancy.[2] Most common age of presentation is around 48-59 years.[3] It presents as a rapidly growing mass with size usually larger than 2 cm^2. Clinically and radiologically more or less it resembles invasive ductal carcinoma (IDC).[4] On ultrasonogram, it may have high density with either circumscribed or irregular and/or spiculated margins. This may appear benign on mammogram.[3]

The cell of origin for MBC is not clear but many studies suggest that myoepithelial cells will differentiate along mesenchymal lines and produce matrix elements.[4] Epidermal growth factor receptor amplification is seen in around 28% of MBC.[4] P53 mutation is seen in 61% in MBC.[3,5] Presence of transitional areas and epithelial differentiation like tight junctions or desmosomes in heterogeneous sarcomatous component is supportive of a metaplastic process.[3] GATA3-regulated genes account for cell-to-cell adhesion, stem cell-like characteristics and epithelial to mesenchymal transition. Decreased expression of these GATA3-regulated genes make any tumor chemoresistant.[6] Like stem cells, tumor cells are positive for CD44 and negative for CD24.[7]

Histologically, MBC is a biphasic tumor containing ductal carcinoma admixed with areas of spindle, squamous, chondroid and osseous elements.[3] MBC with chondroid differentiation is a rare phenomenon.[8] Differential diagnoses include angiosarcoma, fibromatosis, pleomorphic carcinoma,[9] malignant phyllodes tumor, malignant adenomyoepithelial tumor with chondroid matrix and chondrosarcoma. With presence of benign chondroid tissue, chondrolipoma and pleomorphic adenoma are considered.[8] Thorough and extensive sampling is necessary for definitive diagnosis. Immunohistochemistry plays a vital role in confirming the diagnosis.

MBC also shows triple negativity in 90% cases, similar to infiltrating ductal carcinomas, because it is associated with poorly differentiated carcinomatous elements.[9] Chondroid cells are usually positive for pan-CK and S-100 and negative for epithelial membrane antigen (EMA).[5] Axillary lymph node metastasis in MBC is very uncommon. Rather, hematogenous route is preferred with most common distant site of metastasis being pleura, lung, liver and abdominal viscera.[9] Presence of axillary lymph node metastasis indicates a poor prognosis.[1,3]

Prognostic factors of MBC depend on tumor size >5 cm, histological type, degree of differentiation, type and degree of mesenchymal component, presence of axillary lymph node and distant metastasis.[1,9] Increased risk of local recurrence has been reported. Basically, MBC has poorer prognosis than other IDC, but MBC with chondroid differentiation exhibits better prognosis than other subtypes.

Surgical radical mastectomy is considered the mainstay of treatment. Conservative surgery with radiotherapy is followed for tumors <5 cm in size.[5] And total mastectomy followed by chemotherapy and radiotherapy is followed for tumors >5 cm in size with skin or chest wall involvement or >4 axillary lymph node metastasis. Since local recurrence and metastasis is more common, radiotherapy and chemotherapy play a vital role in treatment.[6] Clinical trials on role of targeted gene therapy following genetic profiling have been done.[4] Epidermal growth factor receptor inhibitors act as potent therapeutic agents.[6] Overall 5-year survival rate is around 43%.[1]

CONCLUSION

When a malignant breast tumor with chondroid elements is seen, metaplastic carcinoma with chondroid differentiation is essentially considered, even though epithelial component is minimal or even absent. Extensive sampling and immunohistochemistry will help in differentiating it from other tumors. Surgery with chemotherapy and radiotherapy is considered as most appropriate treatment. Disease-free survival and overall survival is less in metaplastic carcinoma as compared to IDC of breast.

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UK Regulator Found 30 Cases of Blood Clot Events Following Use of AstraZeneca Vaccine

The UK regulators have stated that 30 cases of rare blood clot events have been reported following the use of the AstraZeneca COVID-19 vaccine.

The Medicines and Healthcare products Regulatory Agency added that there were no such reports of clotting events after use of the Pfizer-BioNTech COVID-19 vaccine. The health officials maintained that the benefits of the vaccine in preventing COVID-19 still outweigh any possible blood clot risk.

While some countries have restricted the use of AstraZeneca vaccine, others have resumed its use, amid investigations into the reports of rare blood clot events.

The regulator had stated on March 18 that 5 cases of a rare brain blood clot had been reported among 11 million administered vaccine doses. Recently, it made it as 22 reports of cerebral venous sinus thrombosis, and 8 reports of other clotting events associated with low blood platelets from among 18.1 million doses administered… (*Reuters*)

No Approval for Sputnik V Vaccine in India Yet

An expert panel of the country's central drug authority has asked for additional information from Dr Reddy's Laboratories, which applied for EUA for the Russian COVID-19 vaccine, Sputnik V. The decision on the authorization was deferred till the next meeting.

The company had submitted the interim safety and immunogenicity data of the Gam-Covid-Vac combined vector vaccine from the county, in addition to the interim data from the ongoing Russian study. The Subject Expert Committee (SEC) on COVID-19 of the Central Drugs Standard Control Organisation (CDSCO) has recommended that the company must submit data regarding all immunogenicity parameters, unblinded data of serious adverse events and reverse transcriptase-polymerase chain reaction (RT-PCR) positive cases, and the causality analysis reported till now, for further evaluation… (*ET Healthworld – PTI*)

Covaxin Receives Approval for Trial of Booster Shot

The indigenous COVID-19 vaccine – Covaxin - will now be evaluated for a booster dose, which can be given 6 months following the second dose.

The Subject Expert Committee (SEC) that advises the Drugs Controller General of India (DCGI), has given approval for this and has recommended that Bharat Biotech must carry out the booster dose study only on Phase II trial participants after they have been given 6 μg of Covaxin. The participants have to be followed up for at least 6 months after the administration of the third dose. The approval for the booster dose study has come after Bharat Biotech requested amendments in the approved Phase II trial protocol, to permit administration of a booster dose 6 months after the second dose of the vaccine… (*ET Healthworld – TNN*)

Every citizen of India should have the right to accessible, affordable, quality and safe heart care irrespective of his/her economical background

HEART CARE FOUNDATION OF INDIA
A Not-For-Profit Organisation

Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

E-219, Greater Kailash, Part I, New Delhi - 110048 E-mail: heartcarefoundationfund@gmail.com Helpline Number: +91 - 9958771177

"No one should die of heart disease just because he/she cannot afford it"

About Sameer Malik Heart Care Foundation Fund

"Sameer Malik Heart Care Foundation Fund" it is an initiative of the Heart Care Foundation of India created with an objective to cater to the heart care needs of people.

Objectives

- Assist heart patients belonging to economically weaker sections of the society in getting affordable and quality treatment.
- Raise awareness about the fundamental right of individuals to medical treatment irrespective of their religion or economical background.
- Sensitize the central and state government about the need for a National Cardiovascular Disease Control Program.
- Encourage and involve key stakeholders such as other NGOs, private institutions and individual to help reduce the number of deaths due to heart disease in the country.
- To promote heart care research in India.
- To promote and train hands-only CPR.

Activities of the Fund

Financial Assistance

Financial assistance is given to eligible non emergent heart patients. Apart from its own resources, the fund raises money through donations, aid from individuals, organizations, professional bodies, associations and other philanthropic organizations, etc.

After the sanction of grant, the fund members facilitate the patient in getting his/her heart intervention done at state of art heart hospitals in Delhi NCR like Medanta – The Medicity, National Heart Institute, All India Institute of Medical Sciences (AIIMS), RML Hospital, GB Pant Hospital, Jaipur Golden Hospital, etc. The money is transferred directly to the concerned hospital where surgery is to be done.

Drug Subsidy

The HCFI Fund has tied up with Helpline Pharmacy in Delhi to facilitate patients with medicines at highly discounted rates (up to 50%) post surgery.

The HCFI Fund has also tied up for providing up to 50% discount on imaging (CT, MR, CT angiography, etc.)

Who is Eligible?

All heart patients who need pacemakers, valve replacement, bypass surgery, surgery for congenital heart diseases, etc. are eligible to apply for assistance from the Fund. The Application form can be downloaded from the website of the Fund. http://heartcarefoundationfund.heartcarefoundation.org and submitted in the HCFI Fund office.

Important Notes

- The patient must be a citizen of India with valid Voter ID Card/ Aadhaar Card/Driving License.
- The patient must be needy and underprivileged, to be assessed by Fund Committee.
- The HCFI Fund reserves the right to accept/reject any application for financial assistance without assigning any reasons thereof.
- The review of applications may take 4-6 weeks.
- All applications are judged on merit by a Medical Advisory Board who meet every Tuesday and decide on the acceptance/rejection of applications.
- The HCFI Fund is not responsible for failure of treatment/death of patient during or after the treatment has been rendered to the patient at designated hospitals.
- The HCFI Fund reserves the right to advise/direct the beneficiary to the designated hospital for the treatment.
- The financial assistance granted will be given directly to the treating hospital/medical center.
- The HCFI Fund has the right to print/publish/webcast/web post details of the patient including photos, and other details. (Under taking needs to be given to the HCFI Fund to publish the medical details so that more people can be benefitted).
- The HCFI Fund does not provide assistance for any emergent heart interventions.

Check List of Documents to be Submitted with Application Form

- Passport size photo of the patient and the family
- A copy of medical records
- Identity proof with proof of residence
- Income proof (preferably given by SDM)
- BPL Card (If Card holder)
- Details of financial assistance taken/applied from other sources (Prime Minister's Relief Fund, National Illness Assistance Fund Ministry of Health Govt of India, Rotary Relief Fund, Delhi Arogya Kosh, Delhi Arogya Nidhi), etc., if anyone.

Free Diagnostic Facility

The Fund has installed the latest State-of-the-Art 3 D Color Doppler EPIQ 7C Philips at E – 219, Greater Kailash, Part 1, New Delhi.
This machine is used to screen children and adult patients for any heart disease.

Free Education and Employment Facility

HCFI has tied up with a leading educational institution and an export house in Delhi NCR to adopt and to provide free education and employment opportunities to needy heart patients post surgery. Girls and women will be preferred.

Laboratory Subsidy

HCFI has also tied up with leading laboratories in Delhi to give up to 50% discounts on all pathological lab tests.

Help Us to Save Lives

The Foundation seeks support, donations and contributions from individuals, organizations and establishments both private and governmental in its endeavor to reduce the number of deaths due to heart disease in the country. All donations made towards the Heart Care Foundation Fund are exempted from tax under Section 80 G of the IT Act (1961) within India. The Fund is also eligible for overseas donations under FCRA Registration (Reg. No 231650979). The objectives and activities of the trust are charitable within the meaning of 2 (15) of the IT Act 1961.

Donate Now...

About Heart Care Foundation of India

Heart Care Foundation of India was founded in 1986 as a National Charitable Trust with the basic objective of creating awareness about all aspects of health for people from all walks of life incorporating all pathies using low-cost infotainment modules under one roof.

HCFI is the only NGO in the country on whose community-based health awareness events, the Government of India has released two commemorative national stamps (Rs 1 in 1991 on Run For The Heart and Rs 6.50 in 1993 on Heart Care Festival- First Perfect Health Mela). In February 2012, Government of Rajasthan also released one Cancellation stamp for organizing the first mega health camp at Ajmer.

Objectives

- Preventive Health Care Education
- Perfect Health Mela
- Providing Financial Support for Heart Care Interventions
- Reversal of Sudden Cardiac Death Through CPR-10 Training Workshops
- Research in Heart Care

Heart Care Foundation Blood Donation Camps

The Heart Care Foundation organizes regular blood donation camps. The blood collected is used for patients undergoing heart surgeries in various institutions across Delhi.

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This Fund is dedicated to the memory of **Sameer Malik** who was an unfortunate victim of sudden cardiac death at a young age.

- HCFI has associated with Shree Cement Ltd. for newspaper and outdoor publicity campaign
- HCFI also provides Free ambulance services for adopted heart patients
- HCFI has also tied up with Manav Ashray to provide free/highly subsidized accommodation to heart patients & their families visiting Delhi for treatment.