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Neuroendocrine Tumor of Breast

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ABSTRACT

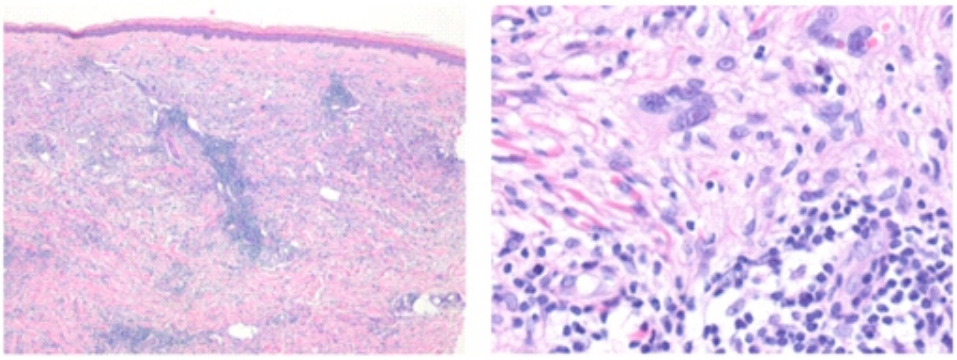
Rare and difficult breast cancer subtype neuroendocrine carcinoma of the breast (NECB). This study includes three NECB case cases to demonstrate its diagnostic and treatment challenges. Case Study 1 is a 34-year-old lady diagnosed with fibroadenoma who later developed neuroendocrine invasive ductal carcinoma. After mastectomy and Tamoxifen adjuvant chemotherapy, she had no recurrence at six months. Case Study 2 is a 48-year-old lady with NECB who responded to surgery and chemotherapy but developed liver and lung metastases. Chemotherapy and hormone treatment reduced metastases. Case Study 3 is a 50-year-old lady with poorly differentiated infiltrating breast cancer with neuroendocrine signs who had adjuvant chemotherapy, radiation, and hormone treatment without recurrence after six months.

INTRODUCTION

Due of its rarity and uniqueness, neuroendocrine carcinoma of the breast (NECB) is difficult to diagnose and cure. The case studies demonstrate this intricacy. Case Study 1's first misdiagnosis emphasises breast lump evaluation. Case Study 2's chemotherapeutic reaction to metastases shows NECB's unpredictability. However Case Study 3's post treatment success shows the value of multimodal therapy.

CASE STUDY -1

A 34-year-old woman saw a drawn outmonth long breast lump. Review uncovered a 3 cm by 3 cm hard, non-delicate lump underneath the nipple and areola. This patient was determined to have fibroadenoma. Mammography showed a sporadic, inadequately characterized hypoechoic cancer that the Breast Imaging reporting and data system portrayed as fifth stage threat. Complete blood counts, liver and kidney capability tests, viral markers and venereal illness research lab tests were negative. These lab tests were ordinary. MRM specimen 16x9x3cm axillary fat cushion. Analyzation uncovered a 2.5 cm × 2 cm dark white unpredictable mass with putrefaction and cystic modification underneath the nipple and areola. Tissue had rubbery, dark and white fibrocystic regions. The axilla fat cushion had thirteen lymph nodes. Histopathological H and E areas showed growth cells in diffuse sheets, groups, and sometimes trabecular pattern with thin fibrous septae. Every cell displayed a homogenous shape, size, hyperchromatic core. Figure 1 (a) and (b) show arrangement of tumor cells. Each of the thirteen lymph nodes had sinus histiocytosis. Immunohistochemistry showed progesterone receptors, estrogen Figure 2 (a), and cytokeratin (CK) 18 in cancer cells. NSE, synaptophysin, and chromogranin A were NE markers that over half of cancer cells displayed positive discoveries for Figure 2 (b). She had negative CK 14, 7.5/6, S-100, 2/neu, and epithelial film antigen discoveries. Ki 67 expansion was beneath 5%. Invading ductal carcinoma-NE breast was the temporary determination, and luminal A was the sub-atomic sort. Research was finished to reject out metastatic NEC. Hence head and neck, chest, and abdomen imaging and processed tomography tracked down no extra-mammary essential growth. In this way, Stage 2A (pT2N0M0) strong essential breast NEC with free took apart lymph nodes was the last finding. The patient had cyclophosphamide, adriamycin, and 5-fluorouracil adjuvant chemotherapy with Tamoxifen. No metastases or nearby repeats were seen all through the half year follow-up.



(a) (b)

Figure :1 Arrangement of Tumour Cells: Diffuse Sheets, Clusters, and Trabecular Patterns with Thin Fibrous Septae (H&E, ×100 and × 400)

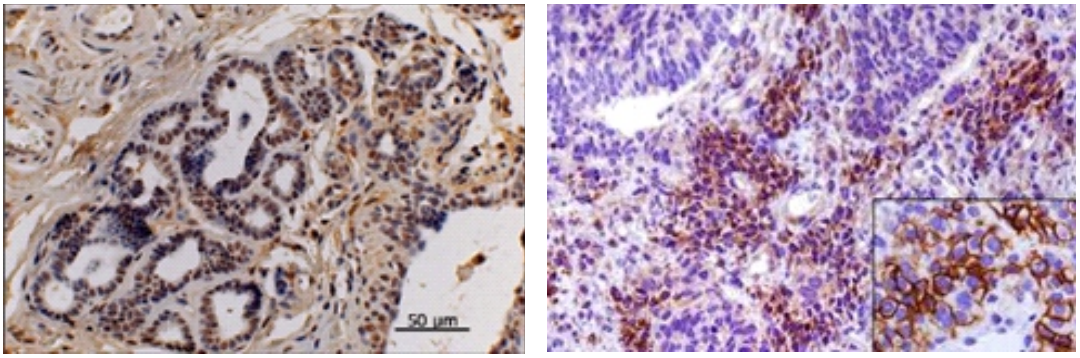


Figure : 2 (a) Estrogen Nuclear Staining and (b) Synaptophysin Cytoplasmic Staining (IHC,× 400)

CASE STUDY 2

A 48 year old lady with clear clinical history gave a knob enduring 2 years. A mammography showed a 23-mm obscure mass with conflicting shapes in the right breast lower quadrants.The ultrasound uncovered a hypoechoic strong development with unpredictable layouts, estimating 21 × 16 mm with a solid Doppler signal showing BIRADS 5.

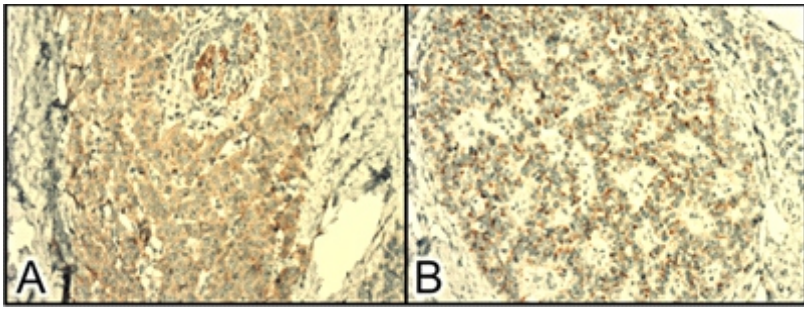


Figure : 3 (a) (Synaptophysin Positivity in Tumor Cells (IHCx) and (b) Chromogranin Positivity in Tumor Cells (b, IHC x 200)

Ultrasound directed right breast knob microbiopsy. Histopathology uncovered a neuroendocrine carcinoma in the right breast. The cancer cells showed solid chromogranin and synaptophysin immunostaining (Fig. 3). Right axillary analyzation and lumpectomy were finished. Naturally visible examination uncovered a strong, white nodular growth estimating 4 × 2 × 2 cm in the extracted tissue. A minuscule assessment showed a grade III neuroendocrine carcinoma. Seven metastatic lymph nodes (7 N +/17 N) had capsular attack and endolymphatic emboli. Immunohistochemistry showed chromogranin and synaptophysin antibodies in the cancer.

Our patient disregarded foundational drug exhortation. She returned a year after the fact with mastodynia in a similar breast, areola withdrawal, and retro areolar solidness. Clinical assessment uncovered two colossal ipsilateral axillary lymphadenopathies estimating 10 and 6 cm and a firm, difficult, 13 cm right breast mass in the infero-outside quadrant, connected to the shallow breast tissues with areola withdrawal. She had SBR grade III neuroendocrine carcinoma once more, as per the cancer biopsy's histology. Chemical receptors were positive (1% progesterone, 80% estrogen). Negative HER2/neu scores had 60% Ki-67 proliferative file.

Radiology uncovered an enormous right breast growth, right axillary lymphadenopathy, liver, and lung metastases on a thoraco-abdominopelvic CT check. No resulting bone sore was seen on bone scintigraphy. Eight rounds of first-line metastatic anthracyclines (epirubicin 100 mg/m2 and cyclophosphamides 500 mg/m2) were given. The growth mellowed and metastatic axillary lymph nodes retreated after treatment. A thoraco-abdominopelvic CT filter showed that her 20 mg/day tamoxifen support chemical treatment decreased her pneumonic and hepatic sores. It was great to see no growth or axillary lymphadenopathy four months after the fact. The liver metastases shrank and the pneumonic sores vanished on a thoraco-abdominopelvic CT filter. Our patient rejected a multidisciplinary meeting mastectomy guidance and took 20 mg of tamoxifen chemical day to day. She fostered a 6 cm hemorrhagic fistulized mass in her right breast, areola penetration, and a hard fixed axillary lymphadenopathy a year after the fact, demonstrating clinical and radiological movement. Bone scintigraphy showed no optional sores. A thoraco-abdominopelvic CT filter uncovered nodular hepatic sores, including a 22 × 13 mm bigger one, and various right breast masses with respective axillary adenopathies and subcutaneous thickening. Organic testing showed CA 15-3 levels at 213.2 U/ml. Our patient got second-line metastatic chemotherapy with 175 mg/m2 paclitaxel and 5 AUC carboplatin. Six rounds of chemotherapy dispensed with axillary lymphadenopathies, shrank the breast growth, and brought CA15-3 down to 180 U/ml. Liver and lung metastases were unaltered. From that point onward, our patient took letrozole 2.5 mg day to day for support hormonal treatment with satisfactory bearableness.

CASE STUDY 3

A 50 year old lady with three gestations and three vaginal births, no menopause, and a mother who died of oropharyngeal cancer She developed a left breast nodule in November 2020 that grew over six months. BIRADS 5 imaging showed a significant left upper external quadrant nodular development. Biopsy revealed poorly differentiated infiltrating breast cancer with vascular emboli. A malignant infiltrating neoplasm with lymph node metastases was found after axillary dissection and surgical tumorectomy. Immunohistochemistry demonstrated significant Chrom ogranin A, localised Synaptophysin, high hormone receptor expression and 70% Ki67 proliferation. Uncertain HER2 expression. Breast large cell neuroendocrine cancer was diagnosed. Adjuvant chemotherapy, radiation, and hormone treatment were given. She has finished chemotherapy, radiation and Tamoxifen with no recurrence after six months.

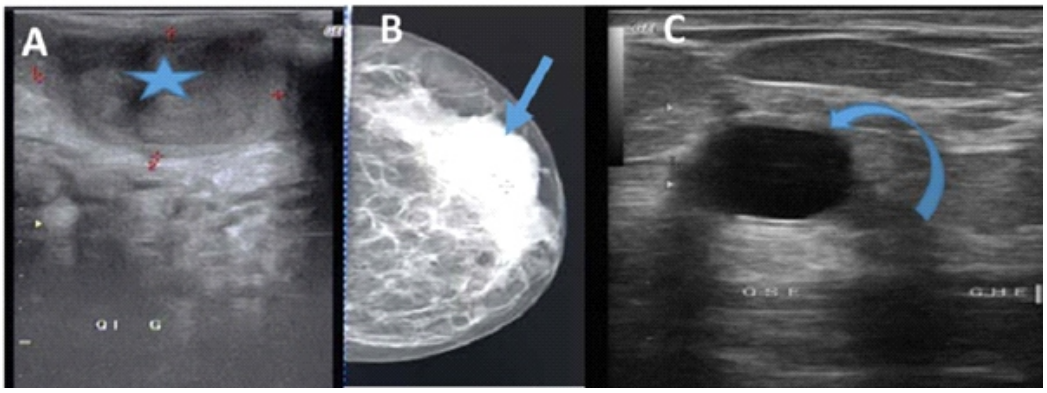


Figure : 4 Mammographic Findings of Left Breast with C Density

DISCUSSION

Volger found mammary tissue NE cells in 1947,[1] and Cubilla and Woodruff previously depicted breast PNEC in 1977.After WHO laid out conclusive models, they were renamed PNEC of breast from argyrophilic breast malignant growth, breast carcinoid growth, or endocrine carcinoma.[2] Few accept the cancer's histogenesis includes endocrine separation of breast disease as opposed to prior breast endocrine cells. Others accepted they came from multipotential undifferentiated organisms that form into NECs.[3] Other than the lungs, small cell carcinomas can happen in the stomach, small digestive tract, uterus, cervix, pancreas, larynx, windpipe, prostate, and breast. In-situ part and immunostaining for estrogen and progesterone receptor energy can lay out NEC overwhelmingly coming from the breast, as for our situation, albeit many recorded occurrences did not.[3] as far as anyone is concerned, the primary report of NEC breast growths was in the third 10 years, albeit broad writing search showed the 6th and seventh many years were the most common. WHO classified breast NEC as strong, abnormal carcinoid, little cell/oat cell carcinoma, and huge cell. Every cell has a circular to ovoid core, salt and pepper chromatin, and little cytoplasm.[4] Immunohistochemistry demonstrates more than half of growth cells positive for NE markers chromogranin, synaptophysin, and NSE. Comparable qualities were available in our circumstance. Akhtar et al. found that grimelius staining shows argyrophilia in NEC and electron thick granules on electron microscopy. Metastatic NEC to breast has been accounted for, so CT of the chest, head and neck, and midsection ought to be finished to preclude essential in the lung or different

destinations. Our CT showed no anomalies. Hoang et al. [4] tracked down indistinguishable sub-atomic changes at Breast Malignant growth quality 1, BRCA-2, p53, and retino-blastoma quality loci in two essential little cell carcinoma cases. Weigelt et al. observed that five of six breast PNECs were luminal An and one was luminal B.Watrowski et al. concentrated on a breast PNEC case and grouped it as luminal B subtype, presuming that sub atomic order helps treatment.[5]

Neuroendocrine breast carcinomas are uncommon, representing under 0.1% of breast malignancies and 1% of neuroendocrine cancers [6]. However commonly connected with the pneumonic and stomach related frameworks, they can likewise be found somewhere else. Uncommon essential mammary organ confinement [6]. Albeit neuroendocrine cancers are in many cases found in Caucasian ladies matured 60-70, more youthful people have been reported in the writing [6]. Men can get these malignancies [7]. Prohibition conclusion: essential breast neuroendocrine cancer. Octreoscan and PET sweeps ought to preclude ENT, lungs, stomach, and cutaneous destinations [8]. These growths have no particular side effects [9]. These sluggish developing growths are most frequently counseled for a single breast injury or one with extra side effects [9]. The writing depicts these characteristics, which our occurrences illustrate. These growths might show up too restricted erythematous and purple skin injuries [9]. The 2003 WHO characterization of breast growths perceives neuroendocrine carcinoma as a particular histological element with similar morphological qualities as gastrointestinal plot, pancreas, and lung neuroendocrine cancers and over half certain immun-ostaining of cancer cells by chromogranin or synaptophysin [10]. Four sorts of neuroendocrine carcinomas are strong, abnormal carcinoids, little cell, and large cell [10]. Mammary -with restricted separation dispersed cancer cells that stain positive for neuroendocrine markers are avoided. Central - separation happens in 2-5% of breast growths [11]. Sapino et al. grouped breast endocrine diseases as firm strong, alveolar, little cell, papillary strong, and mucinous carcinoma [12]. Last two sorts produce bodily fluid and frequently have an in situ part with endocrine separation [12]. Neuroendocrine disease must be analyzed histologically. Visibly, essential neuroendocrine carcinomas of the breast are round or multilobulated, yellowish-shaded, and hard, or thick whenever connected with mucinous part [13]. Histological assessment can propose neuroendocrine separation, yet immunohistochemistry examination should uncover positive staining with neuroendocrine markers by somewhere around half of growth cells to affirm it. The most delicate and explicit neuroendocrine markers are and synaptophysin. Two markers were communicated in our occurrences. Other less unambiguous markers incorporate NSE, NCAM, neurofilament, and bombesin. Cytokeratins with high atomic weight are awful. Like our patients, Her 2 is missing yet estrogenic and progesterone receptors are bounteously

Communicated [14]. Having an in situ part as well as no extramammary restriction are severe histological standards for essential breast neuroendocrine disease. Günhan-Bilgen et al. suggest diagnosing an essential endocrine cancer of the breast in the event that a patient has a thick mammary mass, microlobulated or spiculated shapes on mammography, and hypoechoic and homogenous ultrasonography [15]. Hypoechoic and homogenous ultrasound pictures can likewise be found in other threatening growths like grade 3 penetrating carcinoma or mucinous carcinoma.

Neuroendocrine carcinomas of the breast are rare with the first description in 1983 [16]. They are more common in women around the seventh decade of age, but can occur in younger individuals and men. These tumors are classified into four types based on histology. Diagnosis is confirmed by the expression of neuroendocrine markers and imaging studies like octreoscans or scans with bone scintigraphy. Radiologically, they appear as dense masses with irregular contours on mammography and hypoechogenic and homogeneous on ultrasound, resembling adenocarcinomas.

CONCLUSION

Rare and heterogeneous neuroendocrine breast cancer (NECB) offers distinct issues. This study shows the necessity of correct diagnosis and appropriate NECB treatment through case studies. Current treatments are based on breast cancer in general, but additional study is needed to under-stand NECB's molecular features and develop tailored medications. These instances show that NECB patients need correct diagnosis, interdis-ciplinary therapy, and thorough follow-up to enhance outcomes.

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