Primary Small Cell Carcinoma of the Breast Combined with Invasive Ductal Carcinoma: A Case Report

Yuqi Huang[1], Joyce Wai-Ting Chiu[2], Si Shen[3], Nana Pei[4] and Wei Zhang[1]

[1]*Department of Breast Surgery, The First Affiliated Hospital, Jinan University, Guangzhou, China*
[2]*International School, Jinan University, Guangzhou, China*
[3]*Department of Diagnostic Imaging, The First Affiliated Hospital, Jinan University, Guangzhou, China*
[4]*Department of Pathology, The First Affiliated Hospital, Jinan University, Guangzhou, China*

ABSTRACT

Primary small cell carcinoma (SmCC) of the breast is a rare type of breast cancer (BC) and a histological subtype of neuroendocrine BC. There is no standard treatment method, and the prognosis is unknown. It needs to be differentiated from lung metastases. Here, we report a case of a 52-year woman who was diagnosed with SmCC combined with invasive ductal carcinoma (IDC) of the breast. Whole-body PET-CT and enhanced MRI of the adrenal glands excluded any other primary disease. The patient received an adjuvant chemotherapy regimen of anthracycline combined with cyclophosphamide, sequential cisplatin, and paclitaxel. The changes in the patient's condition remain under close observation. This case report reviews the literature on SmCC to better understand its pathology characteristics and therapy. Due to the peculiarity of the patient's tumour composition, we referred to the treatment plan for small-cell lung cancer and adopted a treatment plan based on cisplatin.

Key Words: *Small cell carcinoma, Invasive ductal carcinoma, Breast cancer, Pathology, Therapy.*

How to cite this article: Huang Y, Chiu JWT, Shen S, Pei N, Zhang W. Primary Small Cell Carcinoma of the Breast Combined with Invasive Ductal Carcinoma: A Case Report. *JCPSP Case Rep* 2024; **2**:117-119.

INTRODUCTION

Neuroendocrine breast cancer (NEBC) is a rare subtype of breast cancer (BC), accounting for approximately 0.3 to 1% of all BCs.[1] Despite being first described more than 40 years ago, WHO did not classify NEBC as a distinct subtype of BC until 2003.[2] Primary small cell carcinoma (SmCC) of the breast is a histological subtype of NEBC with immunohistochemical characteristics similar to those of small cell carcinoma of the lung (SCLC), and the diagnosis is mainly based on pathology. This paper reports a case of SmCC in combination with invasive ductal carcinoma (IDC) of the breast and discusses it in relation to pertinent literature.

CASE REPORT

A 52-year female patient in a postmenopausal state presented with the chief complaint of right breast mass for one month. Physical examination revealed a palpable mass with a 1.5 × 3.0 cm diameter, firm, ill-defined, and poorly mobile and located in the inner lower quadrant of the right breast.

Correspondence to: Dr. Wei Zhang, Department of Breast Surgery, The First Affiliated Hospital, Jinan University, Guangzhou, China
E-mail: zhangwei@jnu.edu.cn

Received: December 01, 2023; Revised: January 20, 2024; Accepted: March 21, 2024
DOI: https://doi.org/10.29271/jcpspcr.2024.117

Ultrasound examination showed a hypoechoic nodule next to the nipple in the 3-4 O'clock position of the right breast, with an echoless dark area inside and multiple hypoechoic masses in the right axilla. Double mammography showed a lump in the lower quadrant of the right breast with a clear margin (Figure 1). A hollow-core needle was used to perform a biopsy of the lump, but intraoperative frozen pathology could not determine the nature of the tumour. Subsequently, a minimally invasive excision biopsy was performed. Based on the appearance and texture of the resected tissue, we considered the possibility of a malignant tumour. The paraffin sections also confirmed our suspicion, suggesting SmCC. After communicating with the patient's family, we performed a radical mastectomy with sentinel node biopsy on the right breast. On pathologic study, IDC (15%) and SmCC (85%) were detected. SmCC cells were relatively uniform in morphology, with little cytoplasm, a high nuclear-to-cytoplasm ratio, and a lamellar or nested distribution. Moreover, a tumour thrombus was seen in the vasculature, but no signs of cancer metastasis in the lymph nodes (0/5). On immunohistochemical staining (Figures 2 and 3), both IDC and SmCC showed estrogen receptor (ER) negativity, progesterone receptor (PR) negativity, HER-2 negativity, Ki-67, approximately 90% positivity, neuron-specific enolase (NSE) negativity, Chromogranin A (CgA), negativity, synaptophysin (Syn), negativity, thyroid transcription factor-1 (TTF-1), negativity, CD56, focal lesions positivity and GATA3, and negativity in IDC, but CD56, positivity and GATA3, and positivity in SmCC. To rule out metastatic SmCC, positron emission tomography-computed tomography (PET-CT) whole-body fusion image (Figure 4) was performed, which showed a strong possibility of adrenal metastases. Subsequently, an enhanced MR scan of the adrenal glands

was performed (Figure 4). After a discussion between the imaging and interventional specialists, it was agreed that there were no abnormalities in the bilateral adrenal glands. The results of the 21-gene test on the blood of the patient were (1) somatic variants, with one somatic variation discovered; (2) *RB1* deletion and *TP53* gene variation. Tumour staging was pT2 N0 M0. The treatment strategy included EC sequential TCb chemotherapy as adjuvant treatment. The patient was being observed very carefully.

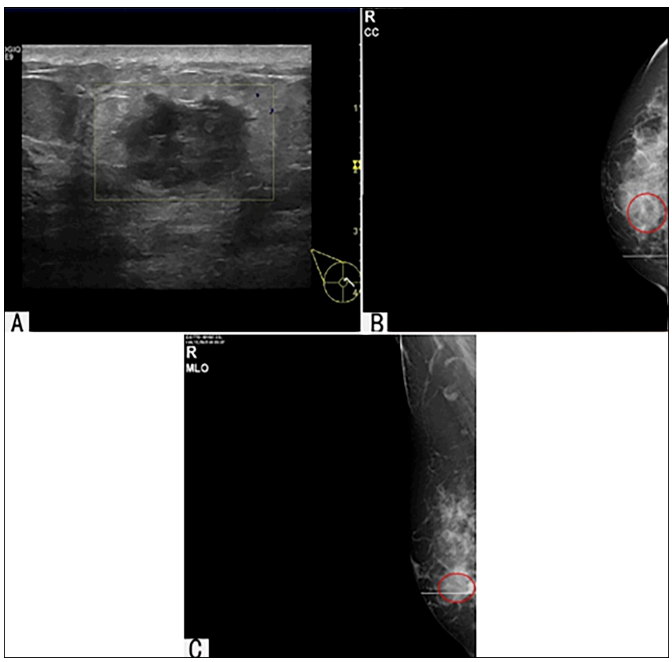

Figure 1: (A) Ultrasound of the right breast: A hypoechoic nodule with an echoless dark area visible within. (B and C) Mammogram of the right breast: Right CC-view and MLO-view showing a tissue mass (circle) in the right breast.

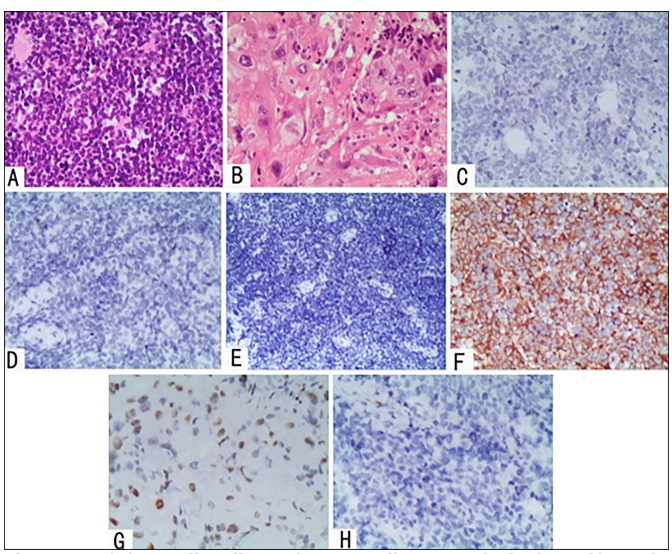

Figure 2: (A) Small cell carcinoma cells are relatively uniform in morphology, with little cytoplasm, a high nuclear-to-cytoplasmic ratio, and a lamellar or nested distribution (HE, ×100) (B) The light microscopy image showing the presence of an invasive ductal carcinoma component (HE, ×200); immunohistochemical staining of small cell carcinoma cells was seen to be negative for NSE (C) Chromogranin A (D) Synoptophysin (E) and TTF-1 (F) and GATA3 (G) (×200) (H) and positive for CD56.

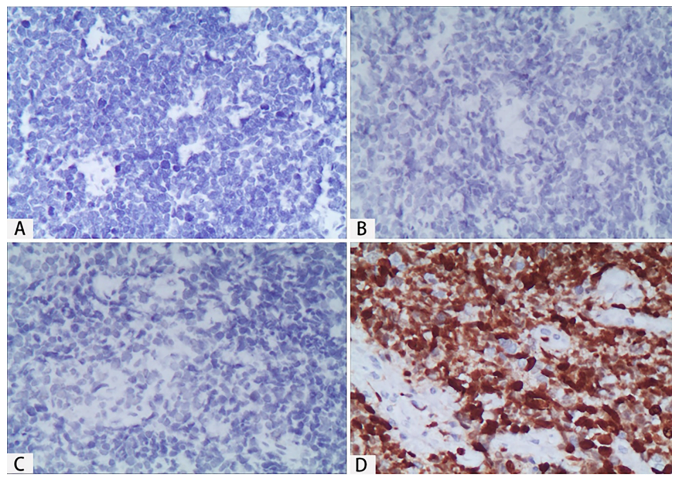

Figure 3: Small cell carcinoma cells stained negative for ER (A) PR (B) and HER-2 (C) on immunohistochemistry and positive for Ki-67 (D) immunohistochemistry (×200).

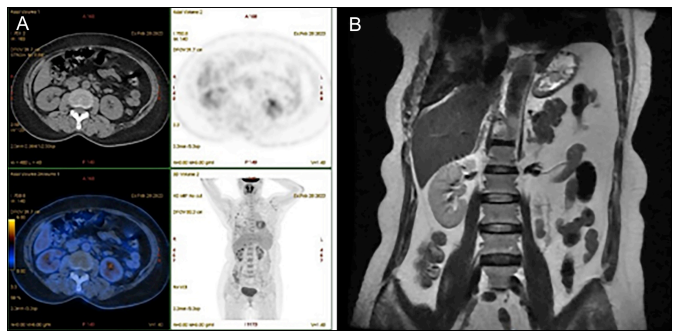

Figure 4: (A) Positron emission tomography-computed tomography whole-body fusion image showing nodular foci in the medial limb of the right adrenal gland. (B) MR scan of the renal region + adrenal glands + angiography enhancement scan suggesting no abnormalities in the adrenal glands bilaterally.

DISCUSSION

SmCC, while commonly occurring in the lung, is a highly aggressive tumour that can also develop in the breast, larynx, trachea, and other locations.[1]

Concerning the pathologic features of SmCC, the WHO defines NEBC as having three criteria.[2] One of these features is the presence of markers of neuroendocrine signatures, such as Syn, NSE, and CgA on immunohistochemistry. However, these markers are not always positive in SmCC.[3] Immune markers play an adjunctive role in the differential diagnosis of primary and metastatic NEBC. Positive expression of TTF-1 indicates a metastatic tumour and positive expression of GATA3 indicates a mammary origin.[2] In the case of excluding other primary cancers, the diagnosis of SmCC can be made by combining the microscopic morphology of the cancer cells with immunohistochemical staining.

To date, the postoperative primary therapy for SmCC is chemotherapy, endocrine therapy, and radiotherapy. There is no standard approach for selecting a chemotherapy regimen to treat SmCC. The 2022 NCCN Clinical Practice Guidelines for SCLC recommend chemotherapy regimens for SCLC, including Irinotecan + Cisplatin or Carboplatin and Cisplatin or Carboplat-

in+Etoposide.[4] The chemotherapy treatment for SmCC of breast relates to the chemotherapy regimen recommended by the aforementioned clinical practice guidelines for SCLC. According to some reports, chemotherapy drugs are based on the expression of Ki-67 protein. When SmCC expresses approximately 10% Ki-67, anthracycline therapy is generally recommended.[5] In the absence of robust data on the role of platinum compounds and etoposide in the adjuvant therapy of SmCC, Inno *et al*. recommended treatment according to the same regimen as for IDC.[3] Therefore, if necessary, anthracycline- and/or taxane-based chemotherapy regimens should be prioritised. Since, 15% of this patient's tumour was IDC, the chemotherapy regimen of anthracycline combined with cyclophosphamide followed by cisplatin combined with paclitaxel was used.

The status of the hormone receptors determines whether to administer hormone therapy as adjuvant therapy. According to one study, ER and PR were positive in 33 to 50% of the diseased tissues in SmCC.[6] No HER-2-positive SmCC has been documented till date.[1] Furthermore, the role of HER-2 in SmCC is uncertain.[7] Targeted HER-2 therapy may be an option for HER-2-positive SmCC, assuming that its function is comparable to that in other invasive BCs.[7] The role of radiotherapy in the therapy of SmCC of the breast is controversial. It has been proposed that the therapy strategy might be personalised. Kanat *et al.* proposed that adjuvant chemotherapy and radiotherapy may be avoided in older postmenopausal individuals with well-characterised malignancies.[8] They reported seven cases of primary SmCC of the breast in females. One of whom was 75 years old, had no lymph node metastases, tested positive for ER and PR, was treated with tamoxifen alone, and had no evidence of recurrence at 20 months follow-up.

In conclusion, this case presented unique features and required a personalised treatment approach given the combination of SmCC and IDC in the same lesion.

FUNDING:
This paper was supported by the Guangzhou Science and Technology Project (2023A03J0599) and the Flagship specialty construction project-General Surgery (The First Affiliated Hospital, Jinan University) (No.711003).

PATIENT'S CONSENT:
The attending physician explained to the patient that the disease is used for publishing case reports, and the patient clearly understood the relevant content, voluntarily cooperated in completing the collection of relevant information, and signed the informed consent form for the publication of case report.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
WZ: Conception and design.
YH, SS, NP: Performed the research and data collection.
YH, SS, NP, JC: Data analysis and interpretation.
WZ, YH: Drafted the manuscript.
All authors approved the final version of the manuscript to be published.

REFERENCES

1. Latif N, Rosa M, Samian L, Rana F. An unusual case of primary small cell neuroendocrine carcinoma of the breast. *Breast J* 2010; **16(6)**:647-51. doi:10.1111/j.1524-4741.2010.00974.x.
2. WHO Classification of Tumors Editorial Board. WHO classification of tumors. 5th Edition. Breast tumours. http://www.iarc.who.int/news-events/who-classification-of-tumours-5th-edition-volume-2-breast-tumours.
3. Inno A, Bogina G, Turazza M, Bortesi L, Duranti S, Massocco A, *et al*. Neuroendocrine carcinoma of the breast: Current evidence and future perspectives. *Oncologist* 2016; **21(1)**:28-32. doi: 10.1634/theoncologist.2015-0309.
4. Ganti AKP, Loo BW, Bassetti M, Blakely C, Chiang A, D'Amico TA, *et al*. Small cell lung cancer, version 2.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2021; **19(12)**:1441-64. doi: 10.6004/jnccn.2021.0058.
5. Murata T, Fujii M, Akahane K, Oda K, Ohama T, Yatabe Y, *et al*. Multidisciplinary management of small cell carcinoma of the breast: A case report. *Nagoya J Med Sci* 2014; **76(1-2)**:173-80.
6. Mirza IA, Shahab N. Small cell carcinoma of the breast. *Semin Oncol* 2007; **34(1)**:64-6. doi: 10.1053/j.seminoncol.2006.10.029.
7. Tan PH, Ellis I, Allison K, Brogi E, Fox SB, Lakhani S, *et al*. WHO Classification of Tumours Editorial Board. The 2019 World Health Organization classification of tumours of the breast. *Histopathology* 2020; **77(2)**:181-5.
8. Kanat O, Kilickap S, Korkmaz T, Ustaalioglu Oven BB, Canhoroz M, Cubukcu E, *et al*. Primary small cell carcinoma of the breast: Report of seven cases and review of the literature. *Tumori* 2011; **97(4)**:473-8. doi: 10.1177/030089161109700410.