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Breast Neuroendocrine Carcinoma Discovered by Lymph Node and Osteomedullary Metastasis: A Case Report

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Abstract **Case Report**

This case highlights a rare presentation of small cell mammary neuroendocrine carcinoma in a young woman, with metastatic spread to the spinal cord. Such a presentation is exceptionally uncommon, particularly in this demographic, and underscores the diagnostic challenges associated with neuroendocrine tumors outside typical locations. Reporting this case adds to the limited literature on mammary neuroendocrine carcinoma with spinal metastasis and may guide early identification in similar cases. We report A 20-year-old female patient presented with persistent lower back pain over three months. Clinical examination revealed cervical lymphadenopathy and bilateral breast masses. Magnetic resonance imaging (MRI) identified a spinal tumor infiltration. A biopsy of the cervical lymph nodes, followed by immunohistochemical analysis, confirmed the diagnosis of small cell mammary neuroendocrine carcinoma. Chemotherapy was chosen as the primary therapeutic approach, given the tumor's aggressiveness and advanced stage at diagnosis. This case underscores the importance of considering neuroendocrine carcinoma as a differential diagnosis for young patients presenting with atypical tumor localizations, such as bilateral breast masses and spinal metastasis. The case highlights the necessity of a multidisciplinary approach in diagnosing and managing rare tumors and demonstrates the potential impact of prompt recognition and treatment to improve outcomes.

Keywords: Breast Cancer, Metastasis, Small Cell Neuroendocrine Carcinoma, Chemotherapy.

INTRODUCTION

Neuroendocrine carcinomas originating in the breast are uncommon tumors, accounting for only 2 to 5% of breast cancer cases. Histologically, they closely resemble small cell neuroendocrine carcinoma of the lung (SCNCL), making it essential to conduct a comprehensive evaluation to eliminate the possibility of metastatic disease from a different primary source. Because of its scarcity, there is a paucity of literature on primary small-cell breast carcinoma (SCBC).

Consequently, documenting each confirmed case is crucial for advancing our understanding of this exceedingly rare and highly aggressive form of breast cancer in future research endeavors.

CASE REPORT

Patient History

This was a case of a 20-year-old woman from Rabat, 2nd of 4 siblings, married without children, 1st-year university student, without any particular personal or family medical history.

Three months before admission, the patient experienced a gradual onset of bilateral lumbar pain and hyperalgesic inflammatory buttock pain. This was followed by the development of multiple cervical adenopathies and masses in both breasts. Concurrently, there was a decline in the patient's overall health, characterized by weakness, loss of appetite, and a measured weight loss of 5 kg. The patient sought symptomatic treatment at the peripheral emergency department on multiple occasions, but there was no noticeable improvement. Consequently, due to the lack

of progress, the patient was referred to the University Hospital of Rabat for further evaluation and treatment.

Clinical Finding

During the clinical assessment, the patient displayed stable hemodynamics and an overall good general condition. The gynecological examination revealed a slightly sensitive, firm mass measuring 60 x 80 mm in the upper and lower external quadrants of the left breast, along with skin infiltration in the superior external quadrant of the right breast. Examination of the lymph node areas indicated multiple superficial cervical lymph nodes that were firm, painless, immobile in both planes and non-inflammatory, varying in size from a few millimeters to 2 cm.

In the osteoarticular examination, palpation of the spinous processes elicited pain, while different peripheral joints had minimal mobilization and were painless to palpation. The rest of the examination, both somatic and otherwise, did not reveal any notable findings.

Paraclinical Examination

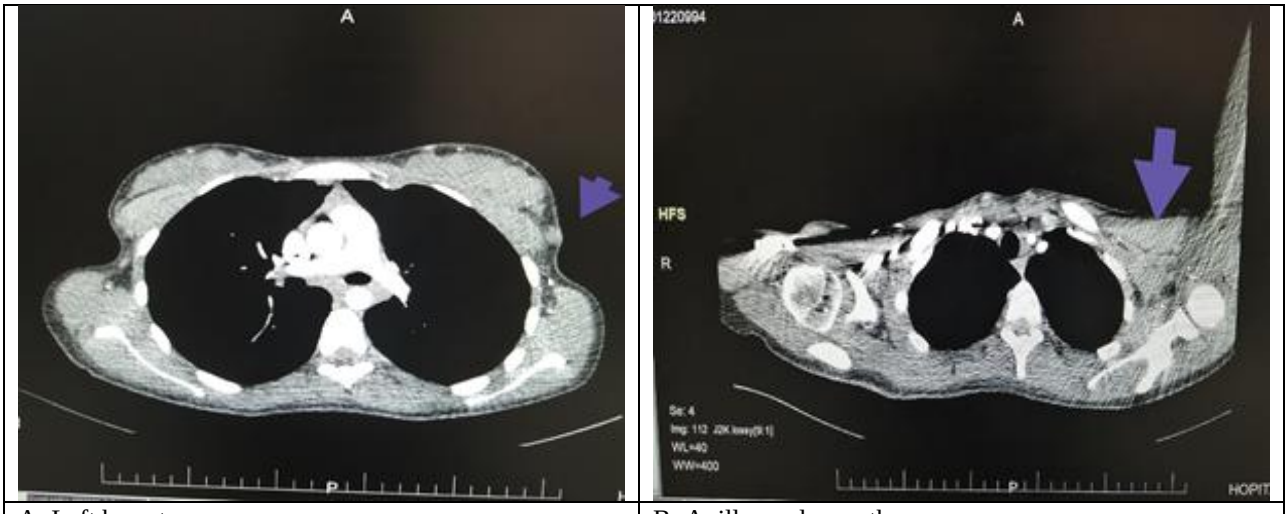
The patient's biology tests showed evidence of microcytic hypochromic anemia (9g/dl) and a macrophage activation syndrome test indicating a low probability (HSCORE less than 1%). Protein electrophoresis analysis revealed a moderate inflammatory syndrome with hypoalbuminemia.

A breast ultrasound demonstrated multiple bilateral breast masses with an oval shape, regular contours, hypoechoic echostructure, and no posterior attenuation. The largest masses were located in the supero-internal quadrant of the right breast at the 2 o'clock position measuring 21 x 12 mm and in the supero-external quadrant of the left breast measuring 26 x 20 mm. There was no evidence of milk duct dilation, and the skin covering was intact. Additionally, bilateral axillary adenomegaly was noted, which appeared oval-shaped without fatty hilum, and had a thickened cortex. The largest adenomegaly measured 9 mm on the right and 5 mm on the left.

The cervical ultrasound showed a normal thyroid with the presence of bilateral lateral cervical and supraclavicular lymphadenopathy. The most significant lymph nodes measured 19mm in the short axis on the right V chain and 16mm in the short axis on the left supraclavicular region. The parotid and submaxillary glands appeared normal.

The thoraco-abdomino-pelvic scan revealed several findings:

- The largest bilateral lateral cervical lymph node was in the left IIb chain, measuring 12x11 mm.
- Bilateral supraclavicular lymph nodes were present, with the largest on the left measuring 26 x 18 mm.
- The largest bilateral axillary lymph nodes were Berg III on the left measuring 29x22 mm and Berg I on the right measuring 12 x 15 mm.
- A rounded, well-defined mass of 10x10 mm was noted in the left axillary extension.
- An internal breast lymph node on the left measured 15x8 mm.
- Lymph nodes at the cardiophrenic angle measured up to 8x6 mm.
- There was a retrosternal tissue nodule measuring 14x8 mm.
- Osteocondensing lesions were observed in the pelvis and the thoraco-lumbar spine.



A: Left breast mass | B: Axillary adenopathy

Figure 1: Axial section of a thoracic CT scan showing in, A: Left breast mass and B: Axillary adenopathy

In the bone scintigraphy results, there was noted increased fixation at the L1 vertebra, which needs to be further assessed morphologically. However, there was no clear indication of secondary bone involvement in the rest of the skeleton.

The magnetic resonance imaging of the pelvis revealed findings consistent with diffuse medullary bone tumor infiltration in the pelvis and lumbar spine, with a significant extension into the soft tissues adjacent to the left hemipelvis. Additionally, there was evidence of endocanal extension with compressive epiduritis next to L5 and the sacrum. Multiple lymph nodes and scattered muscular and subcutaneous involvement were identified in the lumbo-aortic, iliac, and inguinal regions.

A biopsy of the cervical lymphadenopathy indicated a poorly differentiated tumor process, and immunohistochemistry results confirmed the presence of Small Cell Neuroendocrine Carcinoma.

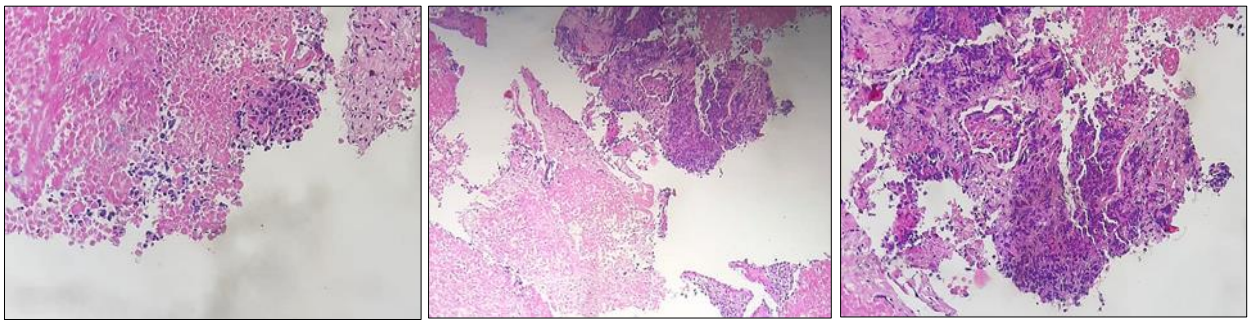


Figure 2: Histological appearance of a small cell neuroendocrine carcinoma: Carcinomatous process made up of round cells often crushed in a fibrous stroma. Presence of necrosis area.

The osteo-medullary biopsy findings revealed a substantial infiltration of the bone marrow by a poorly differentiated malignant tumor. Immunohistochemistry confirmed it to be Small Cell Neuroendocrine Carcinoma. Additionally, a myelogram indicated the presence of a white puncture.

Biopsies of both breasts identified a poorly differentiated malignant tumor without an in situ component or vascular embolism. Immunohistochemistry results indicated a Small Cell Neuroendocrine Carcinoma originating from the mammary tissue, with positive neuroendocrine markers including chromogranin and synaptophysin.

Therapeutic Intervention

Following a thorough discussion at a multidisciplinary consultation meeting, the patient was treated with chemotherapy utilizing anthracyclines and cyclophosphamides.

The potential for surgery will be revisited post-chemotherapy, provided the patient demonstrates positive clinical progress and achieves a complete response. The proposed surgical approach encompasses bilateral partial mastectomy with oncoplasty and bilateral axillary clearance.

The consideration for adjuvant radiotherapy following the surgical procedure will be discussed at a later stage. Additionally, hormone therapy will be contemplated if the anatomopathological analysis of the surgical specimen reveals the presence of hormone receptors.

DISCUSSION

Primary Small Cell Neuroendocrine Carcinoma (SCNEC) of the breast is an exceedingly rare form of breast cancer, with a reported incidence ranging from less than 0.1% to 1-5% of all breast cancers [4]. This type of cancer is typically diagnosed in women who are over the age of 60. It presents a significant diagnostic challenge as it closely resembles small cell neuroendocrine carcinoma of the lung, necessitating a thorough investigation to rule out metastatic disease originating from another primary site.

A population-based study conducted by Wang *et al*., [5], using the SEER database shed light on this aggressive variant of invasive breast cancer. Their analysis of 142 cases revealed that neuroendocrine carcinoma of the breast predominantly affects women over 60 and often manifests with tumors larger than 2 cm. Importantly, the study highlighted a poorer 5-year overall survival rate for neuroendocrine breast carcinomas compared to other types of invasive mammary carcinomas. These tumors tend to exhibit extensive vascular invasion, nodal involvement, a high proliferation index, and frequently lack estrogen and progesterone receptor expression [6, 7].

The treatment of this rare and aggressive breast tumor lacks standardized protocols. Various approaches have been discussed in the literature, including combinations of surgery, chemotherapy, radiation therapy, and endocrine therapy. Early reports suggest modified radical mastectomy as the preferred treatment option, often followed by adjuvant chemotherapy and/ or radiation therapy [1].

Given the aggressive nature of the disease, neoadjuvant chemotherapy is recommended. In the case of our patient, who is notably young in contrast to the typical age described in the literature, she presents with bilateral breast masses, lymph node involvement, and osteomedullary metastases. The disease was diagnosed at an advanced metastatic stage due to her symptoms,

including bilateral lower back pain and inflammatory hyperalgesia buttock pain. This was confirmed by diffuse medullary bone tumor infiltration of the pelvis and lumbar spine on pelvic MRI, necessitating palliative treatment.

The diagnosis was established through the positivity of neuroendocrine markers chromogranin and synaptophysin, confirming the mammary origin of the tumor. It's worth noting that small cell carcinomas tend to be associated with a poorer prognosis when compared to other types of neuroendocrine carcinomas of the breast [8-11].

CONCLUSIONS

Small cell neuroendocrine carcinoma (SCNEC) of the breast shares morphological characteristics with its counterpart in the lung, making it challenging to distinguish based solely on histologic and immunohistochemical features [12]. Therefore, confirming the diagnosis of primary small cell neuroendocrine carcinoma of the breast requires either excluding an extramammary primary site or demonstrating the presence of an in situ component within the breast tissue [13].

Given its rarity and relatively recent recognition as a distinct entity, the current diagnostic and therapeutic approach for this type of cancer is akin to that used for general invasive breast carcinomas. This approach typically involves a combination of treatments, such as surgery, chemotherapy, radiation therapy, and potentially endocrine therapy, tailored to the specific characteristics and stage of the disease.

Informed Consent:

- Informed consent was obtained from the people included in this study.
- Consent for publication of the data was obtained from the patient.

Data Availability: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Ethical Approval:

Not applicable. This study being retrospective, approval by the Ethics Committee of Biomedical research was not necessary according to the local reglementation (Law 28.13, article 2).

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Authorship Contribution Statement: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Declaration of Competing Interest: Authors state no conflict of interest.

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