CDK4/6 Inhibitor in Extensive Cutaneous Metastatic Breast Carcinoma: A Case Report

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Introduction

Breast cancer is one of the most common malignant tumors affecting women worldwide and Mexico. Cutaneous metastases (CM) occur in 0.7 to 10.4% of all patients diagnosed with cancer although they represent only 2% of all skin tumors.

Case-Report

A 68-year-old female with a positive smoking history. Menarche at age 12, menopause at age 45, 2 pregnancies, 2 births, and oral contraceptive use for 6 months. Comorbidities: Chronic obstructive pulmonary disease treated with prednisone 5mg, tiotropium bromide inhaler, salmeterol/fluticasone 50/100 mg inhaled form, and supplemental oxygen at night. Major depressive disorder is treated with paroxetine 20 mg and clonazepam 2 mg daily.

History of unspecified right breast cancer, Clinical stage IIB, in 2000, treated with right radical mastectomy and hormonal therapy with letrozole 2.5mg every 24 hours for 5 years. In 2023, the patient presented disseminated dermatosis, predominantly on the anterior and posterior thorax and skull, bilateral, characterized by multiple subcutaneous neoplasms measuring 1-3 cm (Figure 1: A, B, E), as well as multiple lymphadenopathies in the cervical and retro auricular regions.

In November 2023, an excisional biopsy of a subcutaneous nodule was taken, reporting moderately differentiated infiltrating ductal carcinoma, as well as immunohistochemistry: Estrogen Receptor positive: 95%, Progesterone receptor positive: 90%, negative HER2, and Ki67 positive in 30% of the neoplastic cells (Figure 2: A, B, C, D). She came to the emergency room due to rapidly increasing dyspnoea at rest, not alleviated by drainage of pleural effusion, so she required continued supplemental oxygen. A Computed Tomography scan of the head-neck-chest-abdomen-pelvis also showed evidence of metastatic disease to the lung, pleural effusion, liver, and blastic lesions in the skull, lytic lesions in spine (T3, T9,T11, L1-L3), sacrum, and iliac bones.

The patient was seen for medical oncology evaluation, where she was found to have an Eastern Cooperative Oncology Group (ECOG) score of 2, Karnofsky Performance Status Scale of 70%. PROs (Patient Reported Outcomes) were evaluated at the beginning of the treatment using EORTC QLQ-C30 and EORTC QLQ-BR23 with poor quality of life (QoL), G8 (Geriatric 8) of 13 points (frail patient). She was neurologically intact. Referring to asthenia, adynamia, bone pain in the dorsal and lumbar spine, as well as liver pain. Her scalp showed multiple subcutaneous nodular lesions with alopecia, multiple cervical and retroauricular lymphadenopathy, and a right mastectomy.

Case – Report

She had multiple subcutaneous nodular lesions measuring approximately 1-3 cm, fixed, stony, and painless, in the anterior and posterior regions of the chest. She had bilateral axillary lymphadenopathy, as well as multiple lesions in the abdomen and back.

Her laboratory studies showed hemoglobin 11.2 g/dL, platelets 208,000 ul, glucose 120 mg/dL, creatinine 0.36 mg/dL, increase in LDH level, rapidly increasing bilirubin >1.5× ULN in the absence of Gilbert's syndrome or biliary tract obstruction. An electrocardiogram showed sinus rhythm, HR 70 bpm, and QTc 422.



Figure 1 Disseminated dermatosis, predominantly on the anterior and posterior thora(A, B, E).The subcutaneous nodules with erythematous and brown areas have disappeared from their original location. The scalp lesion has completely disappeared, and hair has reappeared in that area (D and G).

In April 2024, treatment started with ribociclib 600 mg orally every 24 hours and letrozole 2.5 mg orally every 24 hours plus denosumab. The treatment was well tolerated, with no reported toxicity.

During follow-up, all subcutaneous nodular lesions decreased significantly. The lesions were flat and brownish pigmented at that site within the first 3–4 months after treatment. (Figure 1: C and F) Currently, the skin has returned to normal color at the sites where the lesions were located, and most of the nodules are absent. The scalp has completely disappeared, and hair has reappeared at that site. (Figure 1: D and G).

Case – Report

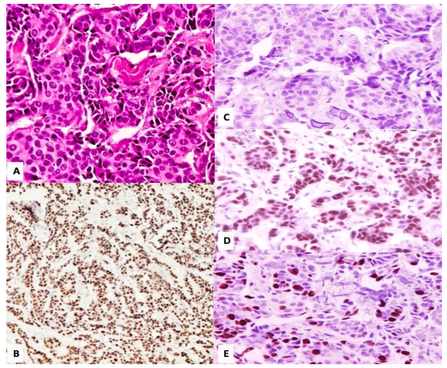


Figure 2
Microscopic examination showed metastatic ductal carcinoma to the reticular dermis with intense and diffuse expression of estrogen receptors. (A, B) Immunohistochemistry revealed Her-2 negative expression (C), intense nuclear expression of estrogen receptors and progesterone receptors (D), and Ki-67 positive expression in 30% of the neoplastic cells (E).

The maging study (CT scan of the head, chest, abdomen, and pelvis with contrast) reports a partial response with a significant reduction in lesions in the lungs, liver, and bones. Currently the patient is on ECOG 1, Karnofsky 90%, EORTC QLQ-C30 and EORTC QLQ-BR23 with improvement in quality of life (QoL), G8 (Geriatric 8) of 13 points (frail patient).

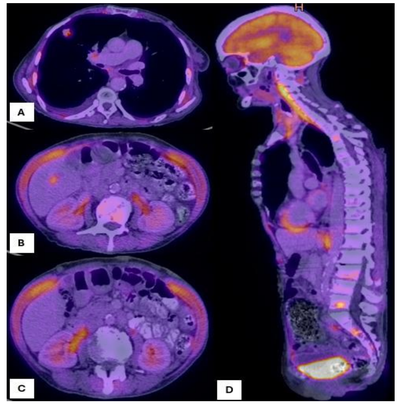


Figure 3 PET CT Scan:
Partial response in lung (A) liver (B), and bone metastases (D). Resolution of pleural effusion (A). Complete response in subcutaneous nodular lesions of the scalp, anterior and posterior thoracic region, and abdomen (A-D)

Discussion

Extensive CMBC hormone receptor (HR)-positive subtypes are generally present late in the course of the disease and treated with hormonal therapy. Cutaneous metastases from breast cancer are relatively common in recurrent disease, but disseminated involvement including the scalp is rare (scalp <1% of patients; disseminated skin + scalp ≈7.8%).

CMBC are usually solitary or multiple nodular pinkish lesions (ranging between 1 and 3 cm). The spectrum of presentation of cutaneous metastasis in breast cancer varies in frequency from the common papulonodular variant to much rarer presentations of dermatitis-like metastases. They usually appear as painless firm nodules, plaques, papules, rashes, or inflammatory lesions that can resemble other skin cancers and may ulcerate or become infected. Breast cancer scalp metastases generally present as one or more inflammatory or nodular lesions, telangiectasias, or irregularly shaped skin lesions that are flesh or reddish, making them difficult to identify from other skin carcinomas.

In our patient, scalp nodules caused alopecia and initially darkened and flattened with treatment, later returning to normal color with complete recovery of the scalp after nine months. The diagnosis of cutaneous and scalp metastasis can be complicated to make, it requires an extensive clinical evaluation, non-invasive imaging techniques like whole-body FDG-PET/CT, as the preferred method when available, or CT scan in specific cases. The gold standard diagnosis remains in the histopathological and immunohistochemical analysis. Our patient is CT scan showed evidence of multiple visceral metastases (liver and lung), as well as multiple bone lesions at the level of the subcutaneous lesions. The use of aromatase inhibitors (anastrozole and letrozole) in CMBC has been reported; however, treatment with modern CDK4/6 inhibitor-based therapy has not been reported, nor is there any experience with this presentation of the disease.

Our case demonstrates that this type of treatment not only acts on visceral and bone disease but also offers adequate penetration at the subcutaneous level, achieving an adequate response in extensive disease with improvement in quality of life (QoL)

Conclusion

This case illustrates an unusual presentation of disseminated cutaneous and scalp metastases from hormone receptor–positive, HER2-negative breast cancer, a pattern typically associated with advanced systemic disease and poor prognosis. Treatment with ribociclib plus letrozole achieved marked regression of the subcutaneous and scalp lesions, recovery of the scalp, and clinical improvement, highlighting the potential efficacy and tolerability of CDK4/6 inhibition even in frail, elderly patients with extensive skin involvement.

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