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Case report

Radiotherapy for a breast cancer patient with Schnitzler syndrome: Report of acute toxicity and early follow-up



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ABSTRACT

This article provides description about acute toxicity and early follow-up of one patient treated for breast cancer and Schnitzler syndrome. There are no previously reported cases exploring this interaction on medical literature.

The expected radiodermitis to occur in the region treated with radiotherapy along with urticarial-like lesions might be challenging in view of the interaction between symptoms and therapeutic measures.

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1. Introduction

Schnitzler syndrome (SS) is a rare autoimmune disease that was first described by Dr. Liliane Schnitzler in 1972¹ by the association between chronic urticaria, bone lesions, and the presence of a monoclonal IgM protein.² After robust research and the consensus from study groups³ in the 1990s and 2000s, the elements for clinical diagnosis actually include urticaria and at least 2 of the following signs⁴: arthralgia, bone pain, skeletal hyperostosis, lymphadenopathy, intermittent fever, visceromegaly, and Kappa-monoclonal IgM gammopathy.

Although some tests might suggest SS, it remains a clinically recognized disease, as there are no specific tests for confirmation. Furthermore, the inhibition of interleukin (IL)-1 pathway leads to rapid recovery of symptoms⁵ and the diagnosis might be under-recognized or confused with other entities.⁶

The most-accepted cause of SS is related to the cytokine network. Interleukin-1 alpha binding activity has been described in patients with SS.⁷ Genetic mutations – NLRP3 gene – have also been correlated in some patients.⁸

Breast cancer (BC) is one of the most diagnosed cancer and highly responsible for cancer deaths throughout the

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world.⁹ The multidisciplinary approach is recommended for treatment guidelines, but usually involves surgery, radiation therapy, and systemic therapy, such as chemotherapy, hormonal therapy, and monoclonal antibodies.¹⁰

Radiation therapy (RT) is indicated for the majority of patients with either in situ or invasive types receiving conservative breast treatment in the adjuvant setting, and for many who undergo radical mastectomy. The benefits include risk reduction of local and regional recurrences, and consequently breast cancer mortality. 11,12 However, RT is associated with some risks and toxicities. Acute toxicities include radiation dermatitis, fatigue, esophagitis, and breast pain. Late complications may involve xeroderma, pneumonitis, arm lymph edema, hypothyroidism, rib fracture, cardiopathy, fibrosis with cosmetic implications in the reconstructed breast, and the risk of radioinduced neoplasia. 13 Several improvements have decreased the frequency of RT toxicities, such as the implementation of tridimensional conformal and intensitymodulated radiation therapy. They provide gains in planning and delivery of RT by sparing healthy surrounding organs while delivering more homogeneous and shaped radiation dose exactly to the target. 14

We report one case of BC patient carrying SS due to the absence of previously published reports involving the interaction of oncological treatments with the manifestations of SS, especially radiodermitis in the irradiated breast. We did not know what the patient's tolerance for treatment would be.

2. Case report

This is a 67-year-old woman who sought medical care in August 2016 due to urticaria skin lesions that caused intermittent pain and pruritus, diffuse muscular pains, arthralgia, and an unwillingness to work.

She was then evaluated by the rheumatology team who considered the likelihood of SS the most probable. At that time, she had undergone several tests:

- Laboratory tests: serum immunofixation test showing monoclonal IgM kappa, and complete blood count showing anemia and leukocytosis.
- 2. Skin biopsy showing neutrophilic urticaria.
- 3. FDG-PET/CT: lobulated mass in the upper inner quadrant of the left breast, measuring 2.6 cm \times 2.2 cm, SUV 4.3; bilateral axillary, external iliac and bilateral inguinal enlarged lymph nodes, measuring up to 2.4 cm with SUV up to 2.8 cm
- 4. Mammography: irregular and isodense nodule with spiculated margins, located in the posterior third of the junction of the upper quadrants of the left breast, associated with pleomorphic calcifications, measuring $2.4\,\mathrm{cm}\times1.8\,\mathrm{cm}$, $5.5\,\mathrm{cm}$ apart from the nipple. Scattered calcifications with a benign radiographic appearance. Free axillary extensions. BI-RADS 5.
- 5. Core biopsy of the left breast nodule: Non-special type invasive carcinoma, histological grade 2, nuclear grade 2, ER100%, PR98%, Ki67 15%, HER2 negative.
- 6. Magnetic resonance imaging of the breasts: irregular nodule, with spiculated contours, with intense heterogeneous

- contrast enhancement, measuring $2.7 \times 1.8 \times 2.5$ cm, at the junction of the upper quadrants. This nodule is 3.8 cm from the skin superiorly, 1.4 cm from the pectoral muscles and 5.2 cm from the papilla. Bilateral axillary lymph nodes, levels I and II, with cortical thickening, measuring up to 2.2 cm on the left axillae.
- Mammotomy of the nodule in right breast + core biopsy of bilateral axillary lymph nodes: all negative for malignancy.

Thus, the rheumatology team recommended therapy for SS (canakinumab monoclonal antibody), and referred the patient for breast surgeon's evaluation.

Subsequently, she underwent left breast conserving surgery plus sentinel lymph node evaluation, and breast oncoplasty. The definitive pathology report showed an infiltrating carcinoma with no other specifications in 2 foci:

- a. Focus 1: Non-special grade 2 carcinoma, histological grade 2, nuclear grade 2, size $2.1\,\mathrm{cm}\times1.8\,\mathrm{cm}$ without angiolymphatic invasion. ER99%, PR80%, Ki 67 23%, HER2 negative, E-cadherin positive
- Focus 2: invasive lobular carcinoma with classic and trabecular patterns, histological grade 2, nuclear grade 2, size
 1.9 cm without angiolymphatic invasion. ER95%, PR70%, Ki67 14%, E-cadherin positive, HER2 negative.

The lower margin was compromised by invasive neoplasia. There were no metastases in axillary lymph nodes (0/2). A high contingency of IgG4 positive plasmocytes was observed through evaluated lymph nodes. IgG4/IgG ratio 20%.

Thus, she afterwards underwent skin-sparing mastectomy plus breast reconstruction by a silicon prosthesis and *latissimus dorsi* interpositions. The pathology report has shown a residual invasive lobular tumor with trabecular and solid patterns, histological grade 2, nuclear grade 2, associated with an in situ component <25%, with cribriform and micropapillary types, nuclear grade 3. The margins were free. The final size of the neoplasm was then $5.8\,\mathrm{cm}\times3.7\,\mathrm{cm}$. The final pathological staging was a pT3, pN0 (ls).

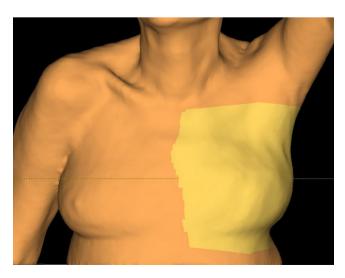


Fig. 1 - Radiation fields' display.

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