

Syphilis, “The Great Imitator”: An atypical presentation of secondary syphilis in a patient with breast cancer

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CASE REPORT

A 40-year-old woman with left-sided, triple negative, invasive ductal carcinoma with metastasis to the left axillary lymph node presented to the medical oncology clinic with five weeks of a whole-body skin eruption. She had previously completed neoadjuvant paclitaxel and was transitioned to neoadjuvant dose-dense doxorubicin and cyclophosphamide chemotherapy for breast cancer. She had completed 3 cycles of dose dense doxorubicin and cyclophosphamide when she reported a non-pruritic, non-tender rash that started on her chest and spread to her face and extremities. There was no pain, itching, or burning associated with the rash. There were no mucosal lesions. She had no other systemic symptoms. The patient had been treating the rash with Neosporin ointment, triamcinolone acetonide 0.1% topical cream, and antihistamines with minimal improvement.

Physical examination was remarkable for indurated, edematous, pink papules affecting her chest, back (Figure 1), face, scalp, arms, legs, palms, and soles. Laboratory testing showed a white blood cell count of $3.79 \times 10^9/L$. Serologies for human immunodeficiency virus (HIV) and Hepatitis B were negative. Gonorrhea and chlamydia nucleic acid testing was negative. Initial differential diagnoses for her undifferentiated rash included neutrophilic dermatosis, chemotherapy-related dermatitis, urticarial eruption, subacute lupus, or other

drug-related eruption. After failure of initial topical therapies, a skin punch biopsy was obtained to investigate further. Histological evaluation of a lesion on the right chest wall and mid-back both showed a superficial and deep psoriasiform lichenoid infiltrate comprised of plasma cells and variable number of histiocytes. An immunohistochemical stain for spirochetes was positive in the epidermis (Figure 2). The initial rapid plasma reagin (RPR) screening test was reactive and reflex RPR titer was 1:128 at time of diagnosis. No VDRL or FTA-Abs testing was done.

At the time of diagnosis, the patient denied any history of syphilis or other sexually transmitted diseases in the past. She denied any high-risk sexual activity or



Figure 1: Evaluation of mid-back showing scattered, erythematous papules, labeled with black arrows.

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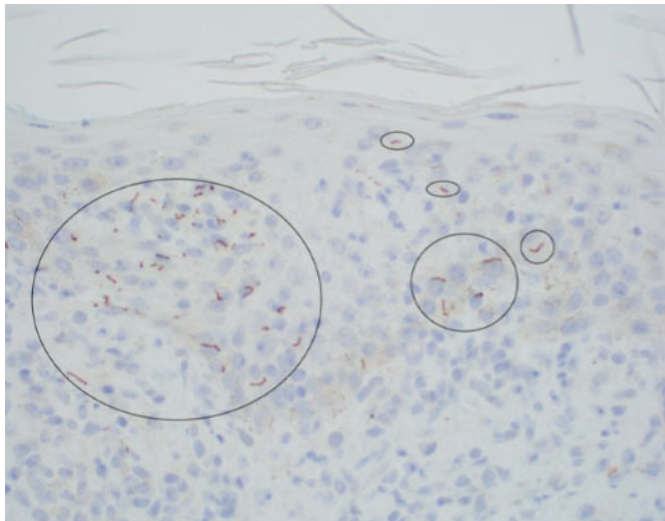


Figure 2: Immunohistochemical stain of papules showing spirochetes in the epidermis.

multiple sexual partners prior to the diagnosis. She did not endorse any neurological symptoms concerning for neurosyphilis. The Dallas County Health Department was notified, and the patient and her husband were treated with a single dose of intramuscular penicillin G benzathine. The patient reported improvement in her rash over the subsequent weeks. Five months following treatment, repeat RPR titer was 1:16. She was able to complete her planned chemotherapy with a complete pathologic response and proceeded with mastectomy and axillary lymph node dissection and adjuvant radiation. Follow-up mammography showed no signs of malignancy and one year after her initial breast cancer diagnosis, the patient continues to do well.

DISCUSSION

Chemotherapy treatments such as doxorubicin and cyclophosphamide are often used as part of standard of care in early breast cancer. The use of doxorubicin, particularly in its liposomal form, can be associated with many adverse skin reactions including hand-and-foot syndrome, diffuse follicular rash, melanotic macules and an intertrigo-like eruption [1–3]. In this illustrated case, the patient's presentation most likely resembles a diffuse follicular rash. Treatment for these skin complications typically involves dose reduction of doxorubicin, supportive care with topical wound care, and pain management and patient education [4]. However, before reaching diagnostic closure, infectious causes should also be fully considered, especially given the patient's immunocompromised status. Both primary infection and reemergence of latent infections are a possibility, with rare cases of reemergence of

latent syphilis after initiation of immunosuppressive medications being reported [5, 6].

Overall, there has been a noticeable resurgence of syphilis cases in the United States over the past two decades despite the prevalence of effective treatment and prevention strategies [7, 8]. Syphilis typically progresses through four clinical stages, primary, secondary, latent, and tertiary. Secondary syphilis, such as in the illustrated case, typically presents with a skin rash involving the palms and soles and/or sores in the mouth and genital areas and may also lead to generalized symptoms of fever, headaches, muscle aches, and fatigue. If left untreated, syphilis progresses to the tertiary stage, leading to severe and irreversible cardiovascular and neurological sequelae. However, syphilis can be readily diagnosed with a combination of non-treponemal [i.e., venereal disease research laboratory (VDRL) or rapid plasma reagin (RPR) tests] and treponemal tests [i.e., fluorescent treponemal antibody absorption (FTA-Abs)]. If present, syphilis can be easily treated with intramuscular penicillin G benzathine. With its perplexing and protean presentation, syphilis should be widely considered for patients presenting with concerning features or risk factors such as high-risk sexual history or immunocompromised states.

CONCLUSION

Chemotherapy-induced skin reactions are common and are typically managed with supportive measures. However, such immunosuppressive medications can predispose patients to infection with dermatologic manifestations that can mimic a drug reaction. In such patients, the infection's course and presentation may be atypical resulting in delayed or missed diagnosis. A skin biopsy should be considered early in the disease course to clarify such diagnosis, particularly when prompt resolution of the skin eruption does not occur with supportive measures.

Keywords: Chemotherapy induced skin reaction, Secondary syphilis, Triple negative breast cancer

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Author Contributions

Sharlene Dong – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Samira Syed – Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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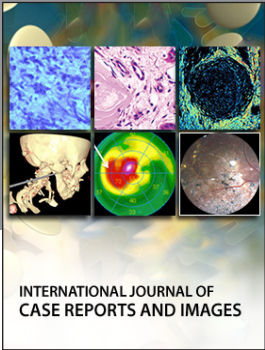
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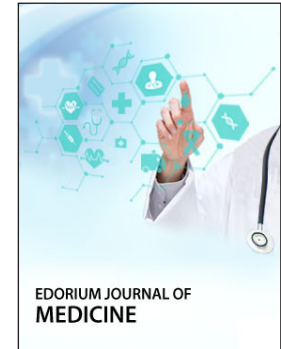
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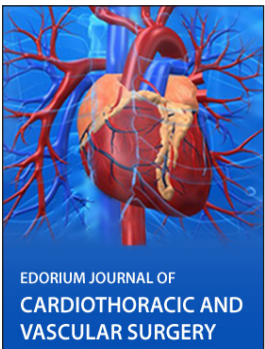
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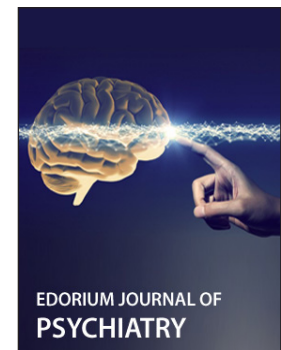
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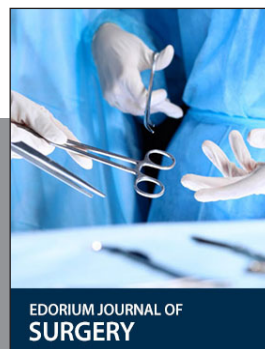
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