Toxic erythema of chemotherapy secondary to gemcitabine and paclitaxel

Erin Jennings[1] BA, Simo Huang[2] MD, Jason B Lee[3] MD, Jisun Cha[3] MD, Sylvia Hsu[2] MD

Affiliations: [1]Lewis Katz School of Medicine, Philadelphia, Pennsylvania, USA, [2]Department of Dermatology, Lewis Katz School of Medicine, Philadelphia, Pennsylvania, USA, [3]Department of Dermatology, Thomas Jefferson University Hospitals, Philadelphia, Pennsylvania, USA

Corresponding Author: Sylvia Hsu MD, Temple Dermatology, 1316 West Ontario Street, Philadelphia, PA 19140, Tel: 215-707-3376, Email: Sylvia.hsu@tuhs.temple.edu

Abstract

Toxic erythema of chemotherapy (TEC) is an infrequently reported cutaneous condition, with diagnosis predominately based on clinical presentation, histologic findings, and known reported associations. Therefore, it is important to both recognize common presentations of TEC and be mindful of chemotherapeutic agents associated with this cutaneous side effect to prevent misdiagnosis and prolonged time to treatment. Herein, we present a patient with TEC occurring in intertriginous skin (malignant intertrigo) with classic clinical and histologic findings. In our patient this was associated with a combination neoadjuvant gemcitabine and paclitaxel therapy, a relationship that, to our knowledge, has yet to be reported in the literature.

Keywords: malignant intertrigo, palmoplantar erythrodysesthesia, symmetrical drug-related intertriginous, flexural exanthema, toxic erythema chemotherapy, drug eruption, graft-versus-host disease, intertrigo, pathogenesis, squamous syringometaplasia, interface dermatitis, epidermal necrosis, inflammatory infiltrate

Introduction

Toxic erythema of chemotherapy (TEC), also reported as malignant intertrigo when occurring in intertriginous skin, typically develops two to three weeks following initiation of chemotherapy. It often presents as an acute eruption of scales, crusts, and erosions with varying degrees of erythema in acral and intertriginous areas. The pathophysiology of the disease is believed to be an accumulation of chemotherapy products in eccrine sweat glands, ultimately causing a local toxic effect in intertriginous areas where eccrine ducts are in higher concentration [1]. Toxic erythema of chemotherapy and malignant intertrigo have been rarely reported in the literature and causative agents primarily associated with this disease state have been limited to cytarabine and pegylated liposomal doxorubicin [2,3]. Herein, we report a patient with toxic erythema of chemotherapy, specifically malignant intertrigo, subsequent to administration of gemcitabine and paclitaxel.

Case Synopsis

A 59-year-old woman presented with a progressively worsening, intertriginous, desquamating, and painful rash six weeks following the administration of neoadjuvant gemcitabine and paclitaxel chemotherapy for pancreatic adenocarcinoma. The rash was first noticed by the patient two days after her second round of therapy (four weeks after initiation) and treatment with fluconazole and nystatin was started by her medical oncology team. The eruption continued to progress, which incited a visit to the emergency room. Upon physical examination at her hospital stay, painful erosions were noted on the lips, oropharynx, axillae, inframammary folds, and under the abdominal pannus bilaterally (**Figure 1**). Upon consultation, a diagnosis of toxic erythema of chemotherapy (malignant intertrigo) was suspected and

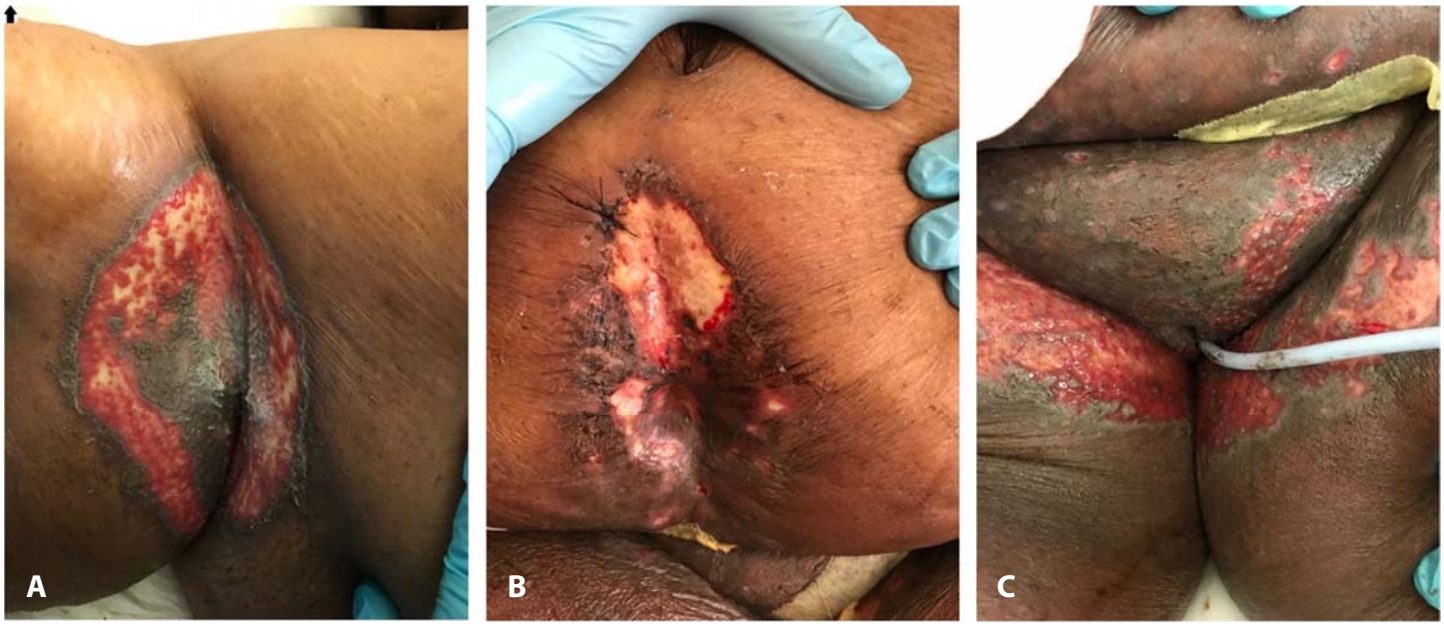

Figure 1. *Intertriginous erosion of **A)** right axilla, **B)** infrappanus fold, and **C)** groin region upon initial patient presentation.*

discontinuing chemotherapy with supportive care of the erosions was recommended.

The patient had a fever of greater than 101 degrees Fahrenheit. Blood tests demonstrated neutropenia, thrombocytopenia, and hyponatremia, believed to be in the setting of chemotherapy administration. In the context of neutropenic fever there was suspicion of systemic fungal or bacterial infection and thus empiric antibiotics, topical clotrimazole, and oral fluconazole were initiated by the primary team. Blood cultures were subsequently found to be negative and systemic treatment was discontinued.

A 6-mm punch biopsy from the infrapannus fold was obtained at the time of initial dermatology consultation. Skin pathology showed interface dermatitis with necrotic keratinocytes and focal eccrine gland necrosis, consistent with toxic erythema of chemotherapy, confirming our initial diagnosis (**Figure 2**). The patient's erosions gradually improved result from discontinuation of chemotherapeutic agents. At the patient's one-month follow-up visit, healing of skin was noted in all intertriginous areas (**Figure 3**). Supportive treatment with petroleum jelly was recommended until areas were fully healed.

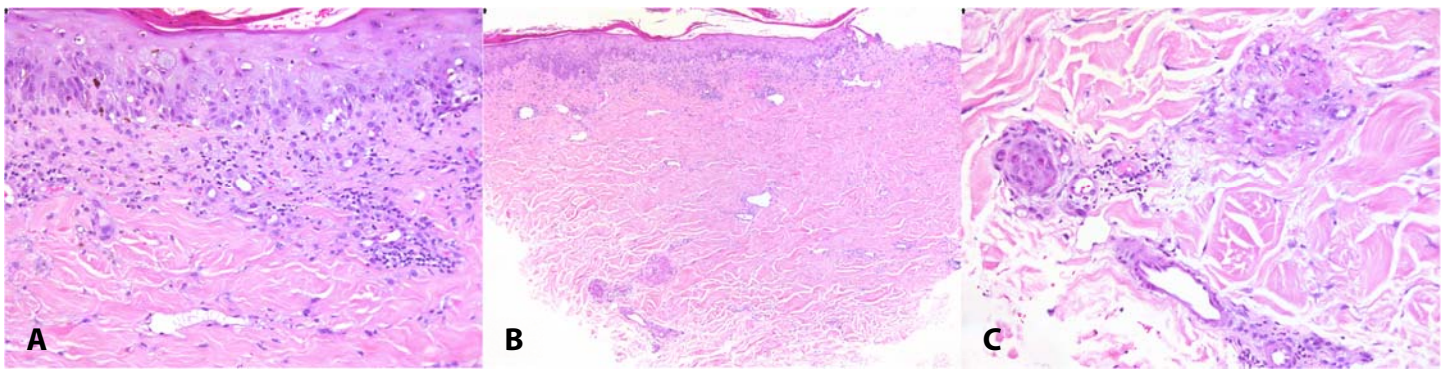

Figure 2. *H&E histopathologies. **A)** 6mm punch biopsy obtained from infrapannus fold, 5×. Interface dermatitis with necrotic keratinocytes and focal eccrine gland necrosis consistent with toxic erythema of chemotherapy. **B)** 6mm punch biopsy obtained from infrapannus fold, 20×. Note the parakeratosis, interface dermatitis with necrotic keratinocytes and vacuolar degeneration of the dermo-epidermal junction, and mild perivascular lymphocytic infiltration. **C)** 6mm punch biopsy obtained from infrapannus fold, 40×. Note the focal eccrine gland necrosis.*

Case Discussion

Toxic erythema of chemotherapy and malignant intertrigo are infrequently reported cutaneous conditions. Toxic erythema of chemotherapy is a rare adverse effect of chemotherapy and diagnosis is based predominantly on clinical presentation, often resulting in misdiagnosis and subsequent mistreatment. Smith et al. reported a case series highlighting six cases of TEC, which demonstrated initial misdiagnosis of TEC as drug allergy, cutaneous candidiasis (as seen in our case), and cellulitis. In each of these cases, time to diagnosis was significantly delayed, resulting in increased hospital stay and unnecessary administration of medication [1]. Therefore, it is important to both recognize common presentations of TEC and to be mindful of chemotherapeutic agents associated with this cutaneous side effect. To date, there is no known association of TEC with use of combination neoadjuvant gemcitabine and paclitaxel therapy. Although rarely reported, the majority of cases have been associated with the use of anthracyclines (most notably doxorubicin), cytarabine, and cyclophosphamide [1,3]. The principle histologic findings associated with this condition are squamous syringometaplasia, interface dermatitis, and epidermal necrosis with inflammatory infiltrate.

These findings are consistent with the histologic findings of the patient reported in our case. In addition to awareness of this condition and its association with certain chemotherapy agents, it is also essential to highlight the variety of treatment modalities for the cases that have been reported thus far. Toxic erythema of chemotherapy is a self-limited eruption after stopping chemotherapy and our patient showed significant resolution with supportive treatment and cessation of chemotherapeutic agents. However, the majority of past cases reported use of topical corticosteroids and occasional use of systemic corticosteroids for resolution of symptoms.

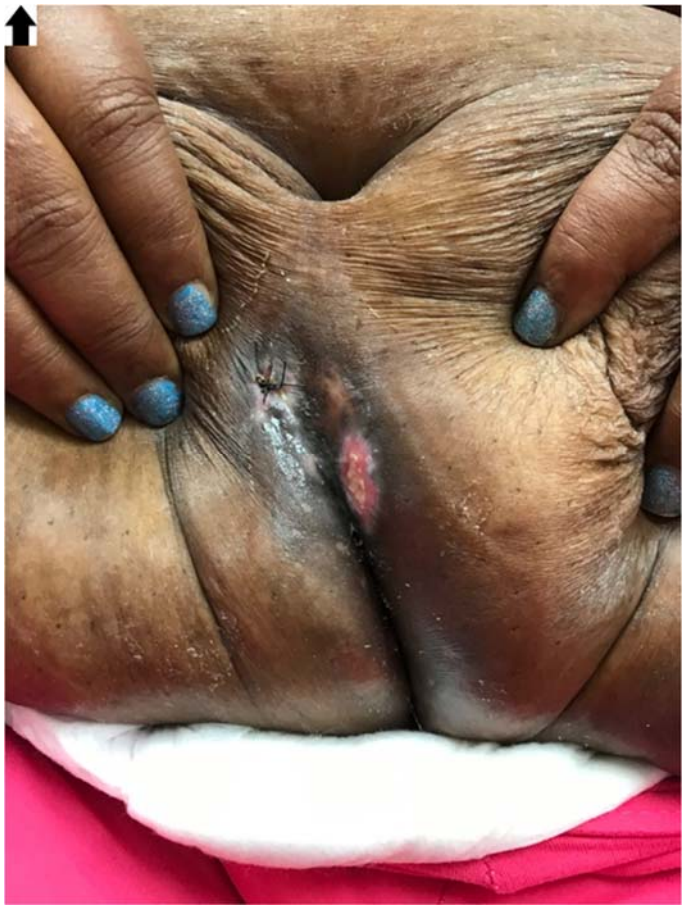

Figure 3. *Healing skin from the infrapannus fold two weeks following discontinuation of chemotherapy.*

Potential conflicts of interest

The authors declare no conflicts of interest.

References

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