

Eccrine squamous syringometaplasia in an allogeneic stem cell transplant patient undergoing chemotherapy

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Abstract

Eccrine squamous syringometaplasia (ESS) is a rare finding defined as metaplastic change of the cuboidal epithelial cells of eccrine glands into two or more layers of squamous epithelial cells. We present a patient who developed ESS after induction of CLAG chemotherapy [2-Chlorodeoxyadenosine (2-CdA) with cytarabine (Ara-C) and (granulocyte-colony stimulating factor) G-CSF] for management of the blast crisis of his chronic myelogenous leukemia (CML). Our patient's ESS eruption presented with a variety of morphologies, thus multiple skin biopsies were taken to determine the possible diagnosis(es). All skin biopsies showed ESS and the eruption resolved with topical corticosteroids after CLAG therapy was finished.

Keywords: chemotherapy, drug eruptions, eccrine squamous syringometaplasia, toxic erythema of chemotherapy, cytostatic agent

Introduction

Eccrine squamous syringometaplasia (ESS) is a condition in which the normal cuboidal epithelial cells lining the eccrine sweat gland undergo a conformational change from cuboidal to two or more layers of squamous cells. The most common etiologic agents are cytostatic drugs, such as cytarabine, vemurafenib, and pegylated liposomal doxorubicin [1-7]. The term used to describe this presentation is chemotherapy-induced ESS, which falls under the proposed umbrella term toxic erythema of chemotherapy (TEC), [1]. ESS has also been described in association with systemic lupus erythematosus, linear scleroderma, diagnostic

procedures involving radiation, cytomegalovirus, herpetic syngitis, phytophotodermatitis, annular elastolytic granuloma, burns, and GVHD [6, 8].

Case Synopsis

A man in his 30s with history of CML for twelve years and unrelated donor allogeneic stem cell transplantation performed two years prior, presented with blast crisis for CLAG therapy. His post-transplant course was complicated with graft-versus-host disease (GVHD) affecting only his skin and manifesting as ichthyosis. His GVHD was stable at the time of admission. His medications included tacrolimus, sirolimus, and corticosteroid eye drops. Tacrolimus dosage was decreased by 50% upon CLAG initiation. A dermatology consultation was requested on day 6 of hospitalization for a new mildly pruritic eruption. Review of systems was positive for fatigue and weakness with subjective fever. At the time of consult, vital signs were stable and within normal limits. Laboratory studies indicated pancytopenia: WBC 0.08 k/ μ L, hemoglobin 7.8 g/dL, and platelets 23 k/ μ L. Comprehensive metabolic panel was normal.

Examination revealed bright erythematous patches on dorsal forearms (**Figure 1**), less pronounced erythematous patches on scalp and ears, indurated erythematous papules coalescent into annular plaques on abdomen (**Figure 2**), thighs, buttocks and gluteal cleft, and dorsal forearms and hands, edematous distal legs with purpuric macules and papules and diffuse desquamation on trunk and extremities. No enlarged lymph nodes were noted. Punch biopsies were obtained from abdomen, left knee, right hand (**Figure 3, 4**), and right forearm. Histopathological analysis in all biopsies demonstrated metaplastic squamous epithelium within the eccrine ducts



Figure 1. Irregular erythematous patches with scattered papules and pronounced scale on dorsal right forearm and hand.

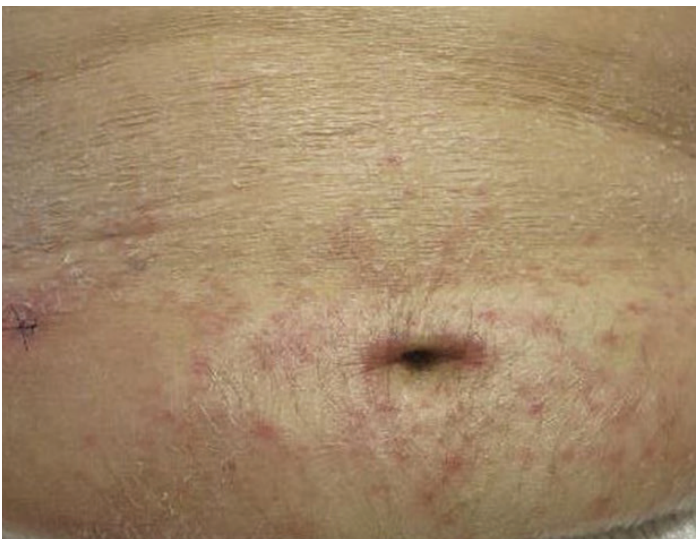


Figure 2. Scattered erythematous papules coalescent into annular plaques on abdomen.

with no significant inflammation. Hyperkeratosis, consistent with ichthyosis, was also noted. The erythematous patches, papules, and plaques, as well as the pruritus, improved with topical triamcinolone and resolved a few days after CLAG therapy was finished. The ichthyosiform GVHD remained constant during hospitalization. KOH, tissue cultures, and workups for viral, bacterial, and fungal infections were negative. The patient was discharged after resolution of the cutaneous eruption. Unfortunately, at the one month follow-up visit, a bone marrow aspirate was repeated and demonstrated relapsed myeloid blast phase. The patient and his family opted for hospice care at that time and he died a month later.

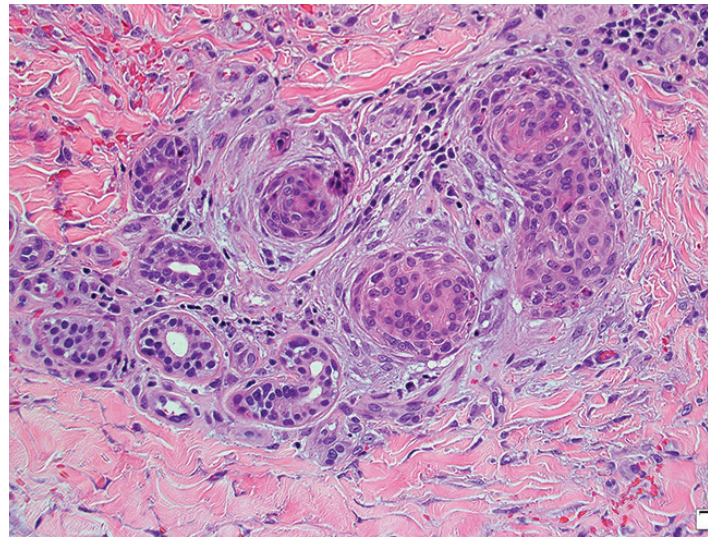


Figure 3. Punch biopsy from right hand shows replacement of eccrine coil/duct with eosinophilic appearing cells. Eccrine glands are in varying stages of metaplasia. No significant inflammation is noted. (H&E, 200%).

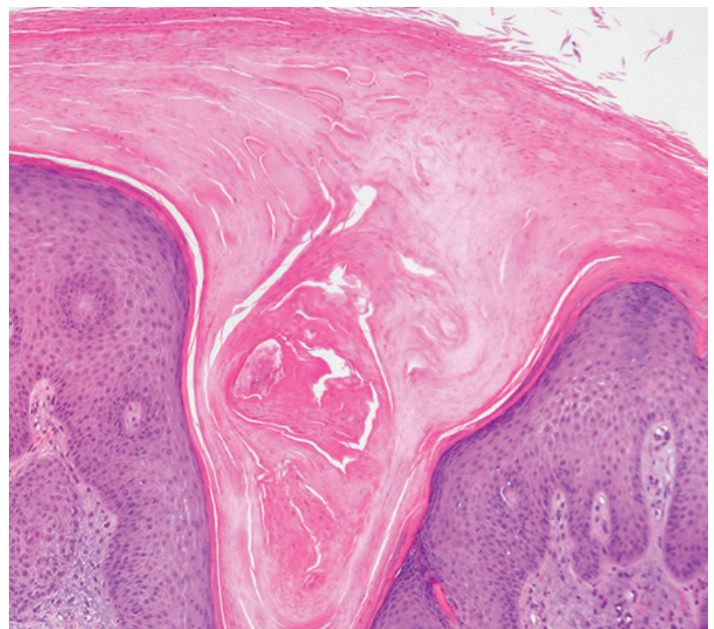


Figure 4. Punch biopsy from right hand reveals hyperkeratosis, consistent with history of ichthyosis. No significant inflammation is noted. (H&E, 50%).

Case Discussion

Clinically, chemotherapy-induced ESS presents most frequently as pruritic or burning erythematodesquamative and edematous papules and plaques, localized acraly or in intertriginous areas [1, 3, 6]. A few cases have been described with generalized distribution [4, 9] or localized to one region [2]. The eruptions usually appear within 30 days of chemotherapeutic infusion, but as early as 2 days have been noted. Lesions resolve spontaneously, but some cases required dose reduction of the

chemotherapeutic agent and/or addition of topical or systemic corticosteroids. With reintroduction of the cytostatic agents, lesions reoccur in up to 50% of patients [3].

Our patient's presentation, specifically the large distribution and varying morphology, does not closely fit with any of the previously described cases of ESS and illustrates the challenges the clinician encounters in this patient population. Given his history of chronic GVHD and immunosuppression, the differential diagnosis for his presentation was broad. Clinically, the erythematous scaly papules with annular distribution on the abdomen may resemble tinea corporis, but a KOH analysis at the bedside and further tissue cultures ruled out the possibility of an underlying infectious process. The fact that the patient's GVHD medications were tapered down prior to chemotherapy initiation could have resulted in worsening of his underlying GVHD and development of secondary ESS [10]. His cutaneous GVHD, however, remained stable while the new lesions resolved after chemotherapy was finished.

The major key for an accurate diagnosis was the histologic analysis of each skin biopsy in which clear eccrine squamous syringometaplasia was present in the absence of inflammatory infiltrate. Chemotherapy-induced ESS can be a diagnosis in and of itself but it also can be associated with other conditions such as neutrophilic eccrine hidradenitis (NEH) and acral erythrodysesthesia [1]. These conditions have tremendous overlap clinically, pathologically, and histologically. In fact, NEH in neutropenic patients and chemotherapy-induced ESS can appear virtually identical histologically [1, 11, 12]. Although NEH, erythrodysesthesia, and ESS have previously been described as distinct entities, Bologna et al. have proposed that these conditions are a spectrum of one another and should be included under the umbrella term "toxic erythema of chemotherapy" (TEC), [1], which describes the non-allergic, non-autoimmune, non-infectious nature of the conditions. The proposed term, TEC, would encompass AraC ears, Burgdorf reaction, ESS (chemotherapy-induced), erythrodysesthesia, NEH (chemotherapy associated), and drug-induced hidradenitis. It has been postulated that a direct toxic effect from eccrine secretions of cytostatic agents

could play a role in the pathogenesis of ESS and NEH. However, the exact underlying mechanisms remain to be elucidated [1, 3, 6, 10].

Conclusion

Though extremely rare, ESS must be kept in the differential for patients with suspicious bilateral erythematous eruptions especially after receiving cytarabine, vemurafenib, or pegylated liposomal doxorubicin. As new cytotoxic drugs become more commonly used, ESS may become more prominent. Dermatologists should be aware of this entity in the oncologic setting and understand the importance of skin biopsy in distinguishing it from infectious causes, other chemotherapeutic drug eruptions, and GVHD.

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