Treatment of Skin Ulcers Secondary to Sneddon Syndrome With Alprostadil (Prostaglandin E1)

Sneddon syndrome (SS) is a rare noninflammatory systemic vascular disease that clinically presents with cerebrovascular disease and racemous livedo. This condition is characterized by obstructive vasculopathy of cutaneous microcirculation, which can lead to the development of painful skin ulcers.

**Report of a Case** | A woman in her 50s with a history of SS of 20 years' evolution came to the dermatology department with ulceration on both legs. The patient had a history of lacunar infarction and was taking acetylsalicylic acid for prevention of cerebral ischemic events. Skin ulcers were previously treated with systemic corticosteroids and clopidogrel with no response. Physical examination revealed the presence of ulcerations of an irregular shape 1 to 5 cm in diameter with retiform purpura in both lower limbs (Figure, A). In addition, racemous livedo was observed on almost all the body surface. Peripheral pulses in upper and lower limbs were preserved bilaterally. No signs of severe chronic venous insufficiency or palpable purpura were observed. Laboratory findings for differential diagnosis of SS were normal or negative. Dermatopathologic analysis showed presence of fibrin thrombi and wall thickening in the papillary dermis with neovascularization phenomena. No fibrinoid necrosis of the vessel wall, neutrophilic infiltrate, or leukocytoclasia was observed. A diagnosis of SS was confirmed.

Treatment with intravenous alprostadil (prostaglandin E1 [PGE-1]) (Prostavasin; Gebro Pharma GmbH) was started at doses of 60 μg every 24 hours for 5 days and then a dose of 60 μg every 24 hours monthly as maintenance. From the first infusion, the patient showed rapid improvement in pain. After 3 months of treatment, complete healing of the skin ulcers was observed (Figure, B). At last follow-up, the patient had been treated for 6 months with a monthly infusion of alprostadil and remained asymptomatic. No adverse effects were observed.

**Discussion** | There are no established guidelines regarding the treatment of SS. Steroids and immunosuppressants have been used, but their effectiveness is still controversial, given the absence of vascular inflammation. Anticoagulant and antiplatelet agents have been used for the long-term prevention of cerebral ischemic events. Antiplatelets are more suitable when findings of antiphospholipid antibodies (aPL) are negative; anticoagulants are more suitable when aPL findings are positive.

Different therapies such as intravenous immunoglobulins, rivaroxaban, nifedipine, or those similar to prostaglandin have been used to treat the cutaneous symptoms. Mittag et al reported the first case of SS treated with iloprost in cycles also obtaining a remission in pain and clearing of the skin ulcers. Mofarrah et al described a case of livedoid vasculitis successfully treated with PGE-1 at dose of 60 μg for 5 days followed by a dose of 60 μg of monthly maintenance. The pain disappeared in the first 2 days, and ulcers healed after 3 weeks of treatment.

Both livedoid vasculitis and SS are cutaneous microcirculation abnormalities characterized by obliterative phenomena in the vessels. Noting this similarity, we used the same treatment regimen for SS. Alprostadil seems to be more effective in occlusive vasculopathy with racemous livedo. In the case reported by Mofarrah et al, iloprost was not as effective as alprostadil.
alprostadil. Alprostadil exerts a vasodilator, antiplatelet, and cytoprotective effect; it is an inhibitor of smooth muscle proliferation and fibrinolytic activity. Potential adverse events can occur, including fever, flushing, hypotension, hypocalcemia, and apnea.

Prostanoids have also been used in patients with peripheral arterial disease (PAD) in association with revascularization to relieve pain or improve ulcer healing. Prostanoids are probably not as effective in treating PAD because this condition is not an alteration of microcirculation as in livedoid vasculitis and SS. In venous ulcers, PGE-1 has also been described to be effective.  

We describe the successful treatment of a case of SS with alprostadil. This drug induces immediate pain relief, complete healing, and prevention of new skin ulcers. Alprostadil may be a therapeutic alternative for other dermatological conditions secondary to obstructive vasculopathy of cutaneous microcirculation.

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Published Online: March 16, 2016. doi:10.1001/jamadermatol.2016.0162.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for granting permission to publish this information. We are also indebted to Karla Tello-Collantes, MD, Department of Anatomic Pathology, Hospital Universitario Puerta del Mar, Cádiz, Spain, who provided expertise in pathology. She received no compensation for her contributions.


Unilateral Axillary Toxic Erythema of Chemotherapy in a Patient With Previous Axillary Lymph Node Dissection: Implications for Pathophysiology and Therapy

Toxic erythema of chemotherapy (TEC) is a cutaneous eruption that occurs with the use of cytotoxic chemotherapy and that presents with painful or pruritic erythematous patches or plaques occurring symmetrically on the hands, feet, and/or intertriginous areas (groin, axilla, neck). The lesions are often red-brown and may have associated blistering or superficial desquamation. The eruption characteristically appears within 2 to 3 weeks of initiating chemotherapy and is dose dependent. The agents most often associated with TEC are cytarabine, anthracyclines, fluorouracil, taxanes, and methotrexate. To our knowledge, this is the first report of a unilateral presentation of TEC, with sparing of an axilla that had previously been exposed to lymph node dissection (ALND) and radiation therapy.

Report of a Case | A woman in her 50s with history of stage II invasive ductal carcinoma of the left breast (upper-outer quadrant), in remission after chemoradiation and lumpectomy, was diagnosed with acute myelogenous leukemia and received induction chemotherapy with mitoxantrone, etoposide, and cytarabine. Eleven days after beginning chemotherapy, she presented with dusky, erythematous patches in the bilateral inguinal and inframammary folds and right axilla (Figure, A). The patches were edematous with areas of desquamation. Histopathologic analysis revealed epidermal dysmaturation, reactive hyperplasia, spongiosis, and mild perivascular lymphocytic inflammation, with negative tissue culture, consistent with TEC. The patient was treated with triamcinolone 0.1% ointment twice daily.

Of note, the eruption was symmetrical except for sparing of the left axilla (Figure, B). Further inquiry confirmed that the spared side had previously undergone irradiation and ALND for breast carcinoma.

Discussion | Though the pathophysiology of TEC is unknown, it is thought that excretion of chemotherapy in sweat leads to direct toxic effects to eccrine glands and keratinocytes. Support for this theory is the typical location of lesions in areas of high concentration of eccrine glands and/or sites of occlusion of sweat, such as the palms, soles, and intertriginous areas. While it has been demonstrated by laser scanning microscopy that chemotherapeutic agents accumulate in eccrine glands in these locations, there is no proof that this directly causes the skin changes seen with TEC.

This is a case of a patient with TEC with unilateral sparing of an axilla that had previously been exposed to radiation therapy and ALND. Though this patient reported little baseline sweating, and therefore did not note hypohidrosis in the left axilla, decreased sweat production in the distribution of the intercostobrachial nerve is a complication of mastectomy and ALND. Sparing of an area of sympathetic denervation in this patient supports the theory that TEC is caused by excretion of chemotherapeutic agents in sweat. Alternatively, it is possible that there are long-term immunomodulatory effects of radiation, resulting in Langerhans cell dysfunction and decreased local cytokine release, perhaps preventing TEC from developing.

Treatment for TEC is limited and mostly supportive. Symptomatic treatment includes analgesics, emollients, and topical steroids. Small studies have shown a potential benefit with...