Tattoo-associated Sweet syndrome

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To the Editor:

Tattoos can potentially be associated with cutaneous adverse events of either acute-onset (such as infections) or delayed-onset (such as skin cancer), [1-3]. Sweet syndrome, also referred to as acute febrile neutrophilic dermatosis, is characterized by pathergy: the development of new skin lesions at the site of cutaneous trauma [4,5]. However, Sweet syndrome occurring at the application site or inoculation site of a tattoo is extremely rare; therefore, the features of tattoo-acquired Sweet syndrome are summarized [6,7].

Sweet syndrome is a systemic condition with mucocutaneous manifestations. The condition is classically associated with a prompt onset of pyrexia and tender red plaques and/or nodules that typically reveal a dense infiltrate of mature neutrophils in the upper dermis, without evidence of leukocytoclastic vasculitis, and overlying edema in the papillary dermis. A preceding upper respiratory tract infection and elevated laboratory studies such as mature neutrophils (neutrophilia), erythrocyte sedimentation rate, and C-reactive protein are also often present. The dermatosis promptly responds to treatment with systemic corticosteroids [4,5].

In addition to infections (such as respiratory, gastrointestinal, and various others), common conditions associated with Sweet syndrome include cancer (more frequently with a hematologic malignancy than a solid tumor), medications (such as granulocyte colony stimulating factor and numerous other drugs), inflammatory bowel disease (such as Crohn disease and ulcerative colitis), and pregnancy. Corticosteroids, colchicine, and potassium iodide are first-line systemic treatments for Sweet syndrome. Alternatively, indomethacin, dapsone, clofazimine and cyclosporin are second-line therapies for patients in whom the condition is recalcitrant [4,5].

Tattoo-associated Sweet syndrome has been observed in two individuals who had recently acquired a black tattoo on their upper extremity (**Table 1**), [6,7]. One of the patients was a 41-year-old woman who initially developed localized Sweet syndrome on a newly inoculated black pigment ink tattoo and subsequently presented with generalized skin lesions that twice recurred during the subsequent two months [6]. Previously, Sweet syndrome had been described in a 23-year-old woman following the application of a black henna tattoo; the tattoo was also associated with allergic contact dermatitis to paraphenylenediamine three days after it was received [7].

Initial cutaneous lesions of Sweet syndrome appeared on the henna tattoo ten days after the tattoo was painted with additional asymmetrically-distributed lesions beyond the tattoo 15 days after receiving the tattoo. In contrast, Sweet syndrome skin lesions appeared on the ink tattoo five days after inoculation and additional lesions spread to the rest of the body eight days after the tattoo was received. Neither patient had antecedent or concurrent drug ingestion, viral illness, or fever; however, the woman with the ink tattoo had a sore throat. The initial and subsequent Sweet syndrome lesions were pruritic. However, the subsequent lesions on the upper arm and shoulder of the woman with the henna tattoo were also slightly painful [6,7].

The Sweet syndrome lesions were erythematous macules and/or papules; the henna tattoo-associated lesions also had a transparent vesicle-like appearance. Biopsy of the skin lesion, for both women, demonstrated a neutrophilic dermatosis. Acute inflammatory markers (such as erythrocyte sedimentation rate and/or C-reactive protein) were elevated in both women; only the woman with the henna tattoo had neutrophilia [6,7].

The Sweet syndrome lesions responded to systemic corticosteroids. However, they recurred twice in the woman with the ink tattoo before completely resolving. At 1-year follow-up, the woman with the ink tattoo-associated Sweet syndrome had no symptoms [6,7].

The pathogenesis of tattoo-associated Sweet syndrome remains to be definitively established. The investigators suggest that Sweet syndrome in their 41-year-old patient was either related (specifically or non-specifically) or independent to receiving the tattoo. In the latter scenario, Sweet syndrome and the tattooing were distinct but simultaneous events. Pathergy, with Sweet syndrome occurring secondary to skin injury during tattoo inoculation, would be a non-specific—yet related—etiology. Alternatively, specific and related tattoo-induced acute inflammation and epidermal necrosis may have attracted Sweet syndrome-associated activated neutrophils initially to the tattoo prior to subsequently spreading to the rest of the body [6].

Henna tattoos are temporary. Henna is derived from the dried leaves and flowers of the shrub *Lawsonia alba* or *Lawsonia inermis*. Black henna refers to plant henna after the addition of a second dye such as paraphenylenediamine in order to darken the red color, improve the pattern definition, and to hasten the drying. Indeed, some of the associated adverse events of henna tattooing have been attributed to the addition of paraphenylenediamine [8-10].

A common cytokine profile has been observed in patients with allergic contact dermatitis and Sweet syndrome. These include granulocyte-colony stimulating factor, granulocyte macrophage-colony stimulating factor, interferon gamma, interleukin 1, interleukin 2, interleukin 3, interleukin 6, and interleukin 8. Therefore, researchers have postulated that the development of Sweet syndrome in a black henna tattoo may have been related to the common cytokines involved in both paraphenylenediamine-related allergic contact dermatitis and Sweet syndrome [7].

In conclusion, tattoo-associated Sweet syndrome has been associated with both a temporary black henna tattoo and a permanent black pigment ink tattoo. The tattoo had been either painted on the distal hand or inoculated on the proximal arm of their left upper extremity; both women subsequently developed biopsy-confirmed Sweet syndrome that originated at the tattoo site and eventually progressed to involve other areas of their body. The etiology of tattoo-associated Sweet syndrome remains to be determined. Allergic contact dermatitis to paraphenylenediamine is suspected in the etiology of the tattoo following the application of black henna, whereas the black pigment is favored to have a pathogenic role in the tattoo that occurred after ink inoculation. Continued surveillance for additional individuals who develop Sweet syndrome in their henna-applied tattoo or pigment-inoculated tattoo may be helpful to further elucidate the pathogenesis of this phenomenon.

Potential conflicts of interest

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Table 1. *Features of patients with tattoo-associated Sweet syndrome.*

Feature	Patient 1	Patient 2
Age	23-years-old	41-years-old
Race	Caucasian	Caucasian
Gender	Woman	Woman
Tattoo type	Henna	Ink
Tattoo color	Black	Black
Tattoo location	Left dorsal hand	Left extensor forearm
Duration to initial symptoms	Three days: edema, erythema, and moderate pruritus over the tattoo area[a] Ten days: black discoloration of tattoo began to fade; itchy, erythematous plaques and scaling on tattoo	Five days: lesion on the tattoo that patient mistook for an insect bite
Duration to subsequent symptoms	15 days: acute skin eruption on left upper arm and shoulder	Eight days: several lesions on the tattoo that subsequently spread to the rest of her body
Recent drug ingestion	None	Not stated
Recent viral illness	None	Not stated
Sore throat	Absent	Present
Fever	None	None
Lesion pruritus	Moderate itch	Mild itch
Eventual lesion location	Asymmetrically distributed on the left upper arm and shoulder	Face, neck, proximal limbs, and upper trunk
Mucosal lesions	Not stated	None
Tender lesions	Slightly painful	Not stated
Lesion morphology	Red papules with a transparent vesicle-like appearance	Erythematous macules and papules
Lesion pathology	Marked edema in the papillary dermis and a diffuse inflammatory infiltrate of neutrophils in the superficial dermis without signs of vasculitis	Neutrophilic nodular infiltrates in the dermis with marked edema and erythrocyte extravasation, but without vasculitis
Laboratory studies	CRP: 19.4mg/L (increased) ESR: 35mm (increased) Hepatic function: normal Leukocytes: 8,620/microliter (normal) Neutrophils: 78% (increased) Renal function: normal Urinalysis: normal	CRP: 87mg/L (increased) Leukocytes: normal Neutrophils: normal
Treatment	Systemic corticosteroids for 11 days	Oral corticosteroids (0.5mg/kg/day)
Response to treatment	Lesions disappeared	Rapid efficacy
Lesion recurrence	None	Two local relapses on her tattoo during the next two months: After rapid prednisolone taper (5mg/day) Immediately after corticosteroid withdrawal
Follow-up	Not stated	No relapse after slower corticosteroid taper No symptoms at 1-year follow-up
Comments	Portuguese standard series patch testing was positive for mixture of henna plus	None

	paraphenylenediamine (in 1% petrolatum) and henna powder History of similar henna tattoo 3-years earlier on left shoulder without any problems; current lesions did not mimic previous tattoo drawing	
Reference	[7]	[6]

CRP, C-reactive protein (normal is less than 5 mg/L); ESR, erythrocyte sedimentation rate; kg, kilogram; L, liter; mg, milligrams; /, per; %, percent.
[a]Symptoms diagnosed as allergic contact dermatitis to paraphenylenediamine.