Does sensitive skin represent a skin condition or manifestations of other disorders?

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Editor,

Sensitive skin or cutaneous sensory syndrome is defined as a skin condition that is hypersensitive to stimuli, which normally do not cause problems in normal subjects.¹ Although this definition has been widely accepted for years, a line of evidence suggests that sensitive skin could be manifestations and/or condition of a variety of disorders, associated with not only impairment of epidermal functions (elevated transepidermal water loss rates, reductions in the stratum corneum hydration, increased skin pH levels, and so on), psychological stress, neuroimmunological dysfunction, but also other cutaneous, and extracutaneous disorders. Here, we briefly relate sensitive skin syndrome with cutaneous and extracutaneous disorders.

In addition to dermatoses, medications, such as topical or systemic retinoid and glucocorticoids can also induce symptoms and signs of sensitive skin. Additionally, sensitive skin can result from adverse reactions to skin care products.²,³ Taken together, evidence indicates that sensitive skin could represent manifestations of cutaneous disorders and of treatment to skin disease. Skin disorders associated with sensitive skin are summarized in Table 1.

1 | SENSITIVE SKIN CAN BE A CUTANEOUS MANIFESTATION OF SKIN DISORDERS

Epidemiological studies have demonstrated a higher prevalence of sensitive skin in subjects with certain cutaneous disorders, such as atopic dermatitis (AD), psoriasis, acne, rosacea, and seborrheic dermatitis.²,³ For example, subjects who claimed sensitive skin were 5 times likely to report skin allergies,⁴ while prevalence of sensitive skin in patients with rosacea can be as high as 100%.⁵ Likewise, over 40% of psoriatic patients experience symptoms and signs of sensitive skin, such as itchy, hot/burning, tender, and cramping.⁶ The odds of having sensitive skin is 3.7 times greater in psoriatic patients than in the controls.² Similarly, odds of having sensitive skin are 2.5 times greater in patients with acne.² To distinguish sensitive skin from them is sometimes difficult. When a patient complains of sensitive skin presented with skin lesion or symptom, a diagnosis of dermatosis should be considered at first. If the complaint of unpleasant sensation cannot be explained by lesions attributable to any dermatosis, a diagnosis of sensitive skin or sensitive skin syndrome could be made.

In addition to dermatoses, medications, such as topical or systemic retinoid and glucocorticoids can also induce symptoms and signs of sensitive skin. Additionally, sensitive skin can result from adverse reactions to skin care products.⁷,⁸ Taken together, evidence indicates that sensitive skin could represent manifestations of cutaneous disorders and of treatment to skin disease. Skin disorders associated with sensitive skin are summarized in Table 1.
For instance, subjects with insulin resistance and hyperglycemia can suffer from sensitive skin syndrome, likely due to a defective epidermal permeability barrier and impaired peripheral sympathetic nervous system. Likewise, diabetic patients can experience skin sensory symptoms, such as itching, stinging, and flushing, possibly due to peripheral neuropathy and angiopathy. Obesity is another exemplar of an association between sensitive skin and systemic condition. The common comorbidities of obesity include itching and burning, which are linked to the fragile skin structure and epidermal dysfunction. In obesity, face roughness was higher than non-obesity, the water content was lower, and significant facial redness accompanied by increased skin blood flow was also observed, all of them were correlated to systemic inflammation, serum insulin, and leptin.

Some disorders, such as hyperalgesia, with damage of cutaneous C-fibers, can increase sensitivity to stimuli because of a reduction in pain threshold. Symptoms of sensitive skin, especially itching, are also common in some autoimmune connective tissue diseases, including dermatomyositis, systemic lupus erythematosus, Sjogren

| TABLE 1  | Association of sensitive skin symptoms with cutaneous and extracutaneous disorders |
|----------|-------------------------------------------------------------------------------------|
| Disorders| Epidemiology/Symptom | References |
| Atopic dermatitis | a history of childhood AD was more frequent in sensitive skin patient (OR: 1.6) | Misery et al, 2009² |
| | 56% of sensitive skin subjects reports a concomitant atopic condition | Richters RJ et al, 2017³ |
| | more self-reported skin allergies in AD patients(OR: 5.0) | Farage MA, 2008⁴ |
| | Itching after exposure to heat, wind, and low humidity | Bonchak JG et al, 2018²⁷ |
| Psoriasis | 1.5% of sensitive skin patient have psoriasis, greater sensitive skin in psoriasis people (OR: 3.7) | Misery et al, 2009² |
| | skin pain, itchy, unpleasant, aching, sensitive, hot/burning, tender and cramping in psoriasis patient | Patruno C et al, 2015⁵ |
| Rosacea | 1.5% of sensitive skin patient have rosacea | Misery et al, 2009² |
| | 100% French rosacea patients complained having very sensitive skin | Misery L et al, 2005⁵ |
| | 78.2% Germany and Russian rosacea patients presented with sensitive skin flushing, erythema, intolerance to stimuli sensitive to burning and stinging | Tan J et al, 2016²⁸ |
| | | Misery L et al, 2011²⁸ |
| | | van Zuuren EJ, 2017³⁰ |
| Acne | 2.5% of sensitive skin patient have acne; Odds of sensitive skin in acne patients is 2.5 times greater itching, dryness, and desquamation related to treatment | Misery et al, 2009² |
| Adverse reactions to skin care products | branded skin care products can cause severe adverse cutaneous reactions | Li Z et al, 2018⁷ |
| | Itching in 59% of patients | Yahya A et al, 2019¹⁶ |
| | Hence, diabetes and skin inflammation | Katayama I et al, 2018²⁶ |
| | dry skin and itching | Yahya A et al, 2019¹⁶ |
| | | Yahya A et al, 2019¹⁶ |
| | Systemic lupus erythematosus | Itching in 61% of patients | Yahya A et al, 2019¹⁶ |
| | Dermatomyositis | Itching in 83% of patients | Yahya A et al, 2019¹⁶ |
| | Systemic sclerosis | Itching in 22% of patients | Yahya A et al, 2019¹⁶ |
| | Mixed connective tissue disease | Itching in 60% of patients | Yahya A et al, 2019¹⁶ |

Abbreviation: OR, odds ratio.
syndrome, systemic sclerosis, as well as mixed connective tissue disease. Collectively, sensitive skin can also be a phenomenon of extracutaneous disorders.

REGARDING THE MECHANISMS BY WHICH SENSITIVE SKIN DEVELOPS IN SOME CUTANEOUS AND EXTRA CUTANEOUS DISORDERS, IT IS NOT CLEAR YET. HOWEVER, EVIDENCE SUGGEST SEVERAL POSSIBLE MECHANISMS.

Firstly, the development of sensitive skin is associated with epidermal dysfunction, which commonly exists in inflammatory dermatoses, diabetes, obesity, and autoimmune connective tissue disease.10,14,17,18 Secondly, some symptoms of sensitive skin syndrome, including itching, stinging, and flushing, could be due to the damage of C-fibers in some disorders, such as diabetic peripheral neuropathy.11 There are also numerous neuromediators involved in the pathogenesis of itch in dry skin, like nerve growth factor (NGF), muscarinic acetylcholine receptors, opiates, serine proteases such as tryptase and their respective proteinase-activating receptor 2 (PAR2).19 Non-neuronal transient receptor potential (TRP) channels also play a central role in the perception and pathophysiology of sensitive skin because they can be activated by heterogeneous physical, chemical, or thermal stimuli, which in parallel act as triggers of sensitive skin.20 On the other hand, transient receptor potential vanilloid 1 (TRPV1) is involved in inflammatory dermatoses like psoriasiform inflammation,21 and some autoimmune diseases.22 Moreover, dysfunction of cutaneous TRPV 2, 3, and 4 expression was observed in rosacea.23 Thirdly, in addition to pro-inflammatory cytokines, TRPV,24 hyperglycemia,25 and hypidrotic in AD and Sjogren syndrome26 can also contribute to skin inflammatory reaction. Finally, increased skin blood flow, redness, and flushing resulting from small vessel dysfunction of sensitive skin are also observed in obesity and diabetic patients.10

In conclusion, above evidence strongly suggests that sensitive skin could represent cutaneous manifestations of various cutaneous and extracutaneous disorders. Therefore, caution should be taken when subjects display sensitive skin because a variety of cutaneous and extracutaneous disorders can accompanied with sensitive skin. For example, screening for insulin resistance and serum glucose is recommended to obese sensitive skin subjects, autoimmune antibody test is recommend to female subjects.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

CONFLICT OF INTEREST
Authors declare no conflict of interests for this article.

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