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Tumor necrosis factor-like weak inducer of apoptosis (TWEAK) in psoriasis and atopic dermatitis: A case-control study

To the Editor: Psoriasis and atopic dermatitis (AD) are common inflammatory, T-cell–mediated diseases. Previous studies suggested a role of tumor necrosis factor–like weak inducer of apoptosis (TWEAK) in psoriasis and AD.[1-5] However, studies are quite limited, with some conflicting results.

This is a case-control study conducted on 90 participants: 30 patients with psoriasis vulgaris, 30 patients with AD, and 30 age- and sex-matched healthy control individuals. All participants were older than 18 years and provided informed consent. Patients were subjected to full history taking and examination of the skin for Psoriasis Area and Severity Index score in patients with psoriasis and EASI score in patients with AD.

Skin biopsy samples were obtained from the lesional skin of patients and normal skin of control individuals. Each skin biopsy sample was weighted and homogenized in phosphate-buffered saline (with a ratio of tissue weight [in grams] to phosphate-buffered saline volume [in milliliters] of 1:9) with a glass homogenizer on ice. The homogenates were then centrifuged for 5 minutes at 5000*g* to get the supernatant. The supernatant was separated to be used for quantitation of TWEAK by using a commercially available enzyme-linked immunosorbent assay kit (catalog No. MBS2511137) provided by MyBiosource, Inc (San Diego, CA.)

Demographic and clinical data of patients and control individuals are summarized in Table I. TWEAK level was significantly higher in patients with psoriasis than those with AD and control individuals ($P = .042$ and $P < .001$, respectively). Also, there was a significant difference between patients with AD and control individuals, with a higher level in AD skin ($P < .001$) (Fig 1).

No significant correlations were detected between the level of TWEAK in patients with psoriasis and each of the age, duration, and Psoriasis Area and Severity Index score ($P = .841$, $r = -0.038$; $P = .64$, $r = 0.089$; and $P = .068$, $r = -0.338$, respectively). Also, there was no relation between TWEAK level and sex ($P = .744$) or family history ($P = .617$).

In patients with AD, the level of TWEAK did not show any association with the measured variables with regard to their age, Eczema Area and Severity Index score, sex, or family history ($P = .736$, $r = -0.064$; $P = .601$, $r = -0.1$; $P = .721$; and $P = .866$, respectively). However, there was a statistically significant positive correlation between TWEAK level and disease duration ($P = .006$, $r = .491$).

TWEAK can have a role in 2 previously known mutually exclusive skin diseases. TWEAK alone cannot produce full AD or psoriasis, but it promotes chemokines common to both diseases from keratinocytes and fibroblasts, in addition to characteristic cytokines of AD and psoriasis such as TSLP and interleukin (IL) 19. Moreover, TWEAK can act in synergy with the disease-specific cytokines IL-13 and IL-17.[5] The absence of correlations with the measured disease variables can be explained by the local production of TWEAK by inflammatory cells. Our demonstration of a positive correlation between the level of TWEAK and duration of AD disease may suggest that persistent activation of TWEAK signaling pathway leads to the harmful effects, causing chronic dermatitis lesions.

In conclusion, TWEAK may have a role in the pathogenesis of psoriasis and AD. Clinical trials studying the blocking of TWEAK signaling in

Table I. Demographic and clinical data of the studied groups

Characteristics	Patients with psoriasis	Patients with AD	Control individuals	*P* value*
Age, y				
Mean	46.13	45.07	47.7	.698
SD	13.87	14.16	6.67	
Sex, n (%)				
Male	19 (63.3)	20 (66.7)	15 (50)	.378
Female	11 (36.7)	10 (33.3)	15 (50)	
Positive family history, n (%)	4 (13.3)	5 (16.6)	—	—
Duration of disease, mo				
Range	1-260	0.5-240	—	—
Mean ± SD	109.90 ± 87.91	54.77 ± 66.06		
Severity of disease: PASI for psoriasis and EASI for AD				
Range	0.9-28.5	1.2-6.6	—	—
Mean ± SD	8.09 ± 6.38	3.92 ± 1.69		

AD, Atopic dermatitis; *EASI*, Eczema Area and Severity Index; *PASI*, Psoriasis Area and Severity Index; *SD*, standard deviation.
*$P < .05$ indicates significance.

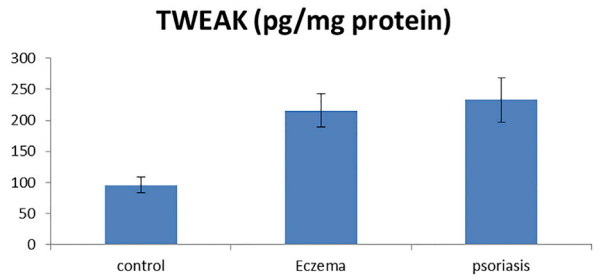

Fig 1. Level of tumor necrosis factor–like weak inducer of apoptosis (TWEAK) in the studied groups.

psoriasis or AD are needed to confirm this hypothesis.

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Patterns of incidental perineural invasion and prognosis in cutaneous squamous cell carcinoma: A multicenter, retrospective cohort study

To the Editor: Perineural invasion (PNI) is rare and usually incidental in cutaneous squamous cell carcinoma (SCC), with an incidence of 2.5% to 14%.[1] Incidental PNI is associated with poor prognosis in cutaneous SCC,[2] and some evidence suggests its outcome differs, depending on the PNI pattern. We evaluated patterns of incidental PNI, using a multicenter retrospective cohort of 140 cutaneous SCCs with incidental PNI to determine the influence of nerve involvement on cutaneous SCC prognosis.

Clinical and histopathologic data were recorded, including the risk factors listed in the *AJCC Cancer*