had low levels of NETosis in circulating neutrophils and increased levels in skin infiltrating neutrophils. Thus, the role of comorbidities in affecting NETosis in skin infiltrating neutrophils seems limited.

On the contrary, in a previous study, aberrant NETosis was detected in skin lesions of all the pyoderma gangrenosum patients that were studied, irrespective of the coexistence of autoimmune disorders.[1,2] Neutrophils extracellular trap are less frequently detected in Sweet syndrome patients compared to pyoderma gangrenosum, suggesting that, despite a similar neutrophilic infiltrate in the skin, neutrophilic dermatoses may differ in the extent of NETosis.[1,2] In pyoderma gangrenosum, the higher number of netting neutrophils is parallel to a higher degree of tissue damage, leading to ulcerative lesions.

Similar results have been reported by Eid *et al.*, analysing a larger cohort of Sweet syndrome patients and a smaller group of pyoderma gangrenosum patients.[2]

Thus, further studies are necessary on Sweet syndrome patients to identify the mechanisms of neutrophil-induced skin damage, and the role of NETosis in the different subsets of the disease.

Declaration of patient consent

Patient's consent is not required as the patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Interleukin 27 in psoriasis: Friend or foe?

Sir,

Several studies have uncovered the pleiotropic role of interleukin 27 in the differentiation and functioning of T-cell subsets. Interleukin 27 was first recognized as an inflammatory cytokine, supported by the fact that it induces expansion of T helper 1 cell.[1] Later on, the immunosuppressive properties of interleukin 27 were uncovered. The cytokine was found to suppress immune responses by inhibiting the development of T helper 17 cells and inducing IL-10 production.[1] We examined the expression of this versatile interleukin in patients with psoriasis, as well as its relation to clinical disease parameters.

This case-control study was conducted on 25 patients with psoriasis and 30 healthy persons without psoriasis, recruited from Kasr Al-Ainy psoriasis unit, Dermatology Department, Cairo University. Each patient was subjected to history taking and clinical examination to document the extent of the disease as well as psoriasis area and severity index. Systemic treatments were stopped for a minimum of four weeks prior to inclusion. Pregnant and lactating females as well as patients with erythrodermic or pustular psoriasis were excluded. Tissue and serum levels of interleukin 27 were measured by enzyme-linked immunosorbent assay.

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Table 1: Demographic and clinical data of patients and controls

Variable	Patients N=25	Controls N=30	*P*-value
Age (years)			
Range	19–67	17–48	0.132
Mean ± SD	38.2 ± 14.894	31.733 ± 9.931	
Sex (N, %)			
Males	16 (64%)	18 (60%)	0.106
Female	9 (36%)	12 (40%)	
Disease duration (months)			
Range	3–404		
Mean ± SD	92.520 ± 90.816		
Extent (%)			
Range	2–60		
Mean ± SD	15.16 ± 15.558		
PASI score			
Range	2–15.3		
Mean ± SD	7.324 ± 4.047		
Onset (%)			
Gradual	23 (92%)		
Sudden	2 (8%)		
Course (%)			
Progressive	10 (40%)		
Regressive	2 (8%)		
Remissions and exacerbations	13 (52%)		

SD: Standard deviation, N: Number

Table 2: Comparison between interleukin 27 levels in patients and controls

	Patients N=25	Controls N=30	*P*-value
Tissue IL-27 (ng/mg)			
Range	93.62–675.18	25.18–195.12	<0.001*
Mean ± SD	347.72 ± 160.07	97.08 ± 48.76	
Serum IL-27 (ng/L)			
Range	62.09–317.49	35.70–114.75	0.005*
Mean ± SD	154.49 ± 75.96	92.75 ± 16.98	

**P*-value <0.05 is significant, SD: Standard deviation, N: Number

The demographic and clinical data of the participants are outlined in Table 1. The mean tissue and serum levels of interleukin 27 were significantly higher among patients with psoriasis in comparison to those without psoriasis ($P \leq 0.001$, 0.005, respectively) [Table 2]. A significant negative correlation between the patients' interleukin 27 serum levels and disease severity (expressed in terms of both psoriasis area and severity index score and extent of the disease) ($P = 0.007$, 0.002, r = −0.528, −0.600, respectively) was observed [Figure 1].

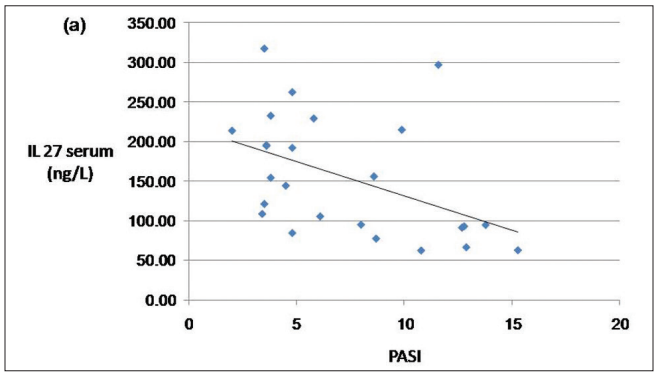

Figure 1a: Significant negative correlation between interleukin 27 and psoriasis area severity index score

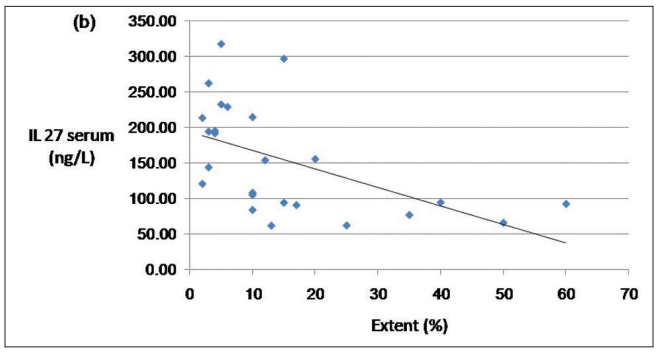

Figure 1b: Significant negative correlation between interleukin 27 and extent of disease

In concordance with our findings, Shibata *et al.*[2] reported significantly higher mean serum interleukin 27 levels in patients with psoriasis. They also reported serum levels of interferon-gamma to correlate positively with serum levels of interleukin 27, indicating that the increased interleukin 27 levels may contribute to the enhanced T helper 1 activity in psoriasis. Interleukin 27 by itself stimulate the in vitro production of chemokine C-X-C Motif Ligand 9, chemokine C-X-C Motif Ligand 10, and chemokine C-X-C Motif Ligand 11 in keratinocytes.[2] However, in the presence of *tumour necrosis factor* α, interleukin 27 exerted anti-inflammatory effects by inhibiting *tumour necrosis factor* α-induced production of IL-1α and chemokine C-C Motif ligand 20. The authors concluded that interleukin 27 is involved in priming the onset of psoriasis by inducing Th1 attracting chemokines Once this is established, with consequently elevated *tumour necrosis factor* α, interleukin 27 may possibly exert its anti-inflammatory effects through the inhibition of IL-1α and chemokine C-C Motif Ligand 20 production as well as its direct suppressor effect over T helper 17 responses.[2]

Nonetheless, it should be noted that this anti-inflammatory effect may be overwhelmed by interleukin 27 mediated enhancement of the expression of the potent pro-inflammatory tumour necrosis factor α; which aids in activation of T helper 17 cells, counteracting the cytokine's anti-inflammatory responses.[2] This was further demonstrated when Shibata *et al.*[3] injected interleukin 27 in rodent models for psoriasis and found a further exacerbation in disease severity and increased messenger ribonucleic acid levels of T helper 1 cytokine/chemokines

and tumour necrosis factor α. Furthermore, the neutralization of interleukin 27 led to a reduction in messenger ribonucleic acid levels of T helper 1 cytokine/chemokines including tumour necrosis factor α and induced improvement both clinically and histologically.

Interestingly, and in contrast to previous studies and the current work, Chen *et al*.[4] reported downregulation of interleukin 27 in both serum and tissue in moderate-to-severe psoriasis. They found that injecting interleukin 27 in imiquimod-induced psoriasis mouse models, decreased the severity of inflammation.[4] Several factors may have contributed to the discrepancy in results across various studies, including ethnic differences,[4] as well as differences in disease activity and stability of the patients recruited between studies, indicating that the function of the cytokine might dynamically change at different stages of disease progression.[4,5]

Our findings show that serum and tissue interleukin 27 is upregulated in psoriasis and this upregulation is negatively affected by the severity and extent of the disease. It may thus be speculated that interleukin 27 is initially upregulated at the onset of psoriasis, but this upregulation is dampened with increasing severity and extent of disease, leading to an inadequate protective role for this cytokine on tumour necrosis factor α induced cytokines in progressive and severe disease. Large scale molecular studies are needed to confirm the dual effect of interleukin 27, in addition to clinical trials that utilize interleukin 27 inhibitors as well as activators, to identify its exact contribution in the pathogenesis of psoriasis and in the various stages of disease progression.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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Switching immune sensitizer agents in refractory alopecia areata as a valuable therapeutic strategy a retrospective case series

Sir,

Alopecia areata is an autoimmune hair disorder that can affect any hair-bearing region of the body. Treatments include topical, intralesional, and systemic medications.[1] When considering immunotherapy, guidelines suggest using diphenylcyclopropenone, with subsequent consideration of squaric acid dibutylester in nonresponders.[2]

After approval by the local research and ethical committee (DE21-00004), a retrospective analysis of cases from the

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