doi:10.36849/JDD.9592e

Hidradenitis Suppurativa in Psoriasis Patients Treated With Biologics

Dennis Chu BS,[a] William Guo MD,[b] Matthew Chen BS,[a] James Briley DO[b]

[a]Renaissance School of Medicine, Stony Brook University, Stony Brook, NY
[b]Department of Dermatology, Stony Brook University Hospital, Stony Brook, NY

To the Editor,

While biologic medications are frequently used to treat inflammatory skin diseases, patients have experienced paradoxical skin diseases arising from treatment.[1] The onset of new hidradenitis suppurativa (HS) has been reported after psoriatic biologic therapy, inciting characteristic deep-seated, inflammatory lesions despite immunosuppression.[1] To investigate the scope of this phenomenon and differences in HS risk between therapies, we conducted a retrospective cohort study utilizing the TriNetX database, a global health research network with aggregated data from over 300 million patients worldwide.

Treatment cohorts included psoriasis or psoriasis vulgaris patients prescribed an approved psoriatic biologic while excluding all other therapies. Certolizumab, brodalumab, tildrakizumab, and bimekizumab were excluded due to low sample size. Controls were patients with psoriasis or psoriasis vulgaris without any biologic use. Groups were propensity-matched for demographics, comorbidities, and comedications. Risk ratios and 95% confidence intervals (CI) were calculated for HS incidence (Table 1). Patients with HS before biologic therapy prescription were excluded.

Psoriasis patients treated with adalimumab (RR: 1.44 |1.16–1.80|) or infliximab (RR: 2.08 |1.29–3.35|) were significantly more likely to be diagnosed with HS compared to controls. Additionally, psoriasis patients on risankizumab (RR: 0.42 |0.24-0.71|) or guselkumab (RR:0.36 |0.17–0.73|) therapy were both associated with significantly decreased risk of HS incidence after treatment. No other biologics demonstrated significantly different rates of HS compared to controls.

The mechanism of biologic-induced HS remains unclear; however, this phenomenon may help explore the complex pathogenesis of HS. Unlike etanercept and certolizumab pegol, adalimumab and infliximab are full monoclonal antibodies to TNF-α.[2] The unmodified Fc region of these biologics can activate the complement cascade,[2] increasing C5a and NLRP3 inflammasome levels, which stimulate interleukin (IL)-1β, a key HS inflammatory marker.[3] On the other hand, unlike IL-17 and IL-12/23 antagonists, IL-23 inhibitors may be protective of HS by avoiding stimulation of compensatory inflammatory markers. IL-23 biologics selectively inhibit the IL-23/Th17 cascade critical in psoriasis while sparing the IL-12/IFN-γ axis, preventing unwanted initiation of other immune responses.[4] Secukinumab and ixekizumab both inhibit IL-17A, but induction of a negative feedback loop in the IL-23/IL-17 axis, can upregulate IL-23 and Th17, balancing out HS incidence.[5] Furthermore, although ustekinumab is also an IL-23 inhibitor, additional IL-12 downregulation may decrease IFN-γ levels, inducing additional stimulation of IL-1β and subsequent HS.[6]

TABLE 1.

Association of Biologic Use in Psoriasis Patients and Hidradenitis Suppurativa Development

Biologics	Biologic		Control		RR (95% CI)	*P*-value
	Patients (n)	HS cases	Patients (n)	HS cases		
Adalimumab	26,193	192	26,796	136	1.44 (1.16-1.80)	<0.001
Infliximab	4257	51	4338	25	2.08 (1.29-3.35)	0.002
Etanercept	10,032	25	10,018	39	0.64 (0.39-1.06)	0.079
Secukinumab	6,666	32	6,783	29	1.12 (0.68-1.85)	0.650
Ixekizumab	4474	15	4497	26	0.58 (0.31-1.09)	0.088
Risankizumab	8687	19	8718	46	0.42 (0.24-0.71)	<0.001
Guselkumab	3987	≤10	2984	28	0.36 (0.17-0.73)	0.003
Ustekinumab	7015	43	7040	42	1.03 (0.67-1.57)	0.900

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Limitations include medication adherence, dosage details, unaddressed confounding variables, and lack of causal conclusions. Greater awareness of paradoxical HS onset is important during psoriasis treatment to discontinue treatment and alleviate symptoms. Our data suggest that adalimumab and infliximab have higher occurrence of paradoxical HS during psoriasis treatment. Furthermore, physicians may consider risankizumab or guselkumab as alternative therapies should paradoxical symptoms occur.

DISCLOSURES

There are no potential conflicts or conflicts of interest.

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AUTHOR CORRESPONDENCE

Dennis Chu BS
E-mail:..... dennis.chu@stonybrookmedicine.edu