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Practical conundrums of immune profiling in Stevens–Johnson syndrome-toxic epidermal necrolysis

To the Editor,

We read the article “Intravenous immunoglobulins, cyclosporine, and best supportive care in epidermal necrolysis: Diverse effects on systemic inflammation” with great interest¹ and congratulate the authors for analyzing the cutaneous and serological patterns of inflammation in Stevens–Johnson syndrome/Toxic Epidermal Necrolysis (SJS/TEN) patients. In fact, the proteomic results gathered at the baseline before initiation of any treatment are one of the most exhaustive reported till date; however, subsequent conclusions drawn may need more refinement, particularly the data on temporal dynamics.

The title of study suggests a study design appropriate to assess and perhaps compare the effect of various treatments on the proteomics. While SJS/TEN does remain very rare, sample size is still small to draw inferences from, and the study composed of subjects with a significantly heterogeneous and varied clinical profile in different groups. The statement that immunological changes observed were therapy-induced may require consideration of additional parameters, since there were important baseline confounding factors including lower age group in cyclosporine treated group, predominant patients of Asian ancestry in best supportive care group vis-à-vis Caucasians in cyclosporine/IVIg group, significantly higher body surface area involvement and higher rates of systemic complications in IVIg group. Although differences in age were not statistically significant, they can be potential confounders owing to differences in the robustness of immune responses with age. The association of severity of SJS/TEN with ethnicity remains unclear but still plausible, due to disparities in their genetic makeup, comorbidity profiles, immune responses, socio-economic factors, and local prescription practices. Interestingly, the SCORTEN values ranged from 0 to 4 with a mean value less than 2 in all the groups with a predictive mortality rate of around 12%.²

Total body surface area at the time of admission was significantly high in the IVIg group and may partly explain the persistent inflammatory response at Days 5–7, preventing one from drawing any concrete conclusion regarding the effect of IVIg per se on the proteomic parameters. The extent of involvement of body surface area would also determine the magnitude of immune responses

and rates of secondary complications like sepsis. The latter, in turn, would affect immune profiles based on pathogen–host interactions and systemic inflammatory overdrive. Blood sampling when done at days 5–7 would also influence the proteomics in IVIg group, where treatment essentially comprised of globulins was administered until a day before the sampling. Overall, the decisive factors for a particular treatment protocol used (best supportive care, cyclosporine, and intravenous immunoglobulin) were not specified, making the groups arbitrary and based on hospital policies.

Timeline for various sampling procedures in the study is considered from the day of hospitalization. However, when studying the patterns of inflammation, timeline as per onset of disease would also become pivotal as not all patients would present on Day 1 of the condition. Also, more intermediate readings may be required like on Day 14, since natural history of disease process is likely to show resolution by 3 weeks in survivors irrespective of treatment. While the reported inflammatory signatures are diverse in the study between different treatment arms, the clinical outcome did not differ. This incongruity may be attributed to a low mean SCORTEN values in the study, which itself has a low predictive mortality rate. Further, as mentioned by the authors themselves, cutaneous inflammation may not necessarily reach the circulation. Perhaps performing serial skin biopsy would have been a better way to assess the disease pathophysiology changes. Interestingly, the equivalence of proteomics on Day 21 has been attributed to the natural resolution course of disease process, while the differences on Days 5–7 attributed to the treatment provided. The latter could rather be attributed to the differences in disease-specific parameters and the severe course of the disease, especially in the initial few days.

Clinical translation of this research would become paramount, since the results seem to compound the controversy whether immunomodulators should be used in SJS/TEN besides supportive care.³ Practical ramifications of inflammatory mediator profiling need to be established for a clinician to draw interpretations from them. Larger cohort, including a wider range of patients, is thus required to justify these important observations and especially correlate with not just the final clinical outcome of mortality, but also with length of hospital stay and duration of re-epithelization.

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CONFLICT OF INTEREST STATEMENT

None of the authors have any conflict of interest.

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REFERENCES

1. Schmidt V, Lalevée S, Traidl S, et al. Intravenous immunoglobulins, cyclosporine, and best supportive care in epidermal necrolysis: diverse effects on systemic inflammation. *Allergy*. 2022. doi:[10.1111/all.15608](https://doi.org/10.1111/all.15608). Online ahead of print.
2. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. *Arch Dermatol*. 1993;129(1):92-96.
3. Jacobsen A, Olabi B, Langley A, et al. Systemic interventions for treatment of Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS/TEN overlap syndrome. *Cochrane Database Syst Rev*. 2022;3(3):CD013130. doi:[10.1002/14651858.CD013130.pub2](https://doi.org/10.1002/14651858.CD013130.pub2)