Serological immune signature changes in SJS/TEN patients during IVIG treatment

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Introduction and Objectives

Steven Johnson Syndrome (SJS) and Toxic epidermal necrolysis (TEN) are rare severe cutaneous adverse reactions with high morbidity and mortality. There is still no consensus on the use of adjuvant treatments such as intravenous immunglobulines (IVIG), TNF inhibitors and systemic glucocorticosteroids for SJS/TEN and little is known about their effects on a cellular/ molecular level. Our aim was to explore the effects of IVIG on the inflammatory response in SJS/TEN and correlate these findings to the clinical outcome.

Patients and Methods

In this prospective study, we included 2 patients with SJS and 6 patients with TEN treated at the University Hospital Zurich between 2014 and 2020 with high-dose IVIG (1g/kg per day) for 3 days. Serum samples were collected from prior (day 0) and 4-5 days after IVIG administration (Figure 1). Serum levels of inflammation-associated proteins were measured with the inflammation I panel of a proteomic multiplex assay by Olink (Uppsala, Sweden), which is a proximity extension assay with oligonucleotide-labeled antibody probe pairs. It measures proteins via an antibody-mediated detection system linked to synthetic DNA for quantification by a real-time polymerase chain reaction platform.

Patient Characteristics		
Gender	female (n=4)	male (n=4)
Mean age (+- SD)	39 (+- 14,90)	57,5 (+- 20,93)
Mean BSA (Body surface area) affected	50%	18,75%
Mucosal involvement	3/4 (75%)	3/4 (75%)
Mean SCORTEN at admission	1,75	2,25
Alive after 6 weeks	4/4 (100%)	4/4 (100%)

Table 1. Sociodemographic data of patients included.

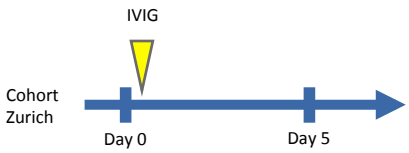

Figure 1. Serum samples were collected before (day 0) and 4-5 days after IVIG administration.

Results

- Substantial decrease of Interferon gamma levels in serum
- Major decrease of factors and mediators of a Th1- and cytotoxic immune response: The Th1 chemokine ligands CXCL9, CXCL10, CXCL11 and CX3CL1, T cell-activation and -differentiation proteins (PD-L1, IL7) and the Natural Killer Cell Receptor 2B4 (CD244)
- Decrease of Th2-inducing cytokine IL33
- Increase in eosinophil chemotactic protein CCL11, sulfate conjugation-catalyzing enzyme SULT1A1 and neurotropic factor artemin
- No significant differences in protein expression prior/post IVIG between SJS and TEN patients
- Improvement of skin detachment and no additional blistering in all patients

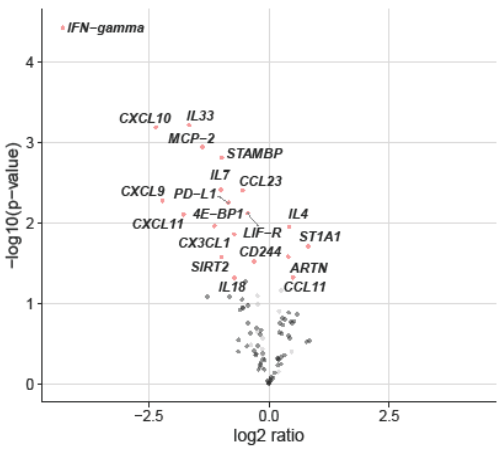

Figure 2. Significant downregulation (< 0) and upregulation (> 0) of protein expression in serum of patients with SJS/TEN after IVIG administration.

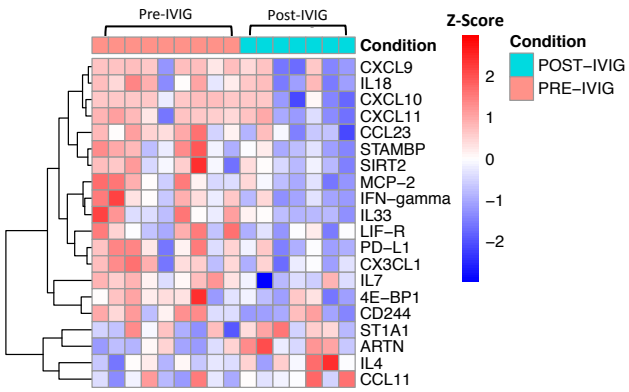

Figure 3. Significant upregulation (red) and downregulation (blue) of protein expression in serum of patients with SJS/TEN and before (orange samples) and after IVIG administration (green samples)

Conclusion

Our study shows that IVIG administration in SJS/TEN patients is associated with major changes in inflammatory mediators in an early phase (day 4-5). The presented data indicate an effect mostly on the Th1-/ cytotoxic immune response. Future studies comparing the molecular effects of IVIG to other adjuvant treatments will enhance our understanding of these therapies in SJS/TEN.

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