INCREASED PLASMA IP-10 LEVELS IN PAEDIATRIC FOCAL SEGMENTAL GLOMERULOSCLEROTIC (FSGS) NEPHROTIC PATIENTS TREATED WITH RITUXIMAB: A PLAUSIBLE MECHANISM IN RITUXIMAB-ASSOCIATED COLITIS

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BACKGROUND

Steroid-resistant nephrotic syndrome (SRsNS) and steroid-dependent nephrotic syndrome (SDNS) are important causes of chronic kidney disease in children worldwide. Of the various underlying histopathologies, focal segmental glomerulosclerosis (FSGS) is the most common histological pattern seen in SRsNS and SDNS.

In recent years, case series have emerged on successful use of rituximab in inducing remission in SDNS and SRsNS patients who have failed therapy with conventional immunosuppressants.

The use of rituximab, however, is not without its inherent set of adverse events, which include inflammatory conditions like rituximab-associated colitis.

Little is known, with regards to the underlying immunological factors predisposing patients who have received rituximab towards the development of these inflammatory conditions.

OBJECTIVE

This study aimed to delineate underlying immunological predisposing risk factors towards development of these inflammatory conditions via examining the cytokine profile in rituximab-treated paediatric nephrotic patients.

MATERIALS & METHODS

Our study population consisted of 13 paediatric FSGS patients who underwent rituximab therapy. Plasma cytokine profiling was performed on each of these patients utilizing multiplexed Luminex® Cytokine Human 27-Plex assay (inclusive of interleukin (IL)-1β, IL-1RA, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12 (p70), IL-13, IL-15, IL-17, eotaxin, basic-FGF, G-CSF, GM-CSF, IFN-γ, interferon-inducible protein 10 (IP-10), MCP-1, MIP-1α, MIP-1β, PDGF-BB, RANTES, TNF-α, VEGF) pre- and post-rituximab therapy.

Statistical analysis was performed using Wilcoxon signed-rank test with a p-value of less than 0.05 considered as statistically significant.

Prospective study involving 13 paediatric FSGS patients who underwent rituximab therapy at the Shaw-NKF-NUH Children's Kidney Centre, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore.

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Two-weekly infusions of 375 mg/m² rituximab x 1-4 doses

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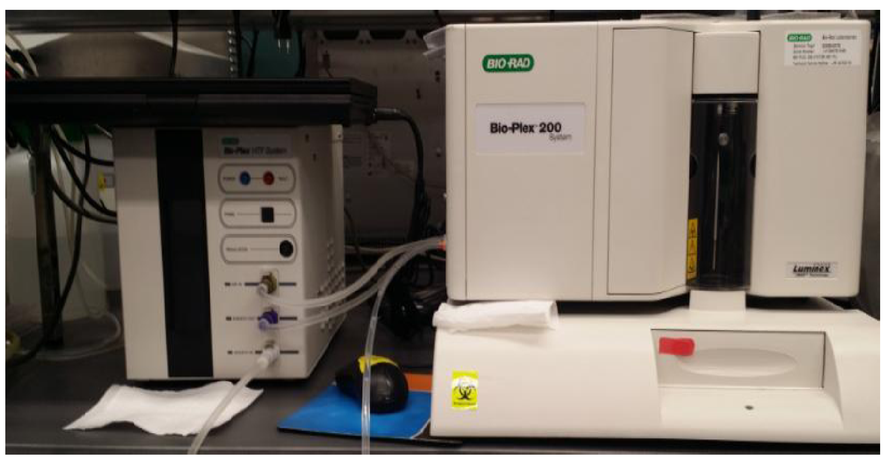
Bloods obtained for plasma cytokine profiling utilizing multiplexed Luminex® Cytokine Human 27-Plex assay pre- and post-rituximab.



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Plasma cytokine profile compared pre- and post-rituximab

RESULTS

1. Comparing the cytokine profile pre- and post-rituximab therapy, patients in the study demonstrated a general increase in plasma IP-10 levels (554.3 62.4 pg/ml vs 793.4 125.5 pg/ml, p=0.008) post-rituximab therapy.

2. Plasma RANTES levels were also noted to be generally increased post-rituximab therapy, albeit not reaching statistical significance (599.9 145.6 pg/ml vs 702.3 161.1 pg/ml, p=0.068).

3. There were no significant difference/observable trends in the other cytokines pre-/post-rituximab therapy.

DISCUSSIONS & CONCLUSIONS

1. Paediatric nephrotic patients seemed to exhibit a pro-inflammatory cytokine profile post-rituximab.

2. IP-10 has been implicated in the causation of inflammatory bowel disease. The increase in plasma IP-10 in patients post-rituximab may account for the predisposition towards development of colitis and possibly even inflammatory bowel disease in genetically predisposed individuals.

3. Further extensive studies, however, are required to validate the above findings.

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