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ORIGINAL ARTICLE

Decline in Number of Elevated Blood CD3⁺ CD56⁺ NKT Cells in Response to Intravenous Immunoglobulin Treatment Correlates with Successful Pregnancy

Marianne J. van den Heuvel¹, Crystal G. Peralta², Kota Hatta³, Victor K. Han¹, David A. Clark⁴

¹ Department of Pediatrics, University of Western Ontario, London, ON, Canada ;

² Departments of Anatomy and Cell Biology, University of Western Ontario, London, ON, Canada ;

³ Departments of Microbiology and Immunology, University of Western Ontario, London, ON, Canada ;

⁴ Departments of Medicine, Pathology, Obstetrics & Gynecology, McMaster University, Hamilton, ON, Canada

Correspondence to David A. Clark, McMaster University Rm 3V39, 1200 Main St. West, Hamilton, ON, Canada L8N 3Z5.

E-mail: clarkd@mcmaster.ca

KEYWORDS

Flow cytometry • IVIG • NKT cells • recurrent implantation failure • recurrent pregnancy loss

Problem



Patients with elevated blood natural killer (NK) cells may be offered intravenous immunoglobulin (IVIG) treatment, but there is controversy about the utility of blood NK cell testing. Human CD56⁺ NK cells include several subpopulations that include the putatively cytotoxic CD56⁺ CD16⁺ subset. In mouse models of pregnant failure, NKT cells appear to be important. However, a mouse model may only be pertinent to a subset of patients, as recurrent pregnancy failure is a heterogenous group.

Method of study

An ethics-approved observational study was done to observe the effect of treatment on total blood lymphoid cells, and subsets of CD56⁺

blood lymphocytes including CD56⁺ CD3⁺ NKT cells determined by flow cytometry, and to correlate with pregnancy outcome. Fifteen fertile women with a history of successful pregnancy and thirty-one women suffering from repeated implantation failure or recurrent spontaneous abortion provided serial blood samples during one menstrual cycle or prior to and during treatment. IVIG was administered to the latter group with or without heparin/aspirin.

Results

Eight of thirty infertile women presented with high numbers of CD56⁺ CD3⁺ NKT cells, which declined after treatment with IVIG. The elevated NKT cell group with or without concomitant autoimmunity achieved a significantly higher successful pregnancy rate over the course of the study, as compared to women with average numbers of NKT cells and no evidence of autoimmunity ($P = 0.018$). Elevated NKT levels alone was an independent predictor of success on treatment ($P = 0.003$).

Conclusion

Elevated NKT cells in recurrent pregnancy loss or implantation failure can be ameliorated with IVIG treatment, and result in successful pregnancy. Assay of NKT cell numbers may identify patients who are more likely to benefit from IVIG therapy and merits further examination in randomized phase II studies.

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