

IMMUNOLOGICAL METHODS TO INVESTIGATE ALLOIMMUNE HABITUAL ABORTION

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Recurrent spontaneous abortion (RSA) is the occurrence of pregnancy loss at 6-12th week of gestation despite normal implantation and normal embryonic development. In several cases where no anatomical, genetic, hematologic or endocrinologic cause or no infection can be found for RSA we speak about RSA of unknown cause. In these cases autoimmune/alloimmune conditions or immune regulation disorders can be the background. The identification of these immunological reasons and their pathologic role is in the focus of several investigations. Clinical observations underlie that immunotherapies used to treat RSA are effective only in those cases, where the immunological cause of RSA is accurately assessed. For this reason a national RSA committee was founded in 2013 at the 2nd Department of Obstetrics and Gynaecology. In cooperation with this committee we introduced a complex protocol for the investigation of immunological RSA that consists of the following measurements:

Flow cytometry crossmatch (between the RSA patient and her partner): Detection of IgG molecules in the patient serum that react with the T or B lymphocytes of the partner showing HLA sensitization or immunoregulation.

Mixed Leukocyte Culture (MLC) and blocking antibody analysis: Describes the amount of cellular reactivity between two donors. By this method we can determine the cellular reactivity of the patient against the partner and we can measure also whether the patients' serum contains any factor that modifies this reactivity.

Determination of T_h1-T_h2 ratio: The determination of T_h1 vs. T_h2 cell ratio is based on measuring their signature cytokines. T_h1 dominance points to elevated cellular immune response while T_h2 dominance represents humoral immune response and suppressive immunoregulation.

Analysis of natural killer (NK) cells: The natural killer cells are responsible for the elimination of foreign or altered self cells (e.g. virus infected or tumour cells) from the body. If elevated NK cell numbers are detected in the blood and/or their reactivity is elevated means a general upregulated immunoreactivity of the patient.

In the present work we summarize our experience with the 91 RSA patients investigated so far in our laboratory. We analyse the efficiency of the different measurements and emphasize the importance of the integrated evaluation of the results. We found that elevated NK cell numbers and Th1 dominance are common in patients. Most informative results were concluded from the MLC measurement, where 32% of the patients showed hyperreactivity against the partner and 77% of patients' serum contained factors that enhanced the reactivity. In contrast, only 21 patients had components in their serum that blocked the reaction against the partner cells. The flow cytometry crossmatch was only informative when evaluated together with the other results.