Decreased ratios of serum Th17/Treg-related cytokines in women with a defect in implantation after in vitro fertilization

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Objective: To compare the ratios of serum T-helper type 17 (Th17) cell/regulatory T (Treg) cell related cytokines between non-pregnant women with repeated implantation failures (RIFs) after in vitro fertilization and embryo transfer (IVF-ET) cycles due to a defect in implantation and those with normal fertility (controls).

Methods: Enzyme-linked immunosorbent assay (ELISA) was used to measure the concentrations of IL-17, IL-6, IL-23, TGF-β and IL-10 in the serum of 28 women with RIF and 23 normal fertile women.

Results: The ratios of Th17/Treg related cytokines, including the ratios of IL-17/IL-10, IL-23/IL-10, IL-23/TGF-β and IL-6/IL-10, were significantly lower in women with RIF due to a defect in implantation than those in controls.

Conclusion: Decreased ratios of serum Th17/Treg related cytokines may play a role in the pathogenesis of a defect in implantation failure.

Key words: T-helper type 17 cell, regulatory T cell (Treg), cytokine, implantation failure

Introduction

Successful human in vitro fertilization (IVF) and embryo transfer (ET) may still result in a low implantation rate. In addition, a certain number of idiopathic sterilities are due to repeated implantation failures. This failure may be due to a defect of implantation as no human chorionic gonadotrophin (hCG) production is ever detected, or an occult pregnancy loss. It may also occur after a transient detection of hCG production, following which an immediate drop of hormone levels can be detected, signifying to early pregnancy loss. During human pregnancy, a semi-allogeneic fetus implants in the uterus. At the feto-maternal interface, inflammatory processes can take place due to the invasion of micro-organisms [1], but also due to a sterile maternal immune reaction against allo-antigens on the fetus or trophoblast [2]. For some years a prevalent theory held that a predominant production of so-called T-helper type 2 (Th2) cytokines, such as interleukin (IL)-4 and IL-10, was a characteristic of normal pregnancy, whereas in miscarriage and recurrent miscarriage (RM) there was a predominant production of Th1 cytokines, such as interferon (IFN)-γ and IL-2 [3]. Th2 cytokines are known to direct the immune reaction towards a humoral response, which may not harm pregnancy, whereas Th1 cytokines direct the reaction towards a cytotoxic response. Elevation of different cytokine concentrations in the maternal serum proved that IFN-γ positive patients had twice the