



P79. INTERLEUKIN-6 CONTRIBUTES TO THE PATHOGENESIS OF ENDOMETRIOSIS BY SUPPRESSION OF NK CELL ACTIVITY VIA REGULATION OF SHP-2 EXPRESSION

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Context: Endometriosis is known to be related to a defect in natural killer (NK) cell cytolytic activity. Additionally, the levels of inflammatory cytokines are elevated in the peritoneal fluid (PF) of women with endometriosis. However, cytokines that contribute to the decreased NK cell cytolytic activity in the PF of endometriosis patients have not been determined.

Objective: To determine cytokines that reduce NK cell cytolytic activity in endometriosis patients, we investigated the effects of PF on the differentiation and functional activity of NK cells in patients with or without endometriosis.

Methods: Cytokines present in the PF were identified by enzyme-linked immunosorbent assay (ELISA). The cytolytic activity of NK cells in the PF was also analyzed using a Calcein-AM release assay.

Patients: Women of reproductive age (between 20 and 40 years of age) who underwent laparoscopic examination for endometriosis were included. This study included 33 women with endometriosis (endometriosis group) and 15 women without endometriosis (control group).

Intervention: PF contains various inflammatory cytokines in addition to interleukin-6 (IL-6), so it is possible that other cytokines affect activity of NK cells.

Main outcome Measure: NK cytolytic activity of PF cells against K562 cells was decreased in endometriosis patients compared to controls. IL-6 levels were increased in PF of endometriosis patients compared to control. IL-6 reduced the cytolytic activity of NK cells and regulated Src homology region 2-containing protein tyrosine phosphatase-2 (SHP-2) expression in NK cells.

Results: PF from patients with endometriosis suppressed the differentiation and cytotoxicity of NK cells compared with PF from controls. Increased levels of IL-6 were found in the PF of patients with endometriosis, and IL-6 levels were negatively correlated with the cytolytic activity of NK cells. Furthermore, IL-6 reduced the cytolytic activity of NK cells, concomitantly with the downregulation of granzyme B and perforin, by modulating SHP-2. Importantly, the addition of anti-IL-6 to the PF of endometriosis patients restored the activity of NK cells.

Conclusion: IL-6 plays a crucial role in the reduction of NK cell activity in the PF of patients with endometriosis by downregulating cytolytic granule components through the modulation of SHP-2 expression.

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