Abstract

Endometriosis is an estrogen-dependent, inflammatory gynecological disorder characterized by the growth of endometrial cells in lesions outside the uterus. Bone marrow-derived cells (BMDCs) engraft lesions and increase lesion size. Do endometriosis cells regulate differentiation of engrafted BMDCs in the pathogenesis and growth of endometriosis? Here, we report endometriosis derived stromal cells promote the differentiation of BMDCs to stromal, epithelial and leukocyte cell fates through paracrine signaling. In-vitro studies demonstrated that both mRNA and protein levels of vimentin, cytokeratin and PD-1 were significantly increased in BMDCs cocultured with stromal cells from endometriosis (ENDO) patients compared to stromal cells from normal endometrium (CNTL). Increased expression of PD-1 has been reported in malignancy where it promotes T cell quiescence and immune tolerance. Increased PD-1 was also confirmed in-vivo where we showed that PD-1 expression was induced in BMDCs engrafted into endometriotic lesions in a murine model of endometriosis. AMD3100, an antagonist for CXCR4 receptor inhibited PD-1 expression in BMDCs suggesting that PD-1 induction requires CXCL12. These results suggest that endometriosis stimulated BMDC differentiation through paracrine signaling and increased T cell PD-1 expression. Increased PD-1 expression may be one mechanism by which endometriosis avoids immune surveillance.