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ORIGINAL RESEARCH

Menstrual blood-derived stromal stem cells from women with and without endometriosis reveal different phenotypic and functional characteristics

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abstract: Retrograde flow of menstrual blood cells during menstruation is considered as the dominant theory for the development of endometriosis. Moreover, current evidence suggests that endometrial-derived stem cells are key players in the pathogenesis of endometriosis. In particular, endometrial stromal stem cells have been suggested to be involved in the pathogenesis of this disease. Here, we aimed to use menstrual blood, as a novel source of endometrial stem cells, to investigate whether stromal stem cells from endometriosis (E-MenSCs) and non-endometriosis (NE-MenSCs) women differed regarding their morphology, CD marker expression pattern, proliferation, invasion and adhesion capacities and their ability to express certain immunomodulatory molecules. E-MenSCs were morphologically different from NE-MenSCs and showed higher expression of CD9, CD10 and CD29. Furthermore, E-MenSCs had higher proliferation and invasion potentials compared with NE-MenSCs. The amount of indoleamine 2,3-dioxygenase-1 (IDO1) and cyclooxygenase-2 (COX-2) in E-MenSCs co-cultured with allogenic peripheral blood mononuclear cells (PBMCs) was shown to be higher both at the gene and protein levels, and higher IDO1 activity was detected in the endometriosis group. However, NE-MenSCs revealed increased concentrations of forkhead transcription factor-3 (FOXP3) when com- pared with E-MenSCs. Nonetheless, interferon (IFN)-g, Interleukin (IL)-10 and monocyte chemoattractant protein-1 (MCP-1) levels were higher in the supernatant of E-MenSCs-PBMC co-cultures. Here, we showed that there are inherent differences between E-MenSCs and NE-MenSCs. These findings propose the key role MenSCs could play in the pathogenesis of endometriosis and further support the retrograde and stem cell theories of endometriosis. Hence, considering its renewable and easily available nature, menstrual blood could be viewed as a reliable and inex- pensive material for studies addressing the cellular and molecular aspects of endometriosis.

Key words: endometriosis / IDO1 / menstrual blood / stromal stem cells / surface marker expression

Introduction

Endometriosis, a benign gynecological disease with a prevalence of 6–10%, is generally described as the existence of endometrial tissues outside the uterine cavity. Common symptoms of endometriosis include chronic pelvic pain, dyspareunia, dysmenorrhea and infertility (Giudice, 2010). The exact etiology of endometriosis is still uncertain. However, a dominant theory put forth by Sampson suggests that during the menstruation phase, endometrial tissue fragments find their way back through the fallopian tubes into the peritoneal cavity, where they implant and establish the lesions (Sampson, 1927). It should be noted, however, that retrograde flow of endometrial fragments occurs in the majority of women as a physiological phenomenon, whereas endometriosis occurs in 10% of these women (Halme et al., 1984); this