Cover Story: Tita Husnitawati Madjid, Bethy Hernowo, Ani Melani Maskoentri Hanggono Achmad Teuku Zulkifli Jacoeb, Achmad Biben. The Relationship of Caspase3, Caspase9, Matrixmetalloproteinase-9 Protein Expression and C-1562T MMP9 Gene Polymorphism in Menstrual Blood as the Etiopathogenesis Marker to Clinical Endometriosis Manifestation in the Establishment of its Diagnosis
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Regular Articles:


The Relationship of Caspase-3, Caspase-9, Matrixmetalloproteinase-9 Protein Expression and C–1562T MMP-9 Gene Polymorphism in Menstrual Blood as the Etiopathogenesis Marker to Clinical Endometriosis Manifestation in the Establishment of its Diagnosis

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ABSTRACT

Endometriosis is an enigmatic disease, with various pathogenesis, uncertain clinical manifestation, invasive and high-risk diagnostic methods, and also various mode of therapy. The endometrium of endometriosis patients shows abnormal protein presentation for protein involved in pathogenesis of endometriosis itself, such as caspases (which is important in apoptosis), and matrix metalloproteinases (which is important in tissue damage, penetration and proliferation of endometriotic lesion, and also in gene polymorphism). The menstrual reflux containing viable endometrial cells affect the development of endometriotic lesion. The aim of this study is to discover non-invasive diagnostic method of endometriosis using menstrual blood, and also to reveal clearer understanding in pathogenesis of endometriosis.

A case control study involving 149 women who visited the Reproductive Endocrinology and Fertility Clinic, FKUP/RSHS and RSHS network hospitals was performed, from February 2007 to February 2008. Screening for suspected endometriosis was performed by history taking, physical examination, and additional examination. Diagnostic laparoscopy or laparotomy and biopsy were performed afterward. The immunocytochemical examination on caspase-3, caspase-9, MMP-9, and mmp-9 gene polymorphism of menstrual blood were performed. Based on the microscopic confirmation of histopathological result, the relationship of endometriotic and non-endometriotic clinical manifestation with menstrual blood biomolecular marker was assessed.
Sixty-three (42.28%) endometriosis cases and 86 (57.78%) non-endometriosis cases were found. From those subjects, 34 endometriosis cases and 48 non-endometriosis cases with complete data were enrolled in this study. The endometrial cells were successfully isolated using preservative solution, and with immunocytochemical assay, all samples from 34 endometriosis subjects could be analyzed for the expression of caspase-3, caspase-9, and MMP-9. The decreased expression of caspase-3 and caspase-9, and increased expression of MMP-9 in endometriosis group were higher than those in non-endometriosis group (82.4% vs 77.1%, p=0.562; 97.1% vs 87.5%, pE,F=0.129; and 85.3% vs 85.4%, p=0.988 respectively). The frequency of allele C in -1562T region of mmp-9 gene was significantly increased in endometriosis group (p<0.039). There is a significant relationship between minimal response to pain treatment and menstrual abnormalities (menorrhagia, polymenorrhea, and menometrorrhagia) with MMP-9 biomolecular marker (p=0.006 and 0.050 respectively). At least 4 from 12 symptoms and 1 from 5 physical signs have strong relationship with the occurrence of endometriosis (OR 3.0 and 2.65 respectively).

The results of this study lead to a conclusion that minimal response to treatment of pain, and menstrual abnormalities (menorrhagia, polymenorrhea, and menometrorrhagia) have diagnostic values for establishing diagnosis of endometriosis. There are no significant relationship between frequency of allele C and allele T in -1562 region of mmp-9 gene with MMP-9 expression. Immunostaining analysis of the menstrual blood endometrial cells can be applied as a non-invasive method for establishing diagnosis of endometriosis in daily practice.

**Keywords:** MMP-9, caspase-9, caspase-3, C-1562T mmp-9 gene polymorphism, menstrual blood, non-invasive endometriosis diagnostic methods.