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Authors
Aghajanova, L
Giudice, LC

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P-1

BALANCE BETWEEN PROLIFERATION AND APOPTOSIS IN ENDOMETRIUM FROM WOMEN WITH FIBROIDS. L. Aghajanova L. C. Giudice. Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco, San Francisco, CA, USA.

BACKGROUND: Fibroids are one of the most common gynecological pathologies in reproductive age women. While fibroid and myometrial biology has been extensively studied, endometrial function in women with fibroids has received relatively little attention, although it is known to be compromised depending on fibroid location and size.

OBJECTIVES: To investigate proliferation and apoptosis in endometrium from women with intramural fibroids (F) compared to controls with no uterine pathology (C).

MATERIALS AND METHODS: Endometrial biopsies were obtained from women with and without intramural fibroids (n=6 and n=4, respectively). Isolated and cultured endometrial stromal fibroblasts (eSFs) were used in the proliferation WST-1 assay assessing metabolic activity of cells, BrDU incorporation assay and TUNEL apoptosis assay. eSF decidualization with 0.5mM of 8-bromo-cAMP for 96 hours was assessed by IGFBP1 and prolactin ELISA. QRT-PCR of pro- and anti-apoptosis and cell cycle genes was performed.

RESULTS: At baseline, there was no difference in eSF proliferation in the WST-1 assay in F versus C, with a significant decrease noted from day 3 in the F group ($p<0.03$). BrDU incorporation significantly decreased upon decidualization in both F and C groups ($p<0.02$), as expected, while no difference in BrDU incorporation was observed between nondecidualized or decidualized eSF from F versus C groups ($p>0.1$). BAX and BCL2 apoptosis-related and cyclin D1 and CDKN1A (p21) cell-cycle gene expression was not different under any condition ($p>0.1$). Yet, the number of apoptotic cells in TUNEL assay increased with decidualization in both groups ($p<0.006$), but was significantly higher in F versus C decidualized eSF ($p=0.0005$).

CONCLUSIONS: eSF from women with fibroid uterus exhibit decreased proliferation potential and increased apoptosis upon decidualization. How this phenomenon might contribute to impairment of endometrial function in infertility/subfertility patients is currently under investigation.

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ASSOCIATION BETWEEN MARKERS OF NON-ALCOHOLIC FATTY LIVER DISEASE AND GLUCOSE TOLERANCE IN POLYCYSTIC OVARIAN SYNDROME POPULATION. Asima K. Ahmad, MD, MPH, Chia-Ning Kao, BS, MS, Monika Sarkar, MD, Marcelle I. Cedars, MD, Heather Huddleston, MD University of California San Francisco.

BACKGROUND: Studies have indicated an increased prevalence of non-alcoholic fatty liver disease (NAFLD) in polycystic ovarian syndrome (PCOS).

OBJECTIVE: We assessed whether elevated liver enzymes were associated with metabolic factors and/or hyperandrogenism (HA) in PCOS.

MATERIAL AND METHODS: This was a cross-sectional study. Women seen in a PCOS clinic from 2006-2014 and diagnosed by 2003 Rotterdam criteria were considered for inclusion. Data collected included: liver enzymes, fasting and two-hour insulin, fasting and two-hour glucose, and homeostasis model assessment of insulin resistance (HOMA-IR). Liver enzymes were evaluated both as a categorical variable divided into normal/abnormal values for alanine aminotransferase (ALT, abnormal >19IU/L) and aspartate aminotransferase (AST, abnormal >40IU/L) and continuously. Analysis of variance (ANOVA) and regression were used for statistical analysis. Testing was performed on the 0.05 level of significance. Body mass index (BMI) and age were controlled for as confounding factors.

RESULTS: A total of 171 PCOS subjects were included in the study, with mean age 28.2years (SD±6.5). ALT values were available for 169 subjects (mean 26.0IU/L, SD±20.0; 83 normal, 86 abnormal) and AST for 166 subjects (mean 22.4IU/L, SD±11.4; 160 normal, 6 abnormal). Using the regression model, ALT was significantly associated with fasting glucose (coefficient 0.16, $p<0.02$). The regression model also showed that AST was significantly associated with fasting glucose (coefficient 0.29, $p<0.01$) and was approaching significance with two-hour glucose (coefficient 0.50, $p=0.07$). Using the ANOVA model, subjects with abnormal AST levels were found to have higher two-hour insulin (coefficient 201.16, $p=0.04$) and fasting glucose levels (coefficient 16.99, $p=0.01$). There were no significant associations found between liver enzymes and HA.

CONCLUSIONS: Our findings suggest a positive association between liver enzymes and fasting glucose levels in PCOS subjects when controlling for age and BMI. Women with PCOS should be routinely screened for NAFLD, especially if they are found to impaired fasting glucose or glucose intolerance.

SUPPORT: We do not have any financial disclosures.

TABLE 1. Liver enzymes and association with metabolic parameters (multiple regression)*

	ALT	ALT	AST	AST
Metabolic Parameter	Regression Coefficient	P-value	Regression Coefficient	P-value
Fasting Insulin	0.16	0.30	0.15	0.56
Two-Hour Insulin	0.57	0.46	1.97	0.17
Fasting Glucose	0.16	<0.02	0.29	<0.01
Two-Hour Glucose	0.15	0.34	0.50	0.07
HOMA IR	0.05	0.18	0.06	0.35

*controlling for BMI and age

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MYELOPEROXIDASE AND ACTIVATED MACROPHAGES HAVE DIFFERING EFFECTS ON OOCYTE SPINDLE MORPHOLOGY. Sana N. Khan, MD,[a] Faten Shaeib, MD,[a] Mahendra Kavdia, PhD,[b] Husam M. Abu-Soud, PhD.[a] [a]Wayne State University, Department of Obstetrics and Gynecology, Detroit, MI 48201; [b]Wayne State University, Department of Engineering, Detroit, MI 48201.

BACKGROUND: Macrophages, ubiquitous inflammatory cells, are major cellular producers of MPO and downstream inflammatory mediators such as cytokines and reactive oxygen species (ROS). Previous assessment systems of the effects of ROS on oocyte quality have focused on parameters such as spindle volume; however we have recently shown that focusing on potentially superior biomarkers such as pattern recognition of spindle morphologic changes may be higher yield.

OBJECTIVE: We attempt elucidate the mechanism behind deregulation of the spindle force balance by monitoring changes in the movement and disintegration of key scaffold proteins such as pericentrin after exposure to myeloperoxidase (MPO) compared to activated macrophages.

MATERIALS AND METHODS: Oocytes with and without cumulus cells were exposed to either 40 nM purified MPO (n=648/648) for 3, 6, 12, and 24 hrs or co-cultured with activated macrophage cells (n=200/200) for 1, 2, 3, and 4 hrs, and resultant changes in spindle morphology and pericentrin were assessed.

RESULTS: Exposure to purified MPO caused the spindles to thin and elongate along the pole-to-pole axis to over double the normal length. In contrast, exposure to activated macrophages caused the spindles to shorten along the pole to pole axis, widen and expand to spherical shape. Although, our results show the deterioration in oocyte quality is likely to be caused by MPO in both cases, opposite movement along the pole-to-pole axis was noted after exposure to purified MPO versus macrophage co-culture. Treatment with purified MPO shows a predominance of outward forces as seen in spindle fiber depolymerization, whereas activated macrophage treatment caused increased inward forces causing shortening and widening similar to a spindle fiber repolymerization effect. Interestingly, the lengthening effect shows persistence of pericentrin near the spindle poles. However, after co-culture with activated macrophages, which produce higher amounts of MPO and importantly, other inflammatory cytokines and ROS, pericentrin is lost.

CONCLUSIONS: These findings are consistent with previous results suggesting ROS implication is spindle fiber breakage and/or disintegration. Pattern recognition and further quantification of these spindle morphologies may provide information as to the condition of the genetic material within the oocyte and serve as a biomarker for functional competence.

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