00213 Tissue Iron Deposition Are Associated With CD68+/CD163+/FPN1+ Macrophages and an Inflammatory Macrophage-like Cytokine Signature

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Aims: Endometriosis is characterized by the persistent presence and growth of endometrial-like implants at extra-uterine ectopic sites. Upon establishment of endometriosis, tissue-resident macrophages may be recruited in response to ectopic iron in the peritoneal cavity. However, the distribution of tissue iron deposition, their association with tissue-resident macrophages, and cytokine profile in endometriosis were poorly described.

Methodology: Perls' Prussian Blue, and immunohistochemical staining for CD68, CD163 and iron exporter ferroportin (FPN1) were performed to analyze iron deposition. Iron-metabolizing macrophages were graded in 24 eutopic and 51 ectopic endometrial tissues. 48 peritoneal fluids cytokines were quantitatively characterized using multiplexed suspension bead immunoassays.

Result: Significantly higher iron deposits were found in endometriotic cysts compared to other ectopic sites (61.5% versus 11.4%; $p<0.001$). A significant correlation of ectopic tissue iron deposition, and CD68+/CD163+/FPN1+ macrophages in endometriosis was observed ($r=0.56$ to 0.83, $p=0.021$ to <0.001). Tissue iron overload was associated with elevated IL-1β, IL-1Rα, IL-6, IL-12p40, IFNγ, and TNFα levels, which resembles an inflammatory macrophage-like signature.

Conclusion: Association of iron, macrophages and an inflammatory cytokine milieu could play a role in the pathophysiology and development of endometriosis. Leveraging on our findings in this study, the modulation of the signalling cascade between iron, CD68+/CD163+/FPN1+ macrophages and the inflammatory cytokine milieu may represent a viable therapeutic strategy to reinitiate repair and prevent the successful establishment of endometriotic lesions.