Preoperative Diagnosis of Endometriosis

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To the Editor: We have enjoyed reading the work of Chen *et al*.[1] which investigated the diagnostic value of circulating (peripheral blood) endometrial cells (CECs) for endometriosis. By modifying their detection technique, Chen *et al*.[1] have demonstrated a high detection rate of CECs in the endometriosis group compared to the control group ($P < 0.001$) with high sensitivity (89.5%) and specificity (87.5%) that was independent of menstrual cycle phases. The authors concluded that CEC may be a promising biomarker for endometriosis for the development of a noninvasive diagnostic assay, but these findings require validation in a larger, multicenter study population.[1]

To date, there is no reliable biochemical marker to screen, diagnose, or stage endometriosis and diagnosis is based on more expensive and/or invasive radiological or laparoscopic procedures. Indeed, the lack of noninvasive diagnostic test significantly contributes to the long delay between the onset of symptoms and the definitive diagnosis of endometriosis.[2] This diagnostic delay often has an adverse impact on women's physical and psychological health, and women often express a sense of relief at diagnosis.[2] Despite many efforts, no single biomarker or a panel of biomarkers have been validated as diagnostic test for endometriosis.[3]

For the above reasons, we see great value in the findings of Chen *et al*.[1] as they have demonstrated a highly sensitive and specific noninvasive test for the diagnosis of endometriosis (subject to prospective validation), which was independent of menstrual cycle phases. The latter is important, as proteins previously identified as potential biomarkers for endometriosis such as the chemokines CXCL8, CCL2, and CCL5 vary during the menstrual cycle which practically limits their diagnostic value.[4] It would have been interesting and helpful if the authors combined CEC and CA125 as a panel of biomarkers to assess whether the combination had increased diagnostic value compared to CEC alone.

Going forward therefore, we believe that CEC, if validated, could be paneled with other promising biomarkers previously identified like CA125 for mathematical modeling with stronger diagnostic or screening potential. Moreover, this biochemical panel could be combined with other parameters (including clinical and/or radiological) for further mathematical modeling with greater diagnostic or screening significance. Such modeling has been applied in the UK in ovarian cancer patients; women with a high risk of malignancy index, which takes into account the levels of CA125, menopausal status, and suspicious radiological features, are referred to tertiary centers for further workup and management.[5]

We agree that such statements are speculative at this stage. They are, however, a valid hypothesis on which to base further research in the field. We still have a long way to go in optimizing biochemical markers for diagnosing or screening for endometriosis. However, the findings of Chen *et al*.[1] and the points raised in this letter should serve as a catalyst in stimulating further validation studies and mathematical modeling for screening, diagnosis, or staging of endometriosis.

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Conflicts of interest

There are no conflicts of interest.

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