Recurrent Pregnancy Loss: A New Algorithm for Evaluation Loss

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The American Society of Reproductive Medicine (ASRM) defines recurrent Pregnancy Loss (RPL) as a disease, distinct from infertility, defined by two or more failed clinical pregnancies. A pregnancy is defined as a clinical pregnancy documented by ultrasonography or histopathological examination. The recommended evaluation from ASRM includes: karyotypes on both partners to look for chromosomal translocations; lupus anticoagulant, anticardiolipin antibodies, and anti-beta-2 glycoprotein-1 antibodies to look for antiphospholipid syndrome; sonohysterography or hysterosalpinography to look for congenital and acquired uterine anomalies; and blood levels of prolactin, TSH, and hemoglobinA1c to look for hormonal imbalances. When all these evaluations are completed, only 45% of all pregnancy losses will have a possible explanation. Results from 55,000 products of conception revealed 55% with genetic abnormalities.

Based on these observations, a new algorithm for the evaluation of RPL begins with a 24-chromosomal microarray analysis (CMA) on the miscarriage tissue after the second documented pregnancy loss. When the result is aneuploid, 25% will have an abnormal finding on the modified ASRM workup (deleting parental karyotypes). When the result reveals an unbalanced translocation, parental karyotypes should be performed in the standard ASRM workup along with genetic counseling and consideration for PGT-A. In the event that the CMA reveals a euploid miscarriage, then the modified ASRM evaluation (without parental karyotypes) will reveal abnormalities in about 80%of couples and would be recommended. Using this strategy, over 90% of all miscarriages in couples with RPL will have a probable or definite cause identified. This new strategy is projected to result in a cost savings to the healthcare system.

Further, with this new strategy, less than 10% of recurrent miscarriages remain truly unexplained. Long term follow-up studies indicate that the prognosis for these patients is very good and can be predicted based on the age of the female partner and number of prior losses. The potential roles of mycoplasma/ureaplasma infections, thrombophilias, progesterone supplementation, vitamin D supplementation, and endometrial receptivity will be considered.