Failed Pregnancy After IVF: Recurrent Implantation Failure and Recurrent Pregnancy

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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, more than 50% of all pregnancy losses will remain unexplained. Many published studies report that 50% to 70% of examined products of conception will display genetic abnormalities.

Based on these observations, a new algorithm for the evaluation of RPL is proposed which begins with a 24-chromosomal microarray analysis (CMA) on the miscarriage tissue after the second documented pregnancy loss. When the result is aneuploid, no further evaluation is advised. When the result reveals an unbalanced translocation, parental karyotypes should be performed along with genetic counseling and consideration of preimplantation genetic diagnosis in subsequent pregnancies. In the event that the CMA reveals a euploid miscarriage, then the modified ASRM evaluation 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 50% savings to the healthcare system.

Further, with this new strategy, less than 10% of recurrent miscarriages remain 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 anti-thyroid antibodies, progesterone supplementation, unfractionated and low-molecular weight heparin, aspirin, natural killer cells, intravenous immunoglobulin, and preimplantation genetic screening (or preimplantation genetic testing-aneuploidy) will be placed into proper perspectives.