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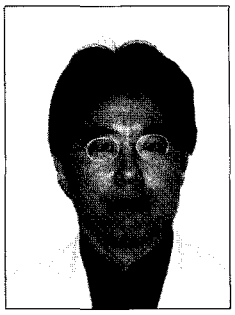

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Similarity between Recurrent IVF-ET Failure and Recurrent Pregnancy Loss

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Clinically, pregnancy test (i.e., hCG test) becomes positive 2 weeks after ovulation (i.e., 4w0d gestation) without ultrasound confirmation, and gestational sac can be seen under ultrasound 3 weeks after ovulation (i.e., 5w0d gestation). Historical miscarriage was natural termination of pregnancy after 5wk of gestation, and natural termination between 4 wk and 5wk is called as 'chemical pregnancy' because only hCG appeared followed by disappeared. Since hCG was tested at 4wk of gestation in usual IVF program, such chemical pregnancies in ART were counted more than those without ART. Similarly, it is not difficult to speculate natural termination between 3wk and 4wk may occur which is called as 'preclinical loss' (Fig. 1). If any pregnancy test can be used at 3wk of gestation, it would be possible to detect such 'preclinical loss'. Only one institute (Wilcox AJ1,2) has reported that they can detect 0.13mIU/ml hCG at the time of implantation (3w0d gestation), and that preclinical loss (21.7%, 43/198) was twice as much as chemical pregnancy (11.6%, 18/155). Therefore, preclinical loss is very common, but counted as infertility in all institutes but Wilcox's. It would be similar to chemical pregnancy or miscarriage (Fig. 1).

Although IVF-ET failure included embryonic damage (growth impairment), implantation failure and preclinical loss, usually we cannot distinguish these three (Fig. 2). Therefore, it is not surprising us that the similar findings observed both in patients with recurrent miscarriage and recurrent IVF-ET failure. Both groups of patients showed elevated autoantibodies such as antiphospholipid

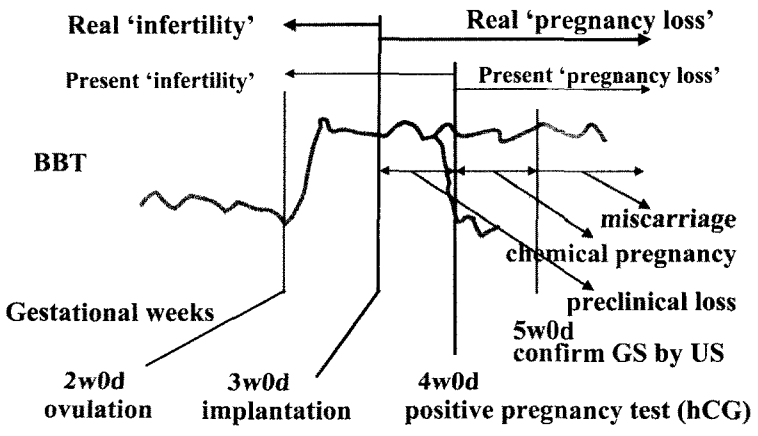

Fig. 1. What is very early pregnancy loss? Historical miscarriage was natural termination of pregnancy after 5wk of gestation, and natural termination between 4 wk and 5wk is called as 'chemical pregnancy'. Similarly, natural termination between 3wk and 4wk may occur which is called as 'preclinical loss'.

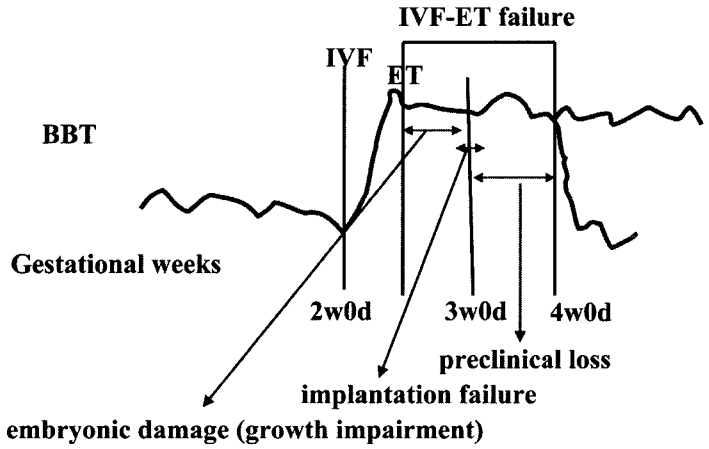

Fig. 2. When IVF-ET is failed? Although IVF-ET failure included embryonic damage (growth impairment), implantation failure and preclinical loss, usually we cannot distinguish these three.

antibodies[3,4] and/or anti-annexin A5 antibodies[5,6], and showed elevated NK activity[7,8]. Sometimes patient with recurrent miscarriage became infertility, or recurrent IVF-ET failure patient experienced chemical pregnancy (Table 1). Therefore, miscarriage and infertility (especially IVF-ET failure) may be the same side of the one coin.

Earlier termination like preclinical loss would be more severe than chemical pregnancy or miscarriage, because they maintain pregnancy for only short period. Even if same type of antibodies detected in both patients, clinical trial failed in infertility patients but succeeded in miscarriage patients. To improve pregnancy rate on IVF-ET, we should focus on the similarity between infertility and miscarriage.

Table 1. Similarity between recurrent pregnancy loss and recurrent IVF-ET failure

1. elevated autoantibodies
antiphospholipid antibodies
anti-annexin A5 antibodies
2. elevated NK activity
3. Sometimes patient with recurrent pregnancy loss became infertility, or recurrent IVF-ET failure patient experienced pregnancy loss.

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