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Rapid Communication

ALTERNATIVE TREATMENT FOR UNEXPLAINED RECURRENT SPONTANEOUS ABORTION

Tetsuo MARUYAMA, Tsunehisa MAKINO, Toshitaka SUGI, Ken-ichi IWASAKI, Masakatsu UMEUCHI, Suguru SAITO and Shiro NOZAWA

Department of Obstetrics and Gynecology, School of Medicine, Keio University, Tokyo

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Introduction

It is generally accepted that an immunotherapy using partner or third-party donor mononuclear cells is efficacious treatment for unexplained recurrent early wastages in pregnancy. Although the success rate of the immunization reported is approximately 80%[4], the mechanism of action of immunotherapy has not been fully elucidated. The prevailing hypothesis assumes that circulating blocking antibodies or factors produced by the mother to protect the fetus are deficient in patients with a history of unexplained recurrent spontaneous abortions (RSA), but can be induced by alloimmunization[4]. In this point of view, instead of "active" immunization with partner's mononuclear cells, "passive" immunization using polyvalent intravenous immunoglobulin (IVIG) treatment could be an alternative therapy for patients with RSA because this products processed from a large pool of donors should contain preformed antibodies of similar specificity like blocking antibodies[1)~3)]. This paper reports our results on three RSA patients treated with IVIG.

Subjects and Methods

Patients

More than 1,350 couples with RSA in our clinic has been investigated for their possible causes of the wastages and 10 of them who fulfilled the following criteria participated in this treatment.

1. Primary unexplained habitual aborter having no possible causes of anatomical, genetic, hormonal, infectious or autoimmune disorders.
2. Patient's partner with blood-transmittable infectious disease such as adult T-cell leukemia (ATL), acquired immune deficiency syndrome (AIDS), non-A,non-B hepatitis and others.
3. No detectable antibodies against paternal lymphocytes.

They gave their informed consent to receive IVIG treatment before subsequent conception and three of them became pregnant. One couple of the three strongly requested IVIG treatment even after they were given full information of standard immunotherapy although they did not fulfill the above all criteria.

Methods

According to the regimen of Mueller-Eckhardt et al.[2)3)], three patients were given 25g IVIG (Sandoglobulin, Sankyo Co. Ltd., Tokyo, Japan) equivalent to 0.5~0.6g/kg body weight, were slowly infused intravenously, as soon as pregnancy was confirmed, usually at 5 weeks of gestation. Reflecting the half-life of IVIG, subsequent administrations of 20g of IVIG (0.3~0.4g/kg) were given every 3 weeks and treatment was terminated by 12 gestational week.

Results

All the three pregnancies continued successfully beyond their critical period of 12 weeks of gestation. The clinical profile of the 3 patients treated with IVIG are summarized in Table 1. No side effect was noted with 9 administrations.

Discussion

Even though lymphocyte immunotherapy has been widely used for patients with RSA, in some cases this treatment offers several disadvantages[2)]: (a) viral infections transmitted from partner (b) HLA immunization which may work favorably in maintenance of pregnancy, while which may be potentially hazardous to the mother in case of

Table 1. Clinical profile of the 3 patients treated with IVIG

Patient No.	Age	Children/abortions (week of gestation)	Indication for IVIG	IVIG infusion week of gestation	Outcome of pregnancy
1	28	0/3 (21, 11, 10)	partner : non-A, non-B hepatitis	5, 8, 11	pregnant, 29wk.
2	30	0/3 (8, 8, 8)	voluntary*	5, 8, 11	pregnant, 27wk.
3	28	0/3 (8, 6, 5)	partner : HTLV-I** carrier	4, 7, 10	pregnant, 14wk.

*See Subjects and Methods

**human T-lymphotropic virus I

future blood transfusions or transplantation (c) ineffectiveness when no generation of blocking antibodies after immunotherapy or subsequent unexplained pregnancy failure with immunization probably due to maternal "nonresponder" or highly histocompatibility in the couple.

In case of (a), it is difficult to select and keep appropriate third-party donor. Furthermore, the success rate of immunotherapy using third-party mononuclear cells were lower than that of immunization with partner's lymphocytes. Mueller-Eckhardt et al. reported that IVIG therapy could be effective in prevention of RSA and the success rate for maintenance of pregnancy was approximately 75%[2)3)]. To resolve these problems, polyvalent IVIG treatment can be available as "passive" immunization for patients with RSA who are confronted with the above cases.

Although a randomized placebo controlled trial remains to be required, the results of this pilot study suggest that IVIG could be an efficacious alternative treatment for patients with unexplained RSA.

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