Selection of patients with habitual abortion for paternal leucocyte immunization


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Summary. After potentiation of the immune response in habitual aborters 75–85% of subsequent pregnancies are claimed to result in healthy term infants. However, all publications to date have either been based on the authors concept of the immune processes involved or an attempt to demonstrate the efficacy of treatment either empirically or by matched trials. As immunization is coming into wider clinical use, it is necessary to determine which patients will benefit from this form of treatment. This paper presents our experience with paternal leucocyte immunization over the period 1985–1988. 207 patients were classified on a clinical basis and by immunological testing. 143 patients have been immunised, 129 pregnancies have occurred in 108 patients. The vast majority of our patients have recurrent missed abortions. Only six women habitually aborted live fetuses. Two had subsequent live births. Secondary aborters seem to do well in subsequent pregnancies, whether immunized or not. The patient most likely to benefit from immunization is the Primary missed aborter who does not possess anti-paternal antibody (APCA), but is induced to produce APCA by immunization. Using these criteria, 75% success rates are observed in the subsequent pregnancy. This success rate is irrespective of HLA antigen sharing or in-vitro mixed lymphocyte reactivity.

Key words: Habitual abortion – Immunopotentiation – Missed abortion

Introduction

Immunopotentiation was first reported as a means of preventing abortion by Beer et al. [3] and Taylor and Faulk [19] in 1981. These early reports were based on the assumption that the habitually aborting woman is either hyporesponsive
or has an aberrant immune response to the paternal antigens presented to her by the pregnancy.

Potentiation of the immune response was attempted in order to improve the outcome of the subsequent pregnancy [3, 19]. Since then numerous reports have appeared in the literature claiming immunization to be highly effective with 75–80% of subsequent pregnancies producing healthy term infants [10, 14, 18, 20]. The double blind trial of Mowbray et al. [13] showed conclusively that 77% of immunised patients had a subsequently successful pregnancy compared to only 32% of control patients. These results have encouraged the wider use of immunopotentiation for habitual aborters, and created an intense demand for treatment. However there is no general agreement as to which patients require immunization. Each center has different indications and uses different regimens of immunization. McIntyre et al. [9] only immunize 1° aborters sharing HLA antigens. (A primary aborter has no children, each pregnancy terminates in abortion.) Unander et al. [20] however immunize 1° and 2° aborters. (2° aborters have one or more children prior to the abortions.) Mowbray et al. [13] immunize all habitual aborters with no more than one child if they do not possess anti-paternal complement dependent cytotoxic antibody (APCA). Beer et al. [3] originally immunized 1° and 2° aborters if the in vitro mixed lymphocyte reactivity of maternal cells was hyporesponsive when stimulated by paternal lymphocytes. As the immune response to pregnancy remains an enigma, it is difficult to accept that the results of immunologic testing should form the sole criteria for immunization. However, if 75% of subsequent pregnancies produce healthy infants, the role of immunization cannot be ignored. Therefore, all habitual aborters presenting to our service were offered immunopotentiation with paternal leucocytes or assigned to a control group if there was no other detectable cause for the abortions. The results of subsequent pregnancies were then analysed according to clinical criteria and immunological criteria such as HLA antigen status between spouses, mixed lymphocyte reactivity and the presence of APCA antibody.

Materials and methods

207 patients with habitual abortions presented to this service between 1985–1988. The clinical features of each patient and her abortions were assessed, paying particular attention to whether the previous abortions were missed abortions or abortions of live fetuses, (when this information was available). Only women with three or more consecutive abortions were included in this trial. Patients were then classified as Primary or Secondary Aborters using the definitions given previously. Some patients could not be classified due to having artificial abortions, prior to or between the spontaneous abortions. These patients were not included in the trial.

Patients were only included in the trial after other presumptive etiological factors were found to be normal, viz:

1. Karyotype of both partners, using Q and R banding techniques.
2. Glucose tolerance test.
3. Toxoplasmosis serology.
4. Hysterosalpingogram thereby excluding anatomical abnormalities, intrauterine adhesions and cervical incompetence.
5. Thyroid function.