STUDIES OF THE ANTIIDIOTYPIC ANTIBODY DETECTED IN THE SERA OF UNEXPLAINED HABITUAL ABORTERS AFTER IMMUNOTHERAPY WITH HUSBAND'S LYMPHOCYTES

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INTRODUCTION
Recently, immunotherapy for unexplained habitual aborters with husband's lymphocytes has been undergone in some institutions and the effectiveness of this treatment has been reported by several investigators. (1)(2)(3)

We have described that blocking antibodies (BAs) detected by mixed lymphocyte reaction (MLR) blocking assay are observed in the sera of all the patients after immunotherapy, and may play an important role in maintenance of pregnancy. (4)

In this paper, we have shown that antiidiotypic antibodies directed to the autologous T cell receptors are detected in the sera of the patients after immunotherapy and during the following pregnancy.

MATERIALS AND METHODS
We have undergone immunotherapy with husband's lymphocytes for the patients who had experienced three or more consecutive early abortions and had no other pregnant history, according to the protocol we have previously reported. (4)

Six patients who had been undergone immunotherapy and had come to be pregnant were chosen to be examined. The serum obtained before first vaccination, about four to eight weeks after second vaccination and during pregnancy of each patient's were tested in MLR inhibition assay to detect antiidiotypic antibodies.

Patients' lymphocytes as responder cells were exposed to the
tested serum with addition of complement, prior to MLR. Pretreated responder cells were mixed with husband's lymphocytes treated by MMC as stimulator cells in AB serum. The response was measured by incorporation of 3H-thymidine into proliferation cells on day 6 of culture. Inhibition was determined relative to the control serum obtained before immunotherapy for calculation of a percentage inhibition. Tested sera were also examined in MLR blocking assay (in which responder cells were not pretreated) to calculate the MLR-Blocking Effect. Details of that were described before.\(^{(4)}\)

RESULTS

Results of MLR inhibition tests and the outcome of pregnancies are listed in table 1. Significant inhibition of MLR assay in which responder cells were pretreated with the serum obtained after immunization compared with control serum obtained before immunization was observed in three cases out of six.\(^{(case \ 1,3,4)}\)(figure 1) These three cases successfully continued their pregnancies beyond their critical period.

In the other three cases in which significant inhibition was not detected, two cases continued their pregnancies,\(^{(case \ 2,5)}\) and one resulted in repeated abortion.\(^{(case \ 6)}\)

TABLE 1

MLR inhibition tests and pregnancy outcome (6 cases)

<table>
<thead>
<tr>
<th>case</th>
<th>history of pregnancy</th>
<th>CPM (responder pretreated)</th>
<th>% inhibition</th>
<th>MLRBE %</th>
<th>outcome of pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>pre vac.</td>
<td>post vac.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0-0-5-0</td>
<td>177050 ±14320</td>
<td>118236 ±13855</td>
<td>33.2</td>
<td>79.4</td>
</tr>
<tr>
<td>2</td>
<td>0-0-4-0</td>
<td>66645 ±9996</td>
<td>64167 ±9572</td>
<td>3.7</td>
<td>52.3</td>
</tr>
<tr>
<td>3</td>
<td>0-0-4-0</td>
<td>96851 ±4734</td>
<td>70655 ±3600</td>
<td>27.1</td>
<td>66.0</td>
</tr>
<tr>
<td>4</td>
<td>0-0-3-0</td>
<td>38043 ±9994</td>
<td>26298 ±4504</td>
<td>30.9</td>
<td>80.6</td>
</tr>
<tr>
<td>5</td>
<td>0-0-3-0</td>
<td>117763 ±5255</td>
<td>109016 ±10730</td>
<td>7.4</td>
<td>94.4</td>
</tr>
<tr>
<td>6</td>
<td>0-0-3-0</td>
<td>143349 ±2787</td>
<td>145203 ±9577</td>
<td>-1.3</td>
<td>26.5</td>
</tr>
</tbody>
</table>
DISCUSSION

In the field of transplantation immunology, pretransplant donor specific transfusion has been widely used for sustaining human renal allograft survival and is shown to generate both blocking antibodies directed against T cell receptors, i.e., antiidiotypic antibodies and suppressor cells. \(^{(5)}\)(\(^{6}\))

In this paper, we have shown that BAs would be produced by immunotherapy and be partly directed against T cell receptors on patients’ lymphocytes. It suggests that antiidiotypic antibodies would be a component part of BAs and that they may play an important role of maintaining pregnancy.

FIGURE 1

The patient (case 3) had experienced four consecutive early abortions and no other pregnant history. She had undergone immunotherapy with her husband’s lymphocytes, and the following pregnancy was successfully terminated at the 40 weeks of gestation. MLR inhibition activity was observed in the sera obtained after immunotherapy and during successful pregnancy.
REFERENCES