PARTIAL OBSTRUCTION, NOT ANTISPERM ANTIBODIES, CAUSING INFERTILITY AFTER VASOVASOSTOMY

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Abstract

Purpose: We determined whether men who may have partial obstruction and antisperm antibodies after vasovasostomy can be distinguished from other infertile men with antisperm antibodies only, and whether repeat microsurgical reversal is beneficial in such patients.

Materials and Methods: A total of 412 patients underwent indirect immunobead testing for antisperm antibodies at our laboratory from December 1991 through July 1996. Of 95 patients with an assay greater than 20% binding 49 had normal partners and were grouped by history of vasovasostomy (20), varicocele (9), cryptorchidism (8) and epididymo-orchitis (12). Semen analysis characteristics and antisperm antibody binding variables were compared across histories. Pregnancy rates were compared between patients treated surgically for partial obstruction and those treated for antisperm antibodies. Mean followup was 33.8 months.

Results: Compared to the other 3 groups, men with a history of vasectomy and reversal had significantly lower sperm concentration (p = 0.002), poorer motility (p <0.001), lower overall binding on the indirect immunobead assay (p <0.001) and lower IgA binding (p = 0.008). The clinical diagnosis of partial obstruction was based on a sense of epididymal fullness by palpation, as well as the aforementioned semen parameters. Of the 20 patients with a history of vasectomy and reversal 14 were diagnosed with partial obstruction and underwent repeat microsurgical reversal and 6 with a history of vasovasostomy but no evidence of obstruction received no further therapy and never established pregnancies. The remaining 29 patients underwent sperm washing and assisted reproduction. Of 14 patients 7 (50%) established pregnancies after repeat reversal compared to only 5 of 29 patients (17.2%) treated with assisted reproduction (P = 0.025).

Conclusions: Antisperm antibodies are not a significant factor in persistently infertile post-reversal cases with the aforementioned criteria. Repeat reversal appears to be the most successful treatment option in this setting.

Key Words: antibodies, spermatozoa, vasovasostomy, infertility, microsurgery

Approximately 38% of men who undergo vasovasostomy will fail to achieve pregnancy despite adequate postoperative sperm concentration. Sharlip proposed the 3 explanations for failure of partner infertility, epididymal dysfunction and antisperm antibodies. Partial obstruction due to an imprecise microsurgical anastomosis or subsequent scarring must also be considered in this differential diagnosis. The situation becomes particularly complicated when any of these factors coexist. When the female partner is normal the role of antisperm antibodies has historically been emphasized. A number of investigators have demonstrated a clear association between the presence of antisperm antibodies in the seminal plasma following vasovasostomy and a reduced pregnancy rate. Conversely, other investigators have questioned the importance of immunological factors in the persistently infertile patient after reversal, arguing that although antisperm antibodies may be present, the continued subfertility in these men may be the result of partial obstruction.

We examined a population of persistently infertile men with an adequate postoperative sperm concentration and normal female partners who may have partial obstruction and antisperm antibodies after vasectomy reversal. The aim of our study is to determine whether these men can be distinguished from other infertile men with antisperm antibodies only and whether repeat microsurgical reversal is beneficial in this setting.
MATERIALS AND METHODS

The charts of all 412 patients who underwent the indirect immunobead assay for antisperm antibodies at our institution between December 1991 and July 1996 were retrospectively reviewed. Of these patients 95 had greater than 20% binding on the assay and, therefore, were classified as testing positive for antisperm antibodies. [7] Of these 95 patients 46 were excluded from study because the partners had infertility risk factors based on examination by a gynecologist. Thus, we identified a population of 49 pure male factor infertility patients with antisperm antibodies. We then classified the 49 patients on the basis of history and risk factor for antisperm antibodies. In addition, patient age at initial presentation, date of presentation and length of followup were recorded.

Semen analysis data were then reviewed for all 49 patients each of whom had at least 2 analyses available for comparison. Semen volume, sperm concentration, motility and morphology were recorded for each semen analysis and then averaged to produce a mean semen analysis for each patient. Sperm concentration and motility were determined manually using counting chambers and morphology assessment was based on World Health Organization criteria. [8]

The results of the indirect immunobead assay were tabulated for each patient. Percent overall binding and percent binding of specific immunoglobulin subtypes (IgA and IgG) were recorded. Data were obtained concerning the therapy chosen and whether pregnancy resulted after therapy. If the medical record did not contain these data, we contacted the patient by telephone to determine the therapy given and outcome.

Using standard analysis of variance testing the sperm concentration, motility, morphology, percent overall binding on the indirect immunobead assay and percent binding of the specific immunoglobulin subtypes (IgA and IgG) were compared across etiologies. If the underlying assumptions of normality and equal variability were in question for a particular performing the analysis of variance. For any variable found to have different means across etiologies with statistical significance, Scheffe’s method was used to perform multiple pairwise comparisons. Using a chi-square test the pregnancy rate achieved by patients treated surgically for partial obstruction was compared to the pregnancy rates achieved by patients treated for antisperm antibodies. For all analyses p <0.05 was considered statistically significant. All data are presented as mean plus or minus standard deviation. The analyses were performed using the statistical software.

RESULTS

Mean patient age was 36 years (range 27 to 50), mean followup was 34 months (range 1 to 55) and mean number of semen analyses reviewed per patient was 2.8 +/- 1.3. The causes of antisperm antibodies, all previously reported to be associated with or a risk factor antisperm antibodies, [9-13] were vasectomy and reversal in 20 cases, varicocele in 9, cryptorchidism in 8, and epididymo-orchitis in 12. For the 20 patients who had undergone vasectomy reversal semen analyses were performed an average of 17 months (range 9 to 68) after the initial reversal surgery. Patients with a history of vasovasostomy had an average obstructive interval of 12.7 years (range 7 to 19).

(Table 1) compares semen analysis and antisperm antibody binding variables by risk factor for antisperm antibodies. Compared to the other 3 groups patients with a history of vasectomy and reversal had a significantly lower sperm concentration (p = 0.002), significantly lower motility (p <0.001), significantly lower percentage of overall binding on the indirect immunobead assay (p <0.001) and significantly lower percentage of IgA binding (p = 0.008) after the initial microsurgical reversal. In addition, patients with a history of vasovasostomy had a lower percentage of IgG binding after the initial reversal but this difference did not achieve statistical significance (p = 0.18).

Therapy and outcome results are presented in Table 2. Of the 20 patients with a history of vasovasostomy 14 were believed to have partial obstruction as well as antisperm antibodies. This diagnosis was based on mild to moderate epididymal fullness on physical examination of each patient with partial obstruction by 1 of the authors (A. J. T.) and results of semen analysis (Table 3). Therefore, these 14 patients underwent scrotal exploration and repeat microsurgical reversal procedure rather than therapy for antisperm antibodies. Six men underwent repeat bilateral vasovasostomies, and 8 underwent repeat unilateral vasovasostomy and contralateral vasoepididymostomy. Of these 14 patients 7 were ultimately able to establish a pregnancy (50%). Average followup was 2.6 years (range 2 months to 4 years).

Table 1. Comparison of semen analysis and antisperm antibody binding according to cause of infertility
The remaining 6 patients with a history of vasectomy reversal but without epididymal fullness received no further therapy. None achieved a pregnancy during a followup of 2.8 years (range 14 months to 4.8 years). Semen parameters in these patients varied somewhat from those in the 14 men with partial obstruction but none of these differences was statistically significant. Specifically, these patients had a slightly higher sperm concentration (20.4 +/- 13.7 X 10^6/ml versus 17.1 +/- 11.8 x 10^6/ml.), marginally better motility (5.1 +/- 4.7 versus 4.4 +/- 4.0%) and a minimally lower number of normal forms (36.7 +/- 17.8% versus 39.7 +/- 14.2%). These 6 patients had greater than 90% binding on the indirect immunobead assay.

Of the 29 patients in the other 3 groups who had antisperm antibodies and no evidence of partial obstruction 17 were treated with intrauterine insemination after sperm washing, 9 were treated with intrauterine insemination and in vitro fertilization, and 3 were treated with intrauterine insemination, in vitro fertilization, and intracytoplasmic sperm injection. Of the 2 treated with intrauterine insemination alone achieved pregnancy, 2 achieved pregnancy after intrauterine insemination and in vitro fertilization, and 1 achieved pregnancy after intrauterine insemination, in vitro fertilization, and intracytoplasmic sperm injection, for an overall pregnancy rate of 17.2%. Corticosteroid therapy was not administered to any patient. The pregnancy rate differed significantly between the 14 patients with partial obstruction treated with repeat microsurgical reversal, and the 29 patients with repeat microsurgical reversal, and the 29 patients with antisperm antibodies treated with sperm washing and assisted reproduction by chi-square testing (p = 0.025, chi-square = 5.04 with 1 degree of freedom).

**DISCUSSION**

The patient with persistent infertility after vasectomy reversal, an acceptable postoperative sperm concentration (defined as greater than 12 x 10^6/ml. by the vasovasostomy study group) [1] and a normal partner poses a diagnostic and therapeutic dilemma to even the experienced urologist. Some observers emphasize the role of antisperm antibodies in these cases. Studies analyzing fertility after vasovasostomy, [6] and emphasize instead the role of partial obstruction. Our study reveals that in the persistently infertile patient after reversal with partial obstruction and antisperm antibodies the infertility more likely results from the partial obstruction and, thus, such patients should be offered a second microsurgical reversal procedure.

Patients with antisperm antibodies after vasectomy reversal are clearly distinguishable from those with no history of vasectomy reversal. In addition, patients with partial obstruction after vasectomy reversal may be separated from those with no evidence of partial obstruction (overall binding less than 90% on the indirect immunobead assay) (see Figure 1). Although patients with a history of vasovasostomy have significantly lower mean overall binding on the indirect immunobead assay than any of the other groups, they also have significantly lower mean motility. Thus, the group in our study with the lowest level of antibody binding also has the lowest level of motility. This finding contradicts the general assumption that the proportion of antibody bound sperm and the percentage of motile sperm in the ejaculate of vas reversal patients are inversely related. [17] This discrepancy can be explained by postulating that the poor sperm motility exhibited by the patients with a history of vasovasostomy results not from antisperm antibodies but rather by the action of some other factor, namely partial obstruction. The differences in IgA and IgG binding across the groups are consistent with the difference seen in overall binding on the indirect immunobead assay, although the difference in IgG binding was not statistically significant.

Comparing the preoperative and postoperative semen analysis results in the 14 patients with partial obstruction revealed that the motility improved markedly after repeat microsurgical reversal from a mean of 4.4% to a mean of 52.3%. In addition, the sperm concentration increased from 17.1 to 35.8 x 10^6/ml. Clearly, these findings suggest that the poor sperm motility seen after the first microsurgical reversal was the result of partial obstruction, not antisperm antibodies, and that repeat microsurgical reversal represents appropriate therapy.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No. Evidence Chronic Partial Obstruction Treated With Repeat Reversal (%)</th>
<th>No. Evidence Chronic Partial Obstruction Treated With Sperm Wash and Assisted Reproduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy</td>
<td>7 (50)</td>
<td>5 (17.2)</td>
</tr>
<tr>
<td>No pregnancy</td>
<td>7 (50)</td>
<td>24 (82.8)</td>
</tr>
</tbody>
</table>

p = 0.025 by chi-square testing.

**Table 3.** Comparisons of preoperative and postoperative semen analysis results in 14 men with partial obstruction treated with a repeat microsurgical reversal procedure

<table>
<thead>
<tr>
<th>Surgical Status</th>
<th>Vol. (ml.)</th>
<th>Sperm Concentration (x 10^6/ml)</th>
<th>% Motility</th>
<th>% Normal Sperm Morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preop.</td>
<td>3.8 ± 1.6</td>
<td>17.1 ± 11.8</td>
<td>4.4 ± 4.0</td>
<td>90.7 ± 14.0</td>
</tr>
<tr>
<td>Postop.</td>
<td>3.1 ± 1.6</td>
<td>35.8 ± 15.6</td>
<td>52.3 ± 38.1</td>
<td>44.8 ± 19.5</td>
</tr>
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</table>

All values are based on the mean of at least 2 separate semen analyses, which were obtained at least 6 months postoperatively.
Unfortunately, this problem cannot be avoided in the study of antisperm antibodies because they coexist with pathological states of the genital tract. [18] While it is theoretically possible that these associated conditions are actually the cause of the infertility, the low pregnancy rate after assisted reproduction in this group would tend to suggest otherwise.

CONCLUSIONS

The patient who has partial obstruction and antisperm antibodies may be distinguished from other infertile men with antisperm antibodies by epididymal fullness on palpation, significantly poorer motility, decreased sperm concentration and lower overall binding on the indirect immunobead assay. These patients are best treated with a second microsurgical reversal procedure.

REFERENCES