

THE INCIDENCE OF ANTISPERM ANTIBODIES IN PATIENTS WITH SEMINAL TRACT OBSTRUCTIONS

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ABSTRACT

Antisperm antibodies are one of the important factors in male infertility caused by vasal obstructions. To investigate the incidence of serum antisperm antibodies in patients with various kinds of seminal tract obstructions, we retrospectively analyzed the sera of 60 patients using the indirect immunobead test (IBT) to find serum antisperm antibodies. Immunoglobulin (Ig)G and IgA class antisperm antibodies were positive in 55% and 18% of those patients with a vasal obstruction caused by inguinal herniorrhaphy and in 60% and 20% of vasectomized patients respectively; whereas these antibodies were positive in 13% and 0% of those patients with an epididymal obstruction of unknown etiology and in 8% and 3% of those patients with congenital bilateral absence of the vas deferens (CBAVD). The incidence of antisperm antibodies was significantly higher in patients with a vasal obstruction than in those with an epididymal obstruction ($p < 0.001$).

Key Words: Antisperm antibody, Vasal obstruction, Male infertility

INTRODUCTION

Antisperm antibodies are one of the important factors causing obstructive azoospermia associated with male infertility after surgical treatment.¹⁻³⁾ It is estimated that 50 to 80 percent of vasectomized men have circulating antisperm antibodies.⁴⁾ However, available information about antisperm antibodies in patients with a seminal tract obstruction caused by factors other than a vasectomy is lacking. Patrizio et al.⁵⁾ reported that the incidence of antisperm antibodies in patients with CBAVD was unexpectedly low. Many infertile patients have bilateral or unilateral vasal obstruction caused by childhood inguinal herniorrhaphy.⁶⁾ In these patients, as well as in patients with CBAVD, vasal obstruction occurred many years before the beginning of the sperm production. Antisperm antibodies were also found in the sera of patients with an epididymal obstruction of unknown etiology. However, the incidence of antisperm antibodies in these patients has not been well documented.

We analyzed the sera of patients with various kinds of seminal tract obstruction using the indirect IBT. The incidence of positive antisperm antibodies was as high in the patients with vasal obstruction caused by childhood inguinal herniorrhaphy as in vasectomized patients, whereas this incidence was low in patients with epididymal obstructions of unknown etiology and those with CBAVD.

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MATERIALS AND METHODS

The patient population consisted of 11 men with vasal obstructions caused by childhood inguinal herniorrhaphy, 5 vasectomized men, 8 men with epididymal obstructions of unknown etiology and 36 men with CBAVD, all of whom were treated at the Nagoya University Hospital from January 1991 to July 1995. The age of the patients with vasal obstructions caused by childhood inguinal herniorrhaphy ranged from 23 to 35 years. These patients had had bilateral inguinal herniorrhaphy before the age of 3, and the period of vasal obstruction was >20 years in all cases. None of the patients showed elevated serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL) or testosterone (T). Testicular volume was normal in all patients. They underwent bilateral vasovasostomy according to microsurgical two-layer methods.⁷⁾ Surgical exploration revealed a vasal obstruction in the inguinal canal in 9 patients, whereas 2 patients had vasal obstructions outside the external inguinal ring. No sperm granulomas were found at the testicular end of the vasa deferentia in any patient.

The age of the vasectomized patients ranged from 37 to 45 years. The period from vasectomy to vasectomy reversal was 8 years in all cases. The longest one was 13 years. None of the patients showed elevated serum LH, FSH, PRL or T except for one patient whose serum FSH level was 13.5 mIU/mL (normal value, 2.9 to 8.2 mIU/mL). Testicular volume was normal in all patients. Surgical exploration at vasectomy reversal showed that sperm granulomas were evident in 4 of 5 patients.

The age of the patients with epididymal obstructions of unknown etiology ranged from 27 to 35 years. Vasography showed normal patency. They had no previous history of urogenital infection. The results of a testicular biopsy in these patients revealed normal spermatogenesis. None of the patients showed elevated serum LH, FSH, PRL or T. Testicular volume was normal in all patients. They underwent microsurgical epididymovasostomy.⁸⁾

The age of patients with CBAVD ranged from 25 to 40 years. On physical examination their testes were bilaterally normal, but both vasa deferentia were not palpable. Seminal volume was less than 0.5 mL and seminal pH was 6 in all patients. The semen analysis showed fructose to be negative. All endocrine panels were within normal limits and testicular volume was normal in all patients. They underwent epididymal sperm retrieval for microfertilization by epididymal micro-puncture technique.⁹⁾

The serum of each patient was analyzed before each operation. Serum taken before the operation was kept at -20°C until assayed. The indirect IBT was performed according to the method of Clarke *et al.*¹⁰⁾ Two hundred microliters of complement-inactivated serum and 25 μL of semen from a fertile donor were incubated for 60 minutes at 37°C . A 7- μL aliquot of the washed sperm was then mixed with 7 μL of Tyrode solution with 5% bovine serum albumin (Sigma Chemical Co., St. Louis, MO) containing anti-human Ig beads (Biorad Laboratories, Richmond, CA). A positive result in the IBT was defined as >20% attachment of motile sperm to the beads. We did not measure the titers of antisperm antibodies. All the tests used sperm (antigens) from the same donors with blood type O who had previously have tested negative for antisperm antibodies. A negative control (obtained from fertile men with blood type AB) was always included in the assay. Statistical analyses were performed using Fisher's direct test.

RESULTS

IgG and IgA class antisperm antibodies were positive in 55% and 18% of those patients with a vasal obstruction caused by inguinal herniorrhaphy, and in 60% and 20% of vasectomized patients respectively; whereas these antibodies were positive in 13% and 0% of those patients with an epididymal obstruction of unknown etiology, and in 8.3% and 2.8% of patients with CBAVD, respectively (Table 1). The antisperm antibodies were positive in all vasectomized patients who were found to have sperm granulomas (4/5). The incidence of antisperm antibodies was significantly different between the patients with vasal obstructions and those with epididymal obstructions ($p < 0.001$). IgM class antisperm antibodies were negative in all patients.

Table 1. Number of Patients With Positive Serum Antisperm Antibodies, Sperm Granulomas and Surgical Outcome

Group	IgG	IgA	Age	Sperm Granuloma	Pregnancy
After herniorrhaphy (n=11)	6(55)	2(18)	28 ± 2.1	0	1
After vasectomy (n=5)	3(60)	1(20)	40 ± 1.9	4	0
Epididymal obstruction of unknown etiology (n=8)	1(13)	0(0)	30 ± 3.4	0	1
CBAVD (n=36)	3(8.3)	1(2.8)	33 ± 4.1	0	6

Values in parentheses are percentages. CBAVD (congenital bilateral absence of the vas deferens). Age is expressed as mean ± SD.

Sperm appeared postoperatively in the semen of 6 of the 11 postherniorrhaphy patients; 5 patients with serum antisperm antibodies, and 1 patient without antibodies. Of these 6 patients, impaired sperm motility $< 5\%$ was found in the 5 patients with IgG class antisperm antibodies, whereas the patient without antibodies had sperm motility $> 30\%$. Pregnancy was achieved by the one patient without antibodies. Sperm appeared postoperatively in one vasectomized patient without antisperm antibodies, but pregnancy was not achieved.

One patient with an epididymal obstruction of unknown etiology achieved natural pregnancy. Serum antisperm antibodies were negative in this patient. Six patients with CBAVD and without antisperm antibodies achieved successful pregnancy by epididymal micropunctured sperm combined with microfertilization.

DISCUSSION

In the present study, a high incidence of positive antisperm antibodies was observed in those patients with a vasal obstruction caused by childhood inguinal herniorrhaphy. Hendry et al. reported on 5 patients with vasal obstruction after inguinal herniorrhaphy who had positive antisperm antibodies in their sera according to the tray agglutination test.¹¹⁾ However, the incidence of antibody-positive patients was not described in their article. Recently, Matsuda et al. reported that a significant percentage of patients with a vasal obstruction caused by infant inguinal herniorrhaphy have serum antisperm antibodies.¹²⁾ Our present data confirm these later results.

When compared with vasal obstructions caused by vasectomy, one of the key clinical characteristics of post-herniorrhaphy vasal obstructions is the long period of obstruction beginning

many years before testicular spermatogenesis. Patients with CBAVD also have the same characteristic. Patrizio *et al.* reported an unexpected low incidence of antisperm antibodies in patients with CBAVD using the indirect IBT.⁵⁾ In their study, pathological evaluation of the epididymal biopsied specimen in CBAVD patients revealed a marked hypertrophied epididymal muscular wall.⁵⁾ On the basis of this finding, Patrizio *et al.* hypothesized that this hypertrophy prevented the leakage of soluble parts of degraded spermatozoa into the periepididymal interstitial tissue and, therefore, inhibited an immunological exposure and subsequent antisperm antibody formation.⁵⁾ In the present study, patients who had undergone childhood inguinal herniorrhaphy had as high an incidence of positive antisperm antibodies as vasectomized patients. It is plausible, as postulated by Patrizio *et al.*,⁵⁾ that some histologic difference in the epididymis between patients with CBAVD and patients with long-term vasal obstruction might be involved in the pathogenesis of antisperm antibodies.

Another characteristic of postherniorrhaphy vasal obstruction is that sperm granulomas are not formed because sperm first appear at puberty many years after the interruption of the vas deferens. In vasectomized patients, it has been reported that positive serum antibodies are correlated with the size of sperm granulomas.¹³⁾ However, the present study demonstrates a high incidence of antisperm antibodies in patients with postherniorrhaphy vasal obstructions in spite of the absence of sperm granulomas. Epididymal blowout caused by increased intraluminal pressure,¹⁴⁾ which may result in secondary epididymal obstruction, can be another cause of autoimmunity against sperm.

In conclusion, patients with vasal obstructions due to childhood inguinal herniorrhaphy have the highest incidence of antisperm antibodies in their sera even though no sperm granulomas exist. The vasectomized patients also have a high incidence of antisperm antibodies in their sera. This incidence is more marked in vasectomized patients with sperm granulomas. In contrast, those patients with an epididymal obstruction or with CBAVD have a significantly lower incidence of antisperm antibodies.

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ANTISPERM ANTIBODIES IN VASAL OBSTRUCTIONS

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