Successful microsurgical vasoepididymostomy for a case of cryptozoospermia

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Asian Journal of Andrology (2022) 24, 436–437; doi: 10.4103/aja202178; published online: 14 December 2021

Dear Editor,

Cryptozoospermia is defined as the apparent absence of spermatozoa from fresh semen samples, but they can be found in centrifuged pellets.1 It is usually caused by a spermatogenic disorder, while cryptozoospermia associated with seminal duct obstruction is less common.2 Because of the extremely low sperm counts in semen samples, men with cryptozoospermia are often reliant on intracytoplasmic sperm injection (ICSI) for paternity. However, for men with cryptozoospermia caused by seminal duct obstruction, reconstructive surgery might be an option. To our knowledge, there is no report of cryptozoospermia caused by epididymal obstruction. Here, we report a man with this condition who impregnated his wife successfully after undergoing microsurgical vasoepididymostomy (mVE). This study was approved by the Ethics Committee of Shanghai General Hospital (approval number: 2021KY084). Informed consent for this study was obtained from the patient.

A 29-year-old man with a 2-year history of infertility presented for treatment in Shanghai General Hospital (Shanghai, China). He was diagnosed with azoospermia by repeated semen analyses but had been confirmed to have active spermatogenesis by fine-needle aspiration in another institution. He had impregnated a previous partner 4 years ago and had a history of epididymitis 3 years ago. He did not have other potential causes of infertility.

The patient had well-developed testes. The bilateral epididymides were plump by palpation. The patient had no evidence of other abnormalities of the genitourinary system. Furthermore, no spermatozoa were found in ejaculates. The seminal fructose test was positive. The level of neutral α-glycosidase was 5.78 U l⁻¹ (reference ≥10.12 U l⁻¹). Endocrine evaluations showed a luteinizing hormone (LH) level of 9.98 mIU ml⁻¹, follicle-stimulating hormone (FSH) level of 3.06 mIU ml⁻¹, and total testosterone (T) level of 3.50 ng ml⁻¹. Scrotal ultrasonography showed tubular ectasia in the bilateral corpus and caudae epididymides (Supplementary Figure 1). He was initially diagnosed with obstructive azoospermia (obstruction of epididymides) and was recommended to undergo mVE. Unexpectedly, the day before scheduled surgery, a semen analysis showed several immotile spermatozoa after centrifugation. Therefore, we revised his diagnosis to cryptozoospermia. After discussion with the couple, the patient elected to pursue conservative treatment to improve his sperm quality. As antioxidant supplements have emerged as a potential therapeutic approach in an attempt to treat male infertility, L-carnitine and vitamin E supplements were prescribed.3 However, his semen quality did not improve after 3 months of treatment, so he returned for surgical treatment by mVE.

Surgery was performed under a Zeiss surgical microscope (Vario 700; Carl Zeiss AG, Oberkochen, Germany). During the surgery, testicular tissue was obtained and delivered immediately to the experienced laboratory experts. Many immotile spermatozoa were found under phase-contrast microscopy (Nikon Corporation, Tokyo, Japan) at 200× magnification. Dilated epididymal tubules in the caudae were identified easily, and many immotile spermatozoa were found in the aspirated fluid. The abdominal vas deferens were unobstructed, as confirmed by dilute methylene blue injection. A single-armed suture longitudinal intussusception vasoepididymostomy technique sparing the deferential vessels was adopted, and anastomosis was performed on both caudae.

During the postoperative follow-ups, semen analyses indicated cryptozoospermia for the first 2 months, but the sperm recovered. The total progressively motile sperm count fluctuated but kept at a relative high level in most tests (Table 1). This indicated the success of the operation. Thirteen months after the operation, his wife conceived naturally, and a baby boy was born in due course.

ICSI has now become an established therapy for cryptozoospermia.3 However, for cryptozoospermia caused by obstructive factors – as in this case – seminal duct reconstructive surgery is recommended. This enables spermatozoa to reappear in ejaculates, making natural conception possible. Compared with ICSI, it avoids oocyte retrieval and reduces medical expenses. In general, we recommend testicular sperm extraction (TESE) during surgery for the following reasons. First, TESE can be used to confirm normal spermatogenesis. Although uncommon, spermatogenic failure may be mistakenly considered normal spermatogenesis. Second, testicular sperm cryopreservation can be carried out for ICSI if the seminal duct reconstruction fails, avoiding reoperation for sperm extraction. In this case, the patient preferred to tolerate his epididymal obstruction. After all the treatment options were informed, the patient only accepted the surgical reconstruction surgery and refused TESE for sperm cryopreservation.

The longitudinal intussusception vasoepididymostomy technique has been recognized as the gold standard to achieve a superior patency.

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Received: 12 May 2021; Accepted: 27 September 2021
rate. A recent systematic review demonstrated that bilateral operations, presence of spermatozoa in the epididymal fluid, and anastomoses of the epididymal corpus or cauda were associated with slightly higher patency rates. The vessels of the vas deferens are typically ligated to facilitate a good anastomosis. The testicular, deferential, and cremasteric arteries are three main arteries in the spermatic cord. Although the testicular artery provides most of the blood flow to the testis, the deferential arteries also make a significant contribution. In addition, the deferential artery also contributes to the blood supply of the epididymis. Therefore, it is better to spare the deferential vessels if the length of the vas deferens allows a tension-free anastomosis. However, well-designed clinical controlled trials should be performed to certify the clinical effect.

Finally, it should be noted that semen analysis is crucial for the diagnosis of cryptozoospermia. Actually, it is difficult to distinguish cryptozoospermia from absolute azoospermia. The detection of spermatozoa in the ejaculates is affected by temperature, laboratory expertise and quality control, centrifugation, sampling, and other factors. Although recommended by the World Health Organization guidelines, all spermatozoa in ejaculates cannot necessarily be centrifuged to form a pellet even at 3000 g for 15 min. Before semen analysis, it is necessary to make sure the semen sample is well mixed, and two slides using pellets should be checked. If spermatozoa are observed in any slide, cryptozoospermia is indicated. If none are observed in either slide, azoospermia is indicated. However, if no spermatozoa can be found in the slides examined, it is still possible that there might be some in the remaining sample. It is recommended that spermatozoa should be searched in repeated ejaculations several times, even before the day of surgery.

In conclusion, we present a patient with cryptozoospermia caused by partial epididymal obstruction. This patient clearly benefited from mVE as his partner conceived. Although this might be unnecessary to consent all patients undergoing mVE for recovering their fertility, it is clearly an alternative treatment.

**AUTHOR CONTRIBUTIONS**

RHT and YHH performed the surgery. RHT, YHH, and HXC drafted the manuscript. PL and ELZ helped to draft the manuscript. CCY conceived of the study and reviewed and edited the manuscript. ZL and CY participated in the testicular tissue and sperm processing. ZL and CY performed the surgery. RHT, YHH, and HXC drafted the manuscript. PL and ELZ helped to draft the manuscript. CCY and CY read and approved the final manuscript.

| Table 1: Semen analysis during the postoperative follow-ups |
|----------------------------------------------------------|
| Postoperative time (month) | Semen volume (ml) | Sperm concentration ($\times 10^6$ ml$^{-1}$) | Progressive rate (%) | Total progressively motile sperm count ($\times 10^6$) |
|---------------------------|-------------------|-----------------------------------------------|----------------------|-----------------------------------------------|
| 1                         | 2.3               | 2 sperm per slides identified after centrifugation | NA                   | NA                                           |
| 2                         | 1.8               | 0                                              | NA                   | NA                                           |
| 3                         | 1.2               | 30                                             | 3.0                  | 1.1                                          |
| 4                         | 3.3               | 13                                             | 20.0                 | 8.6                                          |
| 5                         | 2.0               | 19                                             | 21.0                 | 8.0                                          |
| 8                         | 2.5               | 15                                             | 31.0                 | 11.6                                         |
| 10                        | 3.0               | 8                                              | 3.0                  | 0.7                                          |
| 11                        | 2.2               | 45                                             | 19.0                 | 18.8                                         |
| 12                        | 1.6               | 51                                             | 19.0                 | 15.5                                         |
| 13                        | 2.5               | 12                                             | 27.0                 | 8.1                                          |
| 14                        | 2.5               | 47                                             | 13.0                 | 15.3                                         |

NA: not available

**COMPETING INTERESTS**

All authors declared no competing interests.

**ACKNOWLEDGMENTS**

This work was supported by Clinical Research Innovation Plan of Shanghai General Hospital (No. CTCCR-2019C04 and No. KD007-ly01), Shanghai Sailing Program (No. 20YF1439500), and National Science Foundation for Young Scientists of China (No. 82001530).

Supplementary Information is linked to the online version of the paper on the Asian Journal of Andrology website.

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Supplementary Figure 1: The views of the scrotal ultrasound demonstrate the epididymal tube lesions. (a) Ultrasound image shows tubular ectasia in the corpus (arrows) and cauda (arrowheads) of right epididymis. (b) Ultrasound image shows tubular ectasia in the corpus (arrows) and cauda (arrowheads) of left epididymis.