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ORIGINAL ARTICLE

Male Infertility

Clinical features and therapeutic strategies of obstructive azoospermia in patients treated by bilateral inguinal hernia repair in childhood

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Childhood inguinal herniorrhaphy is one common cause of seminal tract obstruction. Vasovasostomy (VV) can reconstruct seminal deferens and result in appearance of sperm and natural pregnancy in some patients. Secondary epididymal obstruction caused by a relatively long-term vasal obstruction is a common cause of lower patency compared with VV due to vasectomy in adults. From July 2007 to June 2012, a total of 62 patients, with history of childhood inguinal herniorrhaphy and diagnosed as obstructive azoospermia were treated in our center. The overall patency rate and natural pregnancy rate were 56.5% (35/62) and 25.8% (16/62), respectively. 48.4% (30/62) of the patients underwent bilateral VV in the inguinal region, with a patency rate of 76.7% (23/30) and a natural pregnancy rate of 36.7% (11/30), respectively. 30.6% (19/62) of the patients underwent bilateral VV and unilateral or bilateral vasoepididymostomies due to ipsilateral epididymal obstruction with the patency and natural pregnancy rate decreasing to 63.2% (12/19) and 26.3% (5/19). 21.0% (13/62) of the patients merely underwent vasal exploration without reconstruction due to failure to find distal vasal stump, *etc*. Our study indicate that microsurgical reanastomosis is an effective treatment for some patients with seminal tract obstruction caused by childhood inguinal herniorrhaphy.
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INTRODUCTION

The azoospermia is a major concern in male infertility. Compared to nonobstructive azoospermia, which is usually caused by complexed and unexplained reasons, obstructive azoospermia could be diagnosed with clear etiology. Causes of vasal obstruction include vasectomy, inguinal surgery, scrotal surgery, and congenital anomalies. Inguinal hernia repair, particularly when performed at childhood, is one common cause for vasal obstruction and obstructive azoospermia due to vasal injury. According to the published report, the incidence of vasal obstruction could reach as high as 26.7% in subfertile patients with a history of childhood inguinal hernia repair.[1] Although intracytoplasmic sperm injection (ICSI) could mostly solve the problem, some couples still prefer natural pregnancy due to personal or social reasons.

Obstruction of the vas deferens within the inguinal canal can be managed by direct on-site vasovasostomy (VV) which allows the postoperative recovery of sperm in semen, especially with the advanced microsurgical techniques.[2–6] Many factors, such as suspending site, defective length and secondary epididymal obstruction, could influence the treatment outcome.[7] In this study, we reviewed clinical data from 62 patients with childhood inguinal herniorrhaphy who underwent vasal exploration and microsurgical VV. By retrospectively analyzing the clinical characteristics of this obstruction, surgical treatments for reanastomosis, and outcomes in patients, we endeavor to establish a strategy to optimize the diagnosis and treatment of obstructive azoospermia in patients who have undergone childhood bilateral inguinal hernia repair.

MATERIALS AND METHODS

Subjects and laboratory examination

This study was approved by the Ethics Committee of Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University. From July 2007 to June 2012, 62 patients with an average age of 31 years (range: 23–37 years) diagnosed with obstructive azoospermia due to suspected vasal obstruction were included in this study. All patients underwent bilateral inguinal herniorrhaphy at childhood. Forty-five patients underwent herniorrhaphy at the age ranging from 1 to 5 years, other 17 patients at the age older than 5 years, but not above 10 years. Preoperative evaluation included a complete history and physical examination, semen analysis, serum testosterone and follicle-stimulating hormone levels and ultrasonic examination. All the patients had the following common characters: (1) azoospermia in at least two consecutive semen samples collected 6 weeks apart; with normal volume ejaculate and PH. (2) All patients had at least one normal-sized testis and normal or marginally elevated follicle-stimulating hormone (FSH) levels. (3) Scrotal ultrasonography and transrectal ultrasound (TRUS) showed normal integrity of testicular seminal tract (epididymis and scrotal portions of the vas deferens) and abdominal seminal tract (inguinal, pelvic and amputated portions of the vas deferens, and ejaculatory ducts), so as

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to rule out obstruction of the ejaculatory ducts and congenital bilateral vas deferens atresia. In some cases, dilatation in the testicular seminal duct (epididymis and intrascrotal portion of the vas deferens) was detected. (4) In patients undergoing testicular sperm extraction (TESE) or percutaneous epididymal sperm aspiration (PESA), sperm was detected.

Surgical procedure

Under general anesthesia, the procedure was divided into several consecutive steps after preoperative indwelling urethral catheterization: (1) analysis of vasal fluid: vas deferens at mid-scrotal level was identified by a 0.5 cm-length wide incision. A fine-needle aspiration into the vasal lumen was performed; any fluid exuding from the lumen was placed on a slide, mixed with a drop of saline, and sealed with a coverslip for microscopic examination. The presence of sperm in the vasal fluid was graded as follows: Grade 1: motile normal sperm. Grade 2: nonmotile normal shaped sperm. Grade 3: nonmotile sperm, predominately sperm heads (no tails) with some normal shaped sperm. Grade 4: exclusively sperm heads. Grade 5: no sperm.[8] (2) 24-gauge angiocatheterization was put into distal vasal lumen, followed by injection with 1 ml of lactated Ringer solution, then 1 ml diluted methylene blue. Nonblue stained urine in catheter in all the above patients demonstrated that the distal vasal injure was the reason of obstruction. (3) In the case of Grade 5, the surgeon could consider performing testicular biopsy rather than quickly going ahead with VV. (4) In the case of Grade 1, 2, and 3, before proceeding to explore the testicular and abdominal vasal end, the aspiration site in the scrotal vas deferens was closed using 9–0 nylon suture (Ningbo Medical Needle Co., Ltd., Ningbo, China) in an interrupted fashion. Then the inguinal canal was re-opened and the spermatic cord was exposed. The testicular vas deferens was usually identified at or 1–2 cm above the external inguinal ring,[9] then followed upward to the internal inguinal ring until the obstruction site was identified. In the most cases, the disconnected abdominal vasal end was located at the internal inguinal ring, or more distally in the pelvic cavity. After being found, the abdominal vasal end was cannulated with a 24-gauge angiocatheter sheath and injected with 1 ml of lactated Ringer solution with a 1 ml tuberculin syringe to confirm its patency. The testicular stump of the vas was trimmed and vas deferens was separated from the spermatic cord to make anastomosis tensionless. Great care was taken not to injure blood supply to both ends of the vas deferens because devascularlization of the vas deferens is a frequent cause of VV failure. Normally, there was a large difference in the diameter of the vas deferens between the testicular and abdominal ends due to the long period of obstruction. According to Silber, microsurgical two-layer technique under operative microscopy was mandatorily required for VV,[10] which is expected to avoid sperm leakage. The posterior and anterior walls of the inguinal canal were closed, and the patient must subsequently wear tight underwear and sexual intercourse was prohibited for at least 6 weeks. (5) In the case of Grade 4 and 5, if the vasal fluid was devoid of sperm with repeated sampling after milking the epididymis and convoluted vas, secondary epididymal obstruction might occur. Epididymovasostomy following ipsilateral inguinal VV was performed,[11] at the site of epididymis where qualified sperm was detected.

Vasovasostomy

After being freed, the two ends of the vas were cut transversely. An inner layer of sutures was placed to bring the mucosa together and a 10–0 nylon double-armed suture was utilized. Next, an outer layer of sutures closing the seromuscular layers was placed and a 9–0 nylon suture was applied. Six stitches were applied on every layer and all sutures were placed in an interrupted fashion.

Vasoepididymostomy

The vasal fluid was sampled and evaluated under light microscopy. The absence of sperm and sperm parts in the vasal fluid and the presence of abundant motile sperm in epididymal fluid were essential to identify the location of the obstruction. If the vasal fluid was devoid of sperm with repeated sampling after milking the epididymis and convoluted vas, secondary epididymal obstruction might have occurred. Vasoepididymostomy (VE) following ipsilateral inguinal VV was performed. A scrotal incision was applied. The vas was isolated at the junction of the straight so as to allow the maximal length of straight vas to be preserved to allow a tension-free VE to be performed. Four microdots were labeled with a micromarking pen on the vasal ends to demarcate the exit points of the suture needles to be placed on the vas. Double-armed 10–0 nylon sutures were applied to allow inside-out placement of the needles on the mucosa, eliminating the need for manipulation of the mucosa. Under the magnification of × 25 to × 40, one needle from tow separated double-armed 10–0 nylon sutures was longitudinally placed in the epididymal tubule, respectively and left there, then by using a 15° ophthalmic knife, the tubule was incised longitudinally between the two needles, which were then pulled through and placed to the mucosa in the vasal ends in an inside-out fashion through the labeled microdots.

Assessment of surgical results

The treatment outcome was determined by postoperative semen analysis and success of pregnancy through natural intercourse with the minimal follow-up of 12 months. Patency was defined as the presence of motile sperm in the ejaculate in at least one analysis. Pregnancy outcomes were obtained through either follow-up visits or telephone interviews.

RESULTS

Among the 62 enrolled patients, 21.0% (13/62) just underwent vasal exploration without reconstruction because of failure to find distal vasal stump or ischemic atrophy, and the overall patency and natural pregnancy rate were 56.5% (35/62) and 25.8% (16/62). Among them, 48.4% (30/62) of patients underwent bilateral VV in the inguinal region, and sperm was noted in vasal fluid, with patency of 76.7% (23/30) and natural pregnancy rate of 36.7% (11/30), respectively. 30.6% (19/62) of patients underwent bilateral VV and unilateral or bilateral vasoepididymostomies due to ipsilateral epididymal obstruction, because sperm was not found in the vasal fluid on one or both sides. The patency and natural pregnancy rate decreased to 63.2% (12/19) and 26.3% (5/19). Details in subgroups were demonstrated in **Table 1**.

Semen analysis was firstly performed 2 months postoperation, and once per month during following-up. The mean semen concentration at 2 months postoperation was 11.2×10^6 ml^{-1} (4.5×10^6–3.6×10^7 ml^{-1}), mean progressive motility rate was 20.1% (range from 7.8% to 42.7%), with an increase both in semen concentration (range: 9.3×10^6–76.2×10^6 ml^{-1}, average: 1.95×10^7 ml^{-1})

Table 1: Results in different subgroups based on operative styles

Treatment (%)	*Number of patients (%)*	*Number of patency (%)*	*Number of pregnancy (%)*
Bi-VV	30 (48.4)	23 (76.7)	11 (36.7)
Bi-VV+Uni-VE	13 (21.0)	9 (69.2)	4 (30.8)
Bi-VV+Bi-VE	6 (9.7)	3 (50.0)	1 (16.7)
Explo	13 (20.9)	N/A	N/A
In sum	62 (100)	35 (56.5)	16 (25.8)

Bi-VV: bilateral vasovasostomy; Uni-VE: unilateral vasoepididymostomy; Bi-VE: bilateral vasoepididymostomy; Explo: exploration with no anastomosis; N/A: not applicable

and progressive motility rate (range: 17.1%–60.2%, average: 34.7%) at 6 months postoperation.

DISCUSSION

Herniorrhaphy is one of the most common cause of iatrogenic vasal obstruction and also a possible cause of iatrogenic testicular atrophy due to the compromise of testicular blood supply. Vas injury following childhood herniotomy can be caused by cutting, crushing or overstretching. Although the infertile couple can conceive by ICSI combined with TESE or PESA, some couples still seek reconstruction of seminal deferens due to the following reasons: (1) it is a costly procedure and an intense process for the female partner, with associated risks of complications including ovarian hyperstimulation, multiple gestations, and of complications of the procedures for oocyte retrieval. (2) As ICSI bypasses all natural biologic barriers, it raises a concern of passing genetic abnormalities to the offspring. On the contrary to this concern, successful surgical reversal of vas deferens was frequently observed to entitle the infertile couples to have their babies naturally and enduringly by means of high-quality diagnostic and therapeutical techniques.

Treatment of iatrogenic injuries is usually a challenging problem. Compared with VV due to vasectomy, the procedures due to postherniorrhaphy are much more difficult with lower success rates.[12–14] Firstly, surgical exploration of the inguinal region to locate the remnants of the vas deferens for anastomosis has some negative effects. The abdominal vasal end may not be found for the complete injury at very early age, or it may have developed into a kind of membrane cord due to ischemic atrophy. Even if they are found, they may have been devitalized or too separated, making approximation difficult and causing the anastomosis to be under tension. Secondly, it's difficult to estimate the obstructive site before the surgical exploration. The obstruction is commonly inguinal or retroperitoneal and is often associated with severe scaring of the vas deferens and surrounding tissues. When injuries occur in early childhood, the obstruction is usually longstanding, increasing the likelihood of secondary epididymal obstruction which is difficult to detect preoperation. Thirdly, technical difficulty associated with microsurgical anastomosis in the inguinal region, usually at deep inguinal ring, influence the final results.

Although it is difficult to pinpoint the obstruction site in the inguinal region preoperatively, it is still continuously focused and struggled by medical practitioners for its important indicative meaning for prognosis, therefore optimization of treatment protocol, which is also highly considered by patients to make their preferred choice. In this study, transrectal high-resolution ultrasound, as well as scrotal ultrasound with color flow Doppler was used as a useful and potentially diagnostic tool to localize the obstructive site before operation. Dilated vas (larger than 1.5 mm in inner diameter) and thin net-like ectasia (0.3–1.0 mm in inner diameter) or tubular ectasia (>1.0 mm in inner diameter) indicate vasal obstruction. If dilation of epididymis tube was detected,[15] it would be more likely that simultaneous epididymis obstruction has occurred, which may indicate low patent rate after the surgery. Similarly, if abdominal stump of the vas deferens was not detected using scrotal ultrasound and TRUS, it also implied the difficulty even failure of microsurgical reconstruction of ducts. However, ultrasound could not accurately pinpoint the obstruction site for all the candidates. Only the exploration during the surgery could tell the real facts. Before final surgery, all these possibilities should be informed to patients and families.

Intraoperatively in this study, minimally invasive vasal fluid aspiration before the openly explosive procedure to detect the fertile sperm was also very important. It helped the decision-making regarding the following surgical choices. If a large amount of fluid was found in a markedly dilated vas and microscopic examination revealed the presence of normal sperm, the obstruction may have occurred close to the abdominal end of the vas, and VV is usually prescribed to reconstruct the reproductive tract. However, if copious thick white fluid containing no sperm was found in a dilated vas, secondary epididymal obstruction was implied. Besides VV in the inguinal region, ipsilateral VE is also necessary, which leads to much lower patency rate. In some cases, patients may only have epididymal obstruction that is not associated with hernia repair, such as pure epididymitis. This suggests that the vas deferens is probably not injured at all. In these cases, we just need scrotal incision for VE procedure. That is why we firstly use the less traumatic scrotal percutaneous vas puncture to confirm whether vas deferens had been injured and become obstructed. In this study cohort, all the 62 patients had an obstruction at the inguinal portion of the vas, indicating that if patients were selected appropriately, exploration of the scrotal vas with a small scrotal puncture could be bypassed.

Regarding the patients (20.9%, 13/62) who were not suitable for reconstruction because their distal vasal ends were not detected, which was probably due to ischemic atrophy or deeper obstructive site above internal inguinal ring, ICSI cycle using testicular or epididymal sperm is recommended.[16] There are also other exploring approaches such as laparoscopy-assisted pelviscrotal VV, with some advantages in cases where the vas deferens remnants are devitalized or too separated, making approximation difficult and causing the anastomosis to be under tension.[17] Laparoscopic procedures is much more effective to free the vas on the abdominal end, then direct the abdominal vas to or through the external ring to achieve additional length to ensure a tensionless anastomosis. The patency rate for unilateral and bilateral correction could reach 60% and 80%, respectively, much higher than that of the microsurgical two-layer VV (39%).[18] However, the surgical risk and the possible complications must be considered, and much more data are needed.

Accurate localization of obstructive site before explorative surgery, in combination of intraoperatively and minimally invasive aspiration of vasal fluid to evaluate the fertile sperm, is of great importance to effectively treat the obstructive azoospermia secondary to bilateral inguinal hernia repair. Ultrasound, including scrotal and transrectal focus, is a useful and potentially diagnostic method to localize the obstructive sites. Microsurgical reconstruction of the vasal ducts is an effective and competent treatment alternative, based on patients preference and skilled techniques from the practitioners.

AUTHOR CONTRIBUTIONS

XFC and PP designed the experiments, participated in drafting, collecting and interpreting the data and critically revising the paper for key intellectual content. XFC, HXW, KS, PP, and YDL carried out the clinical work. XFC and PP. LXZ, YRH, and ZL reviewed the paper. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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