

# Vas deferens sonographic appearances of tuberculosis lesions of 19 cases of male genital systemic tuberculosis

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## Abstract

To investigate the sonographic findings of the vas deferens in male genital tuberculosis.

The ultrasonographic findings of the vas deferens of 19 cases of genital tuberculosis were retrospectively analyzed.

According to the pathological and ultrasound findings, the ultrasonographic appearances of the vas deferens tuberculosis could be divided into 4 groups, 1 of normal sonograms, 3 of abnormal sonograms. The abnormal ultrasonographic appearances of the vas deferens tuberculosis were considered 3 categories as follows: diffusely thickening of vas deferens, nodular thickening of vas deferens, and space-occupying lesions adjacent to the vas deferens.

The ultrasound manifestations of vas deferens in tuberculosis of the male genital system have certain characteristics. Combination of clinical manifestations, history of tuberculosis, experimental antituberculosis treatment, and ultrasound examination of vas deferens can suggest tuberculosis of vas deferens. Furthermore, it can provide objective basis for the comprehensive and noninvasive evaluation of the impact of genital tuberculosis on the reproductive ability for further treatments.

**Abbreviations:** CDFI = color doppler flow imaging, ED = ejaculatory duct, SV = seminal vesicle, TB = tuberculosis, TRUS = transrectal ultrasound, US = ultrasound, VD = vas deferens.

**Keywords:** abnormality, diagnosis, sonographic appearance, ultrasound, urinary and genital systemic tuberculosis, vas deferens

## 1. Introduction

The vas deferens (VD) originates from the tail of epididymis. It is composed of a mucous membrane, muscular layer, and fibrous membrane. The tube wall is thick and the lumen is small. The inner diameter is about 0.3 mm, while the outer diameter is 1.7 to 2.4 mm. Tuberculosis (TB) of the VD is a rare disease that is often secondary to urogenital TB and can lead to obstruction of the VD, thereby causing infertility in males. The ultrasound (US) can show the testes VD, spermatic VD, groin VD, while transrectal ultrasound (TRUS) can display pelvic VD, especially the ampulla of VD and the segment of VD close to the seminal vesicle (SV).

According to the state of art publication on normative male genital tract US characteristics,<sup>[1]</sup> the whole male genital system can be revealed clearly. The diameter and the volume of testis, epididymis, SV, VD, and prostate can be measured. US is of great value in the male urinary and reproductive system due to the widespread utility of TRUS. Various congenital and acquired vas deferential lesions have been detected and diagnosed, such as congenital bilateral or unilateral absence of VD, VD injury, deferentitis, and so on.

TB of the male genital tract has a considerable impact on fertility and remains a medical challenge.<sup>[2]</sup> Ultrasonography is the best imaging modality for the diagnosis of the diseases of male genital tract. US plays an important role in the diagnosis and treatment of TB of prostate, SV, epididymis, and testicle,<sup>[3–5]</sup> but the ultrasonic manifestations of TB in the VD are rarely reported.<sup>[6,7]</sup> Further observational study is needed to elucidate the ultrasonic changes of VD in patients with genital systemic TB.

Hence, a retrospective analysis of the clinical and US data of 19 cases of TB of the male genital system was conducted in our hospital to reveal the pathological changes of VD in order to systematically and comprehensively assess the disease and provide objective basis for clinical treatment selection.

## 2. Materials and methods

This retrospective study was conducted in accordance with the Declaration of Helsinki, and with approval from the Ethics Committee of Sichuan University (Chengdu, China). A total of 19 patients hospitalized into West China Hospital, Sichuan University between June 2009 and April 2016, diagnosed as male urinary or genital system TB were included. Seven cases were operated. The operation methods included epididymal resection, epididymal orchietomy, and epididymal spermatic

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All procedures complied with the ethical standards of the responsible committee on human experimentation (institution and national) and the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Ethics Committee of Sichuan University (Chengdu, China).

Informed consents were waived off.

There are no financial or other relations that could lead to a conflict of interest.

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cord resection. Acid-fast positive mycobacteria were found in partially resected specimens. And Mycobacterium TB DNA fragments were found by *q*PCR in all cases. Furthermore, in the VD of 3 surgical specimens, acid-fast positive mycobacteria were present and mycobacterium TB DNA fragments were also found by *q*PCR. Two cases were pathologically confirmed to have both prostate and epididymal TB by biopsy. In 12 cases, the lesions were reduced after treatments with anti-TB drugs, which were initially suspected of VD TB. Among the 19 cases, there were 14 cases complicated with epididymal TB, 4 cases complicated with tuberculous epididymo-orchitis, 2 cases complicated with prostatic TB, and 1 case complicated with renal TB.

The age range of patients was 15 to 63 years, the average age was 33.2 years. The clinical manifestations included 11 cases of genitourinary system TB, 4 cases of scrotal spermatic cord pain, 1 case of spermatic cord hardening, 1 case of azoospermia, 1 case of secondary infertility, and 1 case of testicular induration. Nineteen patients received US examination to evaluate the status of the whole urinary and genital system.

Two sonographers who had >10 years experience with conventional US of the small parts and >5 years experience with TRUS evaluation for VD disease were chosen to perform the examinations. All sonographic examinations were performed by an Esaote Mylab Twice unit (Esaote Health Care, Genova, Italy) equipped with a biplane transducer with the frequency band of 3 to 13 MHz (TRT33, transverse plane 3–9 MHz, longitudinal plane 4–13 MHz) and a linear probe with the frequency band of 3 to 14 MHz (LA523). We routinely scanned the testis, epididymis, intrascrotal VD, spermatic VD, and groin VD in transverse and longitudinal planes. The optimized Doppler parameters were used for color Doppler US examination. The power level, threshold, duration, and wall filter were adjusted to maximize the blood flow through the field of view. Next, the same method was used to probe the ampulla of VD and VD segment closing to the SV with the rectal double plane probe in 8 out of the 19 cases.

Sonographic findings were determined by retrospective analysis of the images. Two radiologists interpreted the grayscale and Color Doppler images to determine the location, echogenicity of the lesions, presence of hydrocele, presence of calcification, and presence or absence of blood flow in the lesions. In addition, the presence of combined inflammation of the epididymis and testis were evaluated. The echogenicity of each lesion was compared with that of the ipsilateral VD, testis, and epididymis.

When the epididymal duct was dilated but the VD was not dilated, the obstruction site was located at the junction of the VD and the tail of the epididymis. When the external pelvic VD were dilated and the internal pelvic VD were not dilated, the obstruction site was located in the inguinal channel. Previous studies have suggested seminal criteria and TRUS signs (including midline or eccentric prostatic cysts; ejaculatory duct [ED] dilation or calcifications; SVs transverse diameter >15 mm) suggestive of ED obstruction.<sup>[8]</sup> In addition, ED dilation was defined as >2 mm.

### 3. Results

There were 18 cases with VD abnormal ultrasonographic appearances in the 19 cases of patients with genital systemic TB, 14 cases with unilateral VD abnormal ultrasonographic appearances, while 4 cases with bilateral VD abnormal ultrasonographic appearances.

**Table 1**

**Sonographic appearances in 19 cases of the vas deferens tuberculosis.**

Type	Sonographic appearance	n (%)
1	Nodular thickened vas deferens	4 (4/19, 21.05%)
2	Diffusely thickened vas deferens	11 (11/19, 57.89%)
3	Space-occupying lesions adjacent to vas deferens	3 (3/19, 15.79%)
4	Normal finding	1 (1/19, 5.3%)

According to the pathological and ultrasonic findings, the ultrasonographic appearances of the VD TB could be divided into 4 groups, 1 of normal sonogram, 3 of abnormal sonograms. The ultrasonographic appearances of the VD TB were considered 4 categories as follows: nodular thickening of VD in 4 cases (category 1), diffuse thickening of VD in 11 cases (category 2), space-occupying lesions adjacent to VD in 3 cases (category 3), and normal ultrasonographic appearance in 1 case (category 4), as shown in Table 1 and Figures 1–4.

In the 4 cases with nodular thickening of VD (category 1), solitary nodule was found in 3 cases and multiple nodules were found in 1 case. The echogenicity of the nodules of VD were complicated. The diameter of the nodules was 3 to 8 mm, the boundaries were clear, the internal blood flow signals were poor, calcification was found in 2 cases, and irregular lumen stenosis was found in 1 case.

In the 11 patients with diffusely thickened VD (category 2), sonography showed widening of the outer diameter (about 1.7–9.0 mm) and inner diameter of VD (about 0.2–2.0 mm) of the VD, wall thickness enlargements of VD (about 1.0–2.5 mm) and heterogeneous tube echo. In 2 of the 11 cases, anechoic area was found in the VD. No obvious blood flow signals were found in VD in 9 cases, and internal linear blood flow signals were found in 2 cases. The VD intrascrotal segment thickening was observed in 9 cases. Whole thickening of the total segments was discovered in 2 cases, of which 1 was bilateral and the other 1 was unilateral.

In the 3 patients who had space-occupying lesions adjacent to the VD (category 3), sonography showed hypoechogenicity masses of about 11 × 7 × 8 mm, 22 × 12 × 17 mm, 49 × 35 × 40 mm, respectively, with clear boundary, regular shape, and flowing internal echoes. Internal spot-shaped blood flow signal was seen in 1 case, peripheral linear blood flow signal was seen in 1 case, and no obvious blood flow signal within and around was seen in 1 case.

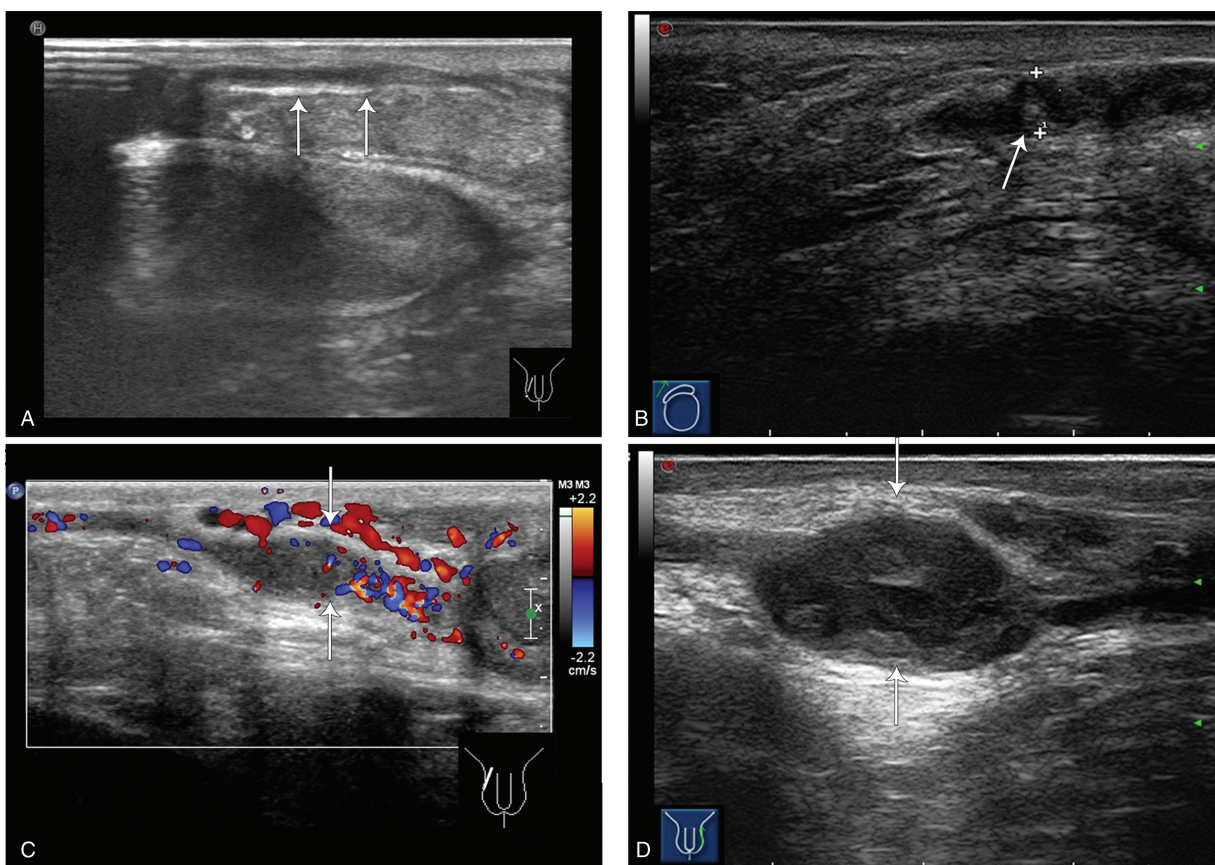
Normal ultrasonographic appearance of VD was seen in 1 case.

Male genital US characteristics of the whole genital system were investigated (Table 2, Fig. 5). Clinical features, andrological characteristics, fertility status, and semen characteristics of the 19 cases of male genital TB were summarized in Table 3.

## 4. Discussion

### 4.1. VD abnormal ultrasonographic appearance in TB of male urinary and genital system

Among cases of male reproductive system TB, epididymal TB is most commonly found in the clinic, while prostate TB is most frequently found in autopsy.<sup>[9]</sup> The VD are located between the prostate and epididymis, so both types of TB can involve the VD. The main pathological changes of the VD TB are tubercular and caseous necrosis, VD thickening, resembling cord-like or string of



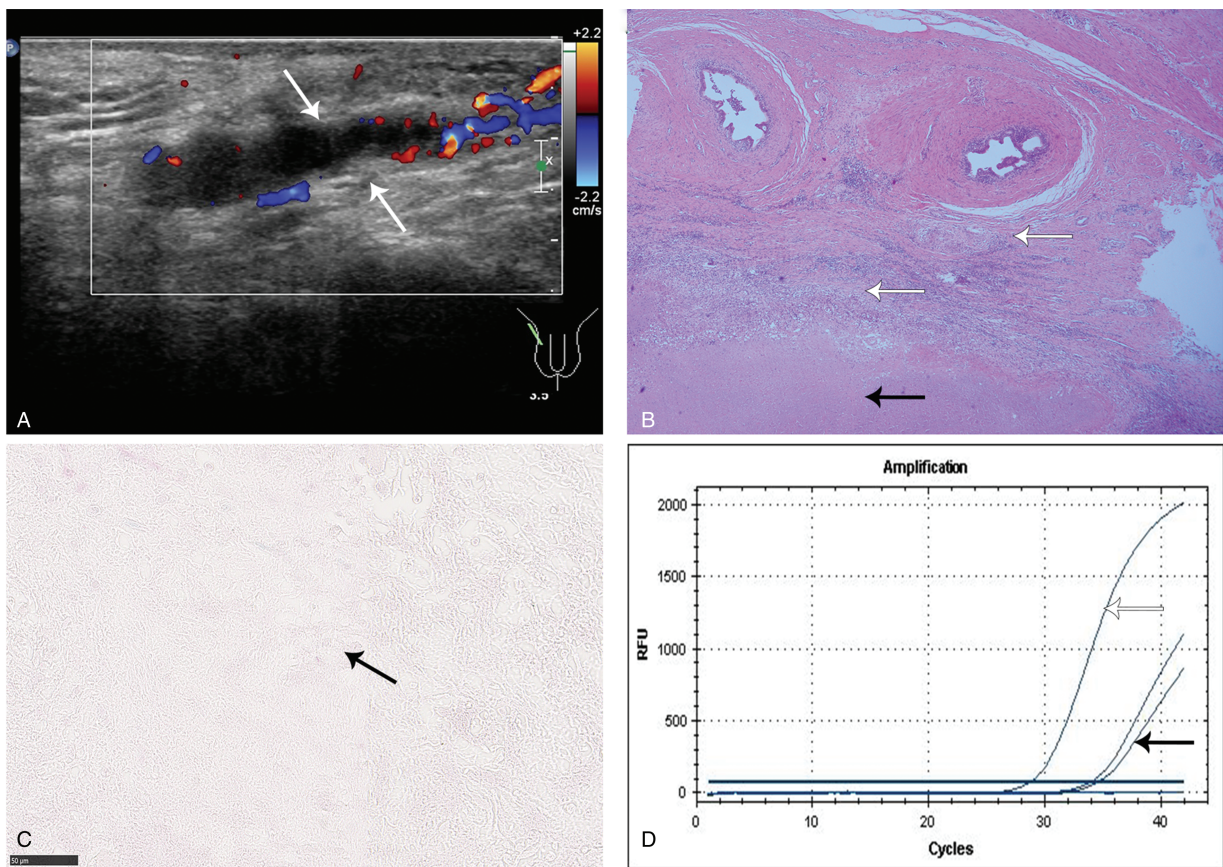
**Figure 1.** Ultrasonographic appearances of the VD tuberculosis. (A) Normal sonogram of VD, (B) Diffusely thickening of VD, (C) Nodular thickening of VD, and (D) Space-occupying lesions adjacent to the VD. (As indicated by the white arrows, respectively.). VD = vas deferens.

beads. The caseous necrosis of the VD subsequently penetrates through the wall of the VD and forms a tuberculous cold abscess near the broken VD. When the lesion of the VD TB is mild, there is no obvious abnormality visible by naked eyes. Eleven cases in the category 2 sonographically showed thickening of VD, heterogeneous hypoechoic, representing edema and proliferation of VD lesions. Four cases in the category 1 sonographically showed nodular thickening of the VD, heterogeneous internal echoes, representing the VD proliferation and necrosis, fibrosis, and calcification with liquefaction. Three cases in the category 3 sonographically showed masses adjacent to the VD, representing disappearance of the normal structure of VD, invasion of the outer membrane of VD by the lesion, and localized abscess formation in the VD side. One case was only diagnosed by pathology. High-frequency ultrasonography can display different types of blood supply of abnormal VD. Ultrasonography is the best imaging modality for the diagnosis of the diseases of male genital tract.<sup>[6]</sup> Yang et al reported<sup>[7]</sup> that the sonographic findings for tuberculous vasitis were heterogeneously hypoechoic with no blood flow in all 3 cases. Transrectal sonography is a useful modality to evaluate seminal duct abnormalities.<sup>[10]</sup> The SVs and the VD can also be affected by TB, and cross-sectional images show wall thickening, contraction, or intraluminal or wall calcifications.<sup>[11]</sup> With the improvement of resolution of ultrasonic diagnostic equipment, all parts of the seminal canal can be optimally displayed on US,<sup>[12]</sup> which makes ultrasonic diagnosis of VD disease a new choice. Inhomogeneity, hypoechoic or hyperechoic pattern, coarse epididymal calcifications, or epididymal hyperemia, which are considered typical CDUS

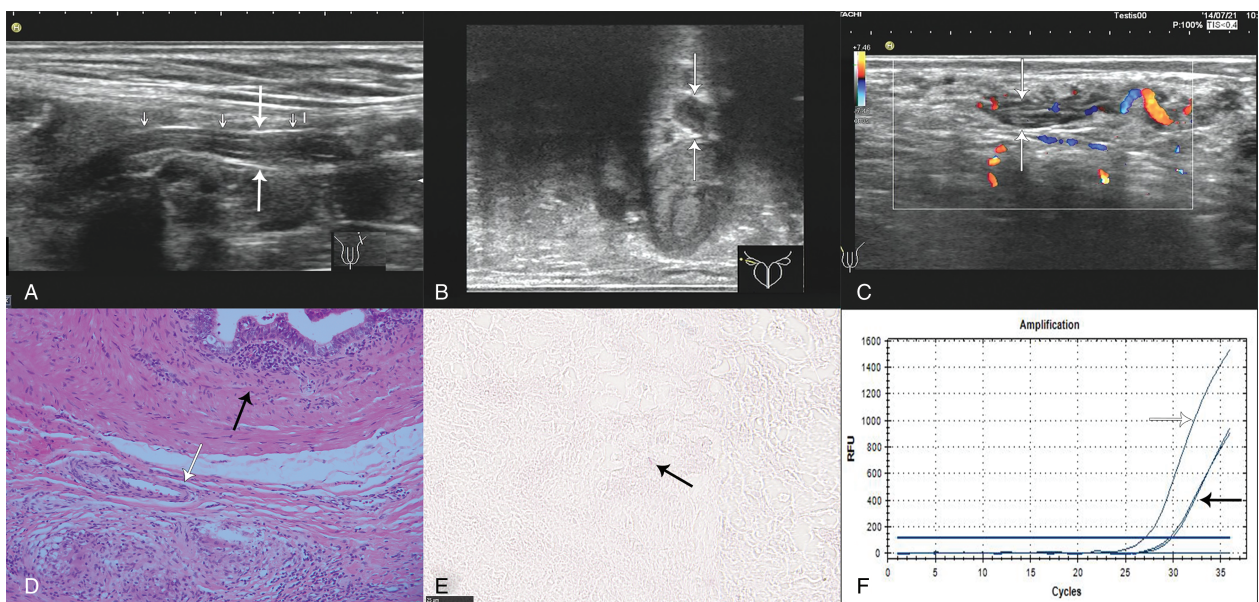
features of chronic epididymitis. Beyond that, an increased size (>6 mm) of the epididymal tail, inhomogeneous epididymal tail, and hyperechoic epididymal pattern are considered by some authors as CDUS features suggestive of male accessory gland infections.<sup>[13]</sup> Testis inhomogeneity and hypoechoic pattern at ultrasonography are suggestive of atrophy and fibrosis and considered important signs of a reduced testicular function and overall impairment of spermatogenesis.<sup>[14]</sup> SV hyperechogenicity is a parameter indicative of fibrosis of the glands, the end stage of an inflammatory process. Furthermore, thickening and calcification of the SV glandular epithelium are considered by some authors as US features suggestive of MAGI.<sup>[15]</sup> A higher prevalence of prostate moderate-severe nonhomogeneity, hypoechoic texture, and hyperemia were observed in prostatitis-like symptoms males of infertile couples.<sup>[16]</sup> There are very few reports of scrotal US for the diagnosis of TB of the VD,<sup>[7]</sup> or only VD TB was reported as part of ultrasonography for the diagnosis of male urinary and genital tract TB.<sup>[6]</sup> In this study, the VD ultrasonographic manifestations of 19 male genital TB patients were examined through scrotum and rectum. Since the VD could only be partially removed for pathological examination, it was not possible for all abnormal VD in US to be directly confirmed by pathological examination of VD specimens.

#### 4.2. Ultrasonic diagnosis and differential diagnosis of VD TB

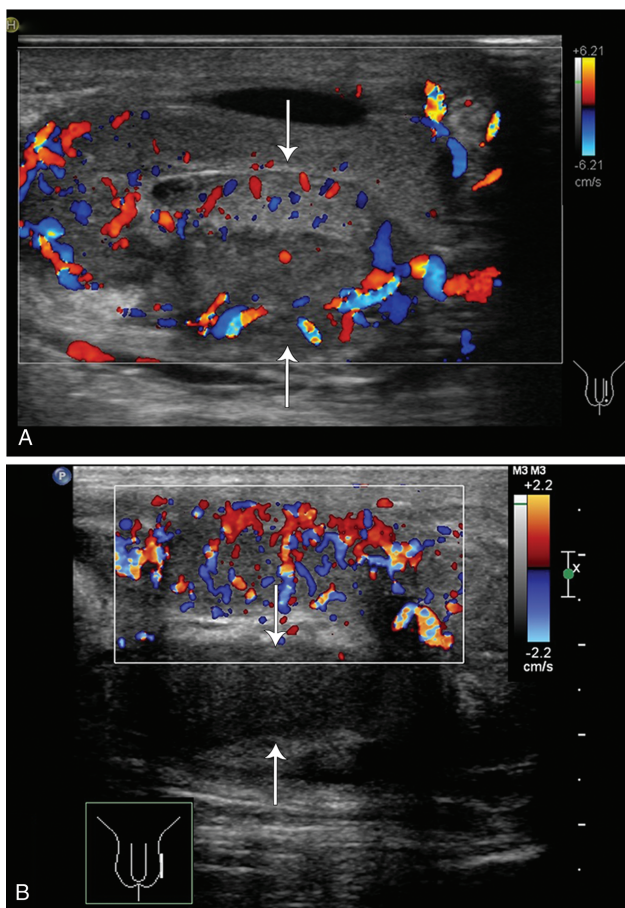
The diagnosis of TB of VD cannot clarify without the history of TB of other organs. In this study, 19 cases of TB of male urinary



**Figure 2.** VD tuberculosis ultrasound findings (category 1, nodular thickening) and pathology results. (A) White arrow shows that the right VD was segmentally thickened in scrotum. (B) The granuloma (white arrow) and caseous necrosis (black arrow) was found at the peripheral region of the VD in the picture of HE staining ( $\times 40$ ) after the vasectomy. (C) In the acid-fast staining picture, the coral-red positive bacillus was visualized (black arrow). (D) The 2 lines represent the amplification of the tuberculosis DNA fragments in the positive control group and the case group which was indicated by the white arrow and black arrow in the qPCR test, respectively. VD = vas deferens.



**Figure 3.** VD tuberculosis ultrasound findings (category 2 diffusely thickening VD) and pathological results. (A) The thickened wall and dilated lumen were indicated in the groin segment of the left VD in a 58-year-old man by the white arrow. (B) The right VD pelvic segment of the patient. Thickened VD wall was indicated by the white arrow, inside which the dilated lumen was revealed. (C) The thickened wall and dilated lumen was also indicated in the groin segment of the right VD by the white arrow. The CDFI picture shows abundant blood signals. (D) In the HE staining ( $\times 200$ ) slides, the black arrow indicates the wall of the VD, white arrow indicates the granuloma. (E) In the acid-fast staining slide, black arrow indicates the coral-red positive bacillus. (F) The 2 lines represent the amplification of the tuberculosis DNA fragments in the positive control group and the case group which was indicated by the white arrow and black arrow in the qPCR test, respectively. CDFI = color Doppler flow imaging, VD = vas deferens.



**Figure 4.** VD tuberculosis ultrasound findings (category 3, space-occupying lesions adjacent to vas deferens). (A) A male 56-year-old genital tuberculosis patient before antituberculosis treatment. The beginning of VD (the white arrow) was obviously enlarged as a spherical mass. Inside the mass, the echogenicity was heterogeneous. (B). In the same patient of Figure 4A, after treatments, the beginning of VD (indicated by the white arrow) was shrunk as rod-shaped mass and the echo was homogenous. VD=vas deferens.

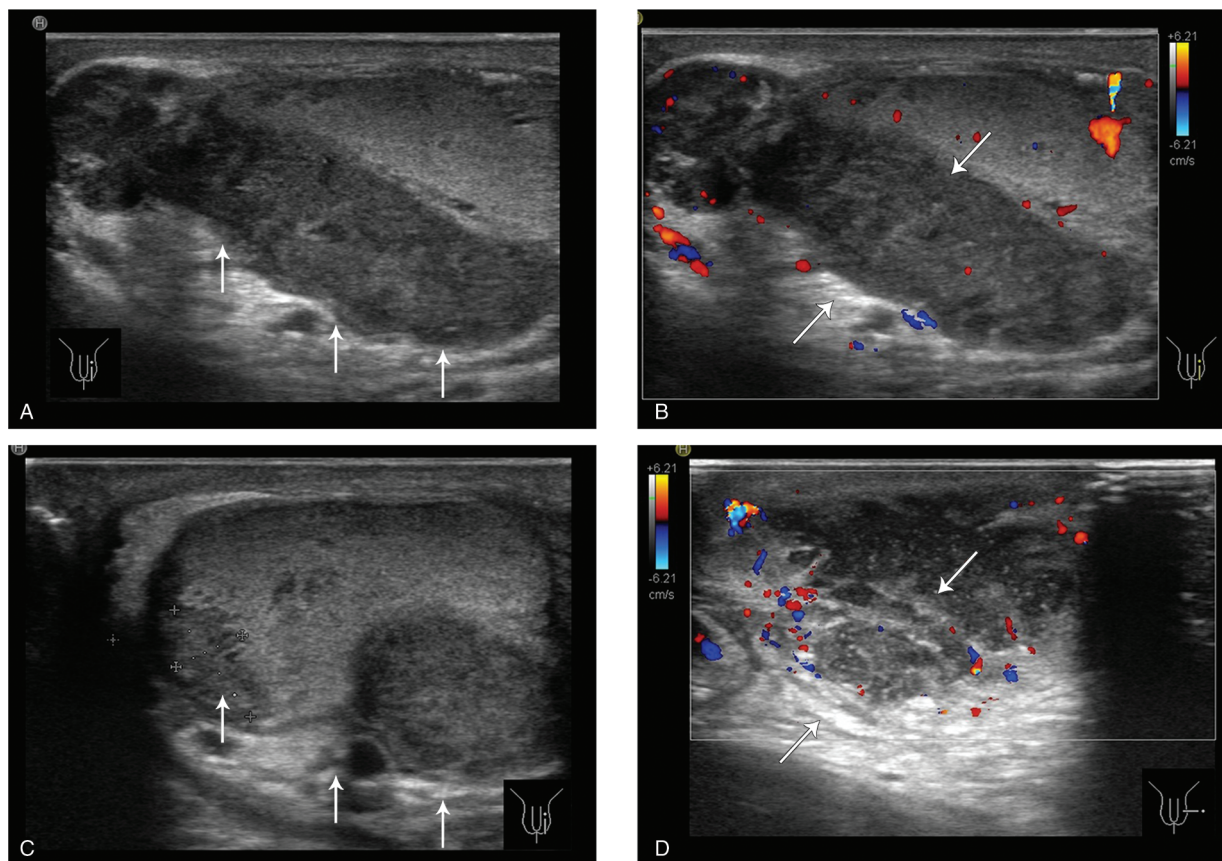
and genital system were accompanied by TB of other organs, and there was no case of simple TB of the VD. The US examination of the male reproductive system is crucial, especially the US imaging of each segment of VD. For ideal results, both scrotal US and TRUS are needed. The sonographic characteristics of testicular TB, epididymal TB are helpful for the ultrasonographic diagnosis of the VD TB. Drudi et al<sup>[17]</sup> and Türkvtan et al<sup>[18]</sup> described multiple small hypoechoic nodules in the enlarged testis as the miliary type and suggested that this sonographic pattern was a feature of TB orchitis. Kim et al suggested that an enlarged heterogeneous epididymis can differentiate TB from non-TB epididymitis.<sup>[7]</sup> A heterogeneously hypoechoic pattern of epididymal enlargement, bilateral epididymal involvement, and concomitant testicular lesion strongly suggest TB, especially in patients with evidence of TB elsewhere in the body and failure of conventional antibiotic therapy.<sup>[19]</sup> The disease usually starts in the caudal portion of epididymis, perhaps due to its richer blood supply as compared to other parts of the epididymis, or because it is the first portion involved by urinary reflux along the VD.<sup>[20]</sup> Therefore, TB of the VD is often accompanied by epididymal TB. Yang reported that the sonographic findings for tuberculous vasitis were heterogeneously hypoechoic in all the examined cases. On color Doppler sonography, no blood flow was

**Table 2**  
**Ultrasound data about the male genital system of the 19 patients with tuberculosis.**

Prostate	
Prostate mean volume, mL	17.6 ± 4.12
Prostate calcifications (n, %)	14, 73.7
Inhomogeneous prostatic texture (n, %)	9, 47.4
Hypoechoic prostatic texture (n, %)	3, 15.8
Prostatic hyperaemia (n, %)	8, 42.1
Seminal vesicles	
Mean anteroposterior diameter, mm	9.90 ± 2.68
Hyper-echoic seminal vesicles (n, %)	7, 36.8
Unilateral (n, %)	5, 26.3
Bilateral (n, %)	2, 10.5
Wall thickening and septa (n, %)	6, 31.6
Ejaculatory ducts	
Dilated ejaculatory duct (n, %)	6, 31.6
Unilateral (n, %)	5, 26.3
Bilateral (n, %)	1, 5.3
Ejaculatory duct calcifications (n, %)	3, 15.9
Unilateral (n, %)	2, 10.6
Bilateral (n, %)	1, 5.3
Testis	
Mean testis volume, mL	13.31 ± 5.88
Varicocele (n, %)	2, 10.5
Unilateral (n, %)	2, 10.5
Bilateral (%)	0, 0
Epididymis	
Mean size of the head, mm	8.38 ± 2.39
Mean size of the tail, mm	8.38 ± 4.57
Inhomogeneous epididymis (n, %)	12, 63.2
Unilateral (n, %)	7, 36.8
Bilateral (n, %)	5, 26.3
Hypo-echoic epididymis (n, %)	12, 63.2
Unilateral (n, %)	7, 36.8
Bilateral (n, %)	5, 26.3
Hyperechoic epididymis (n, %)	3, 15.9
Unilateral (n, %)	2, 10.5
Bilateral (n, %)	1, 5.3
Coarse epididymal calcifications (n, %)	12, 63.2
Unilateral (n, %)	8, 42.1
Bilateral (n, %)	4, 21.1
Hyperaemic epididymis (n, %)	4, 21.1
Unilateral (n, %)	2, 10.5
Bilateral (n, %)	2, 10.5
Increased (6 mm) epididymal tail (n, %)	12, 63.2
Unilateral (n, %)	4, 21.1
Bilateral (n, %)	8, 42.2
Vas deferens	
Mean diameter of the vas deferens, mm	2.43 ± 1.03
Differential ampulla calcifications (n, %)	1, 5.3
Obstruction of the seminal tract	
Obstruction among epididymis tail and vas deferens	
Unilateral (n, %)	13, 68.4
Bilateral (n, %)	3, 15.9
Ejaculatory duct obstruction	
Unilateral (n, %)	5, 26.3
Bilateral (n, %)	2, 10.5
Inguinal obstruction	
Unilateral (n, %)	1, 5.3
Bilateral (n, %)	0, 0

Data are expressed as mean ± SD and as percentages when categorical.

identified within the lesions of the VD.<sup>[7]</sup> There were 11 cases of heterogeneous hypoechoic signals in the VD, accounting for 57.90% (11/19), and 3 cases of internal blood flow signal, accounting for 15.79% (3/19).



**Figure 5.** Ultrasonographic appearance of the epididymis in tuberculosis of the male genital system. (A) The left epididymis of a male 56-year-old male genital tuberculosis patient was visualized (white arrow). (B) The left epididymis blood signal was abundant (white arrow). (C) The enlarged epididymis behind the left inhomogeneous testicle was indicated by the white arrow. (D) The abscess in the left scrotal wall was indicated by the white arrow.

Anatomic obstruction by granulomas or distortion of the normal anatomy by fibrosis surrounding the reproductive tract is the commonest cause of infertility.<sup>[21]</sup> All attempts must be made for early diagnosis and treatment of this condition

**Table 3**

**Clinical features, andrological characteristics, fertility status, and semen characteristics of the 19 cases of vas deferens tuberculosis.**

**All patients (n=19)**

Clinical features	
Chronic pelvic pain (n, %)	4, 21.1
Hemospermia (n, %)	0, 0
Pulmonary tuberculosis (n, %)	5, 26.3
Epididymal mass (n, %)	10, 52.6
Andrological characteristics	
Cryptorchidism (n, %)	0, 0
Varicocele (n, %)	2, 10.5
Prader testicular volume decrease (n, %)	7, 36.8
Scrotal spermatic cord pain (n, %)	4, 21.1
Spermatic cord hardening (n, %)	1, 5.3
Testicular induration (n, %)	1, 5.3
Fertility status	
Primary infertility (n, %)	6, 31.6
Secondary infertility (n, %)	1, 5.3
Semen characteristics	
Azoospermia (n, %)	1, 5.3
Asthenospermia (n, %)	5, 26.3

to avoid unnecessary epididymectomy and adverse effect on fertility.<sup>[19]</sup> Local symptoms are usually insidious and progressive. Systemic manifestations such as fever, chills, and sweat are rare in isolated genital TB. Tuberculous genital infection can be confused with other bacterial (including nontuberculous mycobacterial) infections, fungal disease, tumors, and cysts as well as with numerous uncommon illnesses.<sup>[22]</sup> Some clinical findings, gray-scale sonography, and color Doppler sonography were useful in differentiating tuberculous epididymal abscess from pyogenic epididymal abscess. The presence of long-term scrotal swelling without tenderness and a lower degree of blood flow in the peripheral portion of a large abscess are suggestive of tuberculous epididymal abscess.<sup>[23]</sup> But in our study, the appearance of CDFI of the space-occupying lesions adjacent to VD varied in 3 cases. The manifestation was including internal spot-shaped blood flow signal, peripheral linear blood flow signal, and no obvious blood flow signal within and around, respectively. That may suggest different treatments. Furthermore, spermatic granulomas often require identification with the VD TB. However, sperm granuloma in VD is more common after vasectomy or trauma. There was no history of vasectomy or trauma in 19 cases. Calcification of the VD and SVs has been described in association with genitourinary TB, diabetes, and hyperparathyroidism, amongst other conditions.<sup>[24,25]</sup> For genitourinary TB, the fertility outcome is crucial. Sperm retrieval and cryopreservation should be considered for potential intracytoplasmic sperm injection.<sup>[26]</sup>

### 4.3. Relationship between ultrasonographic abnormal manifestations of VD and reproductive system and treatment options in TB of the genital system

TB of the male genital system should be systematically and comprehensively assessed. Prostate and SV TB are generally conservatively treated.

TB of VD and epididymis with substantial echo, without abscess formation or invasion of surrounding tissues should be conservatively treated. The rich blood supply in lesion or intratunical rifampicin injection has a good curative effect.<sup>[27]</sup> TB of VD and epididymis with mixed echo, abscesses, sinus formation or invasion of surrounding tissues or testicles should be surgically treated, and preoperative and postoperative anti-TB treatment should be given. In this study of 19 surgical cases, preoperative or postoperative anti-TB treatment led to reduction of the VD lesions in 12 cases. The transrectal and trans-scrotal US should be reviewed at 2 to 3 months after anti-TB treatment.<sup>[28]</sup> The treatment plan should be adjusted according to the results of the US examination.

## 5. Conclusions

In summary, TRUS and scrotal US are inexpensive, noninvasive and available in most urology and andrology departments. This study indicated that US manifestations of VD in tuberculosis of the male genital and urinary system have certain characteristics. Combination of clinical manifestations, history of TB, experimental anti-TB treatment, and US examination of VD can suggest TB of VD.

## 6. Limitations

This study had some limitations. It was subject to recall bias owing to its retrospective nature. The number of cases was relatively small, with only 7 surgery cases, and early cases were few.

## Author contributions

**Conceptualization:** Jigang Jing, Hua Zhuang, Yan Luo.

**Data curation:** Jigang Jing.

**Formal analysis:** Jigang Jing, Hua Zhuang, Yan Luo, Yaping Rao.

**Investigation:** Jigang Jing.

**Methodology:** Jigang Jing, Hua Zhuang, Yan Luo, Yaping Rao, Huijiao Chen.

**Project administration:** Jigang Jing, Yaping Rao.

**Resources:** Jigang Jing, Hua Zhuang, Yan Luo.

**Supervision:** Jigang Jing, Hua Zhuang.

**Visualization:** Hua Zhuang, Yaping Rao.

**Writing – original draft:** Jigang Jing, Hua Zhuang.

**Writing – review and editing:** Jigang Jing, Hua Zhuang, Yan Luo, Yaping Rao.

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