Etiology, Diagnosis, and Management of Seminal Vesicle Stones

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Abstract

Background/Aims: Seminal vesicle (SV) stones are a rare, and thus readily misdiagnosed condition in practice. Understanding the etiology, diagnosis, and management are crucial to guide a urologist’s care, and are provided in this literature review. Methods: The inclusion criteria for the literature search, using the search engines MEDLINE® and PubMed was conducted using a combined query of “seminal vesicle stone” and the following keywords: calculi, hematospermia, calcification, and transrectal ultrasound (TRUS). Results: The etiology of SV stones is currently unknown where majority of the patients present with having painful ejaculation and hematospermia. However, clinicians have reported potential etiologies by categorization as an inflammatory or non-inflammatory. A majority of the previous cases had shown multiple stones being present in the SV duct system that are typically diagnosed through radiological examination such as TRUS, MRI, or plain radiographs. Amongst the many imaging approaches, TRUS remains the primary imaging diagnoses of SV calculi. Transurethral seminal vesiculoscopy has shown to be used in an abundant of the case reports to be an ideal surgical approach for managing small SV stones. In regard to larger stones, a transperitoneal laparoscopic protocol is proper. Conclusion: The current imaging techniques have increased the case reports and diagnosis of SV calculi; however, more research is warranted for understanding the pathogenesis of the formation of SV stones. An optimal management of the extraction of SV stones depends on a number of factors such as size and location.

Introduction

Seminal vesicles (SV) are paired secretory glands located posterior to the bladder in men that produce seminal fluid to maintain sperm. This seminal fluid contributes approximately up to 80% of the ejaculate volume [1]. Several benign and malignant conditions such as cysts, infections, abscess, neoplasms, and stones can affect this organ. Presently, we focus on the latter – stones or calculi. White [2] had reported the first SV stone case in 1928, where a 48-year-old man complained of pain in the perineum and rectum along with urinary symptoms. However, SV stones are typically rare occurrences; lim-
limited cases have been reported mainly in adults older than 40 years of age, often associated with seminal vesiculitis, with some reports also in children. Since then, many of the cases have been related to urinary tract infections, anomalies, obstruction, and reflux into the ejaculatory duct [3]. Patients presenting with these stones may also be asymptomatic or symptomatic by expressing symptoms of peritoneal or testicular pain, painful ejaculation, low ejaculate volumes, hematospermia, or infertility. Transrectal ultrasound (TRUS) screening has been introduced in evaluating patients, detecting SV calculi in patients with hematospermia [4]. Due to the rarity of this condition, the etiopathogenesis of the stone formation is unclear to many clinicians leading to misdiagnosis and lack of awareness to various treatment protocols. The primary objective of this review is to facilitate the clinical importance by providing a comprehensive understanding of SV stones as well as compiling recent research to contribute the knowledge of the etiopathogenesis, clinical presentation, and available management options.

### Anatomy of Ejaculatory Pathways

The SVs are part of the male genitourinary system, which is considered to be an accessory glandular structure of the male reproductive system [5]. The male genital organs consist of the penis, testes, excretory genital ducts, vas deferens, SVs, prostate, and bulbourethral glands. These organs work collectively together to generate and excrete semen, containing mature spermatozoa.

The SVs are bilateral glands approximately 5–7 cm in length. They are located dorsally to the bladder, and inferior and lateral to the vas deferens, posterior to the prostate, as well as superior to the rectum [6]. In addition, the SVs lie at the inferior end of the recto-vesicle space in the pelvic cavity. The ducts of the SV join with the ampulla of the vas deferens to form the ejaculatory duct. The ejaculatory ducts extend further inferiorly, which drain into the prostatic urethra through the verumontanum. The primary function of SVs is to secrete a fluid that forms a majority of the ejaculate; however, SVs are not a reservoir of the semen [7]. The fluid that is secreted is composed of proteins, fructose, and various other enzymes that provide nutrition for the spermatozoa.

When evaluating through imaging, a normal SV appears to be elongated fluid-containing structures. The deviations in the appearance are secondary to age and hormonal changes in a patient. Normally, SVs shrink following the age of 70.

| Differential diagnosis |
|------------------------|
| Hematospermia          |
| Inflammatory processes |
| Gonorrhea              |
| Hypoplasia             |
| Prostatitis            |
| SV cysts               |
| Tuberculosis           |
| Urinary tract infection|
| Chronic infection      |
| Diabetes mellitus      |
| Hyperparathyroidism    |
| Neoplasm               |
| Obstructive azospermia |
| Prostate cancer        |
| Reflux of urine        |
| SV and prostatic schistosomiasis |
| Uremia                 |
| Seminal vesicle adynamia [32] |

The nuclei of SV stones are composed of epithelial cells and a mucoid substance that is covered with lime salts [8]. Previous literature reports have shown SV stones to be composed of calcium phosphate, magnesium ammonium phosphate (e.g. struvite), or protein matrix. Menon et al. [9] found that most of the calculi are coated with calcium phosphate, phosphate, urate, carbonate, and struvite. However, Hepburn et al. [10] did not find any abnormality in the urinalysis of the calcium-coated calculi. In addition, Han et al. [11] reported the composition of the SV stone to be calcium fluorophosphate while Yun et al. [3] reported it as carbonate apatite along with urine reflux indicating it as an infectious stone.

### Etiology

The exact etiology of SV stones remains unclear. Analyses of SV stones are conducted through imaging; however, no definite cause has been ascertained to SV stones. Table 1 presents potential etiologies that have been reported [12].

**Calcification of SV**

Calcification of the vas deferens and SV is a rare condition of unknown incidence. Calcification of the SVs was first discovered in the year of 1906 by reporting...
calcium deposition in the right SV as well as in the left vas deferens [13]. In regard to the etiology, calcification cases of SV have been divided into inflammatory and non-inflammatory. The latter type is prevalent in patients of old ages secondary to sclerosis and impaired nutrition of the musculature and connective tissue of the SV, including the ampulla and ejaculatory ducts [14].

In 1951, based on radiographs depicting calcifications of vas deferens, Wilson et al. [15] associated the calcifications with diabetes mellitus (DM) and atherosclerotic changes. In his study, 93% of the patients exhibited DM and 2 patients presented with chronic inflammation of the genital tract as a presumed risk factor towards the calcifications. The role of DM in calcification is suggested to be due to insulin therapy, where patients suffering from DM for many years will exhibit degenerative vascular disease [16]. In regard to the inflammatory type, the calcifications can be mucosal or submucosal and, as a result, there may be partial or complete obstruction of the vas deferens [17–19]. In 2006, the analysis of SV stones by infrared spectroscopy had revealed magnesium ammonium phosphate [19]. However, no present cause has been ascertained towards the pathogenesis of SV calcification. Stasinou et al. [18] reported that the pathogenesis of the calcification of the wall of the SVs should be differentiated from SV stones.

**Hematospermia**

Hematospermia is the presence of blood in seminal fluid. It is a relatively frequent urologic condition, which causes severe anxiety to patients and may be caused by inflammation, obstructive cystic lesions, calculi, benign or malignant neoplasms, and stasis [4, 20, 21]. However, malignancies are rare instances in causing hematospermia. In many patients presenting with hematospermia, calculi of ejaculatory ducts have found to be the root cause [22].

**Impaired Drainage and SV Cysts**

SV cysts are a rare entity that may be congenital or acquired and generally associated with hematospermia. However, SV cysts have been reported in cases where SV calculi have been present [22, 23]. Stones may form secondary to the obstruction caused by the cysts as well as to the drainage of the secretions during ejaculation. Such calculi can contribute to wall thickness in the ejaculatory duct leading to the impaired drainage [20]. This has been noted in 60% of the case reports of patients diagnosed with SV calculi [20]. In a study where pancreatic stones were shown to have similar composition as SV calculi, it suggested that the lack of proteases be linked to SV stone formation [23]. SV cysts appear as large, anechoic masses on TRUS [4].

In addition, a few cases have reported urine reflux into ejaculatory ducts on post-voiding cystography. A combination of impaired drainage of the ejaculatory duct, urine reflux, urinary tract infections, and seminal vesiculitis can lead to the formation of SV calculi [1]. Yun et al. [3] reported that the reflux from the urethra to the SVs was identified in the retrograde urethrogram.

**Clinical Evaluation of Seminal Calculi**

**Physical Examination and Symptoms**

Common symptoms for SV calculi ranges from asymptomatic to patients exhibiting hematospermia, perineal or testicular pain, painful ejaculation, or low ejaculatory volume [19]. Ejaculatory pain and hematospermia are the two most common symptoms that lead patients to seek medical care. SV stones can be distinguished from a condition such as posterior urethral hemangioma as it uniquely presents with dark red blood–semen mixture with ejaculation pain and no blood clots – symptoms which withdraw upon anti-infective treatment [24]. Table 2 displays the diverse profiles of some symptoms occurring in patients associated with SV calculi. The occurrences of each symptom were gathered from case reports.

| Table 2. Symptoms presenting with SV stones |
|-------------------------------------------|
| **Symptom**                               |
| Erectile dysfunction                      |
| Graveluria                                |
| Hematospermia                             |
| Hematuria                                 |
| Infertility                               |
| Low ejaculatory volume                    |
| Pain                                      |
| Abdominal                                 |
| Ejaculation                               |
| Groin                                     |
| Perineal                                  |
| Rectal                                    |
| Testicular                                |
| Urinary tract                             |
| Dysuria                                   |
| Increased frequency of micturition        |
| Urinary tract infection                   |
| Urine reflux                              |
| Voiding                                   |
| Urinary tract                             |
| Spemolithias                              |

**Erectile dysfunction**
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**Testicular**
**Urinary tract**
**Dysuria**
**Increased frequency of micturition**
**Urinary tract infection**
**Urine reflux**
**Voiding**
**Urinary tract**
**Spermolithiasis**
### Table 3. Profiles of reported cases of SV stones

| Year | Country      | Study type      | Age      | Clinical presentation                                                                 | Diagnostic modality                  | Outcome                                                                 | Ref.       |
|------|--------------|-----------------|----------|---------------------------------------------------------------------------------------|---------------------------------------|--------------------------------------------------------------------------|------------|
| 1928 | USA          | case report     | 48       | hematospermia, voiding frequency, and perineal discomfort                               | DRE                                   | first case report of SV calculi and received seminal vesiculoscopic lithotripsy | [33]       |
| 1983 | USA          | case report     | NA       | urine reflux into bilateral ejaculatory ducts                                          | DRE; retrograde urethrogram           | bilateral seminal vesectomy                                              | [34]       |
| 1984 | Japan        | case report     | 7        | terminal pain on urination                                                              | plain radiograph; urethrogram         | stones present in the posterior urethra and in SV                         | [2]        |
| 1988 | USA          | single case     | NA       | hematospermia, ejaculatory pain, and perineal pain                                     | TRUS                                  | NA                                                                       | [22]       |
| 1990 | UK           | single cohort   | 25–77    | hematospermia                                                                         | TRUS                                  | NA                                                                       | [35]       |
| 1991 | China        | case report     | 53       | testicular, perineal, and groin discomfort                                              | DRE; plain radiograph; CT             | transrectal removal of calculus                                            | [36]       |
| 1993 | UK           | case report     | child    | terminal dysuria                                                                     | plain radiograph; fruitless cystolithotomy; followed by seminal vesectomy |                                                           | [37]       |
| 1994 | Japan        | single cohort   | 12–71    | hematospermia                                                                         | TRUS                                  | NA                                                                       | [38]       |
| 1994 | USA          | single case     | 25–77    | hematospermia                                                                         | TRUS                                  | NA                                                                       | [39]       |
| 1995 | South Korea  | single cohort   | 20–59    | hematospermia and perineal pain                                                       | E-MRI                                 | NA                                                                       | [40]       |
| 1997 | UK           | case report     | 7        | recurrent epididymo-orchitis                                                           | CT                                    | extraperitoneal extraction of calculi                                     | [41]       |
| 1997 | USA          | case report     | 25       | pain with ejaculation and hematospermia                                               | TRUS                                  | NA                                                                       | [23]       |
| 1999 | Italy        | single cohort   | 23–71    | hematospermia                                                                         | E-MRI                                 | NA                                                                       | [42]       |
| 2001 | USA          | case report     | 32       | azoospermia and low ejaculate volume                                                   | TRUS                                  | transurethral resection of the ejaculatory ducts and restored fertility post 3 months | [43]       |
| 2002 | Turkey       | case report     | 35       | perineal and testicle pain                                                            | plain radiograph; TRUS                | seminal vesectomy                                                         | [44]       |
| 2002 | Turkey       | case report     | 40       | terminal pain on urination and hematospermia                                         | TRUS                                  | perineal approach                                                         | [44]       |
| 2002 | UK           | case report     | 82       | constant lower abdominal pain, frequency of micturition                               | plain radiograph; CT                 | NA                                                                       | [45]       |
| 2002 | South Korea  | single cohort   | 28–68    | hematospermia                                                                         | TRUS; MRI                             | TRU-SVS                                                                   | [28]       |
| 2004 | India        | case report     | 35       | increased frequency of micturition, dysuria, and lower abdominal pain                  | plain radiograph; symptomatic bilateral large SV calculi where seminal vesiculectomy was performed | endoscopic fragmentation of stones | [19]       |
| 2005 | Turkey       | case report     | 31       | perineal pain, painful ejaculation, and infertility                                  | TRUS; seminal analysis               | endoscopic fragmentation of stones                                      | [8]        |
| 2006 | USA          | case report     | 25       | painful and low volume ejaculation, and complaints of passing “granules” in the semen | TRUS                                  | seminal vesiculscopy with endoscopic laser lithotripsy of calculi         | [46]       |
| 2006 | India        | case report     | 53       | recurrent urinary tract infection and dysuria                                         | TRUS                                  | endoscopic stone removal (cystourethroscopy)                              | [47]       |
| 2007 | Singapore    | care report     | 37       | perineal discomfort and graveluria                                                    | CT                                    | endoscopic fragmentation of calcui (cystoscopy and litholapaxy)           | [48]       |
| 2008 | South Korea  | case report     | 20       | small volume ejaculate, without hematospermia, painful ejaculation and lower urinary tract symptoms | CT; urethrography                     | transperitoneal laparoscopic stone removal and partial seminal vesiculectomy | [3]        |
| 2008 | China        | case report     | 62       | hematospermia, painful ejaculation, perineal pain, and irritable voiding symptoms     | TRUS; CT                              | transperitoneal laparoscopic removal of calculi                            | [11]       |
| 2008 | Brazil       | single cohort   | 25–72    | hematospermia, perineal discomfort, ejaculatory pain                                 | E-MRI                                 | NA                                                                       | [49]       |
| 2009 | South Korea  | single cohort   | 29–67    | hematospermia                                                                         | TRUS; E-MRI                           | TRU-SVS                                                                   | [50]       |
Imaging

Imaging is the conventional way of diagnosing stones present in the SVs. Noninvasive imaging is recommended for essential diagnostic evidence of stones. Modalities for diagnosis include vasoseminal vesiculography, MRI, CT, and TRUS. Vasoseminal vesiculography is an invasive procedure; the lesion of the puncture site may be too narrow which can induce secondary seminal ductal obstruction [25]. The diagnosis of SV calculi can be done through an MRI, which is able to visualize the distal duct system. Nevertheless, its high expense detracts from its preference [20]. Clinicians advise that the combination of an endorectal coil and MRI will provide a more viable diagnosis. However, it has been noted that these examinations yield a false-positive rate as well as diagnostic limitations secondary to the false-negative cases [25]. Thus, clinical applications through the diagnosis of an MRI are limited. It was also previously reported that CT scans are not viable due to the poor visualization of the distal duct system.

TRUS is a noninvasive examination frequently used for diagnosing stones, cysts, increases in SV volume, Mullerian duct remnants, prostatic varices, and inflammatory changes [25, 26]. It has shown to be the most accurate form of visualization of the distal duct system along with assorted abnormalities, which can provide clinicians with a comprehensive visual examination to administer the appropriate treatment protocols [20]. In a single case-control study using TRUS, calculi within the SVs appeared as well-circumscribed, hyperechoic, foci separate from the typical septal architecture of the prostate gland, with or without acoustic shadowing [22]. In children, a retrograde urethrogram or voiding cystourethrogram may be used to distinguish between SV and posterior urethral calculi [19].

Management

Non-Surgical Treatment Protocols

Pre-Operative Sperm Banking

Patients who receive fertility preservation consultation often proceed to sperm banking, which provides a sense of security and reassurance in the future. Sperm banking is a noninvasive procedure that involves the collection and freezing of sperms for potential use in the future [27].

Surgical Intervention

SV calculi must be corrected through surgical treatment in a timely fashion, as they may progress to worsened pain and potentially obstruct the SVs leading to the need for an emergency surgery. Upon diagnosis through
the various noninvasive diagnostic methods, including high-resolution TRUS, MRI, CT, or plain radiographs, the patient is recommended to undergo surgery for the removal of the stones present in the SV. However, the choice of surgical protocol depends on the location and size of the stone.

**Endoscopic Removal** The SV organ is difficult to access. Most open surgical approaches used for treating primary or secondary lesions of the SVs have inherent shortcomings and require a significant incision for access [8]. However, open operation requires extensive dissection which might cause morbidities associated with an exposed operative field, long operative time, and intraperitoneal rupture [11]. Laparoscopic and endoscopic approaches are substitutes to the standard surgical treatments in order to overcome these complications. The first large sample study of transurethral endoscopy technique was conducted in 2002 by Yang et al. [28] where patients were suffering from SV disease, concluding that the method was feasible and safe.

**Transurethral Seminal Vesiculoscopy** The standard recommended therapy includes laparoscopic/open seminal vesiculectomy or transurethral resection of ejaculatory duct (TURED). Previous studies have reported that status post TURED has improved semen parameters by 50–60% in patients, despite being associated with a high risk of complications such as the impairment of semen parameters, retrograde ejaculation, urine reflux into the seminal duct, urinary incontinence, and rectal injury causing urethral fistula [25, 29]. Postoperative complications of TURED are rare but often severe; for this, the procedure requires highly technical skills.

In recent years, transurethral seminal vesiculoscopy (TRU-SVS) has shown to be a safe, minimally invasive surgical procedure for the management of both SV and ejaculatory duct calculi. In comparison to TRUS, TRU-SVS requires surgical skills, anesthesia, and antibiotic cover. A retrospective study of TRU-SVS utilized a 6F vesiculoscope inserted through the orifice of the verumontanum in a retrograde manner. Following insertion, the calculi were removed using grasping forceps or by disrupting the calculi with a holmium laser. Clinicians should be cautious regarding the insertion of the vesiculoscope to avoid secondary injury to the urethra or rectum. Xu et al. [30] had used a 9F rigid ureteroscope in which gaining entry into the SV became challenging where applying excessive force could cause damage to the tissue. Thus, a 6F vesiculoscope is likely safer and more effective than using a 9F ureteroscope. TRU-SVS has shown to be a more attractive option than TURED due to lower complications and having significant improvement in sperm counts and ejaculation volume, thus improving fertility [29]. The avoidance of urine reflux was also postoperatively observed. Furthermore, seminal vesiculography can be performed transrectally in patients who do not want to undergo a transurethral procedure [31]. Many case reports have proven that TRU-SVS can lead to the solution of treating seminal vesiculitis, hematospermia, ejaculatory duct obstruction, and infertility.

**Endoscope Laser Lithotripsy** Seminal vesiculoscopy with endoscopic laser lithotripsy is an efficient and safe minimally invasive surgical approach, where patients are able to recover fully 1 day after.

**Laparoscopic Removal** The transurethral endoscopy approach had been used in cases where patients had stone sizes of less than 3.5 cm and did not undergo the correction of the dilated SV [3]. A 20-year-old male had presented with a stone size of $6.0 \times 3.5 \times 3.5$ cm which consequently dilated the SV wall. However, the transurethral endoscopic removal was too narrow to reach the stone as well as impossible to remove the dilated SV. Yet, the transperitoneal laparoscopic approach allowed for stone removal as well as the anatomical correction of the SV, with respect to larger stones. Laparoscopic surgery may be conducted where the patient must be placed under general anesthesia. The total operative time ranges 80–120 minutes [11].

In the transperitoneal laparoscopic approach, with the camera placed at the umbilicus, 4 auxiliary ports were utilized: 11 mm at the lateral border of the rectus muscle and a 5 mm port on the iliac fossa [3]. Under the direct vision of Cul-de-sac, the left SV, bladder, and rectum were visualized. Further, the retrovesical peritoneum was incised transversely, in which the SV was easily identified. The stone was then extracted upon incision of the SV by dissecting medially to the ampulla, through the extended 11 mm trocar site incision. The dilated wall was dissected and excised at one-third of proximal SV. The remaining vesicle is secured with sutures.

**Conclusion**

Since the first report of SV calculi in 1928, only a few cases have been reported as shown in table 3. Because SV calculi are considered to be rare, the etiology and pathogenesis of the formation of the stone is unclear. It is often associated with hematospermia, ejaculatory pain, and low ejaculation volume. The diagnoses of SV stones have been easily identified due to upcoming diagnostic
modalities. Majority of the case reports had identified the stones through TRUS, where clinicians have proven to be an ideal detection of SV calculi. Several surgical approaches have been described to manage SV calculi. Each surgical protocol is specific for the location and size of the stone due to SV to be a difficult organ to access, requiring significant incisions to access. TRU-SVS is considered a safe and effective method in the management of SV calculi, more specifically when small stones are present in the SV. In regard to larger stones, a laparoscopic approach is advised due to the endoscopic approach is unable to extract the stone. The surgical protocols have been proven to have no recurrence postoperatively. Evaluation through modern imaging is ongoing in understanding the pathogenesis of SV stones.

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