

Salil Tandon and Edmund Sabanegh Jr

Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, OH, USA

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INTRODUCTION

Vasectomy is a very common operation and has been accepted as a method of family planning by ≈42 million couples worldwide. While it is usually a well-tolerated and highly effective form of birth control, it has a risk of significant morbidity in ≈1% of patients [1]. One particularly troubling complication after vasectomy is chronic testicular pain, which has been defined as intermittent or constant, unilateral or bilateral testicular pain for ≥3 months. The pain is intense enough to interfere with the patient's daily activities and prompts him to seek medical attention [2]. The definition of chronic testicular pain after vasectomy has developed with time, as have the names of this syndrome. Various terms have been applied to this condition, including postvasectomy orchalgia, congestive epididymitis, and chronic testicular pain. Currently the syndrome is generally termed postvasectomy pain syndrome (PVPS) [3]. In this article we review the salient diagnostic and therapeutic features of this vexing medical problem.

BACKGROUND

PVPS is disappointingly common and difficult to treat. Although early pain lasting for a few weeks is fairly common after vasectomy (present in up to 30% of men), long-term pain requiring some kind of intervention or surgical therapy occurs in up to one in 1000 vasectomized men [4]. McMahon *et al.* [5] noted that although half of the patients who reported complications after surgery had long-term discomfort, there was no obvious relationship of pain with immediate haematoma or infection.

VASAL ANATOMY

The epididymis consists of a single tubule which traverses from the efferent ducts

leaving the testis at the start of the vas deferens. At its termination the epididymal tubule is invested with a thick muscular wall marking the beginning of the vas deferens. The vas deferens travels superiorly through the inguinal canal and into the retroperitoneum, where it crosses in front of the ureter and behind the medial umbilical ligament. In the retrovesical space it becomes more dilated to form the ampulla of the vas. The terminal narrow segment, the ejaculatory duct, enters the prostate and ends in the prostatic urethra in the region of the verumontanum [6].

PATHOPHYSIOLOGY

After vasectomy, changes occur in all areas of the genital tract which are proximal to the vasectomy site. Adverse testicular histology after vasectomy has been reported in most animal species studied. Pathological histological findings include degeneration of spermatids, thickened basement membranes and increased phagocytosis by Sertoli cells. Quantitative morphometric analysis of testicular histology in men after vasectomy showed dilatation of the seminiferous tubules, interstitial fibrosis, and reductions in the seminiferous cell population [6].

Vasectomy disrupts the blood-testes barrier, resulting in detectable levels of antisperm antibodies in 60–80% of men [4]. Hattikudur *et al.* [7] examined the long-term effect of vasectomy on the humoral antibody response noting the incidence of agglutinating antibodies increased to 60% by 4 years after vasectomy, reaching a stable 76% in 6–8 years. Vasectomy does not appear to lead to cell-mediated immunity to sperm antigens.

The cause of chronic PVPS remains controversial; one leading theory proposes that the obstruction and resulting dilatation of the epididymal duct produces interstitial

fibrosis. It has also been suggested that pain results from perineural fibrosis and inflammation after the rupture of epididymal ducts, with extravasation of spermatozoa around the epididymal tubules and at the site of vasal transection. The nerves in these areas become densely encased in fibrous tissue, with distortion, angulation and lymphatic infiltration [5]. It is unclear why some patients develop persistent symptoms while others only have transient complaints. A different degree of local fibrosis after inflammatory response and the varying extent of epididymal compression might account for the subjective experience of scrotal pain in some patients [8].

The main histological finding in the epididymis of patients with scrotal pain show epididymal engorgement, complex cystic disease and chronic epididymitis [8]. Culture results from epididymectomy series of patients with PVPS support the argument that the cause of this syndrome is not infection [9]. The role of spermatic granuloma as a causative or protective mechanism for PVPS remains controversial.

CLINICAL PRESENTATION

Contemporary studies suggest that chronic PVPS is more common than originally thought. McMahon *et al.* [5] reported chronic testicular pain in 33% of men who had vasectomy, which was troublesome in 15% and caused 5% to seek medical attention. Choe and Kirkemo [10] identified chronic scrotal pain in 18.7% of patients after vasectomy, which adversely affected quality of life in 2.2%. No preoperative (age, socio-economic status, race, environmental factors), operative (technique of vasectomy) or postoperative (particularly related to antibody response) factors have been identified to accurately identify patients at risk of PVPS. The signs and symptoms of PVPS can be quite variable and are listed in Table 1.

| Symptoms/signs | Patients, % | TABLE 1 Symptoms and signs of PVPS [11] |
|--|-------------|---|
| Symptoms | | |
| Orchalgia | 90 | |
| Pain with intercourse | 80 | |
| Pain with ejaculation | 40 | |
| Decrease in libido or decreased erection | 30 | |
| Premature ejaculation | 20 | |
| Pain with lifting | 20 | |
| Signs | | |
| Tender proximal vas | 40 | |
| Tender distal vas | 10 | |
| Proximal vas fullness | 20 | |
| Tender vasectomy site | 40 | |
| Full epididymis | 60 | |
| Tender epididymis | 60 | |
| Tender granuloma | 20 | |
| Non-tender granuloma | 20 | |

While pain can develop immediately after vasectomy, the mean time of pain onset has been reported to be 2 years [11]. Nangia *et al.* [11] reported that 60% of patients with PVPS had tender or full epididymides on physical examination. No objective evidence of infection was identified. West *et al.* [8] reported similar findings in their small series of 16 patients (after vasectomy). On clinical examination, they noted a unilateral swollen tender epididymis in 12 men or bilateral in three. In one other patient testicular tenderness was also present, along with thickening of the epididymis. Findings on scrotal ultrasonography (US) concurred with the clinical impression of epididymal engorgement, thickening or nodularity.

The differential diagnosis of orchalgia after vasectomy must include nerve impingement or injury, varicocele, hydrocele, infection, testicular neoplasm, intermittent testicular torsion, inguinal hernia, referred pain, and psychogenic causes [2]. Although each of these is a potential cause of pain, most can be excluded by a thorough history, physical examination and urine analysis [3]. All men with chronic orchalgia should have high-resolution scrotal US with colour-flow Doppler to evaluate the scrotal contents and exclude any underlying pathological process such as testicular tumour [4]. Only after these diagnoses have been excluded should a patient be deemed to have PVPS.

NON-SURGICAL TREATMENT

Due to the often subjective nature of the pain with PVPS, it remains appropriate for patients

to initially attempt medical therapy and pain management. Various non-surgical options have been used successfully: conservative (scrotal elevation/support; thermal therapy, i.e. heat or cold as needed for comfort; limiting activity (no lifting/sexual activity restrictions): medical therapies, e.g. NSAIDs, narcotic analgesics, antibiotics, neuroleptic drugs, spermatic cord nerve block, biofeedback or a psychiatric evaluation. Conservative therapy with NSAIDs, scrotal support and activity restrictions all have an early role in pain management. Antibiotic therapy, while commonly used empirically, does not appear to be effective in most patients and is certainly not supported by tissue culture results in patients with PVPS [9]. A conservative course of therapy including NSAIDs should be considered for ≥3 months before proceeding with more involved therapies [4].

If there is still no relief after conservative therapy, strategies to manage chronic pain can be used. Spermatic cord blocks or the use of local intralesional steroids by a pain-management specialist can offer relief [4]. Tricyclic antidepressants can be of value for chronic pain management. Transcutaneous electrical nerve stimulation analgesia has been tried with good results in carefully selected patients with chronic testicular pain [12]. Transrectal injections of local anaesthesia (5 mL bupivacaine) and methyl prednisolone into the region of pelvic plexus has been used for managing chronic orchalgia of unknown aetiology [13]. Cohen [14] reported three patients with groin pain or orchalgia who were successfully treated using

pulsed radiofrequency of the nerves innervating the area.

THE ROLE OF DEPRESSION

A psychological evaluation should be carried out on an individual basis. In a large series assessing the satisfaction of patients who had a vasectomy for contraception, there was a 1% incidence of psychosexual problems, including depression. Schover [15] in 1990 reported that many patients who had chronic orchalgia showed signs of major depression and some of these patients had chemical dependencies [16]. Those with intractable symptoms might benefit from a multidisciplinary team approach involving a urologist and a pain-clinic specialist, including a psychologist [16].

SURGICAL THERAPY

While most patients with PVPS can be managed conservatively, those who fail to respond to these treatments might benefit from surgical intervention. Serial examinations to confirm the location of the pain are essential before any surgical intervention is considered.

There are various surgical options available for treating PVPS, i.e. excision of granuloma, epididymectomy, spermatic cord denervation, reversal of the vasectomy (vasovasostomy/vasoepididymostomy) and orchidectomy. Before any procedures are undertaken, thorough counselling and informed consent about the success rate and complications should be reviewed with the patient by the treating urologist.

EXCISION OF SPERM GRANULOMA

Sperm granuloma forms when sperm leak from the testicular end of the vas. Sperm are highly antigenic, and an intense inflammatory reaction occurs when sperm escape outside the reproductive epithelium. The spermatic granuloma's protective or causative role in PVPS is controversial. While the granuloma itself might or might not be painful, epididymal engorgement and pain are more common in its absence. Shapiro and Silber [17] hypothesized that increased hydrostatic pressure leads to expulsion at the vasectomy site and/or epididymis, with subsequent granuloma formation. They theorised that the expulsion relieves congestion and thus lessens the likelihood of chronic epididymal

discomfort. This formed the basis for the open-ended vasectomy modification designed to prevent PVPS; this technique is reviewed below.

By contrast, Schmidt [18] reported an incidence of >50% of pain in men who have granuloma, and of these 76% required surgery for relief of symptoms. When pain is localized to the granuloma on physical examination, excision of the granuloma and occlusion of vas with intraluminal cautery usually relieves the pain and prevents recurrence.

EPIDIDYMECTOMY

Epididymectomy, either partial or complete, is an option for severe PVPS which is resistant to more conservative therapies. Patients who benefit from epididymectomy usually had focal epididymal dilatation and tenderness [8]. The presence of chronic inflammatory changes in the epididymis has been suggested to be a predictor of a poor outcome after epididymectomy. The other indicators of a poor outcome were: atypical symptoms including testicular or groin pain; concurrent erectile dysfunction; and normal appearance of the epididymis on US [8].

Up to half of appropriately selected patients with PVPS were cured by epididymectomy [19]. The epididymectomy specimen should include all of the ductal vas and previous vasectomy site in the excision, along with any other scar tissue [19]. However, epididymectomy renders the vasectomy completely irreversible. In addition, the procedure can also jeopardize the blood supply to the testes, which can result in ischaemic atrophy [4].

VASECTOMY REVERSAL

In appropriately selected patients, vasovasostomy can produce marked improvement or resolution of pain. This therapy has the obvious drawback of restoring fertility. Nangia *et al.* [11] reported that 69% of patients were pain-free after reversal, noting that the selection criteria for surgery are important to the outcome. A careful preoperative evaluation should include serial physical examinations to confirm the site of persistent pain,

consideration of a psychological evaluation to exclude somatization, and scrotal US to assess for occult pathology. Myers *et al.* [20] reported, in a small series, that 84% of patients with PVPS had complete resolution of pain after vasovasostomy.

DENERVATION OF THE CORD

Testicular pain can occur from scrotal and spermatic branches of the ilioinguinal and genitofemoral nerves. Damage to these fibres can cause the sensation of pain in the scrotum and testicle. Levine and Matkov [21] used microsurgical denervation of the spermatic cord in 27 patients who had a normal physical examination and a history of temporary pain relief after undergoing a cord block. The technique described involved an inguinal incision with division of the ilioinguinal nerve and its branches. The vas deferens is also divided, even if there was a previous vasectomy, to eradicate sympathetic innervation. At the end of the procedure, a testicular and/or deferential or cremasteric artery with one or two lymphatic vessels remained while all other tissue was divided. Overall, 76% of men had complete pain relief, with partial relief in an additional 9%. The authors concluded that denervation of the cord is a viable option for patients with PVPS in who fail to respond to conservative treatment.

ORCHIDECTOMY

Unfortunately, a few patients who fail to respond to medical or more invasive treatment will ultimately require inguinal orchidectomy for pain relief. Davis *et al.* [2] compared the results of inguinal vs scrotal orchidectomy for intractable testicular pain and reported better results after the former than the latter, at 73% vs 55% pain relief, respectively. This procedure must be the last resort, and clearly might have life-long repercussions, especially if the patient develops symptoms on the other side [16].

MODIFYING THE VASECTOMY TECHNIQUE TO PREVENT PVPS

Various modifications in vasectomy technique have been proposed to prevent the subsequent development of PVPS. The first is pre-emptive analgesia: Infiltration of the vas deferens with a local anaesthetic such as bupivacaine before its division/ligation might

reduce both immediate and long-term pain. In a small randomized study, the visual analogue scale scores of patients who had their vas infiltrated with 1 mL of bupivacaine 0.5% before vas division and ligation (immediately and 1 year after vasectomy) were significantly lower than those of patients who had their vas infiltrated with local anaesthetic after the vas had been divided and ligated [16].

Open-ended vasectomy was proposed to intentionally allow the development of a spermatic granuloma as way of lowering the risk of congestive epididymitis and orchalgia after vasectomy [17]. In that study, 410 patients had an open-ended vasectomy; sperm granuloma eventually developed in 97% of patients, all of whom were pain-free, and 3% of patients did not develop sperm granuloma, and they complained of epididymal tenderness worsened by examination. It remains to be conclusively confirmed if open-ended vasectomy to purposefully produce a pressure-relieving sperm granuloma will reduce the eventual incidence of PVPS.

PROPER SEALING OF VAS AND FASCIAL INTERPOSITION

Proper sealing of the testicular end the vas at vasectomy might prevent the formation of granuloma. This technique is in stark contrast to the open-ended vasectomy described above, as its purpose is to prevent sperm granuloma formation, which is theorised to be a significant cause of PVPS. Full sealing might be possible by fulgurating the mucosa of the cut vasal end, which leaves the muscular wall intact. If fascial interposition is used, the testicular end of vas should be brought out of the sheath so that if a granuloma occurs, it will be superficial and not involve the vessels or nerves of the spermatic cord [18].

CONCLUSION

PVPS is a rare but serious complication of vasectomy. It remains a challenging and frustrating problem both for patients and urologists. Patients should be informed of this possible complication from vasectomy before selecting this method of contraception. The use of medical, psychotherapeutic and surgical treatment in a stepwise manner represents the best approach available at present for treating this chronic problem.

Controlled studies, particularly targeting the immune response after vasectomy, the protective or causative role of sperm granuloma, and modification of vasectomy techniques, are critical to provide methods to prevent this painful complication and better noninvasive treatments for patients with PVPS.

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CONFLICT OF INTEREST

None declared.

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Correspondence: Edmund Sabanegh Jr, Section of Male Infertility, Glickman Urological and Kidney Institute, Cleveland Clinic, 9500 Euclid Ave./A100, Cleveland, OH 44195, USA.
e-mail: sabaneec@ccf.org

Abbreviations: PVPS, postvasectomy pain syndrome; US, ultrasonography.