Chronic orchialgia: evaluation and discussion of treatment options

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***Abstract*:** Virtually all practicing urologists will encounter patients with a complaint of chronic testicular pain. This can be a frustrating process for both patient and physician, as there is no clearly established effective treatment regimen, nor is there a recognized and accepted standard protocol for evaluation. Many of these patients will see multiple physicians during the course of their evaluation, further increasing their frustration and potentially straining the physician/patient relationship. The etiology of testicular pain is varied and is frequently idiopathic. Easily recognized and reversible causes include spermatocele, tumor, infection, varicocele, and torsion. Chronic orchialgia has been defined as at least 3 months of chronic or intermittent pain. Although the diagnosis of chronic orchialgia is frequently given to these patients, it should be recognized that fairly frequently the patient will not have just testicular pain, but may have pain involving the epididymis, vas deferens, or adjacent paratesticular structures. Therefore a more appropriate term would be chronic scrotal content pain.
This article reviews the current understanding of chronic scrotal content pain, reviewing the etiology, evaluation, and then a systematic review of the published literature on treatment. It should be recognized that the majority of the published literature are cohort studies with limited numbers of patients, rarely placebo-controlled, and without a uniform standard evaluation. Microdenervation of the spermatic cord is emerging as a reasonable and effective outpatient surgical technique to resolve chronic scrotal content pain, and successful results appear to be predicted by a temporary but complete response to a spermatic cord block.

***Keywords*:** chronic orchialgia, microdenervation of the spermatic cord, scrotal content pain

Introduction

Chronic orchialgia is not an uncommon problem seen by virtually all practicing urologists, and yet it remains a treatment dilemma due to its frequent idiopathic etiology, patient distress as a result of not getting ready care to resolve it, and physician frustration as a result of absence of an accepted standard evaluation and treatment algorithm to guide care. It has been defined as intermittent or constant testicular pain, 3 months or longer in duration that significantly interferes with the daily activities of the patient [Davis *et al.* 1990]. In fact, the term chronic orchialgia is used frequently to describe what is better described as chronic scrotal content pain, as the pain may involve the testicle only and/or the epididymis, paratesticular structures, and the spermatic cord. Therefore, the focus of this article is on chronic intrascrotal pain.

A variety of treatments are available, including medical and surgical options with variable results and typically in relatively small, noncontrolled trials. Most authors agree that orchiectomy is a treatment of last resort and that therapy should be based on physiologic as well as anatomic principles. Therefore, an understanding of the afferent innervation of the scrotal contents is critical. This occurs via somatic nerves in the genital branch of the genitofemoral and the ilioinguinal nerves, as well as autonomic branches from the parasympathetic ganglia of T10–12 for the testis, and T10–L1 for the epididymis and vas deferens [Masarani and Cox, 2003]. It should be recognized that there is significant crossover and overlap of sensory input from the ilioinguinal, iliohypogastric and genitofemoral nerves. The mechanism of acute pain is not fully understood, but in general involves nocireceptors which are

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somatic and visceral free nerve endings which are activated by noxious stimuli. These nerves include myelinated A delta fibers, as well as unmyelinated C fibers. Impulses are ultimately carried to the dorsal horn via intraspinal nerve routes and the pain message travels cephalad via the medial and lateral spinothalamic tracts to the brain. Recent research presented at the 2010 AUA annual meeting found a markedly higher number of nerve fibers with evidence of Wallerian degeneration in the spermatic cord nerves in men which chronic orchialgia *versus* those without chronic pain. These investigators also found that the greatest concentration of nerves in the spermatic cord were found around the vas deferens and internal spermatic arteries, as well as within the cremaster muscle and cord fascia [Parekattil *et al.* 2010].

Chronic pain is a more complex process, which is even less well understood, but elegant research is ongoing. Neuropathic pain persists long after the initiating event has healed and is an expression of pathological operation of the central nervous system rather than a reaction to a pathogen [Woolf and Salter, 2000]. It appears most receptors and their neurons display a process known as sensitization following repeated stimulation. This causes peripheral and central modulation where a decreased threshold is necessary to activate the action potential with increased frequency response, decreased response latency, and ultimately spontaneous firing of these nerves. This process has received multiple names, including 'central wind-up' or 'hard-wiring', such that no noxious stimuli are necessary to generate the pain impulse [Bolay and Moskowitz, 2002; Peterson and Brown, 1973].

Etiology and evaluation

Pain in the scrotal contents can be due to direct sources, including infection, torsion, tumor, obstruction, varicoceles, spermatoceles, rarely hydroceles, and can follow direct trauma as well as iatrogenic injury following vasectomy or inguinal hernia repair. Referred pain can occur as a result of a midureteral stone, indirect inguinal hernia, aortic or common iliac artery aneurysms, lower back disorders, and nerve entrapment due to perineural fibrosis. In addition, it should be recognized that up to 50% of patients may present with an idiopathic etiology [Davis *et al.* 1990]. Psychiatric issues, as well as secondary gain with malingering must also be considered in the differential diagnosis. Urologists are most apt to see postvasectomy pain syndrome, which is not a frequent but is a distressing consequence of vasectomy. The prevalence has been suggested to be up to 52%, but it appears that fewer than 10% ultimately seek treatment [Christiansen and Sandlow, 2003; McMahon *et al.* 1993]. It may also present anywhere from immediately, to 7 years after vasectomy [McMahon *et al.* 1993]. Etiology may include congestive epididymitis, sperm granuloma, or nerve entrapment.

Evaluation of the patient with chronic scrotal content pain should include ruling out medically important and reversible causes including tumor, intermittent torsion, infection, and varicocele. It should also be recognized that scrotal pain is not a synonym for scrotal pathology and other sources should be evaluated. History should focus on onset, duration, severity (graded on a 0–10 scale), location, and referral of pain. Other associated factors include prior surgery, trauma, or infection. One should ascertain whether certain activities exacerbate or meliorate the pain, including voiding, bowel movements, sexual, or physical activity, and prolonged sitting, which the author has found to be one of the most common complaints in this population. Past surgeries are important, which may involve the back, inguinal, scrotal, pelvic, or retroperitoneal areas. Psychosocial questions are in order to determine whether there is a disability associated with the pain, if there is potential secondary gain, and if there are signs or symptoms of depression. In addition, it has been recognized that chronic genital pain may be associated with a history of sexual abuse.

As to how to measure and report on pain, this remains one of the many challenges in this field. No clear, accepted gold standard exists. One can simply ask the question 'How would you rate your pain on a scale of 0–10?', or what is most commonly employed is the Visual Analog Scale, a 0–10 and/or cartoon scale. This allows comparison between the patient's pretreatment and posttreatment perceptions of pain, which is the only important measure at this time [Rabah and Fabrozio, 2003]. The PIQ-6 is a validated questionnaire which was developed by the RAND Corporation and is currently available for purchase. It focuses on the impact of pain on quality of life parameters. Clearly future clinical trials offering treatment of chronic scrotal content pain must incorporate a widely accepted evaluation and outcome assessment methodology.

Physical examination should focus on the genitalia. It is recommended to examine the patient standing and supine, starting the genital exam on the nonpainful or less-painful side if bilateral. A detailed examination of the testes, epididymes, and vasa is indicated, and a rectal exam is in order.

Further evaluation includes a urinalysis, urine, and semen culture if indicated. All patients should undergo a duplex scrotal ultrasound. CT scan, intravenous pyelogram (IVP), retrogrades, voiding cystourethrogram (VCUG) and cystoscopies have a very low yield, but MRI or CT scan of the spine should be obtained if there is a history of back or hip pain. A critical diagnostic tool is the spermatic cord block, which is performed by injecting 20 cm^3 of 0.25% bupivacaine without epinephrine into the spermatic cord at the pubic tubercle level. Consideration for a saline control is reasonable.

Treatment

Treatment of this problem remains a therapeutic dilemma. It should start with simple noninvasive and nontoxic approaches including nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, particularly when there is evidence of infection. Doxycycline and quinolones are best, as they appear to have the highest penetration into these structures and may be given up to 4 weeks if indicated. Other oral agents include antidepressants, such as amitriptyline 10–25 mg qhs or nortriptyline 10–150 mg daily may be used, which inhibit norepinephrine release at first- and second-order neurons, or anticonvulsants such as neurontin, starting at 300 mg but titrating up to 3600 mg daily. This drug works as a calcium channel modulator in the central nervous system to reduce neuropathic pain. A recent review by Sinclair and colleagues demonstrated little benefit with these drugs for postvasectomy pain [Sinclair *et al.* 2007]. Nerve blocks as a single injection or in a series have also been used as a form of treatment with or without steroids in an effort to break the pain cycle. A recently introduced form of noninvasive treatment is known as TMR, which is a delivery system for focused, painless, topical, high-intensity pulsed electromagnetic energy, which is receiving increased attention and is currently being studied with encouraging initial results. The problem is, when these nonsurgical approaches fail, no unanimous approach has been established. Psychological counseling may be beneficial to help the patient deal with the pain, but when this fails surgery is frequently the next option.

Epididymectomy should be used when the pain is localized to the epididymis only and appears to have its best outcomes following vasectomy [Hori *et al.* 2009; West *et al.* 2000]. Overall reported success with epididymectomy ranges from 10% to 80% [Siu *et al.* 2007]. Multiple case series have shown poor results with epididymectomy for treatment of chronic orchialgia. Vasectomy reversal has been offered as an open-ended procedure or with vasovasostomy [Nangia *et al.* 2000; Shapiro and Silber, 1979]. The largest report on vasovasostomy for chronic pain was recently presented at the 2010 AUA meeting on a 10-year experience with 45 men where there was a 75% complete relief of pain, 10% experienced partial (>30%) relief, and 10% failed to improve [Werthman, 2010]. Reports on vasectomy reversal are limited and with small cohorts, but do demonstrate pain relief in the 69–84% range [Myers *et al.* 1997]. In addition it is costly and this approach does undo the sterilization process.

Microdenervation of the spermatic cord (MDSC) has received increased attention due to several articles published over the past decade [Strom and Levine, 2008; Heidenreich *et al.* 2002; Levine and Matkov, 2001; Levine *et al.* 1996]. The first case report was in 1978 [Devine and Schellhammer, 1978]. The primary advantage of MDSC is sparing the testicle for both psychological and physiological reasons. The goal of the operation is to divide all structures which may be carrying neural fibers, but to preserve the arteries (testicular, cremasteric, deferential), several lymphatics to reduce the likelihood of hydrocele, and the vas deferens, if it has not already been taken. The key selection measure for this procedure is a positive yet temporary response to a spermatic cord block. Informed consent for this operation is critical, as the pain may be persistent but rarely worse. There is also risk of hematoma, hydrocele, testicular atrophy, and hypogonadism.

MDSC technique

The surgical procedure is performed as an outpatient typically under general anesthesia with the aid of the operating microscope at 8× power. Exposure of the spermatic cord is made at the external inguinal ring, isolating the cord circumferentially, and identifying the

ilioinguinal nerve, which is divided as it emerges out of the ring. The proximal ligated end should be tucked under the external ring fascia to reduce the likelihood of neuroma formation. Division of the ilioinguinal nerve appears to be a valuable part of the procedure, as unpublished reports revealed an unacceptable rate of hypesthesia and allodynia in the inguinal and upper scrotal areas when the ilioinguinal nerve is spared [Carrion, 2009]. The cord is then supported with a Penrose drain and the microscope is brought to the field. The spermatic cord fascia is opened anteriorly, exposing the spermatic cord contents (Figure 1) and then all structures of the cord except the arteries and lymphatics are divided with electrocautery, or between 4-0 silk ties. If the vas deferens has not been divided previously, it should be stripped for approximately 2 cm of its perivasal fascia, as this fascia is richly innervated [Parekattil *et al.* 2010]. If a vasectomy had been performed, the vas and its fascia should be divided again. All spermatic cord veins are divided. Lymphatics are typically found in the central compartment of the spermatic cord, and several should be isolated to reduce the likelihood of postoperative hydrocele. All arteries should be spared and isolated with microvessel loops, and at the conclusion of the procedure all microfascia should be divided with electrocautery. Venous hypertension has not been noted and presumably venous drainage occurs through scrotal veins. However, to reduce the risk of significant prolonged scrotal swelling, it is not recommended to perform this procedure on both sides at the same setting. At the conclusion of the procedure, the remaining structures in continuity include 1–5 spermatic cord arteries, several lymphatics, and the vas deferens, if it has not already been divided (Figure 2).

The most recent published experience on MDSC was on 95 cases in men with a mean age of 40 years and a mean duration of scrotal content pain for 62 months (range 5–252 months). Etiology varied: 43% had unknown etiology, 8% followed vasectomy, 7% followed trauma, 9% after herniorrhaphy, and 9% after epididymitis. In this group, 71% had a complete and durable resolution of pain, 17% had partial relief defined as greater than 50% reduction, and 12% had no benefit. A subanalysis of MDSC cases performed between 2007 and 2009 in men who reported a 90–100% reduction of pain following spermatic cord block, revealed an 88% complete and durable response after surgery. Thus it appears the spermatic cord block can provide useful information for selecting men who are most apt to have surgical success. For those men who had no benefit from MDSC, several explanations exist, including: central sensitization had already occurred, sensory nerves were left intact, a posterior or pudendal source carried the pain stimuli, and malingering cannot be ruled out.

Interestingly, 40% of the men who had complete pain resolution noted immediate postoperative relief, but this may take up to 3 months to occur. Mean follow-up in this patient population was 20 months with a range of 1–102 months. There were 2 men who experienced testicular atrophy with complete pain resolution, and there was no hypogonadism. There was one hydrocele which resolved spontaneously in 6 months. Although one would expect sensory loss in the distribution of the ilioinguinal nerve, this has rarely been noted by the patients, and

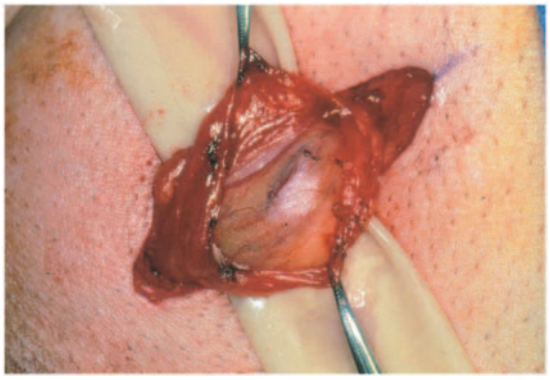

Figure 1. Spermatic cord supported by Penrose drain with cord fascia opened.

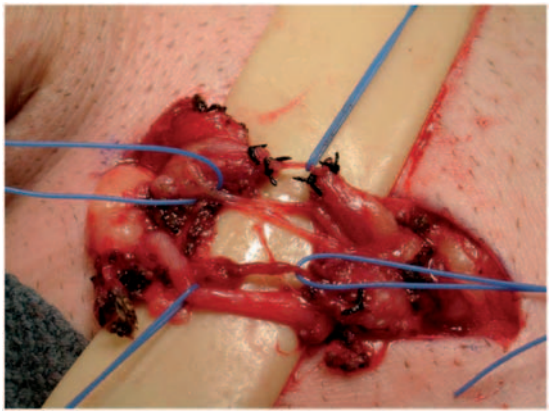

Figure 2. At completion of dissection, only the vas deferens, arteries, and lymphatics remain.

any loss of sensation inferior to the incision has not resulted in any complaints.

Yet to be published but recently presented experience with MDSC at the 2010 Wisconsin Urological Society annual meeting by Daniel Williams, MD, confirms the usefulness and efficacy of this procedure in 26 men in whom a 78% success rate was reported.

Orchiectomy remains a surgical option. This may be considered when other approaches such as MDSC fail and the patient cannot stand the pain any longer. Yet, reported success rates are not encouraging at 20–70%, which may be due to central sensitization or not dividing the sensory nerve input. Pain resolution appears to be higher with an inguinal *versus* a scrotal approach patient [Davis *et al.* 1990].

Conclusions

As further research in this field evolves, more elegant and successful treatment options are likely to emerge. Large-scale, multicenter, controlled trials will be critical for new treatment options, especially for nonsurgical approaches. In the meantime, chronic scrotal content pain is frustrating for both the physician and patient. A deliberate and structured evaluation is necessary. One should rule out reversible causes and recognize that pain in this area is associated with significant psychological factors, including the possibility of secondary gain. A multidisciplinary approach including pain clinic services and psychologists may be beneficial before considering surgery. If surgery is considered, sparing the testicle is possible with the MDSC technique with complete and durable resolution of the pain reported in the 71–89% range.

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Conflict of interest statement

None declared.

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