Nonpalpable Scarring of the Penile Septum As a Cause of Erectile Dysfunction: An Atypical Form of Peyronie’s Disease

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ABSTRACT

Introduction. Men with nonpalpable isolated septal scars (ISS) identified with color duplex ultrasonography (CDU) comprise a group of previously unrecognized patients with wide-ranging sexual concerns.

Aim. We aim to identify the clinical characteristics of patients presenting with this atypical form of Peyronie’s disease characterized by the absence of palpable deformity.

Materials and Methods. Of 482 consecutive patients who presented to a tertiary care erectile dysfunction (ED) clinic and underwent CDU after satisfying inclusion criteria, 27 (5.6%) men with nonpalpable ISS and no dorsal or ventral plaque were identified.

Main Outcome Measures. International Index of Erectile Function (IIEF), CDU, and clinical characteristics.

Results. The median age of the men with nonpalpable ISS was 49 years. The length of time from onset of symptoms to presentation was 22 months, and the pretreatment IIEF score was 14. The remaining 455 men who underwent CDU were of similar age (48 years) but had a markedly lower IIEF score of 9.5 (statistical median). ISS patients presented with decreased penile rigidity (20), penile shortening (13), chronic pain with erection (13; mean 33 months), and the inability to maintain an erection (7). Fourteen men had failed phosphodiesterase-5 inhibitor therapy, and four reported unsatisfactory results. Management options included retraction with oral agents, intracavernous pharmacotherapy, verapamil injections, and surgery.

Conclusions. The clinician should be suspicious for nonpalpable ISS in men with sexual concerns who present with decreased penile rigidity, length loss, and chronic pain with erection. Our findings support the use of CDU for this patient group, particularly when previous treatment has failed, because men with ISS had a greater likelihood of having no palpable deformity or curvature and ongoing penile pain. Bella AJ, Sener A, Foell K, and Brock GB. Nonpalpable scarring of the penile septum as a cause of erectile dysfunction: An atypical form of Peyronie’s disease. J Sex Med **;**:**–**.

Key Words. Impotence; Penile Erection; Peyronie’s Disease; Color Duplex Ultrasonography

Introduction

Current treatment algorithms for the management of erectile dysfunction (ED) advocate a minimalist evaluation prior to treatment [1,2]. Although we support this approach for our general patient population, a comprehensive evaluation seems appropriate in selected patients who present with erectile difficulties of undefined etiology or who request further information about their cause. In these cases, high-resolution ultrasonography is useful in defining penile structure and vascular function. Since its introduction by Lue and associates [3], the role of color duplex ultrasonography (CDU) has evolved to include the evaluation of men scheduled for Peyronie’s reconstructive procedures, penile implants, priapism, and unexplained ED [3–5].

Erectile dysfunction associated with nonpalpable isolated septal scars (ISS) has not been previously described. In contrast to the classical findings of penile curvature, a palpable deformity, and/or pain for Peyронie’s disease (PD), discrete septal scars identified by CDU do not manifest as
a palpable penile induration or plaque [6]. In this study, we identify the clinical characteristics of men with ISS and ED.

Materials and Methods
Between September 2001 and August 2005, 482 patients who presented with ED underwent high-resolution CDU scanning in order to evaluate penile structures and vascular function after satisfying inclusion criteria. A retrospective review of patient records yielded a cohort of 27 patients with CDU-identified penile scarring confined solely to the midline septum without associated dorsal or ventral plaques. Clinical data, including International Index of Erectile Function-5 (IIEF-5) scores, were compiled for all the patients undergoing CDU. Presenting complaints, time interval from symptom onset to assessment, previous treatments, and therapies following diagnosis of ISS were identified. Incidence of hypertension, hypercholesterolemia, diabetes, coronary artery disease, medications, trauma, and smoking history were compared between cohorts. Features distinct from the general ED population, and specifically from patients with Peyronie’s disease, were elucidated for men with ISS.

Results
The median age of the 27 men with nonpalpable ISS was 49 years (range 22–61), similar to the other 455 patients who underwent CDU (48 years). Pretreatment IIEF-5 scores for the study group were 14 (range 10–21) vs. 9 for the control group (median values). A 22-month delay (range 6–66) for the clinical evaluation of ISS patients from the time of onset of symptoms was noted. Median follow-up for ISS patients was 18 months, ranging from 5 months to 4 years.

Color duplex ultrasonography showed that all the patients had discrete lesions isolated to the midline penile septum without associated dorsal or ventral plaques (Figure 1). The vascular response to intracavernous prostaglandin E-1 was abnormal distal to the ISS in 12 men (≤25 cm/second). Median right and left cavernosal artery flows measured 37 (range 16–70) and 32 cm/second (range 15–50), respectively.

The most common presenting symptom in the study cohort was decreased penile rigidity, occurring in 20 out of the 27 men (75%). Penile shortening, inability to maintain an erection, and nonresolving penile pain (median 22 months; mean 33 months) were also reported by the men with ISS (Table 1). A mild curvature of the penis (30° or less), preceded by decreased rigidity and pain upon erection, had developed in three men prior to evaluation.

The most common clinical characteristics of the ISS patients were a history of smoking (6), penile trauma (6), medically controlled hypertension (3), and diabetes (3). No patients with ISS demonstrated Dupuytren’s or plantar fascial contractions, tympanosclerosis, or a familial pattern of Peyronie’s disease. In all cases but one, the development of ED was gradual. Hypertension, hypercholesterolemia, diabetes, coronary artery disease, and medication use were under-represented in men with ED and ISS compared to patients without scarring evaluated for ED refractory to phosphodiesterase-5 (PDE-5) inhibitor therapy.

Twenty patients had been treated with PDE-5 inhibitors prior to referral; 16 sildenafil (Viagra; Pfizer, New York, NY), three tadalafl (Cialis; Lilly ICOS, Indianapolis, IN), and one vardenafil (Levitra; Bayer AG, Leverkuesen, Germany).

Table 1 Presenting complaints of the 27 men with nonpalpable isolated septal scarring (more than one complaint may have been reported)

<table>
<thead>
<tr>
<th>Presenting complaint</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased penile rigidity</td>
<td>20 (74)</td>
</tr>
<tr>
<td>Penile shortening</td>
<td>13 (48)</td>
</tr>
<tr>
<td>Chronic penile pain with erection</td>
<td>13 (48)</td>
</tr>
<tr>
<td>Inability to maintain erection</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Mild penile curvature*</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

*Penile curvature of 30° or less, preceded by symptoms of decreased rigidity and penile pain (median 25 months).
Intracavernous injection (ICI) cohort of men with ED. Patients with ISS represent a unique clinical entity. Nonpalpable ISS of the penis is defined by CDU-identified plaques. Definitive management included intracavernous injection (10), PDE-5 inhibitors (7), and four men progressing to Peyronie’s plaque surgery (Table 2).

**Table 2 Management strategies for ISS patients**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of patients who attempted treatment (%)</th>
<th>Number of patients in whom treatment was successful* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracavernous injection</td>
<td>14 (52)</td>
<td>10 (37)</td>
</tr>
<tr>
<td>PDE-5 inhibitors</td>
<td>20 (75)</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Surgery</td>
<td>4 (15)</td>
<td>4* (15)</td>
</tr>
<tr>
<td>Conservative management</td>
<td>5 (19)</td>
<td>4 (15)</td>
</tr>
<tr>
<td>Intralocular verapamil injections</td>
<td>4 (15)</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

*ICI and PDE-5 inhibitors were used to optimize erectile function for three and one patient, respectively.
†At time of manuscript writing.
‡CDU = intracavernous injection; ISS = isolated septal scar; PDE-5 = phosphodiesterase-5.

Fourteen men failed PDE-5 therapy, and four reported unsatisfactory results.

The treatments for men with ED and ISS included conservative therapy, retrial with PDE-5 inhibitors or a salvage protocol (sildenafil, vitamin E, and folate), intracavernous pharmacotherapy, verapamil injections, and surgical intervention. Therapies progressed step-wise from oral agents to more invasive modalities if symptoms proved refractory to treatment or if ISS progressed. Of note, the mild curvature noted by three patients at initial presentation worsened, and one patient developed a dorsal plaque. Two additional men developed a mild penile deformity consistent with Peyronie’s curvature, but without palpable or CDU-identified plaques. Definitive management included intracavernous injection (10), PDE-5 inhibitors (7), and four men progressing to Peyronie’s plaque surgery (Table 2).

**Discussion**

This report represents the first series of a novel clinical entity. Nonpalpable ISS of the penis identified by CDU are likely present in a significant number of men who experience ED and nonresolving penile pain without evidence of penile deformity. We propose that CDU be considered for cases of ED refractory to PDE-5 treatment, and that patients with ISS represent a unique cohort of men with ED.

To date, the natural history and mechanism of isolated septal lesions remains undefined. The midline septum of the penis acts as an inner supporting frame, resisting dorsal and ventral bending forces during tumescence. In Peyronie’s disease, the cascade of scar formation is likely initiated by buckling trauma, causing injury at the septal insertion of the tunica albuginea [7]. Pressure is focused on the connection of midline septal strands to the tunica, causing delamination of septal fibers at the point of insertion or shear where fibers are interwoven with the inner circular layer [8,9]. Aberrant wound healing in response to the inflammation following injury occurs within the tunical layers, ultimately resulting in a loss of elasticity and plaque formation [10]. A central scar confined to the intracavernous septum could contribute to loss of rigidity distally to the lesion, penile length loss and pain, and changes in cavernosal artery hemodynamics without evidence of deformity. Although it seems likely that traumatic injury to midline septal strands results in scarring, the mechanism by which penile buckling out of column results in ISS has yet to be elucidated.

Presentation for the ISS cohort of ED differs from Peyronie’s disease, as symptoms of chronic penile pain (mean 33 months) and shortening without curvature predominate. Although the initial phase of Peyronie’s disease is also characterized by painful erections, the pain subsides due to the death of trapped nerve fibers or maturing of the inflammatory process [10]. ED is the result of “trapped inflammation” and subsequent fibrosis compromising erectile tissue and tunical elasticity, preventing corporal expansion [10].

In this cohort of ISS, a history of penile trauma was identified in six men, although none of them described a “classical” penile fracture accompanied by extravasation of blood (hematoma or ecchymoses). Blunt or bending injury to the penis during intromission resulted in sharp pain and rapid detumescence for five men; multiple episodes were described by three patients. The fibrosis and contracture of the tunica induced by repeated microtrauma is likely responsible for the penile length loss, decreased corporal compliance, and altered hemodynamics demonstrated for patients with ISS, and may contribute to ongoing penile pain. The decreased cavernosal artery velocities observed distally to a defined ISS are consistent with a previous report describing narrowed vascular caliber, abnormal position, and reduced flow caused by a central penile scar [11].

Organic risk factors, including diabetes, hypertension, hyperlipidemia, and coronary artery disease, were under-represented in the ISS cohort compared to the general ED population [2]. Although both groups of patients were of a similar median age, ISS patients were generally healthier, used less prescription medication, and had fewer risk factors for ED. On the other hand, a history...
of trauma was more common and may suggest that ISS is a by-product of mechanical rather than organic insults. Causality cannot be determined in such a small number of patients, but this observation is intriguing and warrants further investigation.

The clinical feature most commonly shared by men presenting with ISS and ED was the failure of first-line therapy with PDE-5 inhibitors. Of the 20 men initially treated with oral agents, 18 failed or were not satisfied with their improvement. Ultimately, seven out of the 27 men with ISS and ED had chosen PDE-5 inhibitors as their treatment of choice, including four initial failures. As success with first-line agents is multifactorial (patient education, patient/partner involvement in treatment decisions, and lifestyle modification) [2], it is difficult to note whether re-instruction, use of adjuvant agents [12], or other as yet unidentified factors resulted in successful salvage. Testosterone levels should be determined in men initially failing PDE-5 inhibitor therapy [13]; one patient with abnormally low levels was salvaged with the addition of testosterone to his oral ED therapy. Nevertheless, most men with ISS did not respond to PDE-5 inhibitors.

Optimal treatment strategies for patients presenting with ED and ISS are undefined. We believe that making the diagnosis itself may be an important therapeutic maneuver for some men who experience penile pain without evident cause. Identification of ISS and a clear diagnosis may aid in their understanding of the process and facilitate recovery, as evidenced by three patients managed by a conservative approach.

The majority of men were successfully treated with intracavernous pharmacotherapy using a combination of prostaglandin E-1, phentolamine, and papaverine (tri-mix). Failure of PDE-5 and/or intracavernous injection therapies resulted in progression to intralesional therapy or surgery. Intralesional verapamil was administered exclusively by a single urologist (G.B.B.) to four patients to ensure injection accuracy after confirming the ISS location by CDU. Refractory ED accompanied by expanding ISS (2), verapamil treatment failure (1), or difficulty with intromission due to penile curvature (1) necessitated surgical management for four patients, utilizing plaque incision and grafting. Of note, the ISS patient with worsening penile curvature had developed an accompanying dorsal plaque and debilitating deformity almost 3 years after the onset of ISS symptoms. Due to the small number of patients in this cohort, patient characteristics predictive of successful treatment outcomes could not be determined. Future ISS management may include ultrasound-guided injection of novel or current intralesional agents, such as verapamil and interferon-alpha, oral agents, or surgery [14–16].

It is likely that the incidence of ISS will increase as more men are evaluated for ED, especially in patients failing first-line oral therapies. A similar trend has been identified for incidentally diagnosed Peyronie’s disease, as a five-fold increase in the prevalence (16%) for men undergoing standard ED assessment was recently reported [17]. Whether ISS is a precursor to Peyronie’s disease in some patients remains to be determined; follow-up to 4 years in this cohort would suggest that the ISS disease process is distinct for the majority of patients because only one dorsal plaque was identified and 22 of the men did not demonstrate curvature. Future directions should include identifying a larger cohort of patients and allowing for the natural history, risk factors, and treatment options for these lesions to be defined.

Conclusions

The clinician should be suspicious of nonpalpable septal scarring in men who present with penile length loss, chronic pain, and ED, particularly when they are unresponsive to first-line oral therapies. Our findings support the use of CDU for this patient group, because men with ISS had a greater likelihood to present with ongoing penile pain and the absence of penile plaques, curvature, or induration. Definitive management may include conservative measures, pharmacotherapy, and surgical correction.

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Conflict of Interest: None declared.

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