Successful Penile Replantation and the Role of Postreplantation Sildenafil Therapy: Report of 2 Cases and Literature Review

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ABSTRACT
Penile amputation is a rare clinical emergency necessitating urgent urologic and microsurgical intervention. Microvascular replantation has become a conventional form of management, associated with significantly increased viability of the implanted tissue and a lower rate of complications. However, postreplantation treatment intended to promote early recovery of sexual function has been reported only seldomly. Here we report 2 cases of successful penile replantation with postreplantation daily sildenafil therapy. The patients were followed for 24 months and 8 months, respectively, from the date of repair. First intercourse was achieved at 92 days and 105 days, respectively. This is the first report of the use of phosphodiesterase type 5 inhibitors in postoperative care of penile replantation.

INTRODUCTION
Penile amputation may be necessitated by psychotic self-mutilation, circumcision, vicious assault, or accident. In rare cases it necessitates surgical reattachment, which is best performed as early as possible. The external genitals play crucial roles in both physical and mental well-being.

Currently, the standard treatment for penile amputation involves microsurgical anastomosis of vessels and the dorsal nerve along with approximation of the cavernous body and urethra. Improved circulation and sensation lead to a better prognosis, including increased overall penile survival rate, preserved erectile and voiding function, and preserved glans sensation.

In our experience, and as reported previously, most patients who undergo replantation experience partial or even total loss of erectile function. However, there are few references dealing with such clinical issues because of their rarity. Here we describe our experience with 2 patients who received daily oral sildenafil therapy early after replantation, which induced no known adverse effects and appeared to have accelerated the recovery of the patients’ erectile and sexual function.

CASE REPORTS
Case 1
A 49-year-old male arrived at a local hospital 10 minutes after his penis had been amputated with a sharp knife. The penis had been partially amputated approximately 1 cm distal from the pubic area. The local Emergency Department had performed hemostasis with a rubber tourniquet. Four hours later, the patient was transferred to our hospital. After providing informed consent, he was rushed to the operating room.

We assessed the wound on the table. The edge was sharp and clean. The bilateral corpus cavernosum was completely severed and the dorsal nerve along with approximation of the cavernous body and urethra. Improved circulation and sensation lead to a better prognosis, including increased overall penile survival rate, preserved erectile and voiding function, and preserved glans sensation.
Deep dorsal veins and a superficial dorsal vein were then reattached using 9-0 nylon sutures. One branch of the dorsal penile nerve was reattached using 10-0 nylon sutures. Buck’s fascia was approximated using 4-0 Vicryl sutures to reduce tension. The skin was stitched loosely using interrupted 5-0 Vicryl sutures.4,5

Bright-red bleeding from a glans puncture was observed (Figure 1C). Given that the total blood loss did not exceed 500 mL, crystalloid fluid rather than red blood cell transfusion was administered. IV low molecular dextran was given for 3 days, and both intramuscular papaverine and oral aspirin were given for 5 days.

Glans color, skin temperature, and foreskin edema were closely monitored for the first 72 hours postoperatively. The catheter was removed on postreplantation day 14. Oral sildenafil 50 mg/day was started on postreplantation day 28 (half of the penis became erect), and the patient was closely monitored for 2 days.
days before discharge. Daily sildenafil therapy was administered strictly according to our instructions for 2 months after discharge, and when the erection recovered, the patient ceased medication on his own.

Monthly follow-up was conducted. The following data were collected and recorded: penile length and rigidity at erection, frequency of intercourse, and strength of urination. In the sixth week, the patient reported painful nocturnal penile tumescence. The pain decreased over time and was gone by week 12.

Nocturnal penile tumescence (NPT) was first monitored at week 12 using a RigiScan device (Dacomed, Minneapolis, MN, USA), which showed 2 positive NPT periods lasting 10 minutes and 7 minutes, respectively. Then the patient reported his first, albeit unsatisfying, intercourse on postreplantation day 92; his glans remained numb. Sensation and the erection rigidity both continued to improve over the subsequent 3 months. The frequency of intercourse also increased. Data acquired via telephone or clinical interviews and NPT test results are summarized in Table 1.

The patient’s glans remained numb until the third month after discharge, when he reported mild formication lasting for 2 weeks. Two-point discrimination was performed with NPT tests. The patient failed to discriminate the 2 needle points at 12 weeks after replantation. Measurable 2-point discrimination (1.5 cm) was achieved at 24 weeks after replantation. At that time, the patient had regained 70% of tactile sense, according to a self-evaluation.

Case 2

A 31-year-old construction worker whose penis was accidentally severed by a saw blade, presented at our hospital within 2 hours of the accident with gauze compression. The penis was completely severed (Figure 1E) approximately 1 cm distal from the pubic area. The wound was rough and blood resumed pumping when compression was removed (Figure 1D). The distal penis was contaminated with sawdust and had been kept at room temperature during transportation. The scrotum had been cut open though the testicles, and spermatic cords remained intact. The patient was given both crystalloid solution and whole blood transfusion to stabilize his vital signs. A tourniquet was applied. Simultaneously, the amputated penis was washed thoroughly with sterile saline, wrapped in saline gauze, placed in an aseptic bag, and buried in ice chips. The patient was rushed to the operating room, and informed consent was provided by his wife.

Given the roughness of the wound, debridement was performed, after which neurovascular structures were identified. The urethral mucosa was repaired with 5-0 polydioxanone suture over an 18 Fr Foley catheter. Both the urethral and penile cavernous bodies were repaired. Bilateral dorsal artery, deep dorsal vein, a superficial vein, and the dorsal penile nerve were anastomosed using the same techniques as described for case 1. The patient received the same medication regimen as in case 1 (Figure 1F).

The patient’s glans remained numb until the third month after discharge, when he reported mild formication lasting for 2 weeks. Two-point discrimination was performed with NPT tests. The patient failed to discriminate the 2 needle points at 12 weeks after replantation. Measurable 2-point discrimination (1.5 cm) was achieved at 24 weeks after replantation. At that time, the patient had regained 70% of tactile sense, according to a self-evaluation.

Table 1. Contrast between postreplantation status and preamputation status of patients

| Self-scoring and NPT results | Case 1 (partial amputation) | Case 2 (total amputation) |
|-----------------------------|----------------------------|--------------------------|
|                             | Preamputation | 1 | 2 | 3 | 4 | 5 | 6 | Preamputation | 1 | 2 | 3 | 4 | 5 | 6 | 12 |
| Self-scoring                |              |   |   |   |   |   |   |              |   |   |   |   |   |   |    |
| Penile length at erection  | 10           | / | / | 7 | 8 | 8 | 8 | 10           | / | / | 7 | 7 | 7 | 7 |    |
| Penile rigidity at erection| 10           | / | / | 5 | 6 | 7 | 8 | 10           | / | / | 6 | 7 | 7 | 8 |    |
| Frequency of intercourse,  | 3–5          | / | / | / | 1 | 2 | 2 | 2–8          | / | / | 1 | 1 | 2 | 4 |    |
| times/mo                    |              |   |   |   |   |   |   |              |   |   |   |   |   |   |    |
| Strength of urination       | 10           | / | 9 | 10| 10| 10| 10| 10           | / | 9 | 8 | 9 | 9 | 9 | 9|
| Overall satisfaction        | 10           | 5 | 5 | 5 | 6 | 7 | 8 | 10           | 4 | 5 | 5 | 6 | 7 | 7 | 7|
| NPT results                 |              |   |   |   |   |   |   |              |   |   |   |   |   |   |    |
| Total NPT                   | 4            |   |   |   |   |   |   |              | 3 |    |   |   |   |   |    |
| Positive NPT                | 2            |   |   |   |   |   |   |              | 3 |    |   |   |   |   |    |
| Duration of positive NPT,   | 10, 7        |   |   | 12, 11, 9 |   |   |   |              | 14 |    |   |   |   |   |    |

Patients’ self-scored all the parameters on a scale of 1–10 monthly after replantation for comparison with status before amputation. Positive NPT was defined as a maximal penile circumferential change ≥15 mm.

NPT = nocturnal penile tumescence.
his first intercourse postreplantation. The patient reported partial recovery of sensation and the tactile hallucination of “ants walking in a line.” Over the next 6 months, this hallucination gradually disappeared and almost 60% of sensation returned, according to the patient’s self-evaluation.

Interval follow-up was conducted monthly during the first 6 months and biannually thereafter. As the patient’s sexual function returned without complications (eg, urethrostomosis), the patient defaulted, and the actual follow-up period was 1 year. NPT testing was conducted only once, at postreplantation day 91. The data are summarized in Table 1.

DISCUSSION

In our experience with penile replantation, after both incomplete and complete amputations, patients sustain at least partial loss of erectile function after replantation. In the 21 years since March 1997, 24 patients who presented with either incomplete (14 cases) or complete (10 cases) penile amputations were treated in our department. In 20 (83.3%) of these patients, the penis survived with normal erectile function, and the duration of functional recovery ranged from 3 months to more than 2 years. After postreplantation PDE-5i therapy was adopted in 2011, 6 patients (3 with incomplete amputation and 3 with complete amputation) were treated. The total recovery rate of erectile function was slightly higher than reported previously (83.3% vs 77.5%).2,3 Sildenafil was administered at night for rehabilitation after nerve-sparing radical prostatectomy. This led to a significant improvement in and acceleration of the recovery of erectile function.4,5 Given the favorable prognosis of all 6 patients, we conclude that sildenafil may have value in accelerating the recovery of erectile function after replantation. At least our findings show that PDE-5i therapy does not induce adverse complications.

Erection is a complicated physiological reaction that involves multiple avenues of neurohumoral regulation. Nitric oxide (NO) is released by terminals of cavernous nerve and activates guanylate cyclase, which catalyzes guanylate into cyclic guanosine monophosphate (cGMP). cGMP is crucial to the activation of a series of protein kinases that lower the concentration of intracellular calcium ions. Consequently, smooth muscle relaxes, inducing capillary congestion and macroscopic erection. In penile amputation, the cavernous nerve is severed, and local blood sinus sustains mechanical damage. During the early stage of recovery, NO is released at low levels. Previous studies have verified that continuous long-term sildenafil can maintain reversed corporal veno-occlusive dysfunction in a bilateral cavernosal nerve resection rat model.8 PDE-5i may help increase intracellular cGMP levels to improve cavernous microcirculation. Similarly, PDE-5i aids penile rehabilitation. In animal experiments, diabetic rats demonstrated significant increases in cavernous tissue malondialdehyde and significant decreases in glutathione peroxidase and cGMP; the high oxidative and low reductive environment is similar to that of the postreplantation cavernous body. Low cGMP levels lead to erectile dysfunction. With the use of PDE-5i, levels of glutathione peroxidase and cGMP increase and the level of malondialdehyde decreases. Based on the aforementioned theories, we believe that early administration of sildenafil is of great importance in penile rehabilitation after replantation.

Numerous factors affect prognosis, including type of severance, warm ischemic time, quality of blood vessel anastomosis, postoperative venous congestion, and endothelial function.10 Owing to the rarity and diversity of penile amputation injuries, randomized controlled trials are not practical. Likewise, available published studies on management of this condition have only involved single-center cases. This is the first report of early PDE-5i use in postreplantation recovery. According to our initial observation, the early initiation of low-dose sildenafil does not induce erection or any other visible adverse effect. However, more cases and multicenter clinical research studies are needed to further investigate whether early-stage PDE-5i therapy improves the recovery of sexual function. Furthermore, to investigate the underlying mechanism, more objective parameters should be assessed, such as Doppler ultrasound and evaluation of blood oxygen saturation of the glans.

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