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Superficial penile cancer treated with complete excision of the glans epithelium and coverage with a tissue sealant matrix (TachoSil®)

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Introduction The aim of our work was to demonstrate the feasibility and clinical outcomes after partial excision of the epithelial and subepithelial layer of the glans with subsequent tissue sealant matrix coverage (TachoSil®).

Material and methods We enrolled 11 consecutive patients with superficial penile cancer. Under the microscopic guidance, the tumor in the glans area was excised continuously with a minimal lateral margin of 5 mm. The cosmetic result was accessed using a 5-graded scale ranging from very dissatisfied to very satisfied.

Results The median patient's age at the presentation was 46 years (range 38–53). Histopathological examination of the specimen confirmed squamous cell carcinoma and tumor-free surgical margins were obtained in all cases. Overall, the tumors were TaG1 in 3 patients, TaG2 in 1 patient, TisG1 in 2 patients, TisG2 in 2 patient, T1aG1 in 2 patients, and T1aG2 in 1 patient. All patients had clinically negative lymph-node status – cN0 (confirmed by aabdominopelvic computed tomography (CT) scan with contrast). During the follow-up of 6 to 36 months (median 18), local recurrence occurred in 1 patient with carcinoma in situ six months after surgery, which was managed by a second glans-preserving surgery without recurrence. The others showed no signs of local recurrence or metastasis during the period of observation.

Conclusions These preliminary data suggests that glans-preserving surgical technique using TachoSil® as a defect coverage is technically feasible, functionally safe and cosmetically satisfying. However, well-designed prospective-randomized trial is warranted, to further confirm the clinical utility of our approach.

Key Words: organ sparing ‹› penile cancer ‹› superficial ‹› tissue sealant matrix

INTRODUCTION

Cancer of the penis is a rare disease entity in the northern hemisphere (1 per 100000 people in USA and Europe) [1, 2]. Penile cancer (PC) represents 20–30% of all male cancers in some regions of Asia, Africa and South America and is a considerable treatment challenge for some countries, even in the developed countries [3]. Squamous cell carcinoma (SCC) accounts for more than 95% of cases of malignant disease of the penis [4]. PC is a diagnosis that possesses several profound implications for the male self-image and sexual functioning. The choice of the therapy for carcinoma in situ and T1 cancers has to take into account preservation of the organ with its morphology, functioning and cosmetic appearance. Traditionally superficial PC has been treated with many modalities [5]. The current standard treatment strategy with most favorable outcomes has to be yet defined. The major therapeutical concern is

to obtain a clear histological margin. Recently, a 5 mm tumor-free margin in contrast to the old dogma of 20 mm has been proposed [6].
Therefore any treatment modality without possibility to perform few random biopsies, may result in a higher recurrence rate [7]. Complete removal of the superficial penile cancer (SPC) can be achieved by means of excision and microscopic evaluation of the entire subsurface with additional systematic or random biopsies. The microscopic guidance may provide a better tissue preservation and potentially the eradication of the disease [8]. Over the last decade the glans resurfacing using split thickness skin grafting has been proved as a safe alternative to the partial penectomy [9, 10]. The use of prepucial skin graft to cover the glans defect after complete excision of the lesion, is another technique available, although currently less frequently used [11]. However, all these procedures are more complex and potentially carry higher morbidity when compared to the less invasive approaches.
The aim of our work was to demonstrate the feasibility and clinical outcomes after wide excision of SPC of the glans, followed by the defect coverage with tissue sealant matrix (TachoSil®).

MATERIAL AND METHODS

After obtaining the formal approval of the institutional review board, the data on penile cancer management were retrospectively collected. For the final analysis, 11 patients with SPC were further evaluated. All patients underwent partial glans epithelium/subepithelum excision for SPC. As an additional management of the defect, tissue sealant matrix – TachoSil® (Takeda GmbH, Linz, Austria) was applied. In the same setting all patients underwent concomitant circumcision, regardless of the normal macroscopic appearance. The final pathological specimen was evaluated by two senior uropathologists. Staging was performed using the 2002 TNM (tumor, node metastasis) system.
After adequate spinal or general anesthesia, the patient was placed in a normal supine position. A tourniquet was placed around the base of the penis. Under microscopic control and support with magnification of 20–30x a plane was developed to undermine the suspected area with approximately a 5mm healthy margin. Sharp dissection between the subepithelial layer and the corpus spongiosum was performed. After complete excision, a few random biopsies were performed from the base and sent for the frozen section analysis. Afterwards, the defect was covered with TachoSil. Mild compression on the wet sponge fleece for a minimum of 10 minutes was applicated, before releasing the tourniquet. A mild compressive bandage with fat gauze was applied after insertion a foley catheter Ch 14. The catheter was removed after 24 hours and the patient was discharged on the first or second postoperative day. On the very first postoperative day, we had removed the bandage and after careful inspection of the glans we applied a new one with a little bit less compression. TachoSil was attached to the area of excision and left in situ for another 7–12 days, until all the remnants completely fell off. The cosmetic result was assessed using a 5-graded scale ranging from very dissatisfied to very satisfied.

RESULTS

All patients had a single lesion on the glans (mean largest diameter 13; range – 8–15 mm), which was preoperatively histologically verified as a SPC. The median patient's age at presentation was 46 years (range 38–53). The final histopathological examination of the specimen confirmed squamous cell carcinoma and tumor-free surgical margins in all cases. All patients underwent abdominopelvic CT scan with contrast, a clinically negative lymph-node status was confirmed (cL0).
Overall, the tumors were TaG1 in 3 patients, TaG2 in 1 patient, TisG1 in 2 patients, TisG2 in2 patients, T1aG1 in 2 patients, and T1aG2 in 1 patient. During the follow-up of 6 to 36 months (median 18 months), local recurrence occurred in 1 patient with carcinoma in situ six months after surgery, which was managed by a second glans-preserving surgery without recurrence (at 49 months). The others showed no signs of local recurrence or metastasis during the period of observation. A patient with T1G2 SPC refused to undergo modified laparoscopic lymph node dissection, therefore a regular follow-up with CT scan was suggested, despite its limitations and unreliability to detect the micrometastatic disease.
The shape and appearance of the glans penis was preserved in every patient. The cosmetic results were regarded as satisfying/very satisfying by 81.8% (9 out of 11 patients), and the remaining 18.1% (2 of 11 patients) were less satisfied with the final appearance.
Healthy and almost natural appearance of the glans after the procedure helped the patients to regain their self-confidence and managed to revive their sexual functioning (Figure 1). We did not observe, any worsening of the erectile function. However, the exact data on the postoperative glans sensory changes were missing in our database.

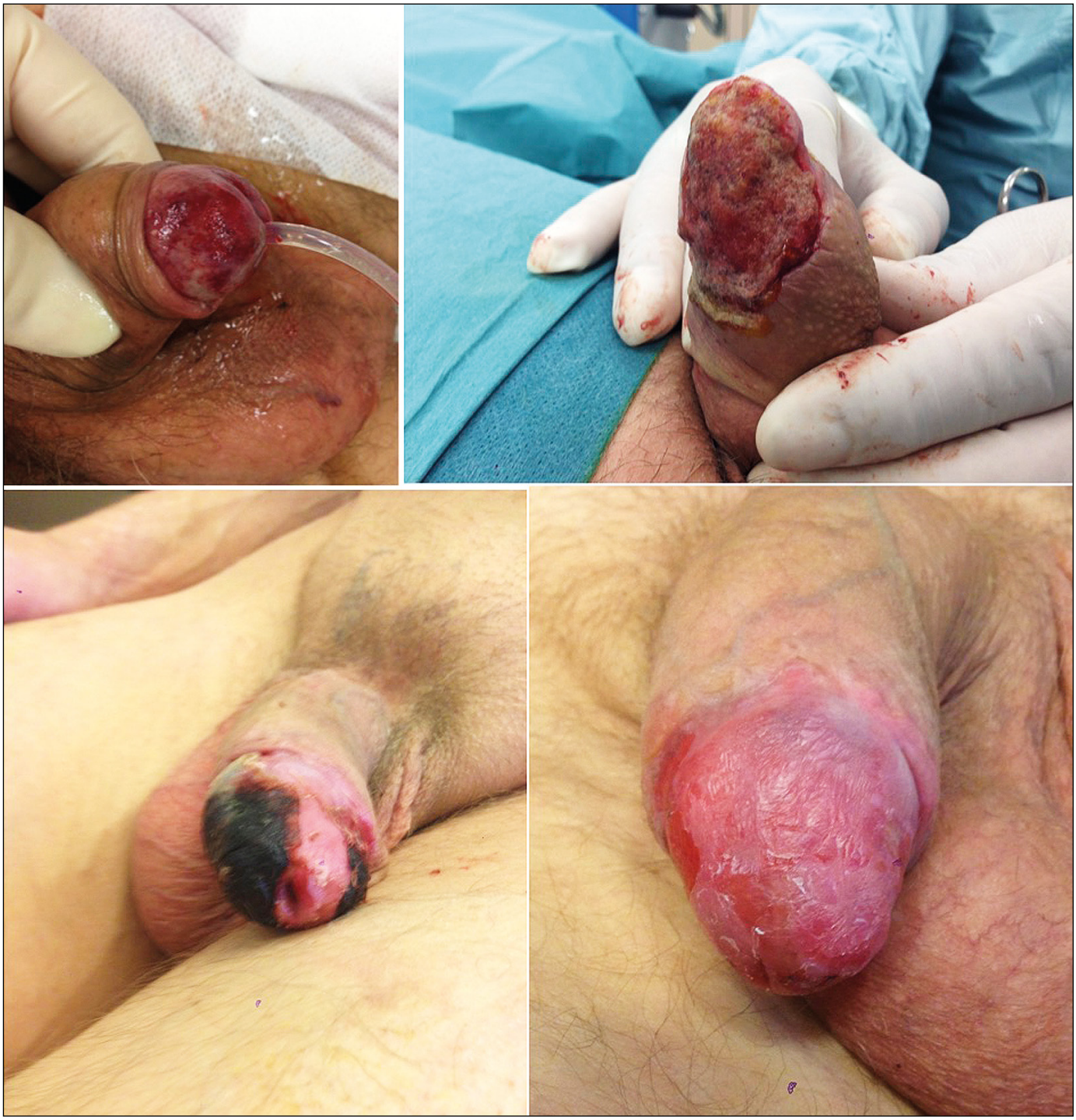

Figure 1. *Superficial penile cancer managed with glans resurfacing and TachoSil as an adjunct for the defect coverage. Within 7–12 days the rest of the TachoSil material fell off, final appearance of the glans after 6 weeks.*

DISCUSSION

The two most common sites for penile cancer are the glans and prepucium. The most common histologic subtype is squamous cell carcinoma, which accounts for 95% of all diagnosed lesions [12].

Phimosis, late circumcision due to chronic inflammatory conditions, lichen sclerosus, smoking tobacco and marijuana, obesity, marital and socioeconomic status, human papillomavirus infection as well as compromised immune system are the known risk factors [13]. Neonatal circumcision,

sufficient hygiene, early interventions in inflammatory conditions are the major prophylactic measures. The direct impact of the HPV vaccine in reducing the incidence of penile cancer in men still remains unclear [13, 14].

Surgical treatment of the penile cancer is generally associated with mutilation and significantly affects the overall quality of life [15].

A recent increasing interest, has broadened the horizons in the clinical management of penile cancer with regard to the organ preserving surgery. Generally, vast majority of tumors are amenable for the organ-sparing procedures [16]. Penile preserving surgery offers acceptable functional and sexual results with satisfactory cosmetic appearance [5, 9, 10].

The adoption of alternative approaches and less-aggressive surgical strategies when compared to the historical penile amputation, has led us to better understand the biological behavior of penile carcinoma. In addition, these approaches tend to improve the patient's quality of life in conjunction to their micturition and sexual functioning without jeopardizing oncological control [17].

Novel interventions include wide local excision, glansectomy with glans resurfacing. These advanced strategies are combining basic principles of reconstructive and plastic surgery. As an adjunct to these techniques, closure using skin flaps and other genital/extragenital grafts, penile lengthening are currently available [5, 18, 19].

TachoSil® is sponge coated with human fibrinogen and human thrombin, widely used and indicated as a support to improve hemostasis and promote tissue sealing. To our knowledge this is the first study to report the use of tissue sealant matrix (TachoSil) as a cover for the defect after partial excision for SPC at the glans area. According to our data we think, that our technique can be a valid alternative to glans resurfacing/grafting techniques or primary suture for smaller lesions.

In general, all of these options can be readily applied, however patient's understanding of the concept, risk of possible disease recurrence, as well as adherence to the close follow-up, are the 'conditio sine qua non' for such a treatment strategy. We have demonstrated relatively high overall satisfactory results with the final cosmetic outcome, which is comparable to other grafting techniques [9, 10, 11]. There was no serious complication sequelae. We did not take into account minimal hematoma in the glans area or penis shaft without requiring any intervention, because the following was not the cause of patient's dissatisfaction.

The overall safety data in conjunction with the local recurrence rates and disease spread is difficult to interprete, because of the small patient's sample and short term follow-up.

For patients with unsatisfactory cosmetics, the redo-surgery should be technically easier when compared to the patients with previously applied genital or extragenital grafts. We assume, that this in particular, can be another hypothetical advantage of the tissue sealant application. We must certainly admit, that the data on revision surgeries for unsatisfactory cosmetic outcomes are missing in the literature.

Last but not least, our approach deserves further evaluation and cost-analysis among other standard treatments. On the contrary, the TachoSil matrix is a ready to use material, which eliminates the risks of morbidity associated with harvesting.

The epithelium of the glans is a mucocutaneous tissue, the outer surface is dekeratinized and is made up of living cells. The glans penis contains of rich supply of nerves and blood vessels responsible for the regeneration properties. Healing occurred by re-epithelialization from surrounding unaffected areas and took several weeks (approx. 42 days). However, as opposed to the split thickness skin grafting techniques, our modality leaves a particular amount of scar tissue behind.

The study is adherent to several limitations, is retrospective in its nature with a very small patient data set. The overall follow-up is short, that is why the oncological safety is difficult to discuss. Our primary study outcome with regard to the feasibility was successfully demonstrated, nevertheless on the very limited cohort. The final aesthetic outcomes, regardless our promising satisfactory rates, should be further evaluated in a randomized design. The satisfactory results were not evaluated with validated questionnaires, in the light of this are prone to subjective biases. Nevertheless, we hope we were able to provide enough preliminary evidence to pose further interest for additional testing of this easy to perform surgical technique. Last but not least, the question remains, if it is really necessary to perform this procedure under microscopic enhancement, as far we were not aware of any related data.

CONCLUSIONS

The present study indicates that our modification of glans 'resurfacing' after partial excision may be of benefit in patients with superficial penile cancer (SPC). Major advantages are decreased operative times and easy ready-to-use application. The hemostatic effect has been widely tested and provided in a great variety of urological procedures, that is

why, the feasibility was considered as the primary outcome of the study. The long-term clinical outcomes are not really important to confirm the utility of this material. On the contrary, long-term local recurrence rates are necessary to evaluate with respect to other penile sparing strategies.
In conclusion, according to our preliminary results we can assume, the defect coverage with tissue sealant matrix seems to be feasible and safe after partial glans excision for SPC.

CONFLICTS OF INTEREST
The authors declare no conflicts of interest.

Research involving humans Informed consent: informed consent was obtained from all individual participants included in the study.

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