Conservative surgery for the treatment of penile carcinoma

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Summary

The rationale for organ preserving surgery in the treatment of squamous cell carcinoma (SCCA) of the penis is based on three key concepts. 1. About 80% of penile carcinomas occur distally, involving the glans and/or prepuce and thus are potentially amenable to organ preserving surgery. 2. Patients with penile carcinomas stages Tis, Ta, T1; grades 1 and 2 are at low risk for local progression and/or distant metastatic spread. 3. The traditional 2 cm excision margin has been challenged as unnecessary for patients undergoing partial penectomy for SCCA. Conservative techniques with surgical margins of less than 10 mm appear to offer excellent oncological control. Circumcision, laser ablation, Mohs' micrographic surgery and partial or total glansectomy associated with various forms of reconstruction have been reported as surgical organ-preserving procedures for the treatment of SCCA. The aim of the present article is to give an overview on the results and indications of penile sparing surgical techniques in the treatment of penile cancer.

For carcinoma in situ (also referred to as erythroplasia of Queyrat or Bowen's disease) laser ablation has been employed successfully.

In case of lesions limited to the foreskin, wide local excision with circumcision is sufficient primary curative therapy, although care must be taken to ensure adequate clearance margins are achieved. If the tumor has involved the glans, the choice of therapy is dictated by tumor size, extent of infiltration, and degree of tumor destruction of normal tissue. All these factors can indicate if organ preservation is a reasonable alternative to amputative procedures. Total and partial glansectomy, with or without grafting procedure, produce good cosmetic and functional results with minimal morbidity without sacrificing cancer control.

Introduction

Penile cancer is an uncommon malignancy with a reported annual incidence of 0,9-1 in 100,000 of the male adult population in Europe and in the USA. Ninety-five percent of penile tumors are squamous cell carcinomas (SCCA) and 78% of all tumors are diagnosed on the glans and/or prepuce [1] [2].

Historically, options for management of invasive penile cancer have included amputative surgery or radiotherapy.

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Amputative surgery, based on partial or total penile amputation and closure of the penile stump using the skin of the shaft to the urethral mucosa, provides excellent local control rates greater than 90% of the primary tumor and, therefore, remains the oncological "gold standard" for all stages SCCA [3] [4]. Nevertheless, this approach invariably leads to considerable cosmetic deformity, psychological traumas and functional loss with resulting sexual and urinary dysfunction with more than 50% of patients developing mental disorders [5-7].

Radiotherapy is an organ-preserving technique but has been used with limited success. Indeed, SCCA is relatively radioresistant and it requires a relatively long treatment regimen of 3 to 6 weeks and a large radiation dose of 6.000 cGy [8]. The local recurrence rate has been reported in over 45% of cases [9]. Almost all patients have acute radiation reactions with necrosis which can lead to amputation of the penis, urethral stenosis, urethral fistula, chronic penile pain and penile oedema that lead to a not negligible drop out rate from the treatment. Moreover, around 40% of patients have chronic radiation reactions that can make harder the early diagnosis of a potential local recurrence [8-12].

The limits of the radiotherapy treatment and the justifiable reluctance of many patients to undergo a mutilating penectomy has promoted the use of penile sparing surgical techniques to maintain penis function and appearance [13] [14]. The aim of the present article is to give an overview on the results and indications of penile sparing surgical techniques in the treatment of penile cancer.

Rationale for organ preserving surgery

The rationale for organ preserving surgery in the treatment of SCCA of the penis is based on three key concepts:

1. about 80% of penile carcinomas occur distally, involving the glans and/or prepuce and thus are potentially amenable to organ preserving surgery [15];
2. patients with penile carcinomas stages Tis, Ta, T1; grades 1 and 2 are at low risk for local progression and/or distant metastatic spread [16];
3. the traditional 2 cm excision margin has been challenged as unnecessary for patients undergoing partial penectomy for SCCA. Conservative techniques with surgical margins of less than 10 mm appear to offer excellent oncological control [17] [18].

Therefore, until more rigorous scientific evidence is available, organ-preserving strategies should be reserved to well-selected patients with low-grade, low-stage disease [15], as in these cases the achievement of good cosmetic and functional results should not compromise long-term oncological outcomes. Circumcision [15], laser ablation [19], Mohs' micrographic surgery (MMS) [20] and partial (PG) or total glansectomy (TG) associated with various forms of reconstruction have been reported as surgical organ-preserving procedures for the treatment of SCCA [1] [2] [21].

The goals of penile-preserving treatments are to maintain penile/glans sensation and to maximize penile shaft residual length when possible.

Circumcision

The majority of men with penile carcinoma are uncircumcised. Small low-stage (Tis, Ta, T1) and low-grade (grades I and II) tumors limited to the distal prepuce can be managed by circumcision alone, with a 2 cm margin of clearance and this procedure can be considered the standard treatment in these clinical settings [13]. If the tumor is closer to the coronal sulcus, the circumcision margin must be extended proximally to the penile shaft to ensure adequate oncological resection, as recurrence rates may be as high as 50% [22]. A careful selection of the patients and the use of intraoperative frozen sections are imperative to reduce local recurrence rates.

Laser ablation

Laser energy for penile lesions was first introduced by Hofstetter and Frank in 1980 [23]. The carbon dioxide laser and neodymium YAG laser are the most commonly used in current practice [19] [24]. The carbon dioxide laser vaporizes tissue with minimal penetration of energy into the deeper layers (only 0.1 mm) as the energy is completely absorbed at impact by the water component of the cell and therefore it is unsuitable for most tumors with a recurrence rates of up to 50% [24]. The neodymium YAG laser penetrates tissue and causes coagulation to a depth of at least 3 to 4 mm [24].

Overall recurrence rates with neodymium YAG laser ablation are stage-dependent. Using this laser, Malloy et al. on 16 treated patients, 5 Tis, 9 T1 and 2 T2 carcinomas, had no recurrences in all patients with TIS, while 33% of the T1 patients and all T2 patients showed local recurrence, at a follow up that ranged between 12 and 36 months [25]. Frinberger et al. in 29 patients, at a mean follow-up of 47 months, had a 5.8% incidence of local recur-

rence in Tis patients and a 10% recurrence rate in T1 patients [19]. Von Eschnbach et al. reported good outcomes for T1 tumors with excellent cosmetic and functional results and high satisfaction rates. Recurrences were noted in 6.9% of patients, which is comparable to recurrence rates after partial amputation (0-8%) [26].

In a recent retrospective study, Meijer et al. reported the results obtained in 44 patients (21 T1, 17 T2 and 6 Tis) after a mean follow-up ranging between 3 months and 16 years. Local disease recurrence in the treated area occurred in 48% of the patients, and in 20% of them, the first recurrence was elsewhere on the glans penis. In 10 cases, nodal metastases were found and 8 of these cases were stage T2. The authors concluded that laser therapy is best for stage Tis and T1 tumors exclusively. Only selected patients with T2 tumors should be treated in combination with early groin lymph node resection, as, with respect to the risk of nodal metastases, the T2 stage represents the stronger prognostic predictor [27].

Overall, these results taken together, demonstrate that laser surgery, who has significant cosmetic and functional advantages over traditional amputation, is feasible. Neverthless, patient selection is extremely important as only those tumors invading less than 4 mm into tissues are suitable for neodymium YAG laser treatment. Therefore, this treatment is best reserved for superficial and small lesions. It is most suitable for Tis lesions and should be done always in conjunction with frozen-section biopsies. It may also be performed in T1 patients, but a close surveillance is mandatory during follow up for early detection of tumor recurrence. A proper surgical procedure should be suggested for T2 patients, unless in very selected cases and in these patients every local procedure should be associated with groin lymph node dissection.

Mohs micrographic surgery

The microscopically controlled surgery represents a reasonable compromise to control local disease while providing organ preservation in patients with small superficially invasive lesions. The tumor is excised, in multiple sessions, in layers and each layer is examined microscopically by systematic frozen sections. Excision is continued until the excised tissue is negative at the histological examination. Reported complications include glans disfigurement and meatal stenosis [28]. Mohs reported 35 cases in 50 years of experience, with a local recurrence rate,

at 5 years follow up, of 14% for T1 lesions, 18% for T2 and 100% for T3 lesions [20].

Brown et al presented the results in 20 patients: 11 with SCCA, 7 with SCCA in situ, 1 verrucous carcinoma and 1 leiomyosarcoma. At a mean follow up of 3 years, local recurrence was noted in 6% and a lymph node recurrence in 24% of SCCA patients. One patient died of metastatic disease and another died of unrelated causes [28].

Bissada and coworkers reported the results on 30 patients: 17 underwent inguinal lymphadenectomy which revealed lymph node disease in 12. At a follow up ranging between 12 and 360 months, 3 local recurrences and 1 cancer related death were observed [15].

Finally, Shindel and coworkers treated 33 patients who underwent a total of 41 Mohs procedures (26 Tis, 4 T1, 7 T2 and 4 T3). Follow up data was available on 25 patients at a mean follow up of 58 months. Eight patients had local recurrence (32%), which was managed by repeated MMS in 7 and by penectomy in 1. There were 2 cases of tumor progression, including 1 from T1 to T3 disease (meatal involvement) and 1 from T1 to inguinal lymph node involvement. Two patients died, of whom 1 had no evidence of penile cancer and 1 had metastatic disease [29].

Overall, taken these results together, MMS can allow for the local complete excision of the tumor with preservation of local penile anatomy and function. However, local failure can occur and therefore this technique should be reserved only for patients with small, distal, superficially invasive tumors [29].

Partial glansectomy

There are three kinds of PG reported in the literature:
1. PG with primary glans closure;
2. PG with graft reconstruction of the glans;
3. PG without grafting.

PG is indicated in localized tumors of the corona or central glans with no surrounding carcinoma in situ or obvious erectile tissue involvement on MRI.

Primary glans closure is suitable for small and isolated lesions. For larger lesions, when primary closure is not technically feasible or might not be oncologically safe, various techniques have been suggested to cover the area. McDougal performed partial glans excision in five patients. All underwent wide excision of the disease, preserving the urethral meatus [30]. In 2 patients a full-thickness graft was used to resurface the hemiglans defect and in 1 a split-thickness graft was applied to the corona

and glans area [30]. Ubrig described a simple technique in which an outer preputial skin flap was used to cover the glans defect [31]. Pietrzak and coworkers suggested the use of a full-thickness flap of penile skin or extragenital (lateral aspect of the thigh) split thickness skin graft [2]. The subtotal glans excision without grafting, reported by Ralph [1], consists in carrying out two circumferential incisions: the first is a skin incision at the level of the coronal sulcus, and the second around the meatus, both with a macroscopic clearance of ≥ 5 mm and confirmed by frozen-section analysis. The tumor and healthy glans, between the incisions, are then excised leaving the urethra intact. The residual glans along with the urethral meatus is then sutured down to the distal corpora and the penile skin closely approximated to it with absorbable sutures. This technique preserves the meatus and gives a better cosmetic and functional outcome. Of the 5 patients treated by Ralph, the postoperative stage and grade were T1G2 and T1G3 in two patients and T2G2 in one patient. At a mean follow-up of 12 months, no patients have had a clinical recurrence, or had voiding difficulties. These men, sexually active before surgery remain so, with cosmetic and functional results acceptable to the patients [1].

Overall taken together, these results showed that, if technically feasible, PG is an effective treatment for penile tumors allowing for a radical removal especially in case of T1 lesions.

Total glansectomy

The surgical technique of TG, first described by Austoni in 1996 [32], consists of a circular incision in the distal shaft skin down to Buck fascia. At this level, a plane is developed to separate the glans from corporal tips. The urethra and the neurovascular bundle are isolated in their distal extremities. The glans is dissected from the corpora cavernosa and the urethra is distally sectioned. The use of multiple frozen sections of the surgical margins is strongly suggested. After removing the glans, the urethra is ventrally opened and the neomeatus fixed to the tip of the corpora cavernosa. The neurovascular bundle is fixed to the albuginea proximally to the neoglans with absorbable sutures.

For distal tumors invading the tunica albuginea and/or corpora cavernosa, a more extensive resection is required and glansectomy must be associated with distal corporectomy and reconstruction of corporal heads. TG without or with distal corporectomy are usually combined with reconstruction of a new glans using a split thickness skin graft (STSG). The STSG is harvested from the inner thigh close to the groin to improve cosmesis with the use of a dermatotome, and then tailored and transplanted to cover the tip of the corpora cavernosa. The graft is repeatedly and multiply incised and fully quilted with the use of multiple Polyglactin interrupted stitches over the top of the corpora cavernosa. Humid compressive dressing can be applied and suture-fixed on covering the penis [21].

Devis et al. treated 3 patients with verrucous carcinoma, angiosarcoma and a melanoma respectively. No patients had a local recurrence and all had normal urinary and sexual function [14]. Hatzichristou and coworkers treated 7 patients with verrucous carcinoma. At a mean follow-up of 65 months only one had local recurrence and all patients had normal urinary and sexual function [33].

Pietrzak and colleagues performed 10 partial glansectomy, 21 glansectomy with reconstruction and 8 glansectomy with distal corporectomy and reconstruction. At a mean follow up of 12 months of the patients who had PG, one had a tumor recurrence on the residual glans. None of those who had the glans removed had tumor recurrence [2]. In our series of 15 patients, treated with TG, between March 2003 and January 2008, only one patient had inguinal lymph node metastases 18 months after surgery, while none had local relapse and our crude disease specific survival rate was 93.3% after a mean follow up of 36 months. All patients were able to maintain their sexual activity starting from 3 months after surgery with a range between 2 and 6 months [21]. Orgasm and ejaculation were preserved in all patients though reduced glans sensitivity was reported by all patients as a predictable consequence of glans amputation [21].

Although the majority of series reports the use of a STSG, some experiences are based on glans replacement with buccal mucosa free grafts [34] and recently Gulino et al. has reported on a new technique of glans reconstruction using the distal urethra, with good functional and aesthetic results [35].

In conclusion, results reported in the literature showed that TG associated with resurfacing is an oncologically sound procedure for pT1 penile tumors and if associated either with distal corporectomy or distal corpus spongiosum excision it can be used also for the treatment of pT2 lesions. Indeed, conventional therapy for pT2 tumors would be a choice of penile amputation of varying degree but these patients can now be offered glansectomy as an alternative.

Discussion

Carcinoma of the penis is a rare tumor with considerable geographical variation [36] [37]. The majority are SCCA (95%) and overall 78% of all tumors originate on the glans, coronal sulcus or foreskin. PG or TG, that provides excellent local control rates greater than 90% of the primary tumor, remains the oncological "gold standard" for all stages [1] [2]. Therefore, the patient with penile cancer is not only challenged by the fear of suffering from a deadly disease, but is also confronted with the threat of losing a part of or the complete penis. The first questions of patients upon hearing the diagnosis usually deal with erectile function and body image, and only secondarily with the disease itself. The justifiable reluctance of patients to undergo a mutilating penectomy has prompted the search for new penis-sparing surgical techniques to maintain penis function and appearance; thus moving from the maximal tissue and organ destruction to the minimal therapeutic tissue removal [12-14]. This represents an oncological and surgical multidisciplinary evolution that has previously been witnessed for chemotherapeutic therapies where medicine moved from the maximal tolerated dosage to the minimal therapeutic dose. Moreover, the "sparing" concept, which has also been proposed for other urological diseases such as kidney cancer, is not peculiar of urologists but represents a surgical multidisciplinary issue being prioritized also in many other malignancies such as melanoma and breast cancer. Circumcision, laser ablation and micrographic surgery aim to remove the diseased tissue, but recurrence of the disease may occur in unrecognized premalignant foci arising within the unstable epithelium following a partial procedure. Circumcision is indicated as the standard treatment in small tumors of the foreskin. However, proper patient selection and attention to intraoperative frozen section margin status are imperative for a successful outcome, because circumcision alone, especially with tumors proximal to the coronal sulcus, may be associated with a recurrence rate of 50% [22]. The laser treatment offers excellent cosmetic results, with low local recurrence rates for Tis tumors [24] [38]. It may also be performed in T1 patients but a close surveillance is mandatory during follow up for early detection of tumor recurrence [24] [38]. Conversely, in stages greater than T1, local recurrence and poor control of the disease are reported [39]. Micrographic surgery, despite good cosmetic results, has failed to gain wide acceptance due to its elevated local recurrence rate also for T1 tumors, and moreover it is very time consuming.

PG and TG [1] [2] [30] [40] [41] are based on a surgical doctrine in which resection margins of 2-3 cm are not necessary to achieve local oncological control [8] [13]. Conventional amputative surgery based on this dogma is associated with unsatisfactory cosmetic results, significant reduction in penile length and thus difficult or impossible vaginal penetration with severe consequences on patients psychology and it has been reported that more that 50% of these patients develop mental disorders [42]. On the contrary, the use of glansectomy in selected patients with carcinoma localized on the glans penis has been proposed to maintain a satisfactory penile length and to improve patients quality of life [14] [40] [42]. Moreover, it is an oncologically safe procedure. Many reports have shown similar 5-year disease specific survival rates for amputative procedures, reducing the width of the resection margins [14] [17] [42]. Moreover, if tumor recurrence occurs it is usually systemic at the inguinal lymph nodes. Cancer specific survival rates are similar to those reported using the conventional surgical treatment [21] [43] [44].

In patients who undergo glansectomy with reconstruction of a new glans, using a STSG, functional results are satisfactory [21]. Thus, the good aesthetic appearance of the penis and functional results that consist in good erectile function, preserved orgasmic sensation and stand up micturition, have a positive psychological impact on the patient and improve the patient's quality of life [45]. The most important disadvantages in the reconstruction of a new glans, using a STSG, are the reduced glans sensitivity, the spraying of urine when voiding and the complications of a more technically complex procedure, including graft failure and infection [21].

To overcome the disadvantages of the reduced sensitivity, a technique of glans reconstruction, using the distal urethra, have been proposed [35]. To avoid the drawbacks of TG and of the grafting procedure, Ralph suggested the use of a subtotal glans excision with the preservation of the urethral meatus and without the need of skin grafting. In such cases, a catheter remains in situ for 24 hours and the patient is discharged the next day. No men had voiding difficulties in his study and the patient sexually active before surgery remains so, with cosmetic and functional results acceptable to the patients [1].

Conclusion

Approximately 20% of patients with penile cancer are under 40 years of age and radical procedures, especially partial or total penectomy, may be psychologically devastating. The ideal surgical procedure

should eliminate the disease and preserve sexual and urinary function. This is still not always possible because of the extent of disease. Circumcision, laser therapy, microscopically controlled surgery, total and partial glansectomy have all been used in an attempt to provide organs sparing alternatives. For carcinoma in situ (also referred to as erythroplasia of Queyrat or Bowen's diseas) laser ablation has been employed successfully.

In case of lesions limited to the foreskin, wide local excision with circumcision is sufficient primary curative therapy, although care must be taken to ensure adequate clearance margins are achieved. If the tumor has involved the glans, the choice of therapy is dictated by tumor size, extent of infiltration, and degree of tumor destruction of normal tissue. All these factors can indicate if organ preservation is a reasonable alternative to amputative procedures. Total and partial glansectomy, with or without grafting procedure, produce good cosmetic and functional results with minimal morbidity without sacrificing cancer control.

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