Penile Tumors: Their Management by Mohs Micrographic Surgery

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FIRST PRIZE

Abstract. Penile tumors represent a difficult group of neoplasms requiring effective and curative treatment while minimizing tissue loss to prevent cosmetic and functional deformity. Over the past 6 years, we have treated 20 patients with penile cancer utilizing the fresh tissue technique of Mohs micrographic surgery. Tumors were excised with an average of 2.25 stages. Most defects (80%) were allowed to heal by second intention. Since surgery, four patients have developed metastatic disease in their regional lymphatic system, and one patient has died from metastatic spread. One patient has developed local recurrence. Micrographic surgery is a very useful treatment modality for patients with penile tumors. Patients with SCC of the penis should be considered for elective regional lymph node biopsy and/or dissection in conjunction with micrographically controlled excision of the primary tumor.

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INTRODUCTION

Surgical treatment of penile carcinoma has primarily been the domain of the urologist. The traditional surgical approach for penile malignancies (most commonly squamous in origin) has been partial or total penectomy, either with or without ilioinguinal lymphoadenectomy.[1,2] This surgical approach often results in marked cosmetic deformity of the penis, with impaired sexual function and body image.

As the benefits of Mohs micrographic surgery become established, there is an increasing tendency for patients with penile tumors to be referred for treatment by this technique. Mohs surgery offers the unique advantages of effective surgical treatment with microscopically controlled tumor-free borders while maintaining cosmetic and functional demands by maximal preservation of normal tissue. The purpose of this paper is to present our experience over the past 6 years in treating penile neoplasms with the Mohs technique. In doing so, we hope to emphasize the advantages of this surgical approach as the preferred treatment modality for localized penile carcinomas.

MATERIALS AND METHODS

Twenty patients with penile cancers were treated by the fresh-tissue technique of Mohs micrographic surgery at the University of Michigan's Department of Cutaneous Surgery and Oncology between 1981 and 1987. Preoperative evaluation included the size and location of the penile tumor, bilateral palpation of femoral and inguinal lymph nodes, and careful inspection of the scrotum and base of the penis to

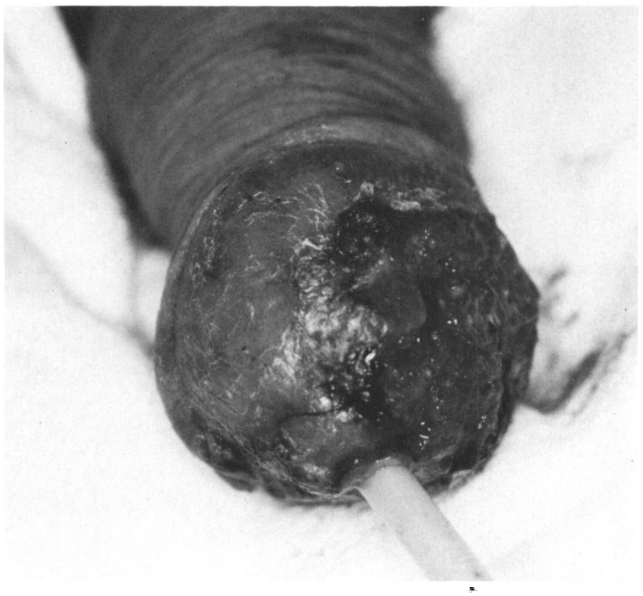

FIGURE 1. SCC on the glans penis, preoperatively.

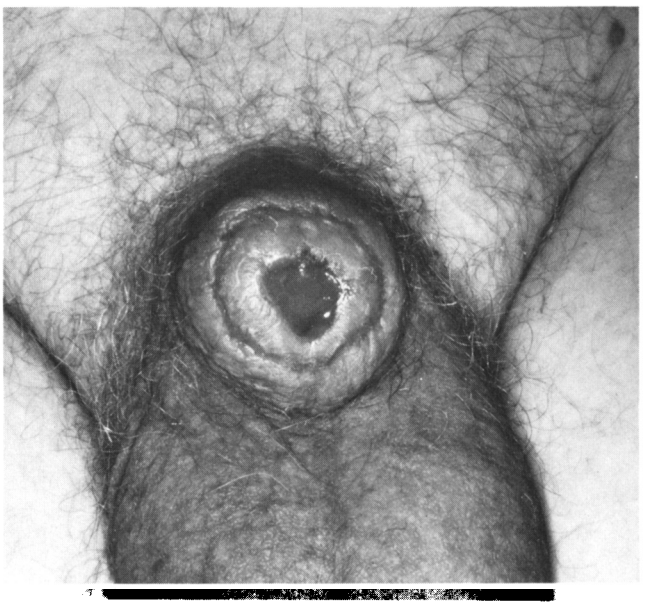

FIGURE 2. Healing by second intention 2 weeks postoperatively.

rule out local extension. All patients were evaluated concurrently by a urologist. The patients were clinically examined during the early postoperative period, and subsequently followed by us or their referring physician. Their progress and clinical outcome was reviewed by examination of inpatient and outpatient hospital records, as well as by telephone survey. Mean follow-up was approximately 3 years for 17 patients; three patients were lost to follow-up.

Mohs surgery was performed in an outpatient setting in the standard fashion. Local anesthesia was achieved with a Carbocaine block. A tourniquet was placed at the base of the penis to minimize bleeding. A foley catheter was inserted for patient comfort and to serve as an anatomic landmark for the urethra and meatus (Fig. 1). Due to the contractile nature of the penile tissue, marking sutures were used to identify the margins of the sections instead of the conventional method of scoring the tissue with a scalpel blade. Hemostasis was obtained with several modalities, including use of a Bovie, spot electrocautery, pressure, and gelfoam.

The average age of our patient population was 55 years, with a range of 35 to 80 years. Histologically, eleven patients had squamous cell carcinoma (SCC), seven patients had Bowen's squamous intraepidermal neoplasia, one patient had a verrucous carcinoma, and one patient had a leiomyosarcoma. Sixteen tumors were confined to the glans penis, and four were located on the distal shaft. There were no palpable nodes at the time of surgery, and there was no clinical extention to the scrotum or base of the penis. Four of these referral cases were recurrent tumors, having been treated elsewhere by non-Mohs therapy. Preexisting conditions were seen in four patients; three patients with SCC had a previous diagnosis of balanitis xerotica obliterans (BXO), and the one patient with a leiomyosarcoma had sustained a previous traumatic event to the penis. Tumor size ranged from 0.5 × 0.5 to 6.0 × 5.0 cm with an average size of 2.3 × 1.8 cm.

RESULTS

All patients tolerated the surgery well in an outpatient setting with no significant perioperative or postoperative complications. Tumor excision was complete in nineteen patients with an average of 2.25 stages. The average postoperative defect size was 3.6 × 3.0 cm, with the largest defect being 6.0 × 7.0 cm. Most defects (16 patients) were allowed to heal by second intention (Fig. 2), three were closed primarily, and one was referred to the urology service for closure and repair.

Of the seventeen patients reviewed, only one has possibly developed local recurrence. Four patients with SCC were subsequently found to have positive regional nodes, despite being clinically negative at the time of surgery. One patient has died of metastatic disease, and one patient has died from unrelated medical causes. Two of the four patients with metastatic disease and the one patient with local recurrence had a preexisting diagnosis of

BXO. Although the number of patients is small, BXO appeared to be a poor prognostic indicator.

DISCUSSION

Penile malignancies account for less than 1% of male cancers in the U.S.[3,4] There is an estimated 1 to 2 new cases per 10,000 population per year.[4] Early circumcision and proper hygiene probably account for this low U.S. incidence, especially when compared to underdeveloped countries. In certain African and Asian populations, where circumcision is uncommon, penile carcinoma accounts for 10 to 20% of all malignancies in males.[4] The development of penile cancer among uncircumcised males has been associated with the chronic, irritative effects of smegma, the by-product of bacterial action on desquamated cells that is retained within the preputial sac. Although smegma has been identified as a carcinogen in animal models, the specific component responsible for malignant degeneration in human males has not been identified.[3] Adult circumcision appears to offer little or no protection against the future appearance of penile tumors.

Penile cancers rarely develop in males circumcised in the neonatal period, but becomes more frequent when circumcision is delayed until puberty. No consistent etiologic relationship has been established for antecedent trauma and/or venereal disease. Precancerous lesions include leukoplakia, BXO, and the Buschke-Lowenstein tumor. Erythoplasia of Querat and Bowen's disease are considered to be carcinomas in situ, and are histologically identical.

Penile carcinoma is usually seen in the 6th to 7th decade, but is not uncommon in the 4th to 5th. In our population, the mean age was 55 years. The tumor is most common on the glans, prepuce, or coronal sulcus, and much less common on the shaft or meatus. Common presenting symptoms include the presence of a tumor mass or phimosis of recent onset. The cancer may appear indurated and erythematous, warty and exophytic, or flat and ulcerated. All these tumors appear to have a similar rate of growth, but the ulcerative lesion has a tendency towards earlier nodal metastases. Initially, the phimosis may obscure the tumor mass and result in a delayed diagnosis. Eventually, a foul odor, discharge, and bleeding may occur. At times, inguinal adenopathy may be the presenting symptom. Pain is not a common symptom, even with extensive local destruction. Likewise, urinary symptoms are uncommon unless the tumor is far advanced with resultant autoamputation.

Unfortunately, many lesions are quite advanced at the time of diagnosis. Possibly due to fear of penile surgery, as high as 50% of patients delay medical care for greater than 1 year.[3] Penile cancer has a relentless progressive course with death in approximately 2 years if untreated. Death usually results from uncontrolled regional lymphatic spread leading to skin necrosis, chronic infection, debilitation, and sepsis.

Because carcinoma of the penis is uncommon in the U.S., there has been a relative scarcity of well-controlled, prospective studies concerning the proper treatment of this cancer. Controversy in disease management includes the appropriate surgical treatment of the primary lesion and the subsequent evaluation and treatment of nodal disease. Selected small tumors that are limited to the prepuce have been treated by circumcision alone. However, tumor recurrence can be unacceptably high, with reports of a 40 to 50% recurrence rate.[3,4] For tumors on the glans and distal shaft, partial amputation with a 2-cm proximal margin is recommended. For more extensive lesions or those located on the proximal shaft, total penectomy is performed.

The desired goal in the treatment of the primary tumor is complete excision with adequate tumor-free margins. Mohs micrographic surgery allows the precise identification of these tumor-free margins, while minimizing tissue loss. It is an excellent alternative to the traditional surgical approach of partial or total penectomy.

Microscopically controlled chemosurgery was introduced in 1941 by Frederic Mohs.[5] A fixation process with zinc chloride paste was utilized to remove thin layers of tissue which were sequentially examined microscopically for evidence of tumor. This procedure was continued, sometimes over a period of days, until tumor-free margins were defined. In 1985, Mohs summarized his results with the fixed tissue technique in the treatment of SCC of the penis.[6] He treated 29 patients with a follow-up of at least 5 years in 25 cases. The primary carcinoma was eradicated in 23 patients (92%) with a 5-year cure rate of 68%. The cure rate was highest for the more distally located carcinomas. There was an 81% cure rate when the tumor was localized to the glans and/or prepuce, but only a 57% cure rate when the penile shaft was involved. The size of the penile lesion also affected prognosis, with a 100% cure rate if less than 1.0 cm, but only a 50% cure if greater than 3.0 cm.

Other poor prognostic indicators included nodal metastases at the time of surgery and previous treatment of the primary tumor by conventional

surgery or radiation therapy. None of the patients treated by Mohs reported a functional deficit, either sexual or urinary. Mohs concluded that except for large and highly anaplastic tumors, which would preclude preservation of a functional penis, and those on the foreskin, which could be excised completely by circumcision, microscopically controlled surgery was the preferred surgical technique for treatment of localized penile carcinomas.

The fresh tissue technique of micrographic surgery was popularized in the 1970s by Stegman and Tromovich.[7] This approach required the surgical excision of fresh, unfixed tissue with subsequent analysis of cryostat sections. The fresh tissue technique is far more rapid and precise and has largely replaced the fixed tissue technique. All of our patients were treated with the fresh tissue technique. Although we cannot yet quote a 5-year survival rate, our results to date have been very satisfactory and encouraging. Only one patient has developed a local recurrence, and it is possible that this represents a second primary lesion. Five to fifteen percent of patients with penile cancer develop a second primary tumor.[4] Our patient had a long standing history of extensive BXO, with a second tumor developing 4 years after the primary surgery. With the preexisting condition of BXO and the relatively long period of time elapsed between tumors, it is likely that this tumor may be a second primary SCC of the penis.

Four of our patients have developed metastatic spread to the inguinal nodes, and one of these patients has died from his metastatic disease. This was 20% of our total population and 35% of the patients with SCC (including the three patients lost to follow-up). Metastatic spread was not suspected clinically at the time of surgery, which was a surprising finding in that an estimated 50% of patients present with inguinal adenopathy at the time of diagnosis. In all cases, metastatic involvement was diagnosed within 1 year postsurgery. The earliest route of spread of penile cancer is metastases to the regional femoral and iliac lymph nodes. There are multiple cross communications throughout all levels of penile lymphatic drainage such that drainage is bilateral to both inguinal areas. In spite of the rich blood supply of the penis and possible spread through the pelvic vasculature, visceral metastases are rare. Clinically detectable distant metastases to lung, liver, bone, and brain occur in less than 10% of patients, usually late in the course of the disease.

Our 20% incidence of metastatic disease raises the controversy of proper management of regional lymph nodes with penile cancer. Approximately 1/3 of patients presenting with penile carcinoma have metastatic spread to the regional inguinal lymph nodes.[8] Because 40 to 50% of patients with positive nodes can be cured by node dissection, it is important to diagnose and treat this metastatic spread in a timely fashion. Unfortunately, clinical evaluation is imprecise and inaccurate with unacceptable false positive and false negative rates. It has been estimated that as high as 50% of patients with clinically positive nodes have no metastatic disease on histologic examination while 20% of patients with clinically negative nodes have occult metastasis.[10–12] To further complicate the issue, approximately 10% of patients with clinically positive nodes that are negative on node biopsy subsequently will demonstrate regional disease.[4] Although bilateral prophylactic inguinal lymphadenectomy is potentially curative and is the most accurate diagnostic staging procedure, it carries a significant incidence of morbidity, including wound infection, skin flap necrosis, pulmonary emboli, and chronic lymphedema.[3,13]

Johnson and Lo[14] compared patients who had late versus early node dissection and found a significant difference in mortality (57 vs. 13% 5-year survival). Therefore, the diagnostic challenge is to identify which patients have metastatic spread and to therapeutically dissect the involved nodes as early as possible. Some authors recommend "watchful waiting" if the regional nodes are clinically negative, especially if the primary tumor is small and located distally on the glans or prepuce.[9,14] Others have strongly recommended bilateral sentinel node biopsies, regardless of whether the nodes are clinically involved.[8,14,15] This recommendation is based on lymphangiographic evidence that a sentinel node located near the junction of the saphenous and femoral veins is the first site of metastatic spread from a penile cancer.[15]

The sensitivity of this diagnostic procedure has been estimated to be 88%.[8] If the sentinel node is positive, then a bilateral deep and superficial ilioinguinal node dissection is warranted. If the sentinel node is negative, no further surgery is recommended. However, close clinical follow-up and observation (preferably by the same physician) for the appearance of unrecognized inguinal metastases in biopsy negative patients is mandatory. There have been several reports of patients with false negative sentinel node biopsies who subsequently developed metastatic spread.[8,12] Nonetheless, the sentinel node biopsy, because of its simplicity and low morbidity, is an attractive method for staging apparently localized penile cancer. The role of the sentinel node biopsy requires continued assessment, as well as establishment of its true sensitivity and specificity.

An alternate proposal is that of a bilateral superficial node dissection. This involves removal of those nodes superficial to the fascia lata with progression to total lymphadenectomy (including nodes deep to the fascia lata contained within the femoral triangle) if the superficial nodes are positive.[4] This approach is based on the fact that iliac lymph nodes rarely become involved unless metastases have first reached the superficial inguinal nodes.

Finally, some urologists recommend bilateral prophylactic and therapeutic ilioinguinal node dissections for penile cancers.[1,16] This approach offers the best chance of cure, but its usefulness is limited by the morbidity of the procedure and the lack of controlled prospective studies to substantiate its benefit.[14] Its best indication may be for large tumors located more proximally on the penile shaft in association with convincing clinical evidence of lymphatic involvement.[9]

Our experience of nodal metastases with clinically negative nodes at the time of primary surgery in 36% patients with SCC of the penis would suggest a more aggressive diagnostic approach than a "watch and wait" policy. In view of the high incidence of lymph node metastases and the probable need for sentinel node biopsy, superficial node dissection or complete ilioinguinal node dissection, it is imperative that a urologist be a member of the treatment team.

SUMMARY

Our experience with 20 patients with penile cancer treated by micrographic surgery has been encouraging. Mohs surgery has several distinct advantages. First and foremost, it is a pricise surgical approach for the removal of the primary penile tumor, with a surgical field microscopically free of invasive tumor or marked dysplastic changes. It offers comparable survival rates with a less radical procedure and may often be curative. Through preservation of penile tissue, there is considerable cosmetic benefit and maintenance of normal sexual function. Surgery is well tolerated with the use of local anesthesia in an outpatient setting with negligible morbidity and high patient acceptance. Follow-up over ensuing years is necessary to define the 5-year survival rate. In the future, closer attention to the depth of invasion, histologic differentiation and intravascular involvement may help to better define prognosis. Our experience and that of others indicates the potential need for sentinel node biopsy and/or lymphadenectomy at the time of primary surgery for prognostic and therapeutic reasons.

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