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ORIGINAL ARTICLE

Carcinoma of the penis: experience from 360 cases

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Summary

Purpose: *To report the therapeutic results of 360 cases of squamous cell carcinoma of the penis treated by surgery.*

Patients and methods: *During the period 1974-1993 the records of 360 patients admitted in our Department with histologically diagnosed squamous cell penile cancer were retrospectively analyzed. Eighty-eight percent of them were uncircumcised. The surgical treatment which was performed included: circumcision 32 patients, local excision 12, partial amputation 227, total amputation 75, and 5 cystostomies in 5 of the 9 inoperable patients. Eighty-two patients had metastases to the inguinal lymph nodes; 30 inguinal,4 ilio-inguinal unilateral, and 35 inguinal,13 ilio-inguinal bilateral lymph node dissections were performed. In cases with partial amputation 1.5 cm margin proximal to the tumor was left.*

Results: *No local recurrence after partial or total amputation occurred. In 19 (8%) patients with partial amputation and in 5 (7%) with total amputation urethral meatus stenosis appeared. Complications after lymphadenectomy were as follows: wound infection in 12 (10%) patients, skin flap necrosis in 14 (12%), lymphocele in 17 (14%) and lymphedema in 19 (16%; 4 unilateral and15 bilateral). The 5-year survival was 91% for patients with stage T1-3 N0, 59% for patients with stage T1-3 N1-2 and 29% for patients with stage T1-3 N3. At 10 years the survival was 80%, 42% and 0%, respectively.*

Conclusion: *As the stage at presentation appears to be the most important prognostic variable for survival, early diagnosis and treatment give the best results. In stage T3 it is better to do primary lymphadenectomy as the possibility for metastasis during 2-3 years after amputation is about 80%. In stage T2 with poorly differentiated tumors, if the patient is not suitable for surveillance, it is also better to do primary lymphadenectomy as the possibility for metastases is about 30%.*

Key words: lymphadenectomy, partial penile amputation, penile cancer, total penile amputation

Introduction

Squamous cell carcinoma of the penis is an infrequent disease representing less than 1% of all neoplasms in males, with yearly incidence of 1-2 cases / 100,000 men [1]. Circumcision has been well established as a prophylactic measure [2]. The development of penile cancer among the uncircumcised has been attributed to the chronic irritative effects of smegma, a product of bacterial action on desquamated cells retained within the preputial sac [3]. Carcinoma of the penis is almost unknown among the Jewish where circumcision in newborn males is customary. On the other had, penile carcinoma among uncircumcised African tribes and Asian populations has been reported to constitute 10% or more of all malignancies in the male [4]. Circumcision in adults offers little or no protection against future appearance of penile cancer. The role of viruses, especially the human papilloma virus (HPV) type 16 and 18 in the etiology of penile cancer is controversial [5]. An interesting point is that patients with penile cancer more than patients with other types of cancers delay seeking medical consultation [6]. The reasons for this delay are ignorance, embarrassment, guilt, fear or personal neglect [7]. No reason appears justified, since the penis is an organ handled and observed on a daily basis.

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Patients and methods

The medical records of 360 patients admitted in our Department between 1974-1993 with histologically diagnosed squamous cell penile cancer were retrospectively analyzed. These patients accounted for 0.5% of all malignancies in men seen in our Department.

The following data were registered and analyzed: age at presentation, previous circumcision, presence of balanitis xerotica and Querat's erythroplasia, exact localization and appearance of primary tumor, presence of inguinal nodal disease, TNM stage and tumor differentiation (G), type of surgical treatment and administration of preoperative (primary) chemotherapy. Registered were also the recurrence rate and 5 and 10-year survival.

Operative treatment methods for the primary tumor included circumcision, local excision, partial amputation and total amputation. In cases with partial amputation 1.5 cm margin proximal to the tumor was left. Postoperatively, the bladder catheter was left in place for 3 days in patients with partial amputation and for 6 days in those with total amputation.

In patients with clinically negative nodes at presentation our policy was not to do prophylactic lymphadenectomy but only follow-up (every 2 months for the first 3 years and every 6 months thereafter).

In those with enlarged lymph nodes (N1-3) at diagnosis, after a 4-week course of antibiotics, unilateral or bilateral inguinal (superficial or deep) or ilio-inguinal lymph node dissection was carried out. During deep inguinal dissection, if only one positive small node (<0.5 cm) with G1 cancer was found, deep inguinal (not ilio-inguinal) dissection was performed. If more than one positive nodes were found, ilio-inguinal dissection was carried out.

In patients with inoperable inguinal nodal disease primary chemotherapy with 3 cycles of cisplatin and 5-fluorouracil were administered in an attempt for disease downstaging. Prophylactic radiotherapy was not used.

Results

The mean patients' age at presentation was 65 years (range 29-91 years). Three hundred sixteen (88%) patients were uncircumcised and 44 (12%) were circumcised some years ago but no one as neonate. Twelve patients had balanitis xerotica and 14 Querat's erythroplasia. In 218 (60.6%) patients the disease was located in the glans, in 42 (11.6%) patients in the prepuce, in 61 (16.9%) patients in the glan and prepuce and in 39 (10.8%) the disease extended to the penis corpora (Table 1). Most commonly (176 patients, 48.8%) the lesion was exophytic (Table 1). At the time of diagnosis 156 (43%) patients had enlarged inguinal lymph nodes detected by palpation and CT scan (after 1981). After antibiotic administration for 4 weeks the lymph nodes disappeared in 28 (19%) of them.

Table 1. Location and type of primary tumor

Location	*Number of patients (%)*
Glans	218 (60.6)
Prepuce	42 (11.6)
Glans and prepuce	61 (16.9)
Penile shaft	39 (10.8)
Type of lesion	
Exophytic	176 (48.8)
Ulcerative	68 (18.8)
Mixed	116 (32.2)

Patients' TNM stage grouping is presented in Table 2. T2N0 cases prevailed, followed by T1N0 (Table 2). Tumor grade of differentiation was as follows: G1 129 (36%), G2 80 (22%) and G3 151 (42%) cases. Patients in our study had symptoms for a median of 6 months before seeking medical examination. After 1986 the admissions for penile cancer decreased compared with those in previous years, with also lower disease stage at presentation. Forty (11%) of the 360 cases had been treated previously in other hospitals. The primary treatment and the treatment after recurrence are presented in Table 3.

The surgical treatment of these 360 cases was as follows: circumcision in 32 patients, local excision in 12 patients, partial amputation in 227 patients, total amputation in 75 patients, and in 5 of the 9 inoperable cases cystostomy was performed only as a palliative treatment (Table 4). In 82 patients with enlarged lymph nodes (N1-2) at diagnosis, after a 4-week course of antibiotics, 30 inguinal (10 superficial only and 20 superficial and deep) and 4 ilio-inguinal unilateral, 35 inguinal and 13 ilio-inguinal bilateral dissections were performed.

Table 2. TNM stage at presentation (number of patients)

	Tis	*T1*	*T2*	*T3*	*T4*
N0	0	69	130	10	0
N1	0	20	21	13	0
N2	0	0	18	34	4
N3	0	0	12	24	5

Table 3. Primary and secondary treatment in 40 cases primarily treated in other hospitals

Primary therapy (in other hospitals)	*Patients, n*	*Secondary therapy (in our department)*	*Patients, n*
Radiotherapy	10	Partial amputation	7
Circumcision	20	Partial amputation	20
Partial amputation	5	Total amputation	5
Partial amputation	4	Inoperable	4
Glandectomy	1	Partial amputation	1

Table 4. Surgical treatment of 360 cases

Type of surgery	*Number of patients (%)*
Circumcision	32 (8.9)
Local excision	12 (3.3)
Partial amputation	227 (63.1)
Total amputation	80 (22.2)
Cystostomy	5 (1.4)
Inoperable	4 (1.1)

In 37 patients with N3, 25 bilateral inguinal and 12 bilateral ilio-inguinal dissection were also performed. Negative inguinal nodes were found in 10 (11%) of 90 inguinal dissections and negative iliac nodes in 6 (21%) of 29 ilio-inguinal dissections. In 9 patients with inoperable inguinal lymph nodes 3 cycles of chemotherapy were given (combination of cisplatin and 5-fluorouracil) with partial remission in 3 patients. From our patients with clinically negative lymph nodes only 2 came back with inoperable nodal disease. Follow-up was documented for 325 patients ranging from 5 to 14 years (median 10.3 years).

No local recurrence after partial or total amputation was observed. Local recurrence was seen in 7 (22%) of 32 patients with circumcision and in 4 (33%) of 12 patients with local tumor excision. All those cases were treated with partial amputation after recurrence.

In 19 (8%) patients with partial amputation and in 5 (7%) with total amputation urethral meatus stenosis appeared which was related to impaired blood supply to the mucosa, with retraction during healing. This complication was corrected with dilatation, and in case of failure with meatoplasty. From 227 patients with partial amputation 58 (26%) retained satisfactory sexual function. All these patients were less than 54 years of age and had distal tumors. All patients had satisfactory voiding and continence after partial amputation.

Complications after lymphadenectomy were as follows: wound infection in 12 (10%) patients, treated with local wound care; skin flap necrosis but small in extension in 14 (12%), and after removing the necrotic area healing was spontaneous; lymphocele in 17 (14%) and lymphedema in 19 (16%) (4 unilateral and 15 bilateral). In 14 patients edema was mild and transient and in 5 patients it was permanent. Postoperative immobilization, elevation of the legs and elastic stockings served to reduce this complication. In the cases with permanent edema intermitted diuretics and elevation of the involved extremity were used. The use of neoadjuvant chemotherapy in cases with fixed inguinal lymph nodes was encouraged as 3 of our 9 patients had a partial remission rendering them into operable cases.

During follow-up inguinal nodal metastases were found in 7 (10%) out of 69 patients with stage T1N0M0, in 35 (30%) out of 120 patients with stage T2N0M0, and in 8 (80%) out of 10 patients with stage T3N0M0. All those patients had G3 primary tumors. All nodal metastases appeared during the first 3 years except in one patient in whom metastases appeared after 9 years. The 5-year survival was 91% for patients with stage T1-3 N0, 59% for patients with stage T1-3 N1-2 and 29% for patients with stage T1-3 N3. At 10 years the survival was 80%, 49% and 0%, respectively.

Discussion

Squamous cell carcinoma of the penis usually originates from the glans, with the next most common site being the prepuce and the shaft [8]. In our series, the age range was 29 to 91 years with a mean of 65 years. Previous studies have reported similar mean ages at diagnosis [9]. Complaints at the time of admission to the hospital include a penile mass, an ulcerative lesion, penile pain or discharge, and few patients will complain of swelling of the penis or of

lymphadenopathy [10]. Although a history of trauma often predates the appearance of carcinoma of the penis, it is felt that this is coincidental rather than causal [11]. There is no relation, however, with exposure to industrial carcinogens, nor is there any association with previous venereal disease [12]. A representative biopsy is taken and histological confirmation of the diagnosis must be obtained before proceeding to therapy. Tumor–like penile lesions most often encountered include leukoplakia, balanitis xerotica, erythroplasia of Querat, Bowens disease, the Buschke-Lowenstein tumor and anogenital Paget's disease [13].The surgical treatment of penile cancer dates back to the times of Celsus [14]. Valsava performed a partial penectomy for a penile cancer in 1761 [15]. The desired goal in the treatment of the primary tumor is complete excision of the lesion with adequate tumor-free margin. For lesions involving the glan and the distal shaft, partial amputation with at least a 2 cm margin proximal to the tumor is necessary to guard against local recurrence although some authors believe that 1 cm margin is also safe [16]. In our cases an 1.5 cm margin was left and no recurrence occurred. Adequate partial amputation in the absence of inguinal nodal metastasis may result in a 5-year survival rate of 70 to 90% [17-19]. Our results for survival are similar to that reported in previous studies. Penectomy provides the best initial control rate, and local recurrence is extremely rare when a proper margin has been obtained [20].

Although the treatment of the primary tumor has been well established, the management of inguinal nodal disease is still a matter of much debate. From our patients 43% (156/360) presented with palpable lymphadenopathy. After 4 weeks with antibiotic therapy, the enlarged lymph nodes disappeared in 19% (28/151) of the patients. From 1990 on we use fine-needle aspiration biopsy without ultrasonography but the results are reliable only if positive [21]. Of the 119 patients who had undergone lymphadenectomy 10(11%) were negative for metastasis. Of our patients with lymphadenopathy at initial presentation 64% had nodal metastases. These results are similar to those of previous reports [22,23]. Most authors recommend primary lymphadenectomy in patients with stage T2 or greater lesion, and in those with G3 tumors, as they found an improved 5-year survival rate among patients with negative findings on lymphadenectomy (87% *versus* 29% in the group with positive findings) [24-26]. On the other hand, there are authors not suggesting primary lymphadenectomy as they did not find any difference in survival [27-29]. In our Department primary lymphadenectomy was not performed until 1990; instead, only surveillance was carried out. From our results it is clear that in patients with stage T3, G2/G3 the possibility of recurrence is very high (80%) and so primary lymphadenectomy began to be performed after that year. In patients with stage T2, G3, if the surveillance is not reliable, primary lymphadenectomy is performed as the possibility for recurrence is 30%. In cases with fixed lymph nodes our experience with neoadjuvant combination chemotherapy is small (only 9 cases) but it appears to provide response in about one third of the patients and seems similar with other series [30,31].

As the stage at presentation appears to be the most important prognostic variable for survival, early diagnosis and treatment give the best possibilities for a successful outcome. The problem with early diagnosis is connected with a usually prolonged delay between onset of symptoms and first medical examination. Improvement in public awareness may result in early diagnosis and longer survival.

Partial amputation with at least 1.5 cm margin proximal to the tumor gives excellent local control and rare recurrences. In stage T3 it is better to do primary lymphadenectomy as the possibility of metastasis during 2-3 years after amputation is about 80%. In stage T2, G3, if the patient is not suitable for surveillance, it is also better to do primary lymphadenectomy as the possibility for metastases is about 30%. During deep inguinal dissection, if only 1 positive small (<0.5 cm) lymph node is found with G1 cancer, only deep inguinal and not ilio-inguinal dissection should be carried out. Neoadjuvant combination chemotherapy in patients with unresectable nodes provides response in about one third of the patients.

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