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METASTATIC PENILE CARCINOMA: A STUDY OF NINE CASES AND REVIEW OF THE LITERATURE

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Objective: Primary penile carcinoma is one of the rarest male genital tract tumors in Turkey, because circumcision is performed routinely. In general, metastatic carcinoma of the penis is the second most common penile tumor. Despite the fact that the penis is rarely affected by metastases, there have been 319 cases reported in the literature. This study was carried out to throw light on the main characteristics of the metastatic disease.

Patients and Methods: Nine patients aged between 32 and 68 years (median 62.9 years) with metastatic tumors of the penis were the subject of this study. The clinical history of the cases was reviewed, and the patients' data were recorded including location, histology of the primary tumor, presence and location of other metastases, clinical findings, treatment and outcome. The microscopic preparations from both the primary tumor and the penile metastases were reviewed in our pathology department to confirm that the penile lesions showed the same histomorphological characteristics as the primary tumor.

Results: The primary tumors were located in the genitourinary system in 7 / 9 patients (transitional cell carcinoma of the bladder), while in the remaining two patients the primary site was the lung (squamous cell carcinoma) and the bone marrow (lymphoblastic leukemia), respectively. Percutaneous needle aspiration cytology was performed in all cases and incisional biopsy in one case for diagnosis. Total penectomy was the treatment of choice in 7 cases and bilateral cavernotomy in the leukemia case. No treatment was given to one patient because of multiple metastases in other organs. Survival after treatment lasted from 4 months to 62 months; the longest survival (5 years) was found in the leukemia case.

Conclusion: Metastatic penile carcinomas are relatively rare and present a challenging problem. Total penectomy and local excision of solitary nodules or distal penile involvement still represent the treatment of choice. However, because of the association of a penile metastatic lesion with advanced disease, survival rates are limited, and the majority of the patients die within one year.

Key words: penile disease, tumors of the penis, metastases, secondary neoplasms, treatment, results

INTRODUCTION

The worldwide incidence of penile carcinoma varies widely and represents a significant health problem with an incidence of 10-20% in some countries[1]. We rarely encounter this malignancy in Turkey, because circumcision is a part of Islamic tradition[2]. Metastatic cancer to the penis is actually the second most common penile tumor[3]. Despite the fact that the penis is rarely affected by metastases, there have been 319 cases reported in the literature[4-7]. The primary lesion is of pelvic origin in 75%; genitourinary or rectosigmoid primaries and extrapelvic metastases constitute 25% of other primaries[8]. Malignant priapism is the main symptom in 40% of the patients[9]. Its optimal treatment remains poorly defined, and the outcome of patients with such metastases is poor. Furthermore, isolated metastases of the penis such as squamous cell carcinoma of the lung and leukemia are exceptionally rare.

Table 1: Patients' Characteristics in this Study

No.	Age	Primary Site	Histology	Treatment	Survival (months)
1	57	lung	SCC	chemotherapy	4
2	60	bladder	TCC	total penectomy and chemotherapy	19
3	65	bladder	TCC	total penectomy	6
4	68	bone marrow	lymphoblastic leukemia	cavernotomy and chemotherapy	62
5	67	bladder	TCC	total penectomy	7
6	63	bladder	TCC	total penectomy	15
7	64	bladder	TCC	total penectomy	9
8	53	bladder	TCC	total penectomy	11
9	55	bladder	TCC	total penectomy	21

TCC = transitional cell carcinoma, SCC = squamous cell carcinoma

The rarity of the event prompted this study which describes 9 metastatic penile carcinoma cases including 7 originating from the bladder and one each from the lung and the bone marrow.

PATIENTS AND METHODS

The medical records of 18 patients with carcinoma of the penis seen between 1985 and 2004 were analysed. Nine out of 18 patients had primary penile carcinoma including seven cases with squamous cell carcinoma and two with Kaposi's sarcoma limited to the glans penis[2,10]. The remaining nine patients aged between 32 and 68 years (median: 62.9 years) had metastatic tumors of the penis. The clinical histories of the metastatic cases were reviewed and the patients' data were recorded including location and histology of the primary tumor, presence of other metastases, location of the metastases, clinical findings, treatment and outcome. All microscopic preparations from both the primary tumor and the penile metastases were reviewed in our pathology department to confirm that the penile lesion showed the same histomorphological characteristics with the primary tumor. The patients' data are presented in Table 1.

RESULTS

The primary tumors were located in the genitourinary system in 7 / 9 patients (transitional cell carcinoma of the bladder). In the two remaining patients the lung (squamous cell carcinoma of the lung) and bone marrow (chronic lymphoblastic leukemia) were the primary sites. In the seven transitional cell carcinoma cases and also in the leukemia patient, the main symptom was malignant priapism. The clinical findings in the patient with metastatic penile carcinoma originating from the lung were painless, multiple and non-ulcerated nodules.

Percutaneous needle aspiration cytology was performed in 9 cases and incisional biopsy in one case for diagnosis. Total penectomy was the treatment of choice in seven cases and bilateral cavernotomy for the leukemia case. No treatment was given to one patient because of other multiple organ metastases. No local recurrence after penile surgery was encountered for any of the nine patients. Therefore, none of the patients has been given local radiotherapy.

The longest survival with up to five years was found with the leukemia case. As a whole, survival after the treatment lasted from 4 to 62 months.

DISCUSSION

The first case of metastatic tumor of the penis was reported by Eberth in 1870[5,11]. When reviewing the literature available on this topic on the Pubmed internet site, we found 319 cases of metastatic penile lesions[1,4,11-22].

Table 2: Primary Sites of Metastatic Tumors of the Penis in 328 Cases Reported in the Literature[1-34] Including the Present Study

Primary Site	No. of Cases	%
Genitourinary	**243**	**73.9%**
- bladder	113	34.3%
- prostate	95	28.9%
- kidney	23	7.0%
- testis	11	3.3%
- ureter	1	0.3%
Gastrointestinal	**62**	**18.8%**
- rectosigmoid	51	15.6%
- colon	6	1.9%
- pancreas	2	0.6%
- stomach	2	0.6%
- anus	1	0.3%
- liver	1	0.3%
Respiratory Tract	**13**	**3.4%**
- lung	10	3.0%
- nasopharynx	2	0.6%
- tonsil	1	0.3%
Others	**10**	**3.0%**
- lymphoma	2	0.6%
- osseous	2	0.6%
- leukemia	2	0.6%
- melanoma	2	0.6%
- sacrococcygeal chordoma	1	0.3%
- basal cell carcinoma	1	0.3%
Total	328	

The most common origin of the primary tumors - with the addition of the cases presented in this study - in order of frequency has been reported to be: the bladder (34.3%), the prostate (28.9%), the rectosigmoid area (15.6%) and the kidney (7%). Isolated metastatic penile neoplasms are exceptionally rare. As a whole, the primary tumor is of pelvic origin in approximately 75% of cases, while extrapelvic metastases constitute 25% of primaries. The ureter, leukemia, sacrococcygeal chordoma, basal cell carcinoma, tonsil, liver and anus head the list of the rarest primary sites of origin of penile metastases and have each been reported only once[1-22] (Table 2). So far, only 9 cases of squamous cell carcinoma of the lung with metastases to the penis have been reported in the literature[1,20]. This study adds the tenth case of metastasis to the penis from the lung which was reported in our country in 1985[23] and, to our knowledge, the second case of metastasis to the penis from leukemia.

The various mechanisms of penile metastases were first studied by Paquin and Roland in 1956[24]. Despite several attempts at describing the possible routes by which the tumor spreads to the penis, this is still controversial. The following routes have been suggested: local direct extension, arterial embolism, retrograde venous, lymphatic or instrumental spread[1-9,11]. Without doubt, more than one route of dissemination may occur in a single case. The most accepted route is direct extension which explains the frequently observed tumoral spread into the proximal corpora cavernosa. The most common histologic feature of the penile invasion by metastatic lesions is the replacement of one or both corpora cavernosa; a ready explanation for the frequent clinical finding of priapism. Both corpora cavernosa usually are involved with the tumor[11]. The glans penis and corpus spongiosum are rarely involved. Solitary cutaneous, preputial and glanular deposits are less common.

Regardless of the location of the primary tumor, the most commonly observed symptomatology of penile metastases in order of frequency are: malignant priapism (40%), urinary retention, penile nodules, ulceration, perineal pain, edema, generalized swelling, broad infiltrative enlargement, dysuria and hematuria[1-4,9-11,23]. In this study, malignant priapism and broad infiltrative enlargement were the most common clinical findings with an incidence of almost 89% and 73%, followed by difficult micturition (64%) and multiple painless nodular involvement (11%). Penile metastases must be differentiated from idiopathic priapism, Peyronie's plaque, venereal or other infectious ulcerations, tuberculosis, syphilitic cavernositis and primary penile carcinomas[3,25].

Various treatment modalities have been suggested and include local excision, penectomy, suprapubic urinary diversion, radiotherapy and chemotherapy. To date, no

therapy has been shown to be superior except for local excision or total penectomy in the case of solitary nodules or localised distal penile involvement. Penectomy is the most accepted and used therapy after failure of other modalities to palliate intractable pain. Treatment with radiotherapy, hyperthermia in combination with radiotherapy and chemotherapy has not been applied in a sufficient number of cases to warrant definitive recommendations[12,21,22,26].

In conclusion, metastatic penile carcinomas are relatively rare and still present a challenging problem. Total penectomy and local excision of solitary nodules or distal penile involvement represent the treatment of choice. Bilateral cavernotomy can be performed for metastases to the penis from leukemia. Because of the association of a penile metastatic lesion with advanced disease, survival after its presentation is limited and the majority of patients die within one year[23,27,28]. Rarely, longer survival can be achieved in patients without other metastatic involvement.

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RESUME

Carcinomes péniens métastatiques: Une étude de neuf cas et revue de la littérature

Objectifs : Le carcinome pénien primitif est l'une des tumeurs génitales masculines les plus rares en Turquie, parce que la circoncision est habituelle. En général, le carcinome métastatique du pénis est la deuxième tumeur pénienne commune. Malgré le fait que le pénis est rarement affecté par des métastases, il y a eu 319 cas rapportés dans la littérature. Cette étude a été réalisée pour déterminer les caractéristiques principales de la maladie métastatique. **Patients et méthodes :** Neuf patients de 32 à 68 ans (médiane 62,9 ans) présentant des tumeurs métastatiques du pénis étaient le sujet de cette étude. L'histoire clinique de tous les patients a été revue, et les données des patients ont été enregistrées comprenant le siège, l'histologie de la tumeur primitive, la présence et le siège d'autres métastases, les résultats cliniques, le traitement et ses résultats. Les préparations microscopiques à partir de la tumeur primitive et des métastases péniennes ont été passées en revue dans notre service de pathologie pour confirmer que les lésions péniennes ont montré les mêmes caractéristiques histo morphologiques que la tumeur primitive. **Résultats :** Les tumeurs primaires ont été trouvées dans le système génito-urinaire dans 7/9 patients (carcinome à cellules transitionnelles de la véssie), alors que dans les deux patients restants l'origine primitive était le poumon (carcinome à cellules squameuses) et la moelle (leucémie lymphoblastique), respectivement. La cytologie par aspiration percutanée à l'aiguille a été réalisée chez tous les patients et dans un cas une biopsie chirurgicale diagnostique. Pénectomie totale était le traitement de choix dans 7 cas et la cavernectomie bilatérale dans le cas de leucémie. Aucun traitement n'a été indiqué chez un patient en raison des métastases multiples dans d'autres organes. La survie après traitement est de 4 mois à 62 mois; la plus longue survie (cinq ans) a été retrouvée dans le cas de leucémie. **Conclusion :** Les carcinomes péniens métastatiques sont relativement rares et présentent toujours un problème diagnostique et thérapeutique. L'excision pénienne locale et totale des nodules solitaires ou la pénectomie totale représentent toujours le traitement de choix. Cependant, en raison de l'association de lésions métastatiques péniennes avec une maladie avancée, les taux de survie sont limités, et la majorité des patients décèdent dans un délai d'un an.

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