Cutaneous Metastases from Squamous Cell Carcinoma of the Ureter

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Key Words

Ureter • Squamous cell carcinoma • Cutaneous metastases

Abstract

Objective: To present an extremely rare case of squamous cell carcinoma of the ureter with cutaneous metastases.

Clinical Presentation and Intervention: A case is presented involving a 67-year-old woman presenting with a clinical history of squamous cell carcinoma of the ureter and who had undergone a nephro-ureterectomy with a bladder cuff excision in May 2004. The pathologic report showed squamous differentiation, as well as keratin pearl formation. A large regional cutaneous lesion on the chest wall was found in January 2006, and a biopsy showed metastatic malignant urothelial tumors consisting of squamous cell carcinomas.

Conclusion: This report describes a case of cutaneous metastasis from a squamous cell carcinoma of the ureter that is extremely rare with a generally dismal prognosis.

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Introduction

Primary carcinoma of the ureter is not rare, and most of these tumors are shown by histologic evaluation to be transitional cell carcinomas. Only about 1% of primary carcinomas of the ureter are reported to be squamous cell carcinomas [1]. Because of its rarity, only a few large series

have examined the natural history and management of squamous cell carcinoma of the ureter [2–4]. It has been suggested that survival is dependent on tumor grade and stage, but not on the treatment administered [2]. Moreover, cutaneous metastases of carcinoma of the ureter are very uncommon. In these rare cases, more than 90% of metastases are shown to be transitional cell carcinomas, with squamous cell carcinomas being extremely rare [5]. Herein we present an unusual case of squamous cell carcinoma of the ureter which metastasized to the skin.

Case Report

A 67-year-old woman was admitted to the hospital in April 2004, complaining of hematuria for 9 months. Urine cytology revealed malignant cells and squamous cell carcinoma-associated antigen, which was elevated in the serum to 38.3 ng/ml (normal range 0–1.5 ng/ml). She had undergone a nephro-ureterectomy with a bladder cuff excision in May 2004. A large tumor, measuring 4.5 × 4.0 × 3.0 cm, was observed in the middle one-third of the ureter, 6 cm distal to the pelvic-ureteral junction. The tumor involved the ureteral wall and extended to the periureteral soft tissues. The area of the ureter infiltrated by the tumor, measuring 1.0 cm, had an erythematous mucosa and a thickened wall. The proximal ureter, measuring 9.5 cm, and bladder cuff were separated from the upper segment of the ureter. The proximal ureter had a normal gross appearance. No lymphadenopathy was detected.

On gross examination, the tumor was tan-colored and firm, and had a gritty surface. On histologic examination (fig. 1), the tumor cells were shown to have undergone squamous differentia-

Fig. 1. Histologic section of squamous cell carcinoma of the ureter (HE).

Fig. 2. Multiple nodules and infiltrated plaques over the anterior chest wall.

tion, as well as keratin pearl formation. The ureteral tissue between the tumor (state site more clearly) also had a nest of tumor cells which had infiltrated into the muscular wall. Vascular invasion was noted in the periureteral soft tissues. The bladder cuff had mild focal dysplasia of the urothelial cells with enlarged hyperchromatic nuclei. Elsewhere, the ureter exhibited a chronic inflammatory cell infiltrate. The final histologic diagnosis was a high-grade, T3-stage squamous cell carcinoma of the ureter. Approximately 3 weeks post-operatively, an abdominal computed tomography (CT) scan revealed a residual mass over the left previous ureteral site and squamous cell carcinoma tumor marker

Fig. 3. ¹⁸F-fluorodeoxyglucose positron emission tomography study revealed multiple hypermetabolic areas of uptake over the chest wall, left lower neck and left supraclavicular, axillary and para-aortic regions.

was still elevated at 12 ng/ml. Therefore, the patient underwent radiotherapy (total dose 5,040 cGy) and chemotherapy with weekly PFL (40 mg cisplatin, 3,300 mg 5-fluorouracil and 200 mg leucovorin) for 6 cycles.

In March 2005, left supraclavicular and axillary lymphadenopathy was noted. A chest CT showed mediastinal, left supraclavicular fossa, and paraaortic and axillary lymph adenopathy. These findings were interpreted as metastatic disease. Consequently, salvage radiotherapy and chemotherapy, consisting of mitomycin (4 mg intravenously) and capecitabine (300 mg orally), was administered twice daily. Three months later, the patient was thought to be in remission as evidenced by moderate regression of the aforementioned lymphadenopathy. However, a skin eruption developed on the chest in January 2006 (fig. 2). Cutaneous examination revealed multiple violaceous nodules and infiltrated plaques on the left aspect of the chest, approximately 15 cm in diameter. Progressive left-arm edema and dyspnea was also noted. A nodal biopsy showed metastatic malignant urothelial tumors consisting of squamous cell carcinomas. Positron emission tomography showed diffusely increased ¹⁸F-fluorodeoxyglucose uptake in the chest wall, left lower neck and left supraclavicular, axillary and para-aortic regions (fig. 3). However, the patient refused further chemotherapy due to her poor overall condition. She was referred to a hospice and died 3 months after admission.

Discussion

Usually, ureteral carcinoma metastasizes to the regional lymph nodes, specifically the retroperitoneal and para-aortic lymph nodes. Distant metastases of ureteral carcinoma (other than the lymph nodes) are rare and are spread by both direct extension, hematogenously and via the lymphatics [6]. The prognosis of patients with cutaneous metastases is very dismal.

The fact that the urothelium normally has no squamous structures makes the pathogenesis quite interesting. The process is assumed to be benign with urothelial metaplasia resulting from a reaction to chronic irritation, which leads to de-differentiation, dysplasia and ultimately squamous cell carcinoma or adenocarcinoma [7]. The relevant medical history often includes episodes of chronic pyelonephritis or nephrolithiasis. However, in our case, the patient had no previous history of urolithiasis nor urinary tract infection. In addition, the patient had never smoked cigarettes.

According to the literature, both the grade and stage of upper urinary tract carcinomas are excellent predictors of survival [2]. Some investigators also believe that the natural history of ureteral carcinoma may be different from that of carcinoma of the renal pelvis; it is often locally advanced and associated with a high local recurrence rate [3, 8]. Because of the high recurrence rate in the

ureter, nephro-ureterectomy and excision of the bladder cuff remain the treatment of choice [8], as was done in this case. If metastasis develops, chemotherapy or radiotherapy is considered. There is anecdotal evidence that survival in metastatic upper urinary tract carcinomas with cisplatin-based chemotherapy may be increased [2]. However, it has little effect on the unfavorable prognosis. In a series of patients with metastatic ureteral carcinomas reported by Das et al. [2], treatment with chemotherapy alone or radiation and chemotherapy had a median survival of 21.5 and 22.2 months, respectively. The overwhelming majority of patients with metastatic disease did not live for 5 years [2]. Currently, the best results are achieved by early diagnosis and radical surgery. One should consider the clinical history and physical findings for the interpretation of cytologic smears of skin lesions, as occurred in this case. We might not have diagnosed this case as metastatic squamous cell carcinoma of the ureter without the clinical history.

Conclusion

This report highlighted a case of cutaneous metastasis from squamous cell carcinoma of the ureter that is extremely rare, and the prognosis is generally dismal.

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