

## The Impact of Squamous Metaplasia in Transitional Cell Carcinoma of the Bladder

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The authors report a case of squamous cell carcinoma of the bladder induced by radiation therapy for transitional cell carcinoma, possibly from sites of squamous metaplasia, which were present at the time of initial diagnosis. Although data in the literature are not sufficient at the moment in terms of implication on prognosis, foci of squamous metaplasia during the initial diagnosis of transitional cell carcinoma must be carefully sought and their presence warrants caution in utilizing irradiation in the management of the disease.

### Introduction

Transitional cell carcinoma may be present as the sole histological finding in patients with bladder tumours or there may be mixed carcinoma and/or accompanying squamous or glandular metaplasia. Mixed carcinomas may represent nearly 6% of all bladder tumours [1].

Squamous metaplasia, which is a well-known histological entity, may frequently accompany transitional cell carcinoma of the bladder and the well-differentiated lesions of squamous cell carcinoma are sometimes difficult to distinguish from severe squamous metaplasia. It may occur in about 20–30% of the cases and transitional epithelium may transform into squamous epithelium with or without keratinization [1, 2].

### Case report

A 66-year-old male patient was admitted to Marmara University Hospital because of right-sided groin pain and swelling of the right leg. He had a history of previous bladder tumour resection at another institution in June 1988 and the pathology revealed that the tumour was poorly differentiated transitional cell carcinoma with areas of extensive squamous metaplasia. The tumour stage was reported as T3, and he was referred to radiotherapy. First control cystoscopy upon completion of radiotherapy was reported to be normal in November 1988.

He was well until February 1989 when pain in the right lower extremity appeared. Physical examination did not reveal any abnormality. A CT scan was

carried out and it revealed a cystic mass within the right lower psoas muscle. A diagnostic CT guided fine-needle aspiration displayed only inflammatory cells and relieved the symptoms. Cultures of the aspirate remained sterile. Whole body scintigraphic examination showed increased uptake at bilateral sacroiliac areas and left femoral head.

The symptoms recurred after 10 days with much severe pain and total oedema of the right leg. Peripheral pulses were absent in this extremity which was hot and tender. A second CT scan revealed the persistence of the cystic mass with a diameter of 15 cm in the psoas muscle along with bilateral obturator and right inguinal enlarged lymph nodes. Ultrasonography of the kidneys revealed right hydronephrosis. The proposed diagnosis was then deep vein thrombosis of the right lower extremity and psoas abscess, and antibiotic and anticoagulant therapy was initiated. An exploratory operation was carried out in March 1989 which revealed abscess formation with a very thick capsule inside the lower third of the right psoas muscle. The lesion was evacuated and multiple biopsies as well as material for microbiological examination were obtained. Microscopic examination of the surgical specimen revealed that the lesion was a squamous cell carcinoma with central necrosis and abscess formation at a metastatic site. Original site of the disease was suggested to be the bladder which had showed extensive squamous metaplasia initially and seemed to respond to radiotherapy. Cultures of the surgical aspirates remained sterile. The postoperative course was uneventful except for low grade fever which was normalized at the end of the first week. Since the patient refused further therapy, he was discharged from hospital on his own request.

### **Discussion**

Metaplastic changes are believed to be an expression of the potentialities of transitional epithelium in response to appropriate stimuli such as chronic irritation, hormonal imbalance or specific infections [3]. Squamous metaplasia may be a physiological finding in the trigone of healthy young women, but keratinizing squamous metaplasia is a more serious occurrence generally accepted as preneoplastic, and has the potential of leading to squamous carcinoma if anaplasia supervenes; thus, neoplastic changes may develop in metaplastic epithelium [2].

The relatively high incidence of squamous cell cancer in females compared to transitional cell carcinoma have led to the speculation that it is the result of higher incidence of squamous metaplasia in the female bladder [4, 5, 6].

Squamous cell carcinoma of the bladder is not very common and accounts for 5–6% of all bladder tumours [2].

Although it is evident that squamous metaplasia may frequently accompany transitional cell carcinoma, until now no clear outlines are given in terms of predictive value of squamous metaplasia in the prognosis of transitional cell carcinoma of the bladder and ultimate histological outcome of the tumour.

Radiation therapy has been an important tool in the therapeutic armamentarium for patients with transitional cell carcinoma of the bladder, especially of

the locally advanced type, with potential advantages and drawbacks [7]. It has been documented that radiotherapy may induce neoplastic changes, without unclear actual risk of a given dose [8, 9, 10, 11, 12]. Li et al. [13] reported a continuing incidence of secondary neoplasms in previously irradiated fields among children cured of their first cancer, and this incidence has reached 17% in two decades.

Recently, progression to advanced squamous cell carcinoma of the bladder in a patient who was treated with radical radiotherapy, with the initial diagnosis of muscle infiltrative transitional cell carcinoma with areas of squamous metaplasia, put forward the probability that squamous metaplasia which accompanies quite frequently transitional cell carcinoma may be stimulated for neoplastic transformation by radiotherapy utilized in treatment. Thus, radiotherapy may be the inducer of squamous cell carcinoma in patients with squamous metaplasia. When the relatively radioresistant nature of squamous cell carcinoma and the great difficulty in distinguishing the well-differentiated type from severe metaplasia is considered [4, 6, 14], escape of metaplastic squamous cells from radiotherapy and progression to carcinoma may not be surprising.

In the series of Peters and Roehrborn [15], 13.9% of patients with squamous cell carcinoma had a history of recurrent bladder tumours and were treated with transurethral resection and radiation therapy before they presented with squamous cell carcinoma.

Therefore, the presence of squamous metaplasia in invasive transitional cell carcinoma of the bladder should have some implications in the management of these patients. It may be wise to utilize radical cystectomy either alone or in combination with chemotherapy in neoadjuvant or adjuvant setting. If surgery is not feasible, radiotherapy may be utilized with neoadjuvant chemotherapy and with a very close follow-up, bearing in mind the probability of progression to squamous cell carcinoma. Chemotherapy may be rewarding in terms of controlling the progression to squamous cell carcinoma.

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