

Squamous Cell Carcinoma of the Urinary Bladder: A Rare Case Report

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Abstract

Case Report

Squamous cell carcinoma of urinary bladder is an uncommon tumor. However its possibility should always be kept in mind especially in people with history of catheterization, stones or repeated urinary tract infections. Histopathology plays an important role in its diagnosis.

Keywords: Histopathology, squamous cell carcinoma, urinary bladder.

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INTRODUCTION

Although urothelial carcinoma (transitional cell carcinoma, TCC) represents the majority of bladder tumours and hence has historically received the most research attention, other types of bladder cancers should not be ignored and include Squamous Cell Carcinoma (SCC), adenocarcinoma, small cell carcinoma and some other less common histologies. SCC of the urinary bladder accounts for 3% to 7% of all bladder cancers in the US and is the most common type of nontransitional cell carcinoma involving the bladder [1, 2]. However, there is a wide variation in incidence in different geographic areas worldwide, being 1% in England while in countries like Egypt where schistosomiasis is endemic; the incidence is up to 75%.¹ Adenocarcinoma accounts for 0.5-2% cases while small cell carcinoma accounts for <1% cases of bladder tumours in the US [3]. These less common histopathological types have been relatively understudied.

SCC of the bladder has been reported to be the most common in the seventh decade of life, and more in males than females [4]. The risk factors for SCC include conditions that induce squamous metaplasia, a process that results from chronic irritation of the urothelium of the bladder such as due to bladder stones, long term indwelling catheter or infection, neurogenic bladder, antecedent infection with *Schistosomiahematobium* or intravesical BCG (Bacillus Calmette-Guerin) [5]. It is usually diagnosed in advanced stage since there are no

specific diagnostic tests. The prognosis, therefore, is poor and most patients die.

We report a case of a 48 year old male patient who presented with a three month history of hematuria and was eventually diagnosed with SCC of the urinary bladder.

CASE REPORT

A 48 year old Indian male, farmer by occupation and a smoker and alcoholic for the past 28 years, presented to the Department of Urology with the chief complaints of intermittent bleeding during micturition since 3 months. It was insidious in onset and was occasionally associated with passage of clots. He also complained of increased frequency of micturition, which was mainly nocturnal. The patient did not give any history of urgency or hesitancy during micturition, nor was there a history of weight loss or anorexia. On enquiring further, he gave history of recurrent urinary tract infections and renal stones for the last 5-7 years for which he did not get operated but gave history of repeated hospitalisation with catheterization. There was no history of any systemic disease. He had no family history of malignancy. His general and systemic examination was otherwise normal except for mild pallor. Laboratory investigations showed a normal serum creatinine of 0.83 mg/dl. Contrast Enhanced Computed Tomography of abdomen-pelvis was done which revealed a large ill-defined mild heterogeneously enhancing polypoidal attenuating mass lesion involving

base and left lateral wall of urinary bladder measuring 6.5 x 3 x 5 cm. There was involvement of the left vesicoureteral junction and full thickness invasion of urinary bladder wall with mild perivesical fat stranding. The lesion was also seen abutting the medial portion of left seminal vesicle with loss of interface. Subcentrimetric sized lymph nodes were seen along bilateral iliac groups. A calculous measuring 1.7 x 1.3 cm was also identified at the lower pole calyx of left kidney with grade III hydronephrosis. Prostate was normal. Other abdominal and pelvic organs including the rectum were normal. On radiology, the diagnosis was given as likely neoplastic aetiology of the bladder (Carcinoma urinary bladder) with no obvious metastatic lesion. The patient then underwent transurethral urinary bladder biopsy at our hospital.

Multiple grey-white to grey-brown soft tissue pieces fixed in 10% formalin together measuring 5.5 x 2 x 0.5 cm and weighing approximately 4 grams were received in our department. These were processed for paraffin embedding and wax blocks were prepared. Serial sections (3-5 microns) were taken using microtome, stained with hematoxylin and eosin for routine histopathological examination and were studied under light microscope. The biopsy revealed features of high grade squamous cell carcinoma with extensive areas of necrosis and associated inflammation in the intervening stroma. Numerous keratin pearls along with individual cell keratinization were noted. At places, the tumour was seen infiltrating into the muscle tissue included in the biopsy.

Our patient refused for any surgical intervention. Presently, he is on chemotherapy and is doing well on regular follow-up.

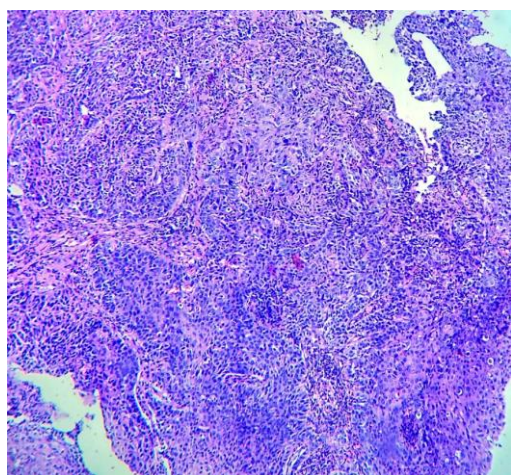


Fig-1: Histologic section showing squamous cell carcinoma (HE;100x)

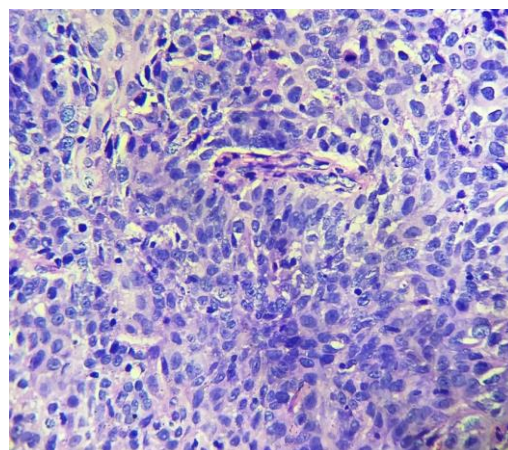


Fig-2: Histologic section showing squamous cell carcinoma (HE;400x)

DISCUSSION

According to global cancer statistics, the incidence of carcinoma of the urinary bladder varies in different geographic areas, being 16.6% in developed countries and 5.4% in less developed countries [6]. Squamous cell carcinoma (SCC) of the urinary bladder is the most common nontransitional cell carcinoma of the urinary bladder accounting for 3-7% of all bladder carcinoma cases [1, 2]. Almost all SCCs are advanced at the time of diagnosis and most have already invaded the muscle. These account for their unfavourable prognosis [7]. The clinical and etiological factors associated with development of bladder cancer are variable. In countries like Egypt where SCC is the most common histopathological type, chronic bladder infection with schistosomiasis has been the most important risk factor in contrast to that in Europe where smoking and occupational exposures are more commonly implicated [8]. Bladder carcinogenesis in case of schistosomiasis is probably related to bacterial and viral infections commonly associated with bilharzial infestation rather than the parasite itself. The mechanism probably involves production of nitrosamine and release of free carcinogenic products through secretion of β -glucuronidase by urinary bacteria like *Escherichia coli*, *Proteus* and *Streptococcus faecalis* which have been implicated in the development of squamous metaplasia [9, 10]. In our patient, schistosomiasis as an associated agent could not be ruled out.

Most patients with squamous cell carcinoma of the bladder present with hematuria. Less common presenting symptoms include symptoms of bladder irritation, urinary obstruction and weight loss. In our patient too, intermittent gross hematuria and increased frequency were the main presenting complaints. There was also a history of chronic urinary tract infection and of intermittent catheterization since 5 to 7 years. Symptoms arising due to a renal stone led him to seek medical help, which eventually led to the diagnosis of bladder cancer.

Various cases reported in literature have shown to have a direct association between bladder calculi and carcinoma [11, 12]. This could be due to continuous irritation and inflammation of the bladder which leads to an increase in growth factors and cytokines in the local environment leading to cell proliferation, angiogenesis and inhibition of apoptosis, thus resulting in squamous metaplasia and dysplasia followed by SCC transformation of the urinary bladder [1, 3]. This risk of cancer development following squamous metaplasia has been reported to be around 21-42 % despite the precise oncogenic pathway being unclear [13]. An increased risk of both bladder SCC and TCC has also been associated with cigarette smoking [3]. In our case too, the patient was a chronic smoker for almost three decades.

The relationship of Human Papilloma Virus (HPV) with SCC bladder is controversial. Being identified as a carcinogenic in various SCCs including those of anogenital and oropharyngeal regions, a potential infectious role in SCC of the bladder is also suggested. Some studies have identified an association [14] while others have reported no association [15] between HPV and bladder SCC pathogenesis. This warrants further investigations to establish the association, if any.

Also, chromosome 9p allelic loss and CDKN2 gene alterations have been found in squamous cell carcinoma of the bladder, in contrast with urothelial carcinomas [16].

In contrast to TCCs which are mostly papillary and non-ulcerating, most SCCs tend to be sessile, nodular, ulcerating and infiltrating. Primary squamous cell carcinoma of the bladder is a relatively rare entity while high grade transitional cell carcinomas commonly show a component of squamous differentiation [6, 16]. For a definite diagnosis of pure SCC, the biopsy should be thoroughly examined and the presence of an invasive high grade component of urothelial carcinoma should be completely excluded. This latter component, if present, marks the diagnosis as a high grade urothelial carcinoma with squamous differentiation instead of SCC [16]. Histologically, the SCCs show varying degrees of differentiation. However, this differentiation in squamous cell carcinoma correlates more loosely with prognosis than in other urothelial carcinomas [1].

SCCs of the bladder, in general, have been reported to have a poorer prognosis. In a study conducted by Newman *et al.*, death occurred in 59% of the patients within the first year [17]. Another study reported a 5-year survival rate of 37% in patients who had SCC with submucosal or muscular invasion and 13% in patients with perivesical invasion [18]. Death in these patients usually occurs due to local progression to either the neck of bladder or to the ureters, causing

obstruction and subsequent renal failure, while distant metastases are rare [12].

CONCLUSION

The worldwide incidence of SCC is decreasing. However, given that bladder SCC presents at a late stage and portends poor prognosis, it is important that future research endeavours support the early detection of squamous cell tumours. The recognition of this rare type of bladder cancer is important to guide the clinician for appropriate treatment of such patients.

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