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Case Report

Muscle Invasive Urinary Bladder Squamous Cell Carcinoma in a Patient with Clean Intermittent Self-Catheterization: A Case Report

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Abstract

In a 37-year-old female patient, an advanced muscle-invasive keratinizing Squamous Cell Carcinoma (SCC) of the urinary bladder was detected during control urethrocystoscopy due to recurrent cystitis in Intermittent Self-Catheterization (ISC). The ISC has been performed since 2002 due to a traumatic neurogenic bladder emptying disorder following craniocerebral trauma with bar lesion. Despite the guideline therapy including cystectomy and adjuvant radiotherapy the patient died as part of tumor therapy within six months. Non-urothelial malignant bladder tumors such as SCC are typically deeply invasive and have a low prevalence within bladder carcinomas. Routine urethrocystoscopic follow-up may allow an early diagnosis of squamous cell carcinoma of the urinary bladder and thus improve the prognosis of the disease.

Keywords: Case report; Intermittent self-catheterization; Recurrent cystitis; Squamous cell carcinoma of the urinary bladder

Abbreviations: SCC: Squamous Cell Carcinoma; ISC: Intermittent Self-Catheterization; MAG-3: Mercapto acetyl glycyl glycyl glycin; e.g.: Exempli Gratia; PD-1: Programed Cell Death Protein 1; PD-L1: Programmed Cell Death 1 Ligand 1; H&E: Hematoxylin and Eosin

Introduction

This case report should explain the importance of the early diagnosis of squamous cell carcinoma of the urinary bladder and its prognosis of bladder cancer in patients with neurogenic bladder emptying disorders. The prevalence and high mortality rate of bladder cancer in neurourological patients emphasizes the significance of long-term follow-up in this specific population. Unfortunately, therefor exists a lack of literature regarding epidemiology, diagnosis, management and prognosis of bladder cancer in this patient population, in order to serve as a basis for future recommendations and research.

Case Presentation

The 37-year-old patient was presented to clarify recurrent cystitis (since 2002 4 to 5 times per year) on ISC and a traumatic neurogenic bladder emptying disorder. Due to detrusoratonia the ISC was performed 5-6 times daily. A macrohaematuria was denied by the patient. Furthermore, the patient complains about a painful ISC with smelly, turbid urine conditions. The urethrocystoscopy did not show a safe exclusion of the tumor due to turbid visibility conditions, so that first a calculated infection therapy was initiated and a transurethral permanent discharge was established. Thereafter, the patient was promptly presented for urethrocystoscopy in transurethral resection readiness of the bladder. The transurethral resection showed a muscle-invasive, keratinizing squamous cell carcinoma of the urinary bladder (pT2 Nx Mx G2) growing above the right ostium. Due to a second urinary obstruction kidney on the right, a renal fistula catheter was additionally inserted. An anterior exenteration with cystectomy, hysterectomy cum adnexe on both sides with the anterior vaginal wall and urethrectomy, pelvic lymphadenectomy on both sides as well as an ileocoecalpouche were performed. A muscle-invasive, lymphogenic metastatic, moderately differentiated, keratinized

squamous cell carcinoma of the urinary bladder (pT4a pN2 (6/13) cM0 L1 V1 Pn1 R1 G2) was diagnosed (Figure 1). An adjuvant radiotherapy (8 gray of planned 59,4 gray total) followed after a short convalescence.

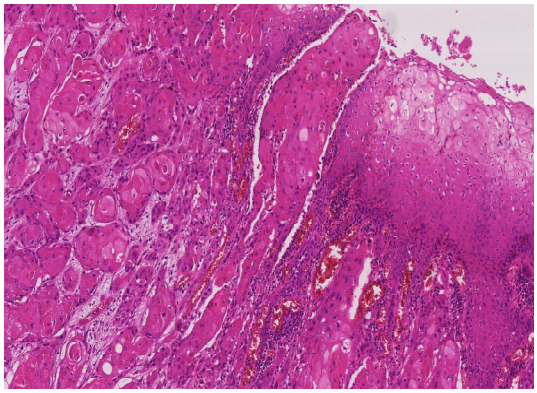

Figure 1: Squamous Cell Carcinoma of Bladder. Irregular invasive nests of neoplastic squamous cells with keratinization. Hematoxylin and eosin (H&E) 10x.

Three months after cystectomy and pouching the patient presented acutely with deterioration of general condition and subileus symptoms. The subsequent laparotomy showed an obstructive ileus, a local recurrence of metastatic squamous cell carcinoma of the urinary bladder and peritoneal carcinoma. After open surgery adhesiolysis, a double-barreled ileostomy was applied, permanent urinary diversion by pouch catheter was established, and a medical palliative service was organized. In addition, after a renal function scintigraphy (MAG-3 with furesis), a urinary transport disorder was detected on the right, for which reason a renal fistula catheter was reattached on the right.

Within the framework of the highly palliative therapy concept and the significantly deteriorated general condition of the patient, enteral tube feeding via percutaneous endoscopic gastrostomy and a port system for parenteral infusion and nutrition therapy were established. After four weeks, the patient died as part of tumor therapy.

Discussion

ISC represents a possibility of bladder emptying in neurogenic bladder dysfunction [1]. Clean intermittent catheterisation with disposable catheters is the standard therapy for primary or therapeutically induced detrusor hypo- or contractility as well as for chronic residual urine formation. As Pannek described, the aseptic lubricants used for ISC are attributed to mutagenic and carcinogenic potency [2,3]. The most common complications of ISC include urinary tract infections, reflux diseases, hematuria, and urethral injury [4-6]. In addition, it has been described that patients with neuro-urological diseases are inevitably at higher for developing bladder cancer [7]. The mortality rate is significantly higher than that of the general population [7-9]. Nahm, et al. demonstrated that patients with spinal cord injuries die 6.7 times more frequently from bladder cancer than the population in general [10]. This fact could be explained by the higher rate of SCC in neuro-urological patients [2,7,8]. Cohen, et al. further describes that especially patients with neurogenic bladder emptying disorders are most frequently affected by this entity [11]. Non-urothelial malignant bladder tumors such as SCC are typically deeply invasive and have a low prevalence and incidence rate of 3-7% of all bladder carcinomas [12,13].

This histological subtype is associated with chronic infections, bladder stones, and indwelling catheters, which can lead to squamous metaplasia (Figure 2). This illustrates why SCC is more common in patients with neurogenic bladder dysfunction.

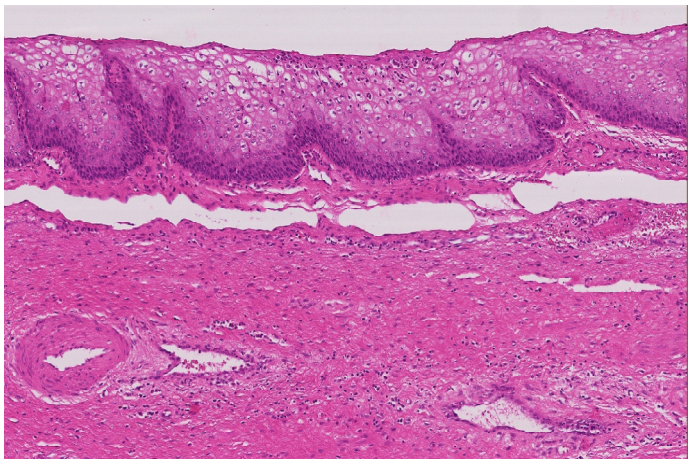

Figure 2: Squamous Metaplasia. Hyperplastic squamous bladder mucosa with inflammation. Hematoxylin and eosin (H&E) 10x.

It is known to be an aggressive and often infiltrating tumor, possibly due to the nature of the tumor itself and the delay in diagnosis [14-18]. Basically, the prognosis for SCC of the urinary bladder is worse than for urothelial carcinoma [15]. This is most likely related to the late time of diagnosis, as at this time local advanced, non-urothelial bladder carcinoma are often diagnosed. Predisposing risk factors of SCC are schistosomiasis (bilharziosis), recurrent/chronic urinary tract infections or inflammations and smoking [18-20]. Chronic inflammation of the urinary bladder due to infection with schistosomes or chronic irritation with permanent catheter treatment may be the cause. In addition to inflammation associated with foreign bodies, e.g. through catheters, bladder stones and diverticula are also risk factors for bladder carcinoma. The early symptoms are often unspecific, so that de novo hematuria or recurrent urinary tract infections caused by urethrocystoscopy should be diagnosed early [21]. SCC of the bladder responds only to a limited extent to chemotherapy and radiotherapy, which

explains its poor prognosis. Most patients therefore die 1-3 years after surgery due to locally advanced tumors and high local recurrence rates [8,22-25].

In order to improve the prognosis, an early surgical approach (radical cystectomy) is recommended. Recent studies have shown that an aggressive cutaneous SCC is characterized by a very high mutation background. Furthermore, the importance of defective immunosurveillance for the growth of cutaneous SCC and the crucial role of programed cell death protein 1 (PD-1) and programmed cell death 1 ligand 1 (PD-L1) interaction in the development of skin tumors provides a rationale for the use of immune checkpoint inhibitors [23]. In view of the circumstances described here as well as the low prevalence of SCC, it is important to urethrocystoscope patients with a young disease age and corresponding predisposing risk factors more closely in order to improve the survival rate in malignant disease [26]. Chronic urinary tract infections in ISC and during ongoing infection therapy should be clarified promptly. Urethrocystoscopy is furthermore the method of choice for follow-up diagnostics. Continued ISC reduces urinary bladder capacity, which affects ISC response. The need for more frequent ISC increases chronic irritation and thus the risk of malignancy.

Conclusions

Patients with recurrent urinary tract infections and regular ISC should undergo urethrocystoscopic. This may allow early detection of malignant diseases and rapid initiation of appropriate therapy. Especially this applies to patients with recurrent cystitis under antibiotic therapy. Consequently, these should be examined as closely as possible, regardless of age and risk factors for squamous cell carcinoma of the urinary bladder. To improve the prognosis, an early surgical approach and possibly the use of immune checkpoint inhibitors is recommended.

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