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NEOPLASM IN A BLADDER DIVERTICULUM

Abstract

Bladder diverticulum is an outpouching of the urothelial mucosa lining from the muscular layer of the bladder. Primary neoplasms arising in vesical diverticula are rare, they occur in around 1% of all bladder carcinoma. Most malignant tumors in vesical diverticula are of transitional type (about 78%), followed by squamous cell carcinoma (17%), a combination of transitional and squamous cell types (2%), and adenocarcinoma (2%). Painless hematuria is the cardinal symptom for diverticular tumors. Modern diagnostic tools like ultrasound, computed tomography (CT) and nuclear magnetic resonance (NMR) enable a more accurate and precise diagnosis of the neoplasm in a bladder diverticulum. From 1961 to 2020, a series of 36 patients with bladder diverticulum cancer was presented and the data show that incidence of tumors today is similar to several decades ago. Most of the patients had p GII and T2 stage disease, therefore the most common surgical treatment was either diverticulectomy or partial cystectomy or radical cystectomy. Recurrent tumor, in our group, was evident in 8 patients with transitional cell carcinoma. Six patients with recurrent tumors were alive for >36 months, while 2 died of the disease within 21 months. No recurrence was noted in 10 patients, and they lived more than 48 months after the operation. We can conclude that therapeutic results are better today than in previous decades due to better diagnostic methods and a more radical surgical approach.

Key words: bladder diverticulum, tumor in bladder diverticulum

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Introduction

Bladder diverticulum is a herniation of the mucosa lacking a muscle layer. This results in a loss of contractility and urine stasis in the diverticulum. Vesical diverticula are congenital or acquired. Acquired diverticula are, by far, more common and are secondary to lower urinary tract obstruction, such as benign prostatic hyperplasia, vesical neck contracture, urethral stricture, or neurogenic bladder. Most bladder diverticula are small and asymptomatic. This lesion may be complicated by inflammation, calculus, infection and malignancy (Kong et al, 2013). Chronic irritation of urine stasis inside the diverticulum results in chronic infection and inflammation and then facilitates the development of neoplasm. In men with bladder diverticulum, mucosal inflammation, ulceration, dysplasia, squamous metaplasia, and leukoplakia were found in 84% of men who underwent diverticulectomy (Kelalis and McLean, 1967).

Painless hematuria is the cardinal symptom for diverticular tumors, as in ordinary bladder tumors. According to Melekos et al (1987), hematuria was present in 87.5% of patients with neoplasms occurring in the diverticula and in 100% of patients with tumors elsewhere in the bladder.

Primary neoplasms arising in vesical diverticula are rare, around 1% of all bladder carcinoma (Idrees et al, 2013). In 0.8% to 13% of patients with vesical diverticulum, neoplasms develop within the diverticulum (Fox et al, 1962; Prakash et al, 2010). As in other bladder tumors, diverticular neoplasms are most prevalent in men above the age of 40. Most malignant tumors in vesical diverticula are of transitional type (about 78%), followed by squamous cell carcinoma (17%), a combination of transitional and squamous cell types (2%), and adenocarcinoma (2%) (Shirai et al, 1984). Prakash et al (2010) reported that the prevalence of bladder diverticulum is more common in men as compared with women (31.6% vs 9%) and also, they found the presence of bladder diverticulum in 23.4% in cadavers.

Due to its rarity, neoplasm in the diverticulum remains infrequently encountered in general practice. Bladder tumors within a diverticulum are difficult to diagnose. Bladder diverticulum neoplasms are characterized by early transmural invasion and a tendency for higher histopathological grades, which allow for prompt diagnosis and crucial treatment. An outpouching in the bladder urothelium through the muscularis propria can complicate the delivery of local therapies, and lack of muscle invasive disease in

a bladder diverticulum can make decisions on extirpation more difficult. Based on ultrasound examination, cystoscopic evaluation, bimanual examination and computerized tomography (CT) or nuclear magnetic resonance (NMR) findings, tumors were classified as superficial (Ta, Tis), superficially invasive confined to diverticulum (T1) or extra diverticular (T3+). Patients with superficial or superficially invasive disease were treated either conservatively with repeat transurethral resection, or with partial or radical cystectomy. Current practice suggests that intradiverticular neoplasm is often stage and treated aggressively as it is thought that it is more likely to disseminate (Walker et al, 2014; Idrees et al, 2013). Unifocal bladder neoplasm limited to the diverticulum and with good bladder function are considered for partial cystectomy, or diverticulectomy. Of course, the finding of carcinoma in situ excludes the partial cystectomy

Materials and methods

We analyzed 96 men with vesical diverticula in the period from 1961 to 1980 (Micic and Ilic, 1983). Of these patients 13 had primary tumors in the diverticulum. Patients with concomitant tumors elsewhere in the bladder were excluded. From 1981 until 2001, we examined 11 patients with primary carcinoma of a bladder diverticulum out of the 101 of patients with vesical diverticulum and 12 out of 88 patients with bladder diverticula were diagnosed with primary carcinoma of the diverticulum from 2001 to 2020. The whole group of men with carcinoma of bladder diverticulum consisted of 36 patients in period of 1961-2020

Results

In our group of patients with diverticular tumor, 25 had symptoms such as hematuria in (69%), urinary tract infection with pyuria in 28 (77%), urinary obstruction in 26 (72%), and fever in 5 (13%). Patients underwent excretory urography from 1961-1998 (Fig 1) and after 1998 they underwent an ultrasound (Fig 2), CT, or NMR with contrast. Cystoscopy was also used in diagnostic evaluation. Tumors were classified as superficial (Ta, Tis), superficially invasive confined to diverticulum (T1) or extra diverticular (T3+). Histopathologic examination revealed transitional cell carcinoma in 28 (77%) patients (4 patients with pG1, 10 patients – pG2 and 14 patients -

pG3), squamous cell carcinoma in 5, and adenocarcinoma in 3. Four patients underwent a transurethral resection of the tumor. Diverticulectomy was done in 10 and partial or total cystectomy was completed in 22 patients.

Recurrent tumor, in our group, was evident in 8 patients with transitional cell carcinoma and was of a higher stage than the primary tumor in 6. Six patients with recurrent tumor were alive for >36 months, while the 2 died of the disease within 21 months. The patients with squamous cell carcinoma and adenocarcinoma died of disseminated disease within 16 and 22 months postoperatively. No recurrence was noted in 10 patients and they remained alive more than 48 months after the operation.

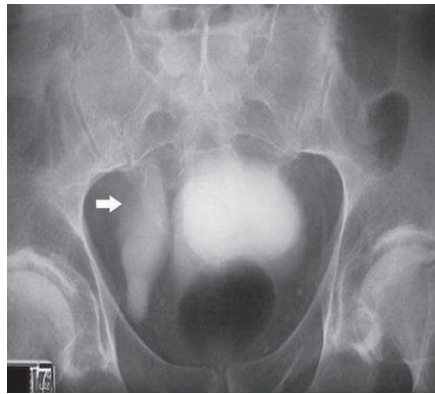


Figure 1. IVF with cystogram showing bladder diverticulum with neoplasm

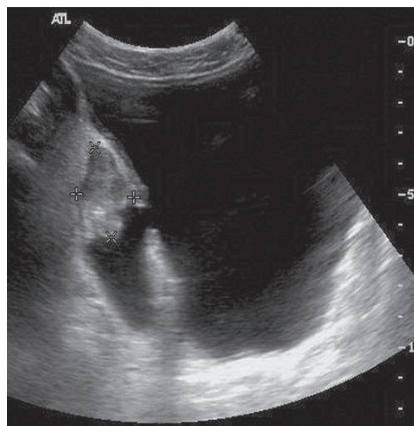


Figure 2. Ultrasound picture of neoplasm in bladder diverticulum

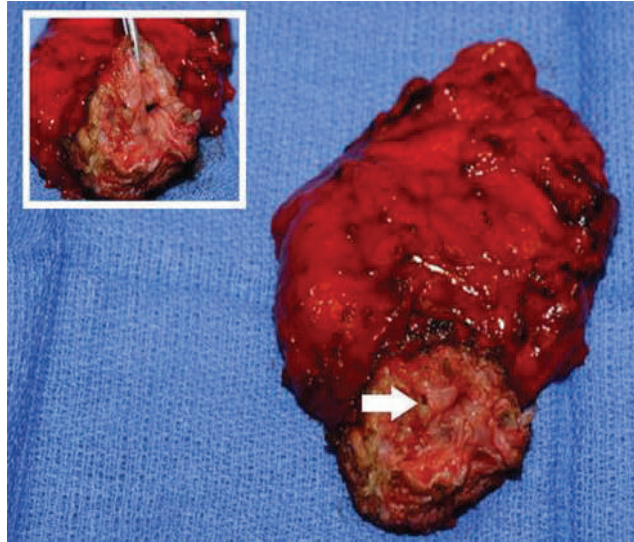


Figure 3. Extracted bladder with neoplasm in diverticulum

Discussion

Intradiverticular bladder carcinomas are malignant epithelial neoplasms arising within a diverticulum of the urinary bladder. Neoplasm arising in urinary bladder diverticulum are uncommon, but not rare and their incidence ranges between 0.8 and 10% (Melekos et al 1987)

These tumors usually occur in aged patients with bladder outlet obstruction, rarely on congenital diverticula. Inflammation, metaplasia, and dysplasia are commonly seen in the vesical diverticula. The urinary bladder is the most frequent site for urinary tract cancers. More than 95% of primary bladder cancers are of epithelial origin, most commonly transitional cell tumors. Squamous cell carcinoma and adenocarcinoma account for a minority of epithelial tumors and mesenchymal neoplasms are rare.

Golijanin et al (2003) published 39 cases, the series on diverticular neoplasms, and found that the most important factor in outcome is the clinical stage, regardless of the histological grade. In their study of 39 patients, 33% presented with superficial disease, 33% with superficially invasive tumors and 33% with invasive (extra diverticular) disease. They treated patients with superficial or superficially invasive disease either conservatively with repeat transurethral resection, or with partial or radical

cystectomy. Patients with extra diverticular extension were treated with partial or radical cystectomy when amenable to surgical extirpation. The 5-year disease specific survival rate for their group was $72 \pm 5.4\%$. Significant differences in the 5-year disease specific survival rate were observed among patients presenting with superficial tumors ($83 \pm 9\%$), superficially invasive tumors ($67 \pm 7\%$) and extra diverticular disease ($45 \pm 14\%$).

Garzotto et al (1996) suggest multimodal therapy, combining diverticulectomy with chemotherapy or preoperative radiotherapy. They showed a disease-specific survival rate of 89%, and they suggested a significant benefit from systemic chemotherapy and RT when combined with surgery for these neoplasms.

In their review of 2,642 patients with radical cystectomy, Hu et al (2014) found 1,991 patients (75 %) who met the inclusion criteria (patients who underwent radical cystectomy for curative intent for primary urothelial cancer). The median follow-up for the urothelial cancer in bladder diverticula group (10.3 years) was comparable to that of patients without urothelial cancer in the bladder diverticula (12.9 years, $p = 0.91$). A total of 77 patients (4%) had urothelial cancer in the bladder diverticula. Of these, 44 (57 %) had the highest pathologic stage of tumors within the bladder diverticula. The remainder ($n = 33$) were found in association with separate, more pathologically advanced tumors.

Considering the risk of the upstaging, therapy decisions should not be based solely on diagnostic cystoscopy and transurethral resection, but should also include radiologic imaging, as was suggested by the “Young Academic Urologist” working group on Urothelial Carcinoma of European Association of Urology (Voskuilen et al, 2018). They found that the upstaging of diverticular tumors was frequent (55%), indicating an inaccuracy in clinical staging in urothelial carcinoma of a bladder diverticulum. Also, the group underline that partial cystectomy may represent a feasible alternative of radical cystectomy in carefully selected urothelial carcinoma of a bladder diverticulum, with equivalent oncological results, but the urologist should be aware of the potential underestimation of tumor extent of carcinoma in a bladder diverticulum.

In review of 36 patients with carcinoma arising from a bladder diverticulum, we demonstrated during the first period of analysis (1961-1980) that treatment, which consisted of transurethral resection and radical

cystectomy, showed a poor survival rate. The last period, the following 30 years, showed better diagnostic possibilities, computed tomography, and nuclear magnetic resonance. In addition, earlier radical surgical procedures enabled better results and survival, especially after 1990, and with the introduction of aggressive chemotherapy the survival rate improved even more. This diagnostic and therapy improvement led to much a better survival rate of patients with urothelial cancer of a bladder diverticulum over the last 20 years.

In conclusion, transurethral resection of neoplasm in a bladder diverticulum seems to be adequate for men with superficial non-invasive urothelial cancer. There is a smaller number of cases, even with modern diagnostic capabilities, due to patients reporting these problems later on to their doctor. We can say that diverticulectomy or partial cystectomy, and radical cystectomy are a safer therapy for patients and provide a better survival rate.

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