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CLINICAL CASE REPORT

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# A Large Bladder Tumor Covered With a Thick ''Shell'' of Necrotic Material

## *Misdiagnosis of a Patient With Spina Bifida*

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**Abstract:** Bladder tumor arising in a spina bifida patient is rare and may be clinically latent.

We report the case of a 61-year-old female patient with spina bifida, neurogenic bladder, and a history of recurrent urinary tract infections. A B-ultrasound and non-contrast computed tomography scan did not reveal any bladder mass, but an unexplained ''well-filled'' bladder was observed, which was confusing as the catheter was present and open. However, a subsequent cystoscopic evaluation revealed a large bladder mass measuring $9.5 \times 9.0 \times 6.5\,cm^3$, which almost filled the entire bladder. The mass had coarse and flocculent surface and seemed to be free from each observed wall of the urinary bladder. It was diagnosed as an infectious necrotic mass based on its appearance.

During transurethral resection of the mass, a bladder tumor was suspected as small blood vessels and bleeding appeared within the inner layer of the mass. Pathological examination revealed necrotic material, inflammatory cells, and urothelial carcinoma cells. Then, a radical cystectomy was performed, and the pathological results indicated stage pT3bN0M0 transitional cell carcinoma. In the gross specimen, the base of the tumor measured $3 \times 3\,cm^2$ on the top of the back wall of the bladder.

Bladder tumors may have atypical presentations in patients with spina bifida. Regular screening is helpful for earlier detection and improving outcomes of bladder tumors in such patients.

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**Abbreviations**: CT = computed tomography, HPF = high power field, SCI = spinal cord injury, UTI = urinary tract infection.

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## INTRODUCTION

Spina bifida is the most common congenital spine abnormality that is defined as any abnormal development of the spine bones with or without the involvement of the brain, nerves, or the meninges. The incidence of spina bifida in the United States is between 1/1000 and 1/4000 births.[1] The neurological deficits vary depending on the subtype of spina bifida, and patients with spina bifida usually have different degrees of neurogenic bladder. The management for neurogenic bladder involves intermittent or permanent catheterization, use of anticholinergic drugs, and surgical intervention, such as augmentation cystoplasty.[2]

Bladder cancer is one of the urologic complications of neurogenic bladder and patients with neurogenic bladder seem to be at increased risk for bladder cancer.[3] Recurrent urinary tract infections (UTIs), bladder stones, and indwelling catheterization were thought to be risk factors.[4] Bladder tumor arising in a spina bifida patient is rare. Up to date, <30 cases of patients with spina bifida and bladder cancer have been reported in the literature.[5–9] Austin et al[6] reported the largest series of 8 spina bifida patients with bladder cancer and reviewed 11 previous published cases. The presenting symptoms may be atypical and a bladder tumor could only been incidentally discovered through biopsy in some of these patients.[10]

We herein report a spina bifida patient with a large bladder tumor. The most interesting point about this case is that this large tumor is covered with a very thick ''shell'' of necrotic material. The presentation is so confusing and misleading that we made a misdiagnosis before operation. To the best of our knowledge, this special presentation of a bladder tumor has never been reported previously.

## CASE PRESENTATION

A 61-year-old female with spina bifida who had complained of aggravated cloudy urine and dull pain in the lower abdomen for 3 months was referred to our urologic center in September 2015. Two years earlier, the patient was diagnosed with neurogenic bladder and nephrarctia of the left kidney (Figure 1A). She underwent a left nephrectomy and was permanently catheterized after the operation because of urinary retention. Her urine became cloudy after catheterization, and this symptom was difficult to cure. *Escherichia coli* was sometimes cultured from the urine. No bladder mass was found in ultrasound examinations. Cystoscopy was not performed during this period.

A physical examination after admission revealed no specific signs. A urine analysis showed leukocyturia (579/high-power field [HPF], normal <5.4/HPF]. Her blood tests were normal, except for an elevated creatinine level of

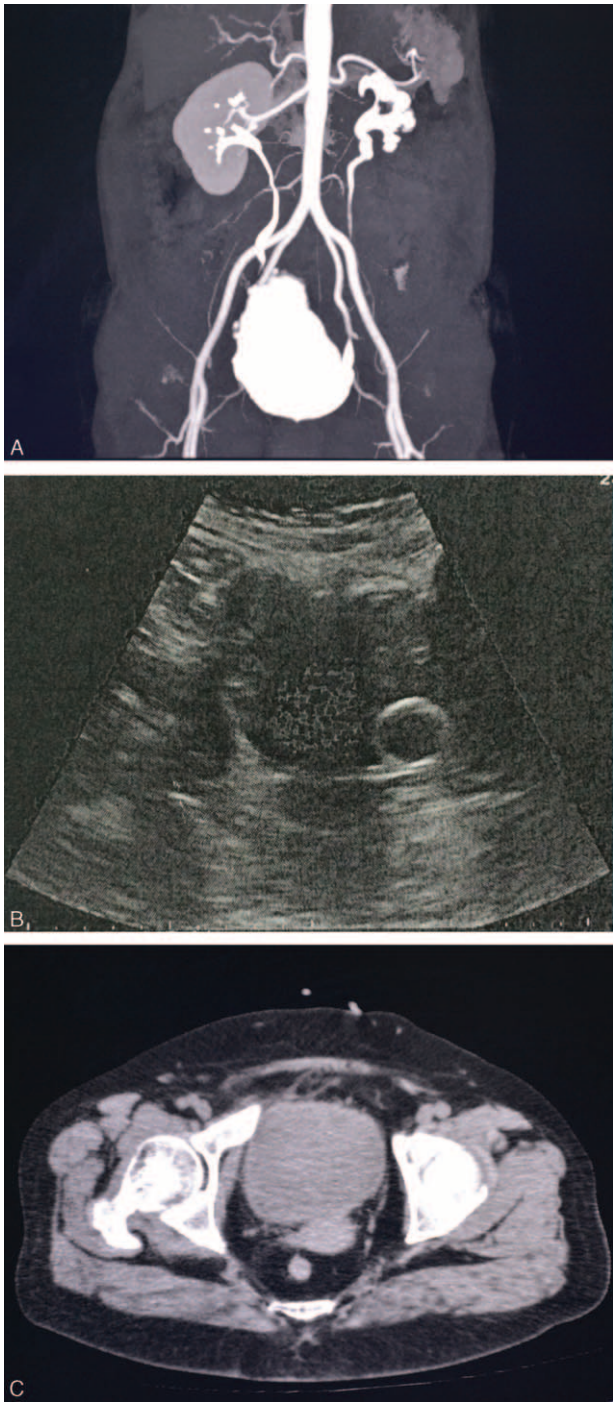


**FIGURE 1.** (A) A constructed CT image of the patient 2 years earlier shows the neurogenic bladder with multiple diverticula and nephrarctia on the left side. (B) A B-ultrasound examination revealed no obvious mass or tumor in the bladder. The bladder, which had a flocculent intravesical echo, seemed to be ''fully'' filled with cloudy urine. (C) A noncontrast CT scan revealed no intravesical mass. However, the ''well- filled'' bladder was unexplained, as the catheter remained open.

145 μmol/L (range: 20–98 μmol/L). Urinary cytology was negative. *Enterococcus faecium* was cultured from the urine. A B-ultrasound examination revealed no bladder mass or tumor (Figure 1B). Noncontrast computed tomography (CT) revealed no intravesical mass, but an unexplained ''well-filled'' bladder was observed, despite that the catheter remained open (Figure 1C). Cystoscopy was then employed and revealed a large, sphere-shaped, grayish-yellow mass measuring $9.5 \times 9.0 \times 6.5\,cm^3$ that almost fully filled the entire bladder (Figure 2A,B). The surface of the mass was coarse and flocculent. The mass was free from each observed wall of the urinary bladder, but the back wall was difficult to observe using rigid cystoscopy because of the size of the mass. A large amount of debris composed of infectious and necrotic material was diagnosed based on its appearance.

A transurethral resection of the mass was performed several days later. During the operation, the thick outer layer of the ''mass'' was found to be composed of pale necrotic material. However, as the operation progressed, small blood vessels and bleeding (arrows) appeared within the inner layer of the ''mass'' (Figure 2C). A bladder tumor was therefore suspected, and the ''root'' of the tumor seemed originate from the top of the back wall of the bladder. The surgery lasted for 110 minutes, and 165 g of tissue were resected (Figure 3); however, one-third of the mass remained. A pathological examination revealed that 60% of the mass was composed of necrotic material infiltrated with inflammatory cells, whereas the other 40% contained high-grade urothelial carcinoma cells (Figure 4). Two weeks later, a radical cystectomy and a right cutaneous ureterostomy were performed. In the gross specimen, the base of the tumor measured $3 \times 3\,cm^2$ on the top of the back wall of the bladder (Figure 5). The TNM tumor stage was pT3bN0M0.

The postoperative recovery was uneventful. The patient received adjuvant gemcitabine and cisplatin chemotherapy postoperatively. A review at 4 months after the operation showed no evidence of tumor recurrence.

## DISCUSSION

We present the case of a patient with spina bifida and a neurogenic bladder who developed bladder cancer. The bladder tumor, which was fully covered with a thick ''shell'' of infectious necrotic material, was misdiagnosed preoperatively, even after a CT scan and a cystoscopic examination. To the best of our knowledge, this should be the first report of a bladder tumor with such a confusing and misleading presentation.

Previous studies have shown that patients with a neurogenic bladder are thought to be at increased risk for bladder cancer[3]; however, many recent studies have reported a comparable incidence of bladder tumors in neurogenic patients and in the general population.[11–15] The reported incidence varies between 0.11% and 0.39% in different studies.[11,15] Transitional cell carcinoma is still the predominant overall pathological pattern,[16] but the incidence of squamous cell carcinoma has increased dramatically, especially in patients with chronic catheterization.[11,13–15] Austin et al[6] reported 19 patients (8 of their own and 11 previous published cases) with spina bifida and bladder cancer and concluded that these patients presented with an advanced stage (frequently muscle invasive) at a young age and exhibited poor survival. Pannek et al[11] also found that >60% of patients with spinal cord injuries (SCI) initially presented with muscle-infiltrating bladder cancer. It is unclear whether this aggressive biological behavior is because

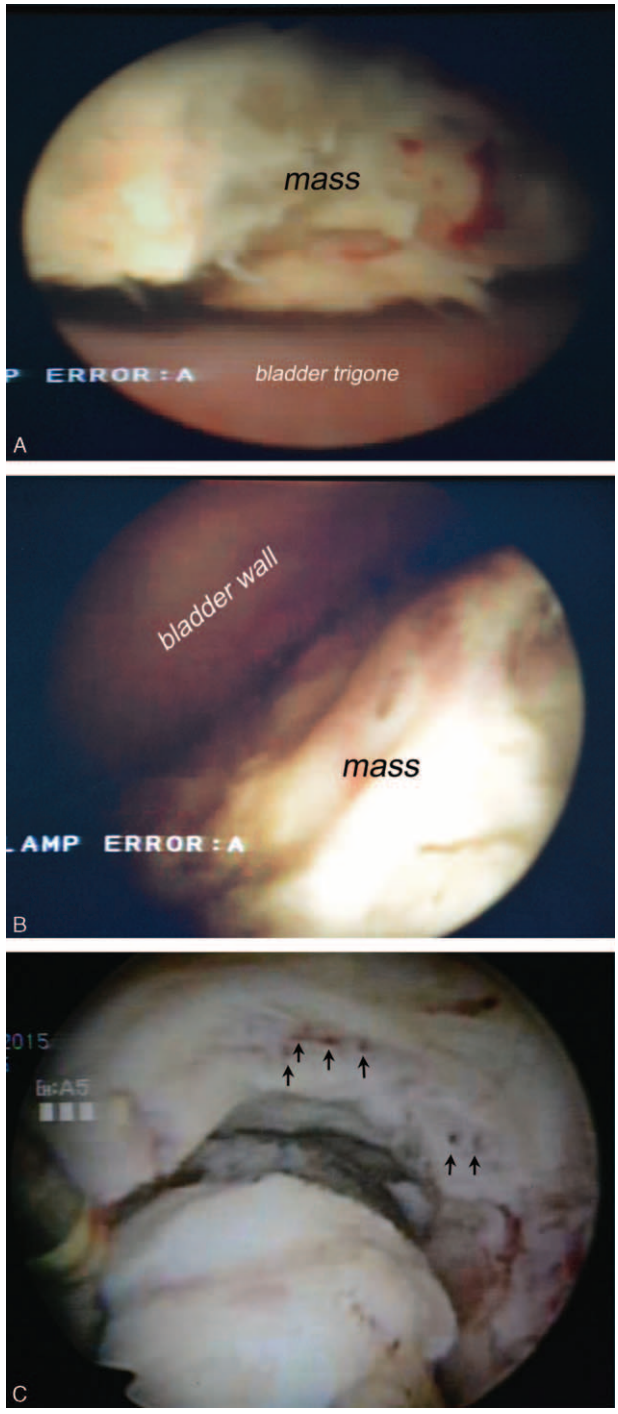


**FIGURE 2.** (A) A large sphere-shaped mass with flocculent necrotic debris on its surface, which almost filled the entire bladder, was revealed by rigid cystoscopy. (B) The intravesical ''mass'' seemed to be free from all of the bladder walls that could be observed. (C) As the transurethral resection progressed, tiny blood vessels and bleeding (arrows) appeared within the inner layer of the ''mass.''

of the chronic inflammatory response leading to prolonged exposure of the bladder to carcinogens or because of the altered immunological function of these patients. Given the high mortality and percentage of patients with advanced stage

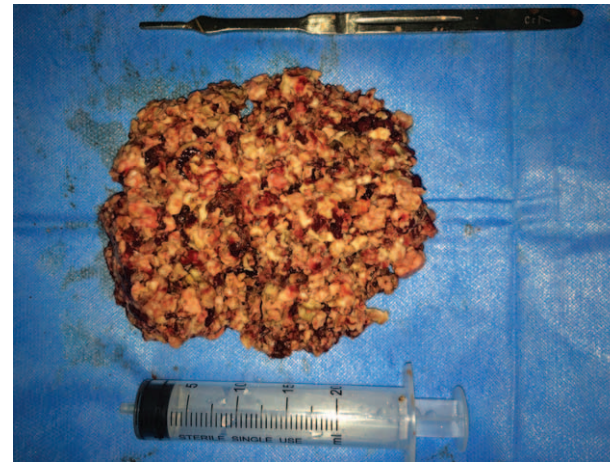

**FIGURE 3.** Tissue resected during the transurethral operation.

disease, screening patients with a neurogenic bladder has been advocated.[17] Some scholars[10] have even advocated annual serial bladder biopsies for patients with neurogenic bladder.

UTIs, bladder stones, and indwelling catheterization are risk factors for cancer in patients with a neurogenic bladder. Micturition disorders are common in these patients; thus, different approaches to drainage are applied clinically. Stonehill et al[18] showed that a history of long-term indwelling catheterization was a statistically significant risk factor for bladder tumors in SCI patients. West et al[15] confirmed that patients with SCI managed with clean intermittent urethral catheterization have a lower incidence of bladder cancer and squamous cell subtypes than those managed with an indwelling urethral catheter. Overall, indwelling catheters are thought to cause mechanical alterations that lead to increased bladder tumors, most notably squamous cell carcinoma.[11,18] Chronic or recurrent UTIs have been reported to be another risk factor for bladder tumors in patients with neurogenic bladder.[11] Some reports have stated that UTIs might be more important than the mode of bladder evacuation for the development of bladder cancer.[11]

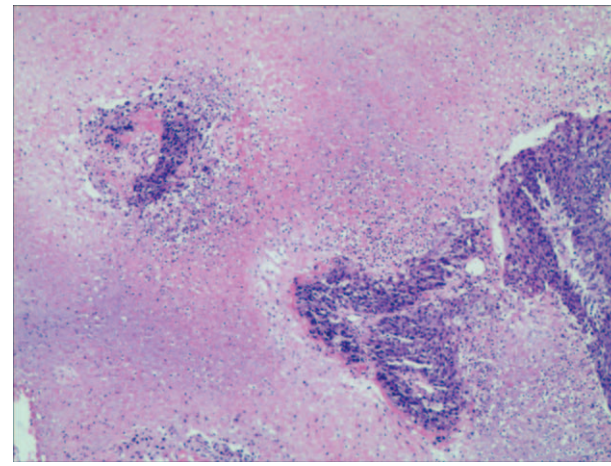

**FIGURE 4.** A pathological examination showed poorly differentiated invasive transitional cell carcinoma, a large necrotic area, and inflammatory cell infiltration (H&E ×40).

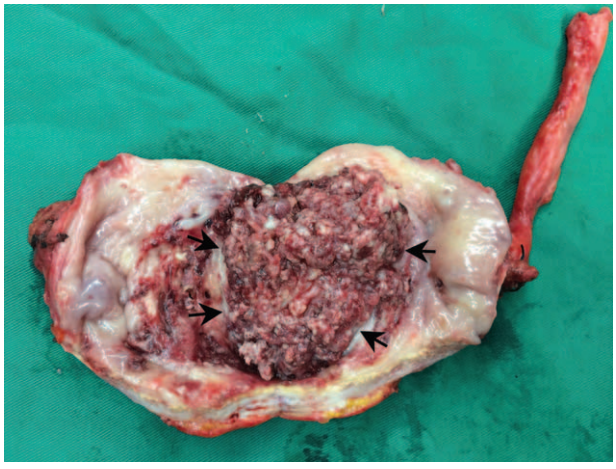

**FIGURE 5.** Using radical cystectomy of the gross specimen, the base (arrows) of the tumor measured $3 \times 3\ cm^2$ on the top of the back wall of the bladder.

For our patient, no evidence of a bladder mass was found in an enhanced CT scan performed 2 years earlier. We propose that the tumor exhibited rapid growth within the previous 2 years. During this period, 2 adverse factors were present: a perpetual indwelling catheter and recurrent UTIs. The UTIs in this patient were recurrent, severe, and poorly controlled, which caused the thick ''shell'' of infectious necrotic material to grow rapidly. The bladder tumor was closely surrounded by necrotic material, which may explain the patient's negative urine cytology and lack of hematuria. The tumor and its ''shell'' were large enough that they filled the entire bladder, and thus no urine was retained in bladder, which caused the mass to be easily missed during the ultrasound and noncontrast CT examinations. An enhanced CT examination, which was not performed on this patient because of her elevated creatinine level, might have been helpful for finding the tumor preoperatively.

In conclusion, bladder cancer in spina bifida patients may have an atypical presentation, as was demonstrated by our case. Based on our patient and previous cases, we recommend that clean, intermittent, self-catheterization should be used preferentially, as an indwelling catheter is a risk factor for bladder cancer in neurogenic patients. We suggest that regular screening with a urinary test, cytology, an imaging examination, cystoscopy, and an active biopsy would be beneficial for earlier detection of bladder tumors and improved outcomes in spina bifida patients with risk factors.

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