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CLINICAL STUDY

Inflammatory pseudotumour of urinary bladder – a rare cause of massive macroscopic haematuria

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Abstract: *Purpose:* Authors analyzed their experience with urinary bladder tumours. This article discusses clinical and histopathological diagnostics and treatment procedures, and follow up of patients with rare benign urinary bladder tumours.
Methods: 406 patients with bladder tumours were treated in our department between January 2000 and December 2008. 322 patients had superficial tumours and 84 had primary invasive tumours. All patients who underwent transurethral resections of these tumours were operated under general or spinal anaesthesia. The resected specimens were histologically examined in the department of Pathology.
Results: 399 of the 406 patients had urothelial bladder cancer, 7 patients had a histologically uncommon type of bladder tumour, one female was diagnosed with sarcomatoid bladder cancer, one patient had a histologically confirmed feochromocytoma of the urinary bladder. Two males had epidermoid carcinoma. One female had a histologically described uncommon benign pseudoneoplastic lesion, chararacteristic for endosalpingiosis. Another two patients were diagnosed with inflammatory myofibroblastic tumour of the urinary bladder. Both patients presented with gross macroscopic haematuria. Authors performed complete transurethral tumour resections, which required several sessions and the deliberation of a blocked ureter through nephrostomy in one case.
Conclusion: More than 98 % of all treated patients had urothelial bladder cancer in different stages and grades. Two patients had rare benign inflammatory proliferation of the bladder wall which formed large tumorous bleeding masses obstructing the ureter in one case. These types of bladder tumour could be treated conservatively with meticulous long term follow up similarly to patients with bladder cancer *(Tab. 1, Fig. 4, Ref. 15)*. Full Text in PDF *www.elis.sk.*
Key words: haematuria, urinary bladder, inflammatory pseudotumour.

The inflammatory pseudotumor of the urinary bladder or pseudosarcomatous fibromyxoid tumor is a benign proliferative mesenchymal spindle cell process, usually polypoid. First described in 1980 by Roth (1), it can mimic malignancy on clinicoradiological and pathological examination (2). It has been suggested that an inflammatory pseudotumor is the manifestation of a fibroblastic or myofibroblastic spindle cell and granulation reparative response of uncertain cause. Although some tumors have been associated with urinary tract infections, trauma and surgery, most are idiopathic. Inflammatory pseudotumors predominate in females (2:1), are described in literature in patient between 2 and 80 years of age, and range in size from 1 to 9 cm in diameter or rarely more (3, 4). The differential diagnosis of benign inflammatory pseudotumors primarily includes the spindle variant of urothelial carcinoma and several types of bladder sarcomas. Immunohistochemical staining has to be used to distinguish spindle variants of carcinoma from benign inflammatory pseudotumors (5).

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Methods

406 patients with bladder tumours were treated at our department between January 2000 and December 2008. 322 patients had superficial tumours and 84 had primary invasive tumours. All patients who underwent transurethral resections of these tumours were operated under general or spinal anaesthesia. The resected specimens were histologically examined in the department of Pathology. There were these specimens examined also imunohistochemically.

Results

399 of the 406 patients had urothelial bladder cancer (328 males and 78 females). The remaining seven patients had a histologically uncommon type of bladder tumour. One female (56 years) was diagnosed with sarcomatoid bladder cancer, one patient (80 year old male) had a histologically confirmed feochromocytoma of the urinary bladder, which was clinically asymptomatic of hormonal activity. Twomales (71 and 63 year old) had epidermoid carcinoma. One female (49 years) had a histologically described uncommon benign pseudoneoplastic lesion, chararacteristic for endosalpingiosis with presence of glandular structures with ciliary cylindrical epithelia. The tumour had atypical tubular and flat cellu-

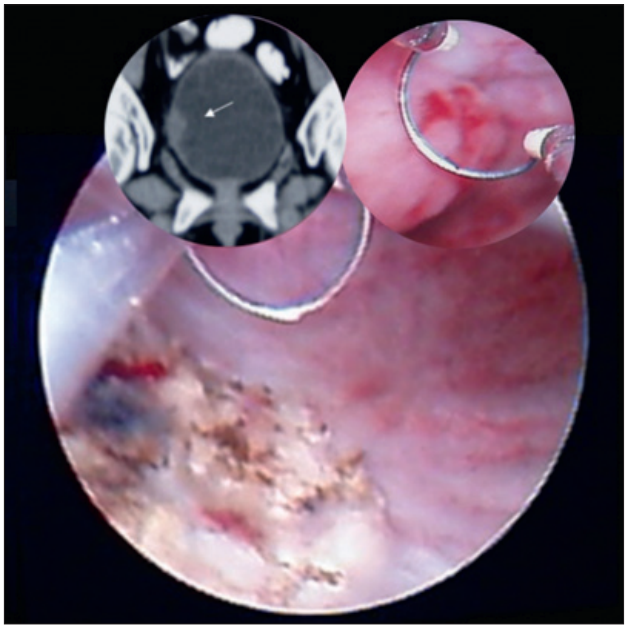

Fig. 1. Case No 1. Non-contrast CT scan of a 48 year old female, endoscopic image and complete resection of the tumour.

lar elements located in the muscularis propria.We present two cases of inflammatory pseudotumor verified histologically, and treated by endoscopic resection. The presenting complaint of these patients was macroscopic hematuria. The first patient, a 48 year old female had been treated with cyclophosphamide and prednisone for six years. This was due to systemic Scleroderma which affected her esophagus and lungs. Her urinary problems commenced in 2003, where cystoscopy confirmed diffuse hemorrhagic cystitis. This was repeated on several occasions, and treated with electrocoagulation over the last years. Due to possible correlation between cyclophosphamide therapy, and hemorrhagic cystitis, we stopped this treatment. In February 2006 she presented, and was admitted with gross hematuria, and was found to have a broad-based polypoid bladder tumor (3x4 cm, on right bladder wall). Prior to surgery she received 5 units of blood transfusion, because of anaemia (Hb 5.1 g/dL). We performed a native CT scan of the urinary tract, which showed a solid tumorous lesion on the right bladder wall, without extravesical invasion . The tumor was endoscopically resected (Fig. 1). Histological examination confirmed a rare entity – inflammatory myofibroblastic tumor composed of spindle cells mixed with extracellular collagen, lymphocytes, and plasma cells. Three months later, she again presented with gross haematuria, due to recurrence of the bladder tumour (4x 5cm), which was localized close to the bladder trigone, and obstructed both ureters. The tumor was again resected transurethrally, which showed the same histological features. Due to fibrotic processes in the bladder wall, likely induced by previous long term treatment with cyclophosphamide and repeated electrocoagulations, the bladder capacity was remarkably decreased. Due to obstruction of both ureters, JJ stents were inserted bilaterally. Despite histologically the tumor appeared benign, clinically it showed a malignant course, which made the patient a candidate for cystectomy.

The patient refused cystectomy, and after a total of six transurethral resection procedures, there has been no recurrence of the inflammatory bladder tumor. The patient is regularly reviewed (every 3 months) endoscopically and biochemically. Symptoms of severe urgency improved after treatment with anticholinergics. The bladder capacity is only 130 ml, and the obstruction of the ureteric orifices surprisingly changed to bilateral vesicorenal reflux grade III with renal impairment (Fig. 2). Her blood creatinine is mildly elevated above normal range (140μmol/l) and her general status is stable.

The second case, a 37 year old male with Sclerosis multiplex, presented (May 2006) with haematuria, anaemia, and left flank pain. A huge intravesicular mass (5x6 cm) was identified on bladder ultrasound, IVU, CT, and cystoscopy. The left ureter was involved in this tumour, with dilatation of the renal pelvis (Fig. 3). Deep complete transurethral resections (3 sessions) were performed and histological results confirmed (with light microscopy and immunohistochemical staining) inflammatory fibromyxoid tumor. Due to obstructed left kidney percutaneous nephrostomy was performed. After resection of the residual bladder tumor and an antegrade insertion of a guidewire into the bladder nephrostomy

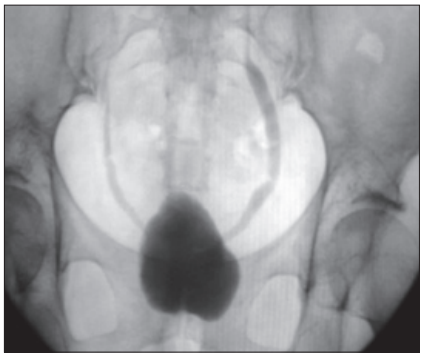

Fig. 2. Case No l. Voiding cystogram shows small fibrotic urinary bladder (with 130ml capacity) with bilateral vesicorenal reflux of grade III (B).

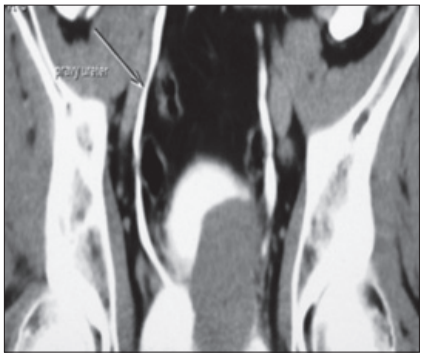

Fig. 3. Case No 2. CT scan: A large intravesical tumor 5x5cm in size with partial blockade of the left ureter.

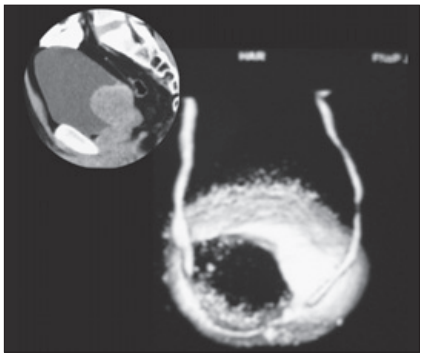

Fig. 4. Case No2. 3-D CT reconstruction of bladder wall showing invasiveness of tumor which suggests high malignant bladder tumor growth.

Tab. 1. Main immunohistopathological differences between inflammatory pseudotumors, sarcomatoid carcinomas and bladder sarcomas.

Inflammatory pseudotumor	spindle cells are positive for vimentine, ALK-1 desmine and muscle specific actine, no reaction for cytokeratine
Sarcomatoid carcinoma	positive reaction for cytokeratine and epithelials antigens
Bladder sarcoma	Leiomyosarcoma: vimentin+, aktin+, H-caldesmon+, CK- Liposarcoma: vimentin+, S-100 protein+, aktin-, h- caldesmon-, CK- Rhabdomyosarcoma: vimentin+, desmin+, myogenin+, MyoD1+, CK-

tract, the derivation of urine has been converted to JJ stent. The initially considered management of partially resecting the bladder wall with reimplantation of the left ureter was rejected because of the good result of the above mentioned procedures. Two years later, the patient is now stent free, with a normal functioning left kidney, and no recurrence of bladder tumor (Fig. 4).

Discussion

The inflammatory pseudotumor – also known as a pseudosarcomatous or atypical fibromyxoid tumor is a benign mesenchymal tumor (6). The benign nature of this rare bladder tumour warrants conservative surgical management, either transurethral resection or partial cystectomy (7, 8, 9). The risk of recurrence of inflammatory pseudotumors following surgical excision is low (3). Because of the histological similarity of inflammatory pseudotumors to some malignant tumors, most authors recommend close surveillance (10, 11, 15). Hematuria is the most common presenting complaint, although dysuria, frequency, and suprapubic pain have also been reported (5). Laboratory abnormalities include microcytic hypochromic anemia, thrombocytosis, polyclonal hypergammaglobulinemia, and elevated erythrocyte sedimentation rate (4).Our first reported patient presented with complex symptoms because of systemic scleroderma and toxic impact of long term treatment with cyclophospamide. Oral cyclophosphamide is associated with substantial urotoxicity including development of transitional cell carcinoma of the urinary bladder, mainly in terms of long exposure. The most frequent manifestation of side effect of cyclophosphamide is haemorrhagic cystitis (12, 13). Our patient suffered from repeated gross hematuria caused by bleeding from benign inflammatory bladder tumor most probably induced by cyclophospamide treatment as well. The cause of the inflammatory bladder psedotumor in the second presented patient is unknown. CT findings of these benign bladder tumors are usually nonspecific, but CT is a staging modality capable of revealing a neoplastic infiltration into the deeper layers of the bladder and local structures (14, 15) (Tab. 1).

Conclusion

In our two cases we presented diagnostic and therapeutic procedures of inflammatory bladder tumors with large and deep infiltration of the bladder wall. We found a correlation between cyclophosphamide induced haemorrhagic chronic cystitis, and the proliferation of the bladder mesenchymal structures into benign inflammatory bladder lesions.

For definitive confirmation of its benign character, special immunohistochemical analysis should be performed to clearly differentiate their inflammatory origin from malignancy. Such bladder tumors could be treated conservatively with meticulous long term follow up. In case of recurrence or histopathological doubts, partial cystectomy eventually radical cystectomy is indicated.

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