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CASE REPORT

Mycobacterium tuberculosis and bovis as causes for shrinking bladder

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ABSTRACT

Urogenital tuberculosis (UGTB) is the second common form of tuberculosis (TB) in countries with severe epidemic situation and the third common form in regions with low incidence of TB. UGTB is complicated by bladder TB in more than half of cases; late diagnosis and/or absence of pathogenetic therapy leads to the development of shrinked bladder. The intravesical bacillus Calmette-Guerin (BCG) after transurethral resection (TUR) in Ta and T1 bladder cancer provides a significantly better prophylaxis of tumour recurrence than TUR alone. Nevertheless alongside with positive results many complications of BCG therapy, including lethal, were noted. We describe two cases of shrinked bladder TB – one was caused by M. tuberculosis, and second – by M. bovis.

Key words: urogenital, tuberculosis, bladder, mycobacterium

INTRODUCTION

Urogenital Tuberculosis (UGTB) is complicated by bladder tuberculosis (TB) in more than half of cases[1]; late diagnosis and/or absence of pathogenetic therapy leads to the development of shrinked bladder up to full its obliteration. It is known, that TB is an antropozoonotic disease. Reciprocal contamination of humans and animals, mainly cattle, is with M. bovis. In 80-th years of past century 16% of all nephrotuberculosis in Siberia were caused by M. bovis; now this form of UGTB is revealed sporadically.[1]

From 1976 intravesical instillation of bacillus Calmette-Guerin (BCG) were used in the therapy for Ta and T1 bladder cancer.[1-3] 26 publications comparing transurethral resection (TUR) with TUR + BCG showed that TUR with intravesical BCG provides a significantly better prophylaxis of tumour recurrence in Ta and T1 bladder cancer than TUR alone.[4] Two another meta-analyses demonstrated statistically significant superiority for BCG compared with mitomycin C (MMC) for the prevention of tumor progression.[5-7] Nevertheless alongside with positive results many complications of BCG therapy, including lethal, were noted.[8-16]

Typical scenario of development of natural bladder TB grade 4 (classification of E. Kulchavenya[1]), caused by M. tuberculosis, is demonstrated by case 1, and a case 2 demonstrates the iatrogenic bladder TB as a complication of BCG therapy.

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CASE 1

Patient BLM, 62 years, inhabitant of Altay. For 8 years he complained of flank pain, which was interpreted by his doctors as radiculitis. He was treated with non-steroid anti-inflammatory drugs with incomplete efficiency. In 2008 he found the increasing of the size of right testis, scrotal pain, frequency urination, and pyuria. The patient received some courses of antibiotics for "urogenital infection" without effect.

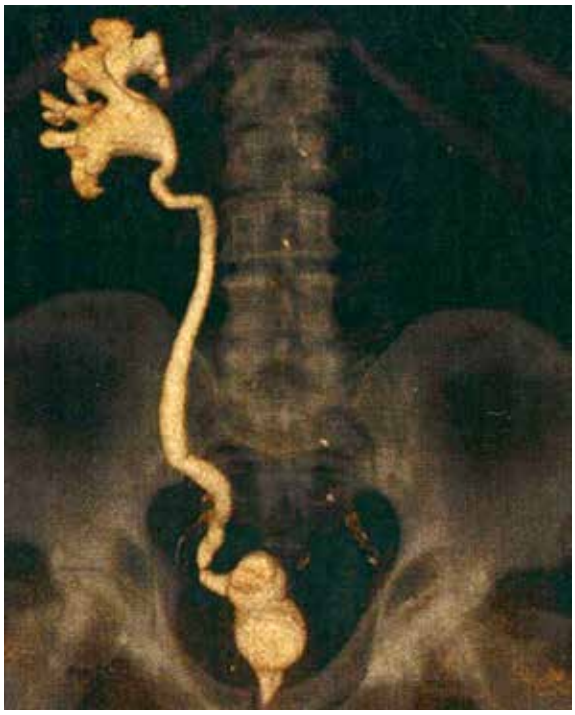

Figure 1, Spiral computer tomography: tuberculous papillitis of single right kidney,
bladder tuberculosis grade 4, mictocystis.

When intervals between micturitions got 30 min., his urine was investigated for Mycobacterium tuberculosis (Mtb) with positive result. The urinalyses, biochemical blood analyses, culture and microscopy of urine, X-ray, spiral computed tomography and ultrasound examination revealed generalized UGTB: policavernous TB of left kidney, non-funtion of left kidney, tuberculous papillitis of right kidney, bilateral TB of ureters, bladder TB grade 4 (microcystis), right-side vesico-renal reflux. Renal failure. TB orchiepididymitis on the right, TB of the prostate, Mtb+.

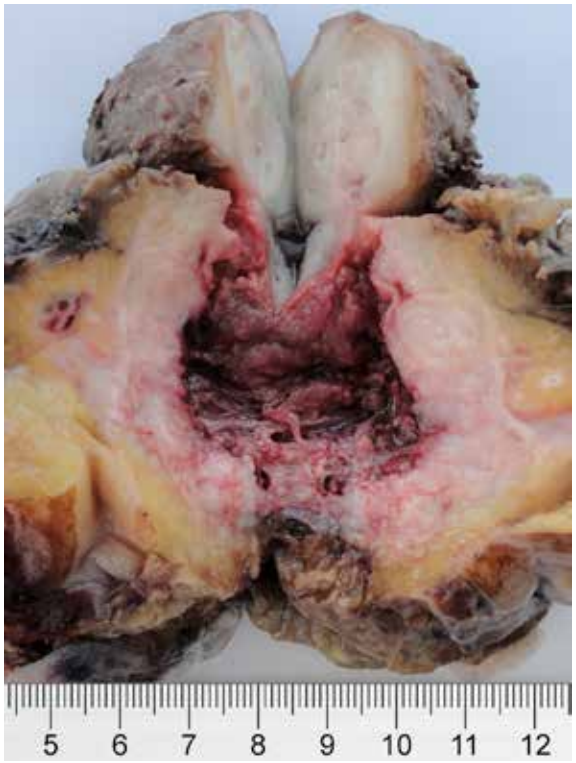

Figure 2, Removed bladder and prostate – longitudinal section. Bladder capacity very low, walls are thickened, fibrotic.

Complex chemotherapy with four drugs (isoniazid, rifampicin, pyrazinamid, streptomycin) was begun. In two months none effect was noted, so the patient underwent nephrectomy on the left, epididymectomy on the right. Chemotherapy was continued till 14 months. Severe disturbance of urination, low bladder volume were indication for hydrodistension, but it resulted in deterioration of his condition.

The patient was admitted in Urogenital Clinic of Novosibirsk Research TB Institute on 29.09.2009. Laboratory examination presented pyuria, haematuria, bacteriuria (Klebsiella pneumoniae $5x10^4$; Pseudomonas aeruginosa 10^5). White blood cells – $7.9x10^9$/l, urea – 13 mmol/l, creatinin – 270 mkmol/l, PSA – 1.9 ng/ml. The prostate biopsy was performed 14.12.09; pathomorphologically – chronic non-specific prostatitis with intensive sclerosis of the stroma were found. Microcystis complicated by vesico-renal reflux was considered as a reason for a progression of renal failure, so for urine derivation on 19.11.2009 trocar cystostomy was performed. A level of a creatinin in 4 weeks decreased till 167 mkmol/l, and on 15.01.2010 cystprostatectomy, ileocystoplastic by Studer technique was conducted.

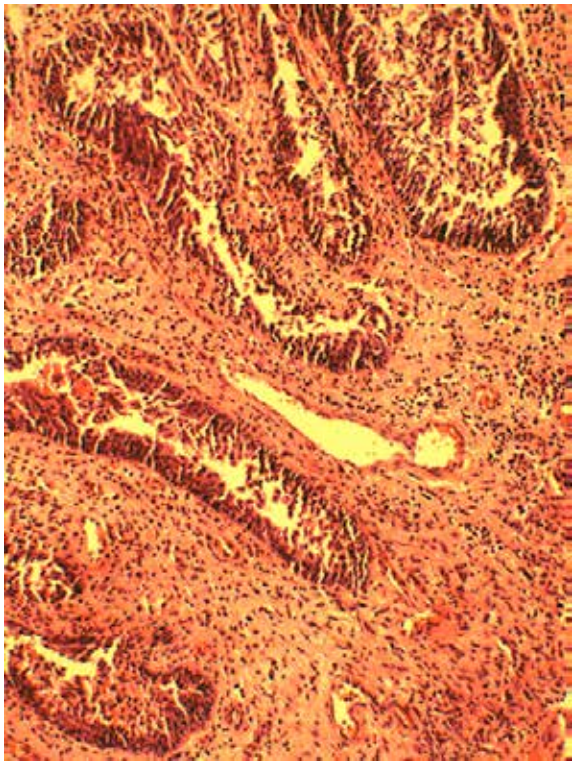

Figure 3, Bladder - papillary cystitis, mononuclear infiltration and stromal fibrosis.
Hematoxylin and eosin. x150.

The right ureter was dilated, but its wall was elastic, with peristaltic waves. The bladder was reduced in size, the surrounding fatty tissue was sclerotic. Histological findings: prostate – focuses of caseous necrosis surrounded by irregular layer of granulomatous tissue with multinucleated giant cells (Langhans'); small granulomas, massive fibrosis, chronic inflammatory cell infiltrates and nonular glandular hyperplasia with cyst formation around. Seminal vesicles – cystic atrophia and pericanalicular fibrosis. Bladder – chronic nonspecific inflammatory infiltrate, massive fibromatous transformation of stroma. Diagnosis: active tuberculosis of prostate, progression phase. Chronic fibrosing cystitis.

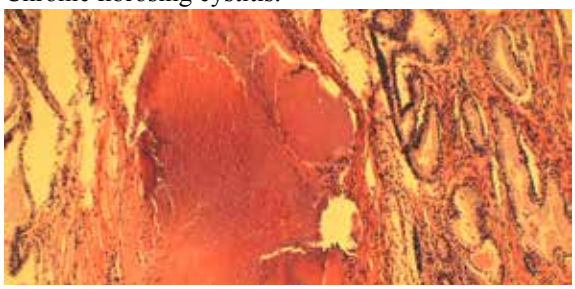

Figure 4, Prostate - granuloma-like eosinophilic amorphous mass, contacting (top right) with rounded deposition (corpus amylaceum). The mass is surrounded by mature fibrous capsule. Stromal fibrosis and mononuclear interstitial infiltrate. Hematoxylin and eosin. x150.

Just after the operation some improving of renal function was noted (creatinin – 124 mkmol/l. Volume of artificial bladder was 480 ml. Episodes of incontinence, mostly at night, were rarely. Pyuria and bacteriuria were the same despite of complex antibacterial therapy.

Spiral computer tomography of a urinary system of the patient BLM is presented on picture 1; pictures 2, 3 and 4 demonstrate his bladder macro and micro.

CASE 2

Iatrogenic bladder TB, caused by M. bovis. Patient B.A.I., 50 years. In 2003 superficial urothelial carcinoma of a bladder was diagnosed, TUR was performed without any adjuvant therapy. Control cystoscopy in 2004 presented relapse of the tumor in 4 sites. TUR was repeated and pathomorphologically urothelial carcinoma without invasion of lamina propria was found. After this operation the patient left the city and didn't address to a doctor during 6 years. In March 2010 he was admitted in urological clinic because of gross-haematuria. Cystoscopy presented multitude (more than 10) tumors of 5 – 20 mm in diameter. TUR was repeated again; pathomorphologically – low grade urothelial carcinoma T1 was found. In one month BCG-therapy in dose 100 mg weekly was started. After 3rd instillation dysuria, fever appeared. Levofloxacin 500 mg was prescribed, and in one week temperature became normal, but dysuria was the same, bladder capacity decreased till 50 ml, intervals between urination were about 30 minutes.

In August, 2010 control cystoscopy revealed a solitary ulcer, tubercles. This picture was estimated as bladder TB and anti-TB therapy was recommended. But the patient got sick in myocardial infarction, underwent cardio-surgery and only 07.09.2010 he was admitted in urogenital clinic of TB Institute. Pathologic examination. Bladder urothelium with focal thinning down to 1-2 epithelial cells. Lamina propria is obviously edematous, hyperemic, contains petechia.

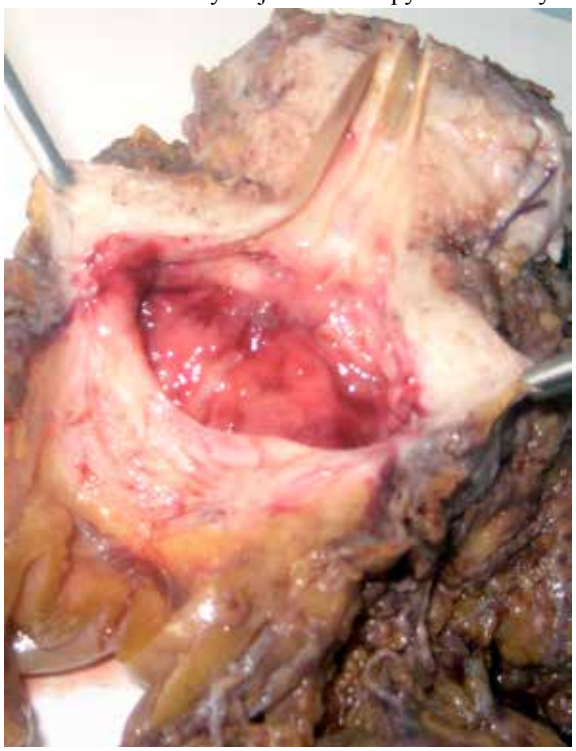

Figure 5, Removed bladder and prostate of B.A.I. on sagittal section. The diameter 4.5 cm, thick walls. Mucous membrane is reddish with hemorrhages. Prostate is grey, dense, at a glance without pathology.

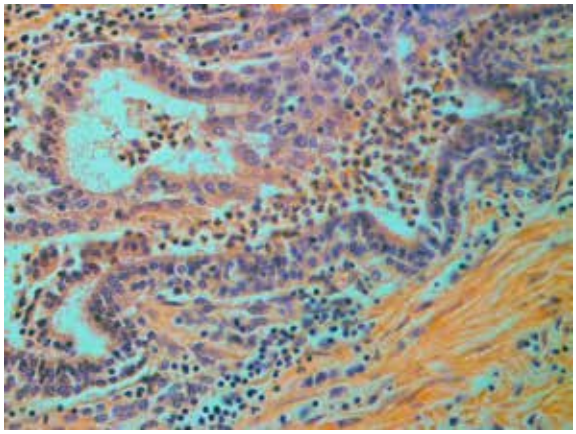

Figure 7, Prostate. Polymorphocellular interstitial infiltration, granulocytes fill dilated ductular lumens. Hematoxylin and eosin. x600.

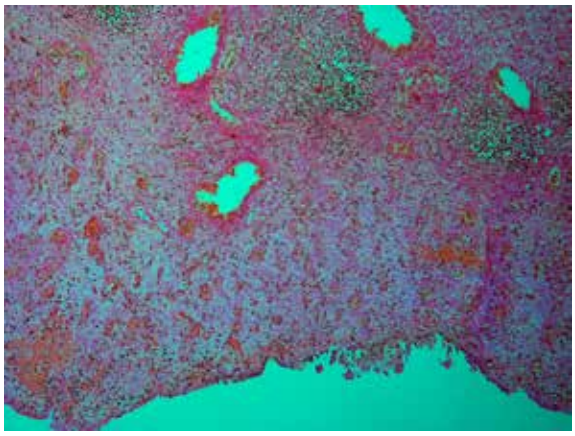

Figure 6, Chronic erosive cystitis. Wide erosion of bladder epithelium (bottom). Lamina propria shows neoangiogenesis (granulation tissue), edema and early collagenic fibrosis. Focal mononuclear inflammatory infiltration, formation of lymphoid follicles, and more mature fibrosis (top). Van Gieson, x120.

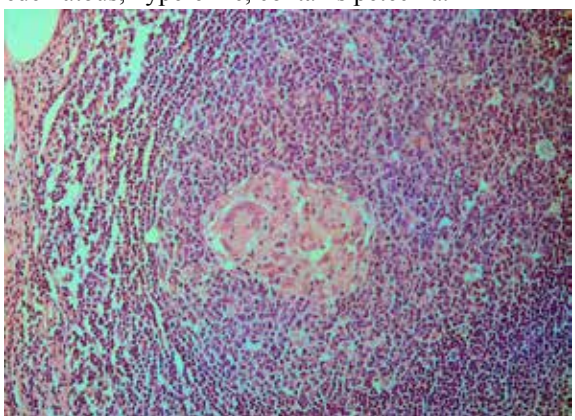

Figure 8, Appendix. Granuloma is located within germinal center of lymphoid follicle and consist of epithelioid and giant multinucleated Langhans cells. Hematoxylin and eosin. x300

Diffuse lymphocytic and neutrophilic infiltrates in mucosa, some lymphoid follicles occur. Papillary lesion is identical of other mucosa by structure. Bladder wall is significantly desorganized by sclerotic expansion, smooth muscle fascicles are thin and fragmented. Prostate: nonspecific chronic inflammatory infiltrate with significant focal neutrofilic component, especially intra- and periductular. Stromal fibrosis in prostate, atrophic and cystic ductal changes. Appendix contain few epithelioid- and giant (Langhans') cell granulomas, including one within follicular germinal center. Thus, BCG therapy provoked local TB as well as generalized TB. Nevertheless histological signs of neither TB nor cancer were not found.

On control examination in 2 months the capacity of an artificial bladder was 400 ml, urination free, but sometimes there was night incontinence.

DISCUSSION

Presented cases of bladder TB differ on etiology (in first case infectious agent is M. tuberculosis, in second case – M. bovis) and on pathogenesis (in first case – hematogenous dissemination with total involvement of organs of urogenital system, in second case – local TB inflammation caused by absorption of infectious agent). Nevertheless both outcomes were identical – formation of severe fibrosis, development shrank bladder, microcystis.

Bladder TB is a complication of kidney TB, the situation when patient has a healthy kidney and bladder TB is impossible at all. Bladder TB in UGTB patient mostly is confirmed by clinical and radiological findings as well as results of provocative tuberculin test, not by culture. Specific histology in bladder biopsies is rare. It is unknown the degree and duration of contact Mtb with urothelium in case of natural bladder TB.

In case of iatrogenic bladder TB as result of BCG instillation there was unconditional contact of mycobacteria with urothelium. Sometimes, when a patient presents co-morbidity, immunodeficiency, inflammation etc, infection agent may absorb and provoke local bladder TB – primary site of infection, which impossible in natural bladder TB. Low resistance of macroorganism may lead to the spread of TB - especially in the prostate, the abdominal organs, regional lymph nodes, and in some cases it is possible generalization of infection with a fatal outcome.

CONCLUSION

These two cases of natural and iatrogenic bladder TB emphasize the actuality of UGTB. Flank pain with dysuria is an indication for excluding of UGTB, especially in the region with high incidence of TB. And second point – it is necessary to estimate all real and potential contraindications for BCG-therapy before first instillation, careful maintenance of technique and surveillance for the patients during the therapy.

The authors declare that they have no conflict of interest

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