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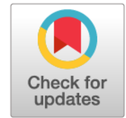

Is neoadjuvant chemotherapy necessary for the surgical treatment of renal tuberculosis?

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The relevance of urogenital tuberculosis remains high as well as its social significance. With the advent of anti-tuberculosis drugs it became possible to perform organ-preserving surgeries, both anti-tuberculosis chemotherapy in the preoperative period and after surgery is extremely important. Violation of this principle leads to the development of severe complications, which is demonstrated by clinical observation. Patient I., female 40 years. Diagnosis: polycavernous tuberculosis of the right kidney, cavernous tuberculosis of the left kidney, bladder tuberculosis of stage 4 (microcystis). Her anti-tuberculosis therapy was irregular and occasionally. In the general urology department a laparoscopic nephrectomy on the right and nephrostomy on the left were performed. Anti-tuberculosis therapy was discontinued, which led to the progression of renal failure and repeated attacks of pyelonephritis. In this regards she was re-operated in the Avicenna Medical Center: laparoscopic cavernotomy of the left solitary kidney and cystectomy with enterocystoplasty by Studer were performed. In the postoperative period a reservoir-uterine fistula was formed. She did not receive anti-tuberculosis therapy. The patient returned to the Avicenna Medical Center after 9 months, laparoscopic removal of the shrunken intestinal reservoir was performed with the formation of Bricker ileal conduit with a good short-term and long-term (follow-up period of 10 months) result.

Keywords: anti-tuberculosis chemotherapy; surgical treatment of renal tuberculosis; urogenital tuberculosis; nephrotuberculosis; laparoscopy.

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Нужна ли неоадъювантная химиотерапия при хирургическом лечении туберкулеза почек?

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Актуальность урогенитального туберкулеза остается высокой, равно как его социальная значимость. С появлением противотуберкулезных препаратов появилась возможность выполнения органосохраняющих операций, однако крайне важным является противотуберкулезная химиотерапия — как в предоперационном периоде, так и после хирургического вмешательства. Нарушение этого принципа приводит к развитию тяжелых осложнений, что демонстрирует клиническое наблюдение. Пациентка И., 40 лет. Диагноз: «Поликавернозный туберкулез правой почки, кавернозный туберкулез левой почки, туберкулез мочевого пузыря 4-й стадии (микроцистис)». Противотуберкулезные препараты принимала нерегулярно и бессистемно. На этом фоне в урологическом отделении общего профиля выполнена лапароскопическая нефрэктомия справа, наложена пункционная нефростома слева. Терапия противотуберкулезными препаратами прекращена, что привело к прогрессированию почечной недостаточности и очередным атакам пиелонефрита. В связи с этим повторно оперирована в МЦ «Авиценна»: лапароскопическая кавернотомия единственной левой почки, цистэктомия, энтероцистопластика по Штудеру. В послеоперационном периоде сформировался резервуарно-маточный свищ. Противотуберкулезное лечение не получала. Пациентка вновь обратилась в МЦ «Авиценна» через 9 мес., было выполнено лапароскопическое удаление сморщенного кишечного резервуара с формированием уретероилеостомы по Брикеру с хорошим ближайшим и отдаленным (срок наблюдения 10 мес.) результатом.

Ключевые слова: противотуберкулезная химиотерапия; хирургическое лечение туберкулеза почек; урогенитальный туберкулез; нефротуберкулез; лапароскопия.

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INTRODUCTION

Globally, tuberculosis is one of the major causes of death from a single infectious agent for most of the documented history of mankind [1, 2], although the coronavirus pandemic has made adjustments to its epidemic indices. Tuberculosis is also considered a serious social problem due to its pronounced negative impact on demographic indicators and through decreased fertility [3–6]. In addition, tuberculosis causes approximately 40% of mortality among patients with human immunodeficiency virus (HIV) [7]. The World Health Organization estimates that 10.0–10.4 million people worldwide developed tuberculosis in recent years, 1.3–1.8 million died, and 40% of patients remained undiagnosed and did not receive treatment in 2017 [8, 9].

Tuberculosis of the lymph nodes, pleura, bones, meninges, and the urogenital tract is diagnosed most often in the range of extrapulmonary localizations [10–12]. The term "urogenital tuberculosis" (UGT) includes tuberculosis infection affecting the kidneys, ureters, bladder, prostate, urethra, penis, testes, epididymis, vas deferens, ovaries, fallopian tubes, uterus, cervix, and vulva [13–16]. In some regions, UGT remains the second most common localization of extrapulmonary tuberculosis (EPT) [17–19].

EPT does not have pathognomonic symptoms. The mycobacteria excretion in these forms of diseases is meager, inconsistent, and elusive, and in some localization, is absent (for example, tuberculosis of the adrenal gland, spleen, and pericardium). Histological verification is not always possible; in some cases, the risk in collecting tissue for pathomorphological examination exceeds the possible benefit and is fraught with a generalization of the process [11, 13, 19, 20]. Thus, EPT is often diagnosed at the stage of severe complications or intraoperatively in the general medical network, as well as in urgent surgeries for severe complications (liver abscess, pyonephrosis, uterine bleeding, etc.). Concomitant HIV infection completely changes both the clinical and pathomorphological presentation of EPT, which introduces additional difficulties in its timely diagnosis [11, 12].

Since the beginning of the century, 40%–56% of EPT cases were registered as UGT, but in 2008, osteoarticular tuberculosis ranked first [11]. Nevertheless, the relevance of UGT remains high, as well as its social significance [4]. Diagnostics of UGT, as a rule, is delayed, which can lead to fatal consequences. One of the main reasons for this is low alertness to tuberculosis, inability to recognize it among other urological diseases, under which UGT is successfully disguised [11–13]. UGT diagnostics, especially in the early stages, is extremely difficult. Despite the mild severity of symptoms, the disease progresses inexorably and ends with obstructive uropathy, pyonephrosis, and renal failure.

Until the middle of the XIX century, the "white plague," as tuberculosis was also called, was one of the most terrible diseases, annually killing thousands of people worldwide and making hundreds of thousands disabled. Effective treatment development, including surgical treatments, has been one of the most pressing concerns of professional medicine. It was a breakthrough time in understanding the etiology and pathogenesis of tuberculosis. In 1872, George Absalom Peters (1825–1894, St. Luke's Hospital in New York) was able to remove a tuberculous kidney for the first time, and rather by accident. Initially, nephrectomy for tuberculosis caused controversy, and surgical treatment of renal tuberculosis was one of the most important tasks of renal surgery in urology at the beginning of the XX century. In 1902, Victor Schmiden (1874–1945) summarized all cases of surgical interventions for renal tuberculosis in Bonn. A total of 1118 nephrectomies were performed, wherein 301 patients died. In 1925, James Israel (1848–1926) devoted a separate chapter in his textbook to the surgical treatment of renal tuberculosis [21].

Late diagnostics leads to the development of serious complications that cannot be eliminated by therapeutic intervention. With the advent of anti-tuberculosis drugs, performing organ-preserving surgeries became possible [13, 22]. Thus, surgical aids for UGT are still relevant. Modern capabilities of medical science significantly expanded the range of surgeries performed, most are minimally invasive. The absence of pathognomonic symptoms, a tendency to self-healing through caseous calcification, and low alertness lead to late diagnosis at the stage of organ loss [11–13, 21, 22].

Surgical treatment consideration is always a temptation, especially in the case of organ-resecting surgery, sufficient to cure a patient with tuberculosis, as after all, the focus of infection was removed, then what will be the reason for long-term chemotherapy prescription. However, this is a misconception, and the following clinical case demonstrates this.

CLINICAL CASE

Patient I., a 40-year-old female and a citizen of the state of Central Asia, has been sick for approximately 5 years. The first manifestation of the disease was frequent urination during the day and night; over time,

the frequency of urination increased. During the day, the patient urinated every 15 min and 7–8 times at night. When gripes occurred during urination, she consulted a doctor. The patient lived in an epidemically unfavorable region for tuberculosis; therefore, the doctors' alertness was high, and within 2 months, she was diagnosed with polycavernous tuberculosis of the right kidney, cavernous tuberculosis of the left kidney, and stage 4 bladder tuberculosis with the formation of microcystis. However, polychemotherapy was not prescribed and surgical treatment was not offered (reasons could not be established due to the language barrier). The patient came to Novosibirsk, where her brother lives, for medical help. Since she did not have Russian citizenship, hospitalization in a municipal or federal hospital or provision of a free full-set of anti-tuberculosis drugs at the dispensary was impossible. On the recommendation of a phthisiourologist, the patient received anti-tuberculosis therapy on an outpatient basis, with treatment interruptions.

In the urology department of the general profile, a right laparoscopic nephrectomy was performed. The surgery was associated with a large blood loss, which indirectly indicated its complexity. The left kidney was drained by a puncture nephrostomy, which often stopped functioning, and then the patient had voluntary frequent urination (after 15 min), which caused severe discomfort and significantly reduced the quality of life. The body temperature increased to febrile values. A Foley urethral catheter was installed to relieve these complaints.

In June 2019, the patient turned to the private clinic in Avicenna MC, Novosibirsk for further surgical treatment.

On 03.07.2019, laparoscopic cavernotomy of the solitary left kidney was performed. For the surgery, the patient was placed on the operating table in the right side position. The traditional placement of the optical and working trocars was performed and the lower pole of the solitary left kidney was mobilized from the perirenal fatty tissue, where the cavern with a diameter of approximately 6 cm was located. Using an ultrasonic dissector, the wall of the cavern was opened; the contents were a transparent liquid of light yellow color. The cavern wall was excised using an ultrasonic dissector (Fig. 1). The neck of the lower calyx was visualized at the bottom of the cyst. The neck was not sutured. The bottom of the cavern was treated with bipolar coagulation. A drainage tube and a glove-gauze tampon were brought to the bottom of the cavern to delimit the bottom of the cyst from the free abdominal cavity.

The patient was placed in the supine position for stage 2 of the surgery. The surgery was continued through the lower midline laparotomy, wherein the uterus with the fallopian tubes and the right ovary was amputated. The left ovary was preserved. The cervical stump was sutured with a continuous 2–0 Vicryl suture. Then, a subtotal cystectomy was performed with bladder mobilization by electroligating the surrounding tissues with the Ligasure apparatus and transecting the ureter of a solitary kidney.

Extracorporeal formation of the artifactual bladder according to Studer was performed. Thus, a 60 cm long segment of the ileum was isolated at a distance of 25 cm from the ileocecal angle. The integrity of the intestine was restored by the imposition of a hardware interintestinal anastomosis side-to-side. Detubularization of the distal portion of the isolated segment was performed by longitudinal dissection of the intestinal wall along the antimesenteric edge for 40 cm using monopolar coagulation. The proximal part of the intestine was left without tubularization. The formation of an S-shaped spherical reservoir was made with a continuous vicryl 3–0 suture. On a 7 Ch single-loop ureteral stent, a Wallace ureteral-intestinal anastomosis was formed with a continuous 4–0 vicryl suture between the ureter of a solitary left kidney and the proximal end of the non-detubularized section of the intestine. Between the reservoir and the urethra, 20 Ch anastomoses were formed on a urethral silicone catheter.

The immediate postoperative period was uneventful. On a postoperative day 1, thromboembolic complications were prevented, as well as analgesia with non-narcotic analgesics and ropivacaine administration into the epidural space through an infusion pump. On postoperative day 3, the administration of anesthetic into the epidural space was discontinued. Antibacterial therapy with carbapenem was performed for 7 days. On day 1, the patient was allowed to drink water. From postoperative day 2, Nutrizone enteral nutrition was allowed. Bowel function recovered on postoperative day 3, after which normal food intake was allowed.

The patient was discharged for outpatient treatment on day 10. On an outpatient basis, a single-loop ureteral stent was removed on day 14, a reservoirostome was removed on day 20, and the urethral catheter was removed on day 21.

The histological study revealed a renal fragment with foci of necrosis, with granulations along the periphery, lymphoid nodules, and macrophage granulomas with Pirogov–Langhans cells. The preparations revealed

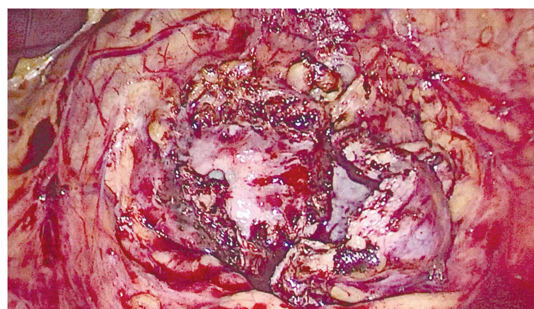

Fig. 1. Laparoscopic cavernotomy of a solitary left kidney: the bottom of the cavity and the excised wall of the cavity are visible
Рис. 1. Лапароскопическая кавернотомия единственной левой почки: видно дно каверны и иссеченная стенка каверны

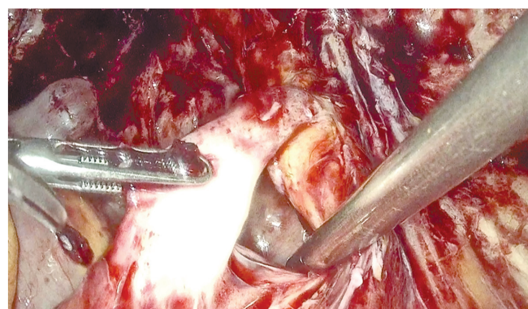

Fig. 2. The ureter flows into the scar-altered reservoir
Рис. 2. Мочеточник, впадающий в рубцово-измененный резервуар

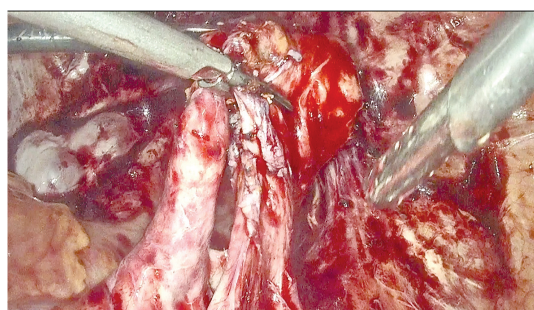

Fig. 3. Intersection of the mesentery of the wrinkled reservoir
Рис. 3. Пересечение брыжейки сморщенного резервуара

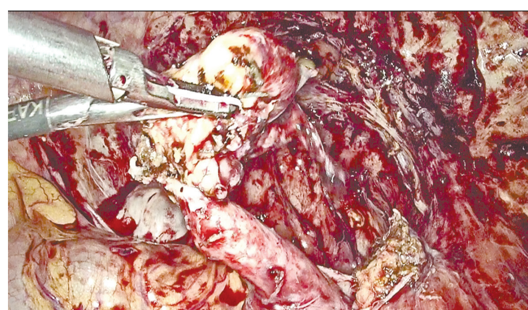

Fig. 4. Remains of the reservoir into which the left ureter flows
Рис. 4. Остатки резервуара, в который впадает левый мочеточник

a cavity wall with a three-layer structure, necrosis, granulation, and fibrosis. The bladder wall had mucous membrane atrophy, hemorrhages, focal fibrosis, multiple lymphoid accumulations, focal growths of granulomatous tissue, and single epithelioid tubercles. The ureter wall had focal fibrosis, with weak lymphohistiocytic infiltration. UGT with kidney damage with a cavity-cavern formation, bladder damages, induration, and scarring were histopathologically concluded.

After the catheter removal, the patient developed an involuntary vaginal discharge of urine in addition to voluntary urination. Examination revealed the discharge of urine from the cervical canal of the cervical stump as a reservoir-uterine fistula. Conservative patient management was recommended, as well as the continuation of anti-tuberculosis therapy and, after the postoperative inflammatory process remitting in the small pelvis, reconstructive surgery was performed.

The patient went home, and anti-tuberculosis therapy was performed with long breaks due to insufficient anti-tuberculosis drugs. Spontaneous urination gradually ceased and urine began to be completely excreted from the vagina. The pain was experienced in the lumbar region, and the creatinine level increased. The patient used an indwelling urethral catheter to drain urine for a long period.

She applied for an examination at the Avicenna medical center in April 2020, 9 months after the surgery. A multispiral computed tomography was performed, of which, results revealed solitary left kidney ureterohydronephrosis. The creatinine level at the time of hospitalization was 226 μmol/L. Therefore, a second surgery was decided.

On July 4, 2020, laparoscopic removal of the wrinkled intestinal reservoir was performed with the formation of a Bricker ureteroileostomy. The traditional placement of trocars was performed above the navel and an optical trocar was installed, as well as two working trocars, each in the right and left iliac regions. During the laparoscopy in the abdominal cavity, a moderately pronounced adhesion process occurred and small intestinal loops were fixed to the small pelvic walls, which were separated by blunt and sharp dissection. After separating the adhesions, a dilated ureter was visualized, of which a wrinkled intestinal reservoir anastomosis was revealed (Fig. 2).

The walls of the reservoir were tightly fixed to the pelvic bones. The reservoir mesentery was separated, clipped, and transected (Fig. 3). Figure 4 shows the remains of the artifactual reservoir where the left ureter ends.

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The reservoir was transected from the ureter and immersed in an extraction bag. The mucous membrane of the reservoir remains, fixed to the pelvic walls, was coagulated using bipolar energy. Bricker ureteroileo-cutaneostomy was formed in a typical manner. The remains of the reservoir with the ureteral segment were removed.

On day 7, the ureteral stent catheter was removed, and the patient was discharged for outpatient treatment. Deterioration of renal function and exacerbations of pyelonephritis was not noted in the patient (follow-up period for 10 months).

Histological examination revealed fragments of the ureter and reservoir wall. The ureter had symptoms of mucosal atrophy, wall fibrosis, and diffused lymphocytic infiltration. No epithelial lining was found in the reservoir wall; an area with desquamated intestinal epithelium, stroma fibrosis, and diffused lymphoma-macrophage infiltration with multinucleated cells of the foreign body type was noted. The morphological presentation of chronic nonspecific granulomatous inflammation of the uretero-reservoir segment was histologically concluded.

DISCUSSION

This case demonstrates the possibility of fibrosis of the artifactual reservoir with inadequate anti-tuberculosis therapy. Excessive post-tuberculous scarring is the source of many complications in genitourinary tuberculosis. Until now, the opinion of V.D. Grund is relevant that we get “desirable scarring in an undesirable place” [23]. Sclerotic processes prevail with inadequate and haphazard polychemotherapy without simultaneous pathogenetic treatment.

Reservoir-vaginal fistula is a described complication of ileocystoplasty in women. Surgical treatment of these fistulas leads to good results. The optimal time for suturing the fistula is 3–4 months since its inception. The surgery is best performed with a transvaginal approach. The fistula can be disconnected and sutured with laparotomic access if suturing is possible with a transvaginal approach. The presence of a fistula does not explain the reservoir shrinkage. A compensatory value of the fistula can also be assumed. The fistula preserved the residual function of the solitary left kidney.

CONCLUSION

Surgical success depends not only on surgical skills but also on adequate preoperative anti-tuberculosis therapy. To prevent the recurrence of genitourinary tuberculosis, most phthisiourologists recommend intensive anti-tuberculosis chemotherapy for at least 4–8 weeks with continued therapy in the postoperative period.

Lack or inadequate therapy can lead to the recurrence of urogenital tuberculosis, reconstructive surgery failure, and renal failure progression.

ADDITIONAL INFORMATION

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