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OVERVIEW

Overview of urological complications before, during and after kidney transplantation

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ABSTRACT
The result of a kidney transplantation may be affected by certain congenital or acquired urological diseases that need to be addressed before, during or after the kidney transplant. Complications accompanying kidney transplantation are not fundamentally different from the events that accompany other difficult surgical procedures. However, their course is usually modified by adverse circumstances in the recipient – uremia, dialysis treatment, immunosuppression. The incidence of urological complications is reported in the range of 1 to 30 % of the transplants, and they represent up to one half of all surgical complications. They can cause a significant morbidity and mortality and can lead to a delayed onset of the function and even to a loss of the transplanted kidney.
Urological complications that need to be addressed before kidney transplantation include anomalies or pathological changes in the lower urinary tract, pelvic involvement in atherosclerosis or previous kidney transplants, infectious foci in lithiasis or pyonephrosis, large polycystic kidneys and malignancies. During the kidney transplantation itself, vascular complications, and complications connected with the reconstruction of the lower urinary tract can occur. Other complications are bacterial and viral infections and malignancies. All these complications require a rapid and accurate diagnosis and subsequent targeted treatment with intention to maintain a functional kidney transplant *(Fig. 11, Ref. 36)*. Text in PDF *www.elis.sk*
KEY WORDS: kidney transplantation, urological, vascular, infectious, bleeding, complications.

Abbreviations: CMV – Cytomegalovirus, CT – Computed Tomography, ESWL – Extracorporeal Shock Wave Lithotripsy, MRI – Magnetic Resonance Imaging.

Introduction

The result of kidney transplantation may be affected by certain congenital or acquired diseases of the urogenital system that must be addressed before, during or after transplantation. Complications accompanying kidney transplantation are not fundamentally different from the events that go along with other difficult surgical procedures. However, their course is usually modified by adverse circumstances in the recipient – uremia, immunosuppression, dialysis treatment with the use of anticoagulants (1, 2, 3).

The incidence of urological complications is reported in the range of 1 to 30 % of transplants. Urological complications account for about one half of all surgical complications after kidney transplantation. They can cause a significant morbidity and mortality in patients, can lead to a delayed onset of function, as well as a loss of the transplanted kidney.

The aim of preoperative urological examination of patients included in the waiting list for kidney transplantation is to identify and address in time possible congenital and acquired pathological changes affecting the kidneys and the upper and lower urinary tracts of the potential kidney recipient. It is also necessary to detect any changes in the pelvic arterial bed. In this way, the occurrence of serious urological and vascular perioperative and postoperative complications can be minimized. Therefore, it is appropriate that patients undergo at least a basic and, if necessary, specialized urological and vascular examination before kidney transplantation.

Complications before kidney transplantation

Patient's own kidneys can cause subjective problems and postoperative urological complications. These diseases include autosomal dominant inherited polycystic kidneys, sometimes

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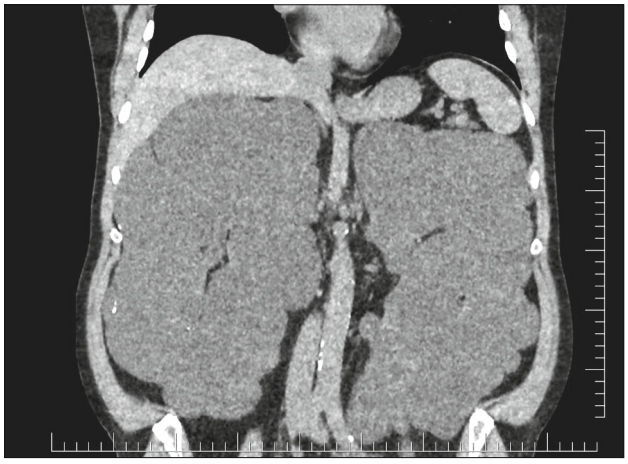

Fig. 1. Native CT scan showing giant polycystic kidneys.

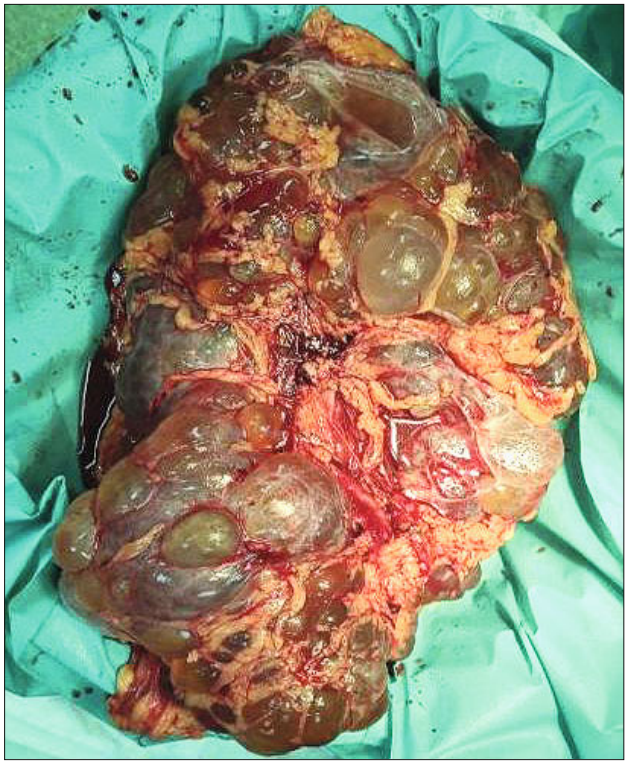

Fig. 2. Removed left polycystic kidney, weight 6000 g – same patient as shown in Figure 1.

giant ones, which can be a mechanical barrier to the placement of the transplanted kidney and cause pain, temperature, or bleeding (Figs 1 and 2).

Other diseases of the kidneys can be malignant tumours, nephrolithiasis with subsequent hydronephrosis and infection, uncontrollable hypertension, or a therapeutically uncontrollable nephrotic syndrome. Standard visualization examinations are used to diagnose pathological changes in patient's own kidneys before or after kidney transplantation. Subsequent urological treatment depends on the specific impairment of the kidneys. Since the patient's own kidneys are worthless in terms of their function, nephrectomy is usually indicated when pathological changes in the kidneys are detected. The method of nephrectomy (open surgery or laparoscopy) is decided by the urologist according to the nature of the kidney disease and its size.

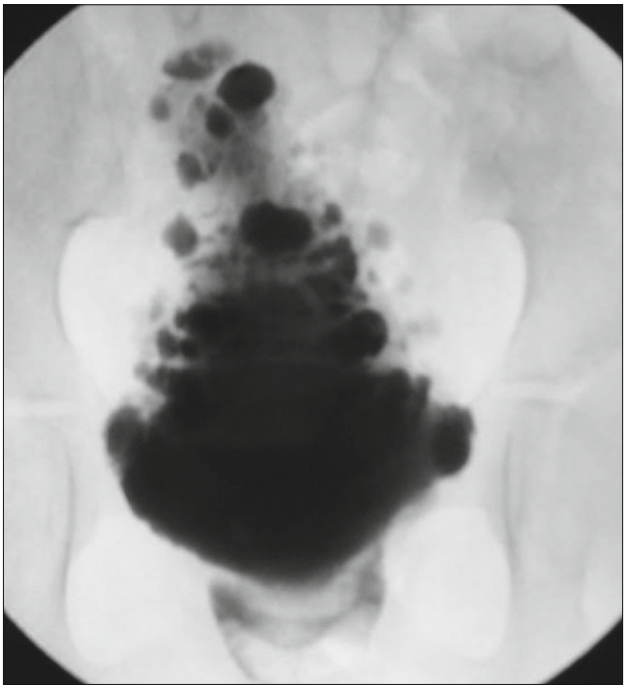

Fig. 3. Neurogenic bladder.

Regarding the lower urinary tract of patients before kidney transplantation, information on repeated operations on the vesicorenal reflux or megaureter is important. The wall of the bladder changes, scarring after repeated operations, which can lead to shrinkage of the bladder with a significant reduction in its functional and anatomical capacity. The functional and anatomical capacity of the bladder is also decreased in anuric patients. However, the histological structure of the bladder wall is usually unchanged, and such a bladder, after kidney transplantation and restoration of diuresis, can restore its function of storing and emptying urine. An alternative method of draining urine from the transplanted kidney directly into the bladder is uretero-ureteroanastomosis between the transplanted kidney ureter and the own ureter of the transplanted kidney recipient. In the case of pathological changes in the lower urinary tract, or a missing bladder, it is necessary to address the situation in a suitable way of urine derivation (4, 5, 16).

The category of pathological changes of the lower urinary tract also includes a neurogenic bladder with all functional and clinical consequences (ureterohydronephrosis, cystolithiasis) (Fig. 3).

Complications during kidney transplantation

Exceptionally, during kidney transplantation, it is necessary to decide whether to transplant a kidney injured or damaged at col-

lection. The injured removed kidney must be inspected precisely in an ice bath. It is necessary to check its blood vessels, the integrity of the kidney surface and assess any cracks, their extent and depth. A blunt kidney injury may result in a contusion in the kidney parenchyma. If the kidney vessels are not injured, such a kidney can be safely used and transplanted. The contusive lesion in the parenchyma heals even without a further specific treatment (Fig. 4).

In the event of a conflicting finding, the transplant team leader is required to assess the nature of the kidney and vascular injury and decide whether the kidney can be used for transplantation. Patient's safety must be paramount in making this decision.

Urological complications after kidney transplantation

Surgical and urological complications after kidney transplantation can be divided into early and delayed. Early complications occur immediately after surgery or during the first postoperative days (6, 7, 8).

Bleeding after a kidney transplantation

The most serious early complication after kidney transplantation is bleeding, which can be mild but also clinically very severe with hemodynamic alteration and rapid anemia of the patient. Massive blood secretion from the drain in the surgical wound, sonographic or CT evidence of hematoma around the transplanted kidney, but especially the clinical condition of the patient indicating hemorrhagic shock are indications for an urgent surgical revision. After aspirating the liquid blood and clots from the wound, all structures are gradually inspected. The most common sources of bleeding are leaking vascular anastomoses or vessels injured in the kidney hill during its collection. Tiny blood vessels often bleed from the surface of the kidney. The source of bleeding is then treated accordingly. Rarely, vascular reanastomosis is required in the case of a tortuous or kinked artery or vein of the transplanted kidney. Exceptionally, the transplanted kidney needs to be removed for massive and unstoppable bleeding.

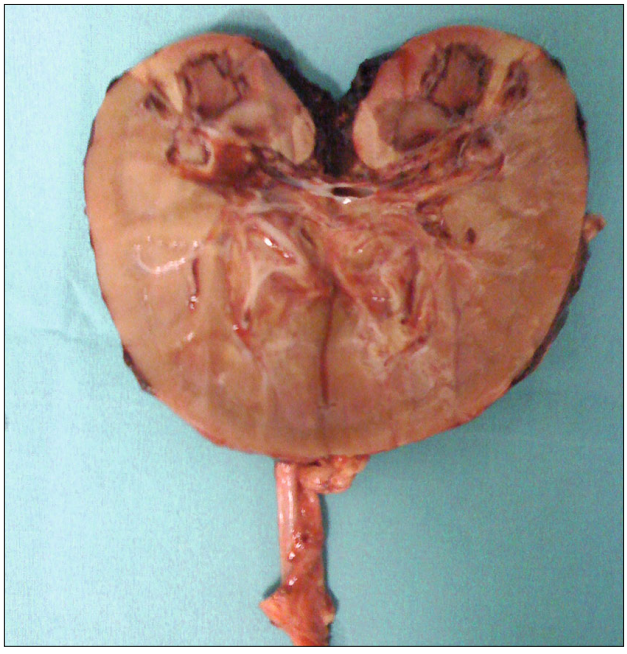

Fig. 4. An injured removed kidney – contusive lesion in the parenchyma of its upper pole.

Hematuria after kidney transplantation

A relatively common complication after kidney transplantation is macroscopic hematuria of varying intensity and clinical severity. Macroscopic hematuria occurs in 1 to 34 % of the patients after surgery. Bleeding most often occurs from the bladder wall injured during ureteral implantation or from the ureter stump of the transplanted kidney. Less severe hematuria can be managed conservatively, by ensuring a perfect bladder drainage, sometimes even with permanent flushing. In cases of massive hematuria, cystoscopy and endoscopic fulguration of the bleeding site are indicated. Rarely, the cause of hematuria is injury to the kidney by endoprosthesis or bleeding after biopsy of the transplanted kidney.

Other early complications after kidney transplantation

Early complications after kidney transplantation include the primary dysfunction of the transplanted kidney. It is the result of acute graft necrosis and is observed in 5 to 40% of kidney transplants taken from dead donors. Problems in the donor (circulatory instability with renal hypoperfusion), mistakes in kidney collection, perfusion and preservation are involved in the development of this disorder. Acute tubular necrosis affecting the epithelium of the renal medullary tubuli is in most cases reversible (8, 9, 10).

The histological pendant of the avital kidney is necrosis of the cortex. If cortical necrosis is detected on bipsy after kidney transplantation, a delayed onset of function cannot be expected, and such a kidney should be removed.

Lymphocele after kidney transplantation

Another complication after kidney transplantation is the formation of lymphocele. A lymphocele is a pseudomembrane-bounded deposit of fluid, lymph, near the transplanted kidney. Lymphocele usually leads to lymph leakage from the injured lymphatic pathways running along the recipient's iliac vessels. Lymphatic vessel injuries occur during the preparation of iliac vessels and their preparation for vascular anastomoses with the vessels of the transplanted kidney. Injured lymphatic vessels in the removed kidney, decapsulation of the removed kidney or oedema of the transplanted kidney caused by acute transplant rejection can also be a source of lymph leakage. Diabetes mellitus in the kidney recipient or treatment with m-TOR signalling pathway inhibitors may also be involved in the development of lymphocele. Lymphocele develops several days to weeks after kidney transplantation. Its incidence is 0.8 to 22 %. The incidence of small asymptomatic lymphoceles with a volume of up to 50 ml, which can be found during sono-

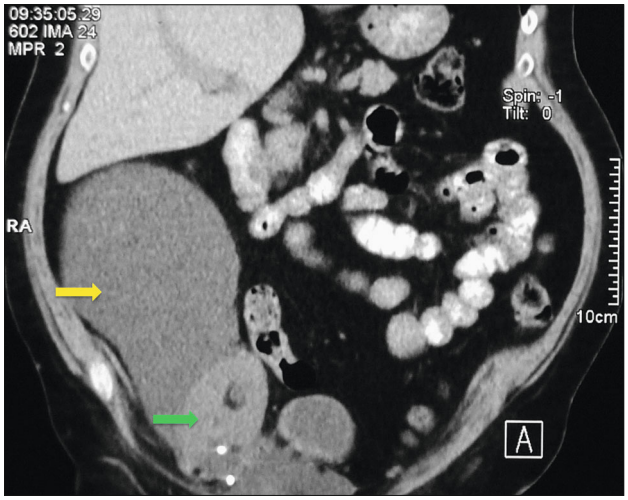

Fig. 5. CT picture of large lymphocele (yellow arrow) over the transplanted kidney (green arrow).

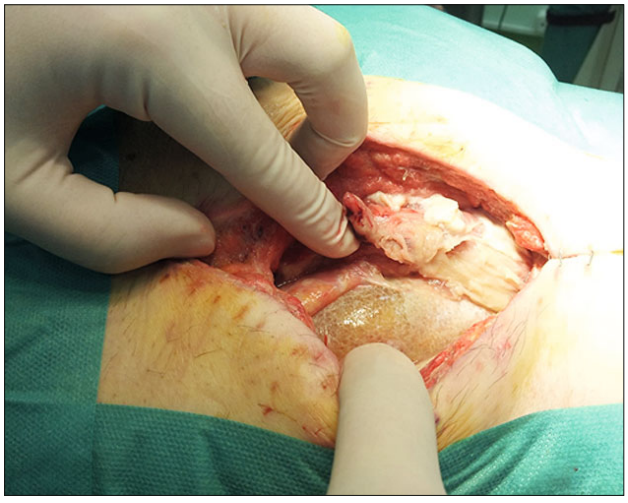

Fig. 6. Clinically important lymphocele near the transplanted kidney.

graphic control of transplanted kidneys, is up to 50 %. Most of them do not cause problems and resorb spontaneously (11, 12).

Significantly more severe are the large lymphoceles whose pressure on the surrounding structures leads to clinical symptomatology. The most common symptoms are impaired kidney function with elevated serum creatinine in ureterohydronephrosis due to lymphocellar pressure on the transplanted kidney ureter and ipsilateral lower limb oedema with subsequent phlebothrombosis of the iliac vein at lymphocellar pressure on the venous pelvic system.

Lymphocellar diagnosis usually does not cause problems. Ultrasonography and CT provide information on the presence, size and location of the lymphocele and its relationship to important structures of the transplanted kidney (Fig. 5).

The sole evacuation of the lymphocele sometimes leads to a rapid adjustment of the function of the transplanted kidney. The success of laparoscopic marsupialization, in which the lymphocele opens into the peritoneal cavity, depends on the size and location of the lymphocele. The last way of treatment is an open drainage of the lymphocele into the peritoneal cavity through the lower middle laparotomy (Fig. 6).

Urinary fistula after kidney transplantation

A serious urological complication is the urinary fistula, which can occur in any part of the urinary tract. This may lead to the loss of the transplanted kidney. The cause of urinary extravasation around the kidney may be a technical mistake in the reconstruction of the lower urinary tract or necrosis of the ureter. In the first case, the fistula is due to a leaky suture at the site of ureteral implantation. Its solution lies in the reimplantation of the ureter into the bladder. Ureteral necrosis is the result of a disruption of its vascular supply that occurs in the case of careless removal and damage to the ureteral vessels during kidney collection, less often during kidney transplantation or due to rejection. Urinary fistula in ureteral necrosis typically occurs around the 7th to 10th day after kidney transplantation (13, 14) (Fig. 7).

The incidence of urinary fistulas after kidney transplantation is reported to be in the range of 1.3 to 5.4 %. The incidence of urinary fistulas in ureteral necrosis is reported to be in the range of 0.4 to 3.2 % of kidney transplants.

Diagnosis of the cause of urinal fistula must be rapid and accurate. Biochemical examination of the secretion leaking from the drain or surgical wound distinguishes urine from blood serum. The presence and extent of the fluid collection and its relation to the transplanted kidney will be confirmed by visualization – ultrasonography, CT, and MRI. Under ultrasonographic control, the hollow system of the transplanted kidney can then be punctured in a targeted manner and antegrade pyeloureterography can be performed, which confirms the leakage of urine and the location

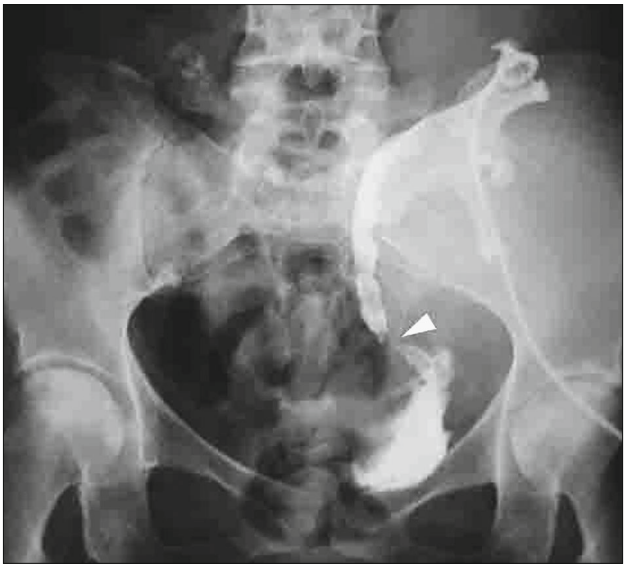

Fig. 7. Urinary fistula in ureteral necrosis of the transplanted kidney.

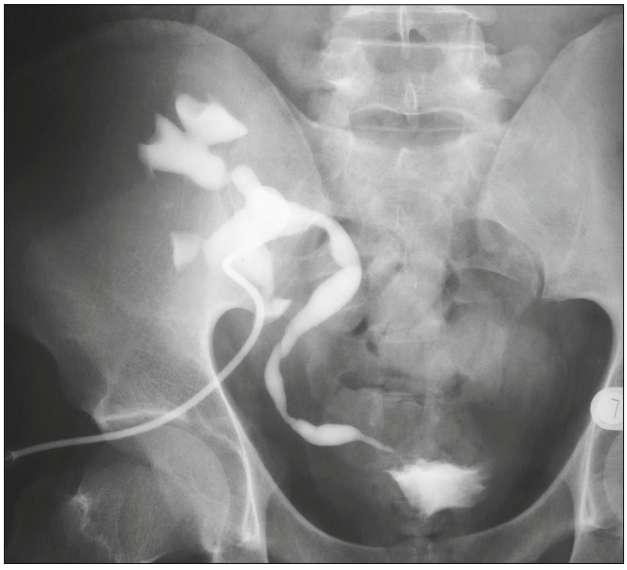

Fig. 8. Urinary drainage via nephrostomy in the transplanted kidney.

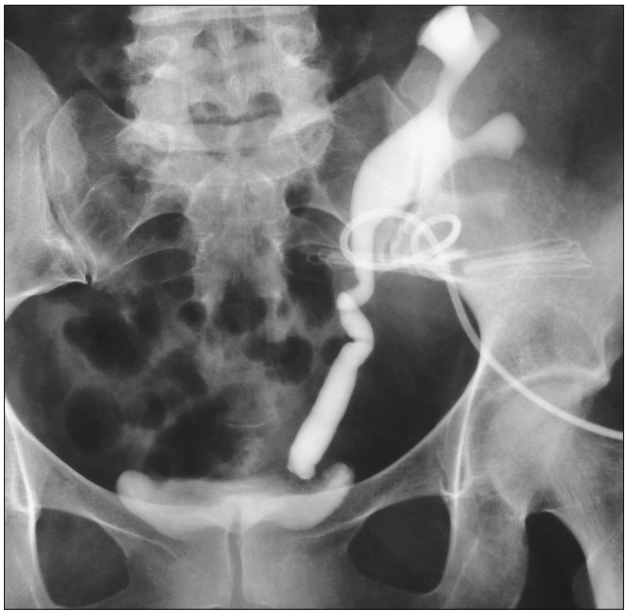

Fig. 9. Ureterohydronephrosis of a transplanted kidney caused by a stone in the intramural part of the ureter.

of the leakage of urine with a great accuracy. Surgical revision is indicated in patients with urinary fistula resulting from ureteral necrosis. It is a complex and technically demanding reconstruction of the urinary tract.

Upper urinary tract obstruction

A serious urological complication is the blockage of the upper urinary tract of the transplanted kidney that is the result of an obstruction in the ureter of the transplanted kidney. The most common and most significant cause of an impaired urine drainage from the transplanted kidney is chronic ischemia of the distal ureter wall with subsequent fibrotic changes and stricture formation. Urinary stricture occurs in weeks, months, to years after surgery. Subsequently, ureterohydronephrosis of the transplanted kidney occurs. Symptoms of ureteral obstruction are usually absent. However, a dramatic clinical situation can occur with urosepsis resulting from the combination of bacterial infection and urinary stasis in the transplanted kidney. In ureterohydronephrosis, the function of the transplanted kidney gradually deteriorates, and the level of serum creatinine increases. Precise information about the function or dysfunction of the kidney is provided by gammagraphy of the transplanted kidney. Percutaneous puncture-ureterography and subsequent nephrostomy of the hydronephrotically altered transplanted kidney are of both diagnostic and therapeutic importance. Antegrade pyeloureterography can accurately locate the site and type of the ureteral stricture. Urinary drainage via nephrostomy will allow not only an accurate examination of the anatomy of the upper urinary tract but provides also a "relief" to the kidney by reducing the hydrostatic pressure in its hollow system and thus improves kidney function and effective treatment of concomitant urinary tract infections (14, 15) (Fig. 8).

Treatment of a ureteral stricture with ureterohydronephrosis of the transplanted kidney depends on the patient's clinical condition. In the case of oligo-anuric and uraemic patients, sometimes with temperature, urine derivation in the form of puncture nephrostomy, rehydration of the patient and targeted antibacterial treatment is indicated as the first step. After stabilization of the clinical condition, definitive treatment consisting in removing or circumventing the obstruction in the ureter by endoscopic or open surgical intervention is possible.

Urolithiasis after kidney transplantation

Urinary stones are rare in transplanted kidneys, occurring in 0.2 to 1.7 % of transplants. Due to the frequent impairment of the concentrating function of the transplanted kidney, a new stone is rarely formed in the kidney. Urine stasis and the presence of a foreign body (eg endoprosthesis) in the transplanted kidney also contribute to the formation of stones in the transplanted kidney. More often, the kidney is removed from the donor and transplanted with a stone. The disease is usually asymptomatic because the transplanted kidney is denervated. The patient usually observes hematuria, oliguria or anuria in supravesical urinary retention as the consequence of the presence of a stone in the ureter of the transplanted kidney.

Standard radiological and ultrasonographic methods are used to diagnose nephrolithiasis after kidney transplantation. The exact method for diagnosing nephrolithiasis and ureterolithiasis is spiral native CT. After kidney transplantation, both nephrolithiasis and ureterolithiasis are treated with standard urological techniques such as percutaneous stone extraction and ESWL (7, 8) (Fig. 9).

Vascular complications after kidney transplantation

Part of the urological examination before kidney transplantation is also the detection of possible pathological changes of the pelvic arterial bed. In relation to preoperative examination, the principle is that all pathological changes of the pelvic arterial system and the lower urinary tract should be addressed before kidney transplantation, not after it.

Vascular complications after kidney transplantation are rare, but serious because they can result in the loss of the graft. They are most often related to the affected vessels of the transplanted kidney, but they can also affect the recipient's vessels. Vascular complications in the early post-transplant period include renal artery or vein thrombosis, later stenosis, extra- and intrarenal pseudoaneurysm, and arteriovenous fistula.

Renal vein thrombosis is more common than arterial thrombosis, with the incidence of about 2 %. It is an early postoperative complication, possibly due to technical problems with venous anastomosis, vein compression by fluid collection, twisting or torsion caused by a long vein. Hypovolemia and coagulopathy in the recipient are considered risk factors. Renal vein thrombosis is manifested by primary anuria or a sudden decrease in diuresis, and the transplanted kidney is enlarged and tense. Ultrasonographically, in addition to graft enlargement, typical changes in terms of reverse arterial flow in diastole can be observed. Delayed diagnosis leads to graft ischemia. Graft rescue is only possible if early renal vein thrombosis is detected, followed by an immediate surgical revision and thrombectomy.

Renal artery thrombosis has the same symptomatology as venous thrombosis – anuria or a sharp decrease in diuresis. Colour Doppler ultrasonography provides an accurate differential diagnostic information. Rarely, CT or MRI renoangiography is required to confirm renal artery thrombosis, usually as part of urgent invasive radiology, which involves a direct transcatheteral local thrombolysis of the thrombus in the graft with or without stent-induced percutaneous angioplasty. Thrombolysis is successful within 24 hours of the renal artery occlusion by the thrombus (Figs 10 and 11).

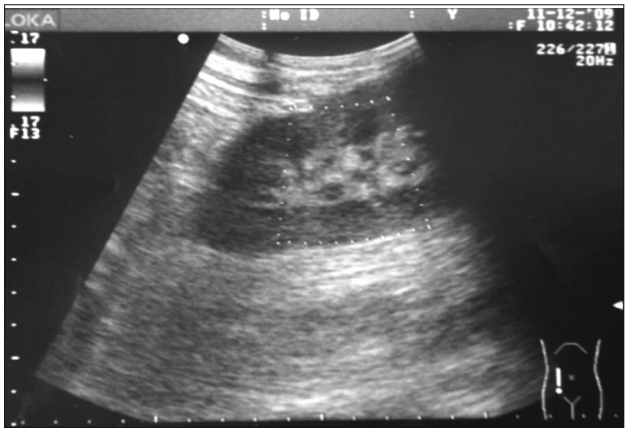

Fig. 10. Renal artery thrombosis of transplanted kidney diagnosed by Colour Doppler ultrasonography.

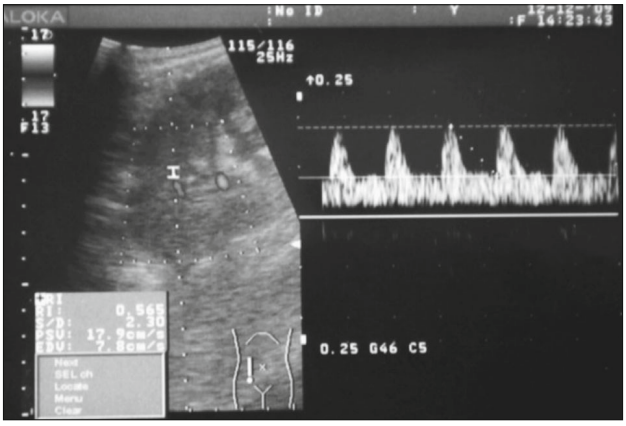

Fig. 11. The same transplanted kidney as in Figure 10 – after direct transcatheteral local thrombolysis of the thrombus with stent-induced percutaneous angioplasty.

Saving of the transplanted kidney is possible only with an early diagnosis of this complication. Urgent surgical intervention with thrombectomy is indicated. Renal artery thrombosis often ends in graft nephrectomy (16, 17, 18).

Kidney transplant infections

Despite significant advances in the treatment of infections, infectious complications are still a common and serious cause of morbidity and mortality in kidney transplant patients. Most infections occur in the early post-transplant period. Approximately 70 % of serious bacterial, viral, and fungal infections occur within the first three months after transplantation, and up to two-thirds of patients overcome the infectious complication in the first year after transplantation, with urinary tract infections accounting for up to 40–50 % of all infectious complications. In the second year after kidney transplantation, the incidence of urinary tract infections is halved (about 35 %), and in the fourth year it occurs in 21 % of the patients.

Infections after kidney transplantation are usually similar to infections after other major operations, but their course is usually modified due to a number of adverse circumstances in the transplant recipient (uremia, immunosuppression, urinary tract drainage). These include bacterial infections of the urinary tract, wound infections, lung infections, sepsis. During the first year after kidney transplantation, the incidence and especially the severity of infections depend on the graft function and the intensity of immunosuppression (19, 20, 21, 22).

Cytomegalovirus (CMV) infection can be a major cause of increased morbidity and mortality in renal transplant patients. Because of the high mortality and risk of graft loss, symptomatic CMV disease should always be treated with antiviral drugs ganciclovir or valganciclovir (24, 25).

Malignancies after kidney transplantation

A serious complication of long-term immunosuppressive treatment is an increased incidence of cancer. The incidence of malignancies in kidney transplant patients is significantly higher compared to the general population. In addition to cardiovascular and infectious complications, malignancies are among the most common causes of death in the patients with functional kidney transplants. While infectious complications occur most often during the first year after transplantation, when the level of immunosuppression is highest, malignancies (other than post-transplant lymphoproliferative disease) usually do not appear until the first year after transplantation.

Malignancy in the patient after kidney transplantation may be due to the transfer of an unknown tumour from the donor, recurrence of the tumor in the patient previously treated for malignancy, or de novo cancer. The risk of de novo malignancies in kidney transplant patients is 3 to 5 times higher compared to the patients in the general population of comparable age and sex. Malignancies after kidney transplantation have a more aggressive progression and a worse prognosis compared to the general population. The etiopathogenesis of cancer after kidney transplantation is multifactorial and similar to the general population.

The aim of pre-transplant screening is to identify the patients with possible cancer and to exclude these patients from the transplant program. After an early detection of malignancy, curative treatment is possible with the prospect of subsequent inclusion of the patient in the transplant program. After successful treatment of most malignancies, a safety interval of 2 to 5 years is recommended before enrolling a patient for kidney transplantation, depending on the type of malignancy.

Conclusion

Kidney transplantation is an organ-specific operation in the sense that it draws on the experience and knowledge of those medical disciplines that treat kidney diseases causing chronic renal failure (urology, nephrology, pediatric nephrology, diabetology and other disciplines). Specialists in other fields (anesthesiology, neurology, neurosurgery, traumatology, radiology, pathology) are involved in solving the complex issue of kidney collection and transplantation, thus coordinated multidisciplinary cooperation is necessary (26, 27, 28, 29, 30).

Mutually meaningful cooperation of doctors from different fields is typical for the diagnostics and treatment of complications that accompany the process of selecting a suitable donor-recipient pair, solving possible health problems of the recipient of the transplanted kidney before as well as long after transplantation (31, 32, 33, 34, 35, 36).

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