A CASE OF ANASTOMOTIC LEAK DUE TO *CANDIDA ALBICANS* INFECTION IN A 64-YEAR-OLD FEMALE RENAL TRANSPLANT PATIENT TREATED WITH AN EMERGENCY SUPRAPUBIC ILIOFEMORAL BYPASS GRAFT

Przypadek nieszczelności zespolenia wywołanej zakażeniem *Candida albicans* u 64-letniej pacjentki po przeszczepieniu nerki, leczonej w trybie nagłym poprzez wszczepienie pomostu biodrowo-udowego z dostępu nadłonowego

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Abstract

Introduction: Vascular complications are a rare but important risk factor for failure and loss of kidney graft, increasing the mortality of renal graft recipients. **Case report:** We present the case of massive haemorrhage due to the rupture of the arterial anastomosis caused by *Candida albicans* infection in a 64-year old female kidney graft recipient managed with suprapubic iliofemoral bypass during emergency life-saving graft nephrectomy performed in our unit. The postoperative period was complicated by femoral vein thrombosis and intraabdominal fluid collection. After 33 days, with a well-functioning iliofemoral bypass, the patient was discharged to the nephrology unit. At the 12-month follow-up, the patient is functioning well, receiving nephrological care and haemodialysis treatment. **Conclusions:** Routine fungal cultures of graft preservation fluid and radiological follow-up in high-risk patients after transplantation may be helpful in the prevention of fatal complications in the high-risk patient group – especially if digestive tract injury occurred during organ harvesting. Nevertheless, histological examination remains the gold standard for the detection of fungal arteritis. Negative culture samples from the preservation fluid, blood and urine before the transplantation do not exclude the risk of fungal infection. Urgent allograft nephrectomy with resection and reconstruction of changed vessels seems to be the safest approach in ruptured anastomotic pseudoaneurysm, as shown in our case.

Streszczenie

Wstęp: Powikłania naczyniowe są rzadkim, ale istotnym czynnikiem ryzyka niepowodzenia i utraty przeszczepu nerki, zwiększającym śmiertelność u biorców tego narządu. **Opis przypadku:** Przedstawiamy przypadek 64-letniej biorczyni przeszczepu nerki, u której doszło do masywnego krwawienia w następstwie pęknięcia zespolenia tętniczego wywołanego zakażeniem grzybem *Candida albicans*. Podczas ratującego życie zabiegu nefrektomii przeszczepionej nerki, wykonanego w trybie nagłym na naszym oddziale, pacjentce wszczepiono pomost biodrowo-udowy z dostępu nadłonowego. Przebieg pooperacyjny był powikłany zakrzepicą żyły udowej i gromadzeniem się płynu w jamie brzusznej. Po 33 dniach pacjentkę z prawidłowo funkcjonującym pomostem przeniesiono na oddział nefrologiczny. Po 12-miesięcznej obserwacji stan pacjentki jest dobry. Chora pozostaje pod opieką nefrologiczną, jest leczona hemodializami. **Wnioski:** Rutynowe badania posiewowe płynu do przechowywania narządów przeznaczonych do transplantacji w kierunku zakażenia grzybiczego oraz radiologiczne badania kontrolne po zabiegu transplantacyjnym u chorych wysokiego ryzyka mogą być przydatne w zapobieganiu śmiertelnym powikłaniom w grupie wysokiego ryzyka – zwłaszcza jeśli podczas pobierania narządu doszło do uszkodzenia przewodu pokarmowego. Niemniej jednak badanie histologiczne nadal pozostaje złotym standardem w diagnostyce zapalenia tętnic wywołanego zakażeniem grzybiczym. Ujemny wynik posiewu płynu do przechowywania narządów oraz krwi i moczu przed wykonaniem przeszczepu nie eliminuje ryzyka zakażenia grzybiczego. Przedstawiony w pracy przypadek wskazuje, że pilna nefrektomia przeszczepionego narządu wraz z resekcją i rekonstrukcją zmienionych naczyń stanowi najbezpieczniejszą metodę postępowania u chorych, u których doszło do pęknięcia tętniaka rzekomego w obrębie zespolenia.

Keywords: pseudoaneurysm, kidney transplantation, fungal arteritis, renal artery rupture

Słowa kluczowe: tętniak rzekomy, przeszczep nerki, zapalenie tętnic wywołane zakażeniem grzybiczym, pęknięcie tętnicy nerkowej

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Introduction

Kidney transplantation (KTx) increases the survival rate and quality of life in patients with end-stage renal disease (ESRD). Vascular complications are a rare but important risk factor for failure and loss of kidney graft, increasing the mortality of renal graft recipients [1–3]. We present the case of massive haemorrhage due to the rupture of the arterial anastomosis caused by *Candida albicans* infection in a 64-year old female kidney graft recipient managed with suprapubic iliofemoral bypass during emergency life-saving graft nephrectomy performed in our unit.

Case report

A 64-year-old female patient with ESRD secondary to polycystic kidney disease, after three months of peritoneal dialysis, was first admitted to an external institution in Poznan city for her primary deceased donor KTx; the hospitalisation lasted 11 days and proceeded without complications, with the serum creatinine level of 1.2 mg/dL on the day of discharge. The immunosuppressive regimen included tacrolimus, mycophenolate mofetil, and prednisone. Additionally, the patient was under the care of specialists on account of hypertension (treated pharmacologically with bisoprolol, doxazosin, clonidine) and papillary thyroid cancer (after surgical and iodine-131 treatment in 2001; on the substitution therapy with levothyroxine). Moreover, she was taking the following medications: acetylsalicylic acid, aciclovir, sulfamethoxazole, trimethoprim, allopurinol, omeprazole, alfacalcidol, calcium carbonate. There were no available data on donor status prior to organ harvest, and no microbiological assays of the preservation fluid the graft was stored in.

Thirty days after discharge, the patient presented to the emergency room with symptoms of hypovolaemic shock. On admission, she was in a serious condition – conscious, on the verge of circulatory and respiratory efficiency, pale, and drenched in cold sweat.

Computed tomography (CT) of the abdomen performed on admission showed a 145 × 112 × 45 mm haematoma along the right iliolumbar muscle (fig. 1), ischaemia of the kidney graft, and a 40 × 41 × 49 mm pseudoaneurysm/arteriovenous fistula between the right external iliac artery and vein (fig. 2). Laboratory tests revealed leukocytosis (11.6 G/L) with neutrophilia (10.1G/L), lymphopaenia (0.3 G/L), and eosinopaenia (0 G/L); and elevated levels of inflammatory markers – C-reactive protein (104.7 mg/L) and procalcitonin (2.38 ng/mL), serum urea (79 mg/dL), and serum creatinine (1.83 mg/dL). The patient was referred for urgent surgery by transplant surgeons assisted by vascular surgeon.

An incision through the KTx scar in the right iliac fossa was performed to reach the graft site. Shortly after the procedure began, the patient suddenly collapsed, which led to cardiac arrest. An effective cardiopulmonary resuscitation was carried out, making the continuation of the surgery possible. A huge haematoma was evacuated from the retroperitoneum and graft site,

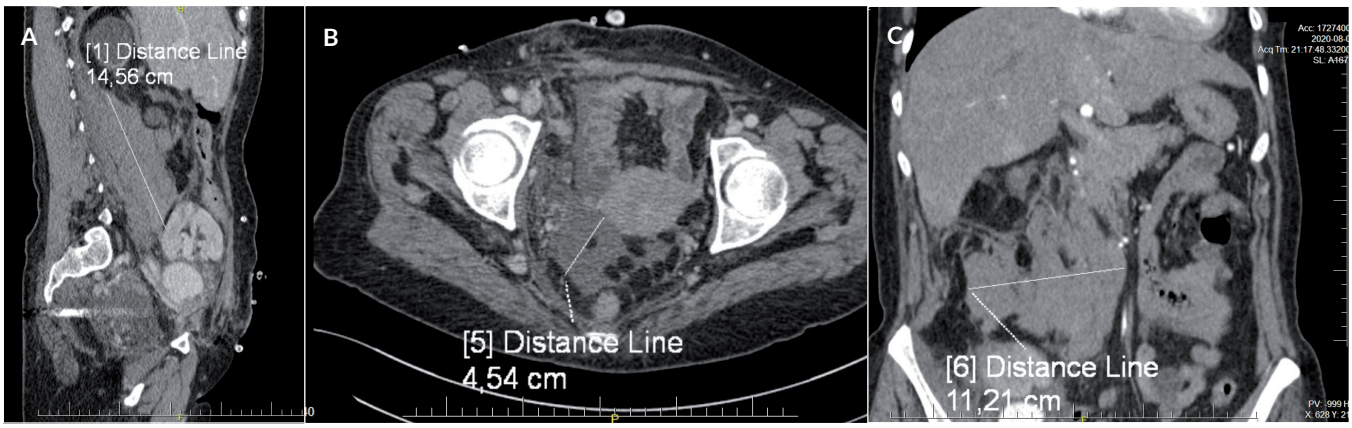

Figure 1. CT scan of the abdomen performed before admission, showing 145 × 112 × 45 mm hematoma along the right iliolumbar muscle and ischemia of the kidney graft. **A.** Sagittal section **B.** Horizontal section. **C.** Frontal section

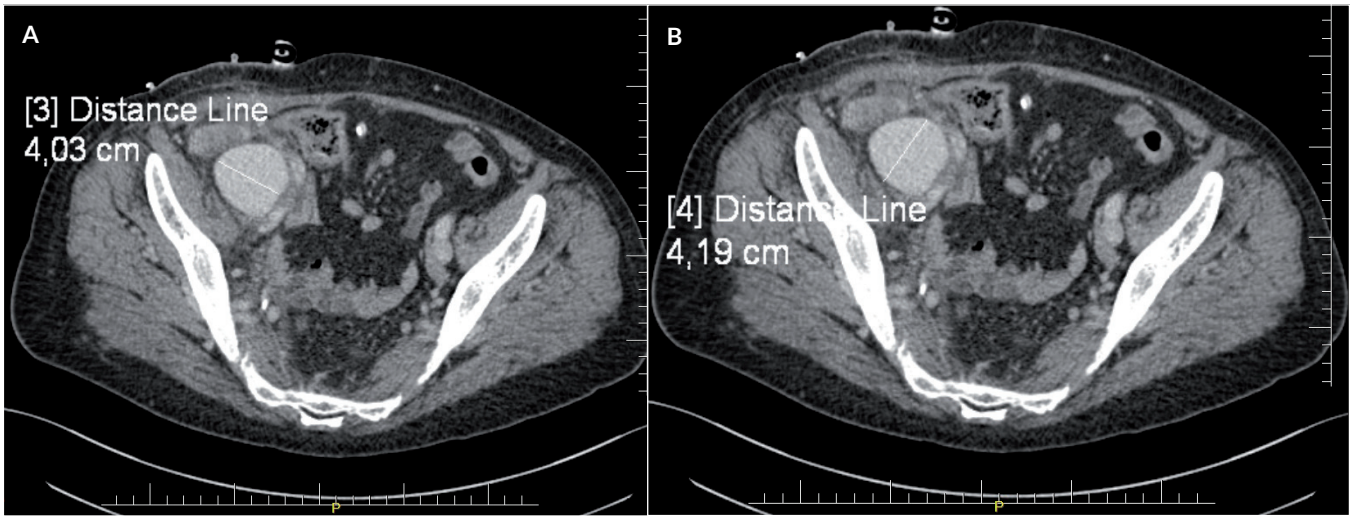

Figure 2. CT scan of 40 × 41 × 49 mm pseudoaneurysm of the arterial anastomosis between the external iliac artery and kidney graft artery. **A.** Transverse dimension in horizontal section **B.** Longitudinal dimension in horizontal section

and the place of active bleeding from the external iliac artery was found in the area of arterial anastomosis. The graft was pale, and the vessels, including the fragile disintegrating external iliac artery and the external iliac vein, were infiltrated by a massive inflammation. However, the blood flow in the iliac vein was normal, with no signs of leakage.

The graft vessels were ligated and cut, and then the graft was removed, denuding a perigraft abscess, which was evacuated after sampling the swab for microbiological testing. To achieve control of the haemorrhage, the surgeons opened the peritoneal cavity through a midline incision to clamp the aorta, which made the identification and dissection of the right common iliac artery possible. The right common iliac artery was clamped above the inflammation, and the aortic clamp was removed. The incision was extended towards the right groin. The right inguinal ligament was cut to expose and clamp the right femoral artery. The stump of the right external iliac artery was ligated, and the pathologically changed part of the artery was removed for histopathological and microbiological examinations. In the meantime, the Tenckhoff catheter was removed.

In order to ensure proper blood supply to the right lower limb, a suprapubic iliofemoral bypass was performed by a vascular surgeon. Impra Carboflo STRAIGHT CARBON-LINED stent was successfully implanted end-to-side with the left external iliac artery and end-to-end with the right femoral artery. Both anastomoses were sealed using a fibrin sealant patch. The blood flow to the right femoral artery was achieved with well-palpable pulse. Drainage was applied at the site of the removed graft. During the surgery, four units of red blood cell concentrate and two units of fresh frozen plasma were transfused. Empirical broad-spectrum antibiotic and voriconazole therapy was administered. After the surgery, the patient was admitted to the intensive care unit, where she spent three days.

The early postoperative period was complicated, with fluid collection at the site of the removed graft and near the stent. Doppler ultrasound (Doppler USG) imaging four days after the surgery showed good blood flow in the unobstructed suprapubic stent, with two irregular fluid reservoirs near the anastomosis (63 × 25 mm on the right side and 14 × 46 mm in the left side). On day 11 after surgery, a computed tomography angiogram (angio-CT) showed compounding of the fluid reservoirs. Due to ineffectiveness of drainage of the removed graft area, ultrasound-guided percutaneous drainage was performed, evacuating 110 mL of cloudy, blood-tinted fluid.

On day 16 after surgery, the patient reported pain and swelling of the right lower limb. Doppler USG showed a 10 mm wide clot extending about 6 cm below the inguinal ligament, closing the right common femoral vein. Fortunately, thrombosis resolved after conservative treatment, and after 33 days spent in our department the patient was discharged to the nephrology unit.

Histopathological examination of removed tissues confirmed fungal invasion and inflammation of the iliac, renal, and femoral arteries (fig. 3, 4). Microbiological evaluation of the swab collected from the perigraft site revealed *Candida albicans* and methicillin-resistant *Staphylococcus epidermidis* (MRSE).

After six months, in January 2021, the patency of the aorta, both common iliac arteries, the graft, and both femoral arteries was confirmed by Doppler USG examination; after one year, the patient is functioning well, receiving nephrological care and haemodialysis treatment.

Discussion

A broad array of organisms may be transmitted with the living cells of transplanted organs. In order to lower the risk of donor-derived infectious diseases, microbiological a ssays should be performed prior to transplantation. Procurement organisations recommend screening organ donors for CMV, EBV, HIV, HBV, HCV, syphilis, and toxoplasmosis. Blood and urine cultures should be obtained. Additional tests may be advised based on local epidemiology (i.e. serological test for Histoplasma and *Coccidioi-*

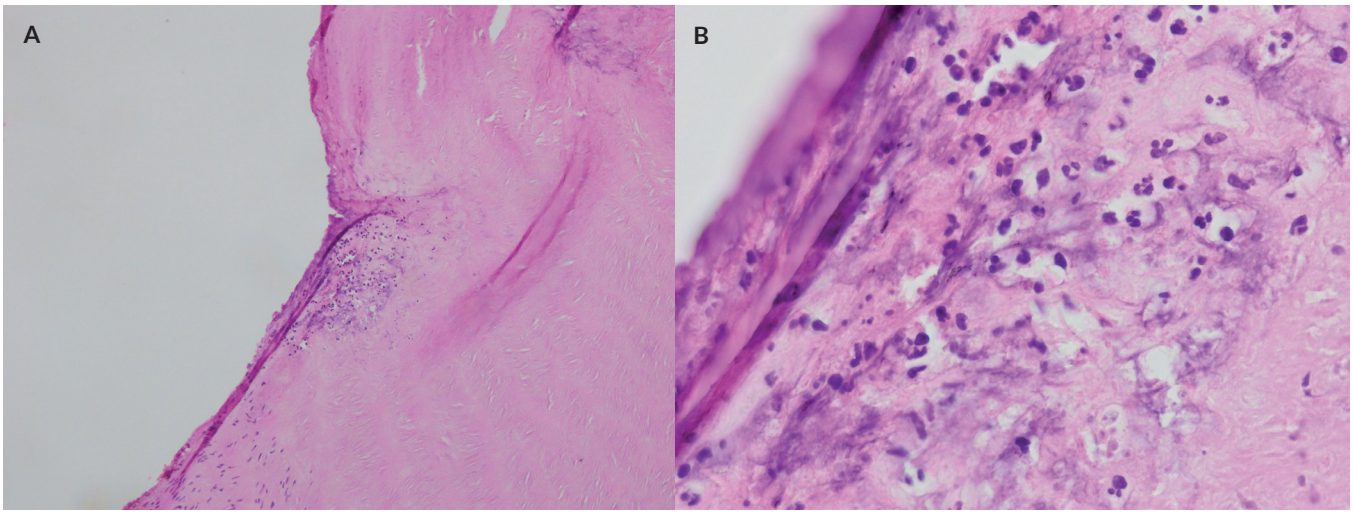

Figure 3. Microscopic images of the kidney graft artery aneurysm caused by fungal infection – Haematoxylin and eosin staining. **A.** Wide view **B.** Detailed view

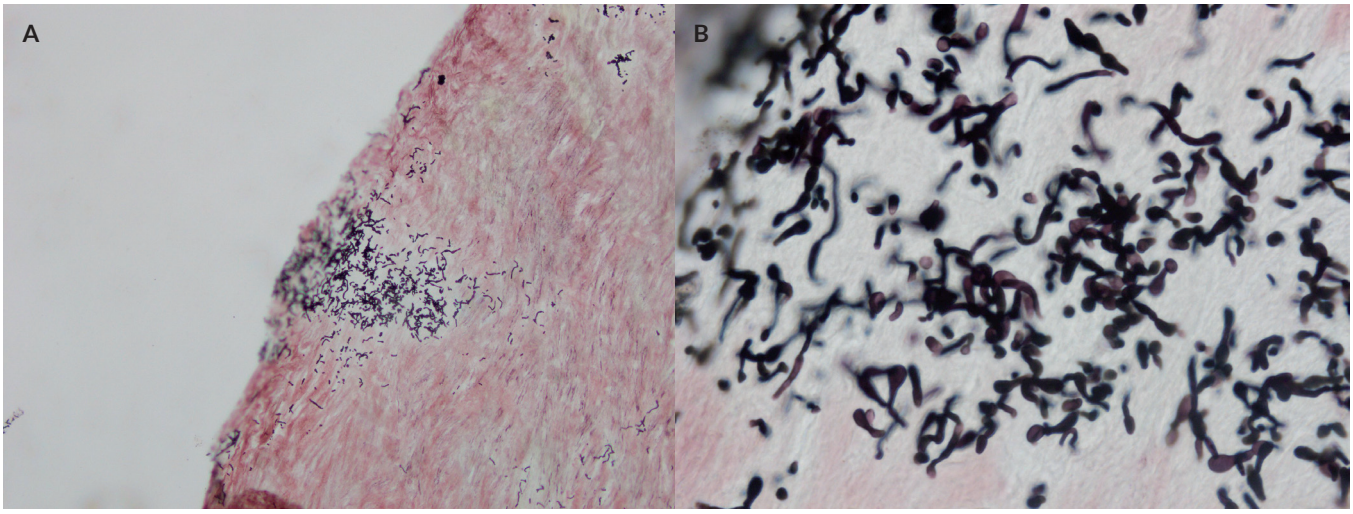

Figure 4. Microscopic images of the kidney graft artery aneurysm caused by fungal infection – Grocott staining. **A.** Wide view **B.** Detailed view

des spp.). Thanks to ongoing improvement of microbiological assays, the incidence of donor-derived infectious diseases is low [1, 2]

Nevertheless, contamination during graft procurement should always be taken under consideration, as it might cause life-threatening complications. Metaanalysis performed by Oriol et al. shows that the overall incidence of preservation fluid-related infections is 4% [3]. In nearly 80% of cases, mycotic arteritis in kidney graft recipients is caused by contamination with *Candida* and *Aspergillus* species during donation, storage or handling of the graft [4–7]. Preservation fluid cultures were found to be positive for *Candida* spp. in 8.6% samples. Of those, one-third of patients developed fungal arteritis and needed a transplantectomy [8]. Although fungal infection of the arterial anastomosis in kidney graft recipients is an extremely rare complication [4, 5], it might result in chronic rejection in 60% of cases [4].

Multi-organ donation, death related to multi-organ trauma, broad-spectrum antibiotic therapy, and long stay in the intensive care unit are among the donor's risk factors for fungal infection of the graft site [5]. Kidney graft recipient's risk factors for fungal infection include immunosuppressive therapy, treatment with broad-spectrum antibiotics, diabetes mellitus, multi-organ transplantation, permanent catheters, malnutrition, and repeated kidney transplantation [4, 5].

Pseudoaneurysm of the graft artery caused by fungal infection in this group of patients usually occurs at a median of 36.2 days after transplantation (range: 1–150 days) [5]. Early presence of this complication is connected with higher mortality. Maozhi Tang et al. reported that in 10 patients who died the median was 9.5 days (range: 4–18 days), and in 40 survivors the median was 43.5 days (range: 1–150 days) [5]. It may be asymptomatic, and cause renal dysfunction or hypertension due to compression of graft vessels [5, 9]. It may also manifest as abdominal pain with a well-palpable pulsating mass in the graft site and haemorrhagic shock [5, 9]. While small, non-infectious and asymptomatic pseudoaneurysms, commonly diagnosed incidentally, do not require urgent invasive treatment, symptomatic, rapidly progressing or ruptured ones require immediate surgical management [10].

The treatment of choice should include invasive procedures and antifungal therapy [4].

Aneurysms with a narrow neck, and those in extraanastomotic locations may be eligible for stenting or embolisation. Reports of graft-preserving operations, including excision of mycotic aneurysm (MA) and vascular reconstruction, have also been published. It seems that in selected patients such management should be taken under consideration by transplantologists [6].

Graftectomy seems to be the safest option for MA in cases where the aforementioned therapeutic strategies cannot be employed. Especially in emergency life-threatening situations, as shown in this case, when dealing with haemorrhagic shock, cardiac arrest, destruction of both allograft artery and the patient's iliac arteries, preservation of the transplanted kidney may not be feasible.

Conclusions

Fungal arteritis in kidney graft recipients is a very rare but life-threating complication which in many cases leads to emergency life-saving graft nephrectomy. Its early detection still remains a challenge due to a long asymptomatic course [4]. Routine fungal cultures of the graft preservation fluid and radiological follow-up in the high-risk group of patients after transplantation may be helpful in the prevention of fatal complications among high-risk patients especially if digestive tract injury occurred during organ harvesting [7], but still the gold standard for the detection of fungal arteritis is histological examination [5]. Negative culture samples from the preservation fluid, and blood and urine before the transplantation do not exclude the risk of fungal infection [5].

Urgent surgical treatment, including allograft nephrectomy with resection and reconstruction of changed vessels, seems to be a life-saving procedure in patients with a ruptured pseudoaneurysm of the arterial anastomosis, as in our case [4, 10, 11].

This is a rare case of iliofemoral bypass performed for fungal arteritis in a renal transplant patient.

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