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An exacerbation of hemorrhagic vasculitis with the development of hemorrhagic necrotizing pancreatitis in a patient at an early stage after kidney retransplantation (Case Report)

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The clinical case report covers rare complications of hemorrhagic vasculitis manifested in the form of macrofocal hemorrhagic pancreatic necrosis that occurred in a patient at an early stage after kidney retransplantation. We have presented clinical and laboratory findings and therapies that helped to avoid serious infectious complications in the course of induction immunosuppressive therapy.

Keywords: kidney transplantation, hemorrhagic vasculitis, pancreatic necrosis, immunosuppressive therapy.

Introduction

Hemorrhagic vasculitis (HV) or Henoch-Schönlein purpura (HSP) Henoch-Schönlein Purpura (HSP) is one of the most common hemorrhagic diseases originating from multiple microthrombotic vasculitis that affects blood vessels of the skin and viscera [1].

Currently, HV has been proved to belong to complex immune diseases characterized by aseptic inflammation of small vessels with more or less deep damage of their walls, thrombosis and the formation of circulating immune complexes (CICs) that are deposited on the inner surface of blood vessels, thereby causing their damage. CIC-induced vascular damage in HV is not specific. It may be caused by various factors: viral, bacterial infections, cold, drug allergy [1, 2].

Case report

Patient K., born in 1987, was admitted to the Department of Kidney and Pancreas Transplantation on 20.08.2014 with the clinical diagnoses of hemorrhagic vasculitis (musculo-cutaneous with reno-intestinal involvement), end-stage chronic renal failure (CRF); condition after live related kidney transplantation of 2010, recurrent CRF of the kidney allograft; a renal replacement therapy (hemodialysis program) performed since 2012.

As known from previous medical history, the signs of typical HV in the form of cutaneous abdominal purpura were first diagnosed in the patient at the age of 13, with nephritis developed a year later. Meanwhile, microhematuria had been the main symptom of the disease for years. Proteinuria in association with nephrotic syndrome and hypertension were also observed, and the patient received a glucocorticoid therapy. Persistent arterial hypertension and microhematuria had been observed from the age of 18. The signs of end-satge CRF were identified in the patient at the age of 21, and a renal replacement therapy was started. Two years later, a live related kidney transplantation was performed, her mother being the donor. An early graft function was seen after surgery. The patient was discharged

from hospital on the 29 postoperative day having normal creatinine and urea levels, without abnormalities in urinalysis. She received a dual immunosuppressive therapy (IST). After a year, a fine-needle aspiration biopsy (FNAB) of the kidney graft was performed for increasing proteinuria and deteriorating graft function. The biopsy revealed the signs of chronic rejection for which a pulse methylprednisolone therapy and plasmapheresis (PA) sessions were undertaken. After repeated plasmapheresis session in the course of therapy, angioedema, hemorrhagic rash, pain in the major joints, and an acute cerebrovascular disease were observed. Considering the above clinical symptoms, the infusion of plasma-replacement fluids and plasmapheresis sessions were withdrawn, and the IST was continued. Five months later when blood creatinine reached 820 mmol/L and the urine output abruptly decreased, the planned hemodialysis was administered. After 4 months, the renal replacement therapy was hardly feasible due to vascular thrombosis of access sites, and a poor tolerance of hemodialysis (occurrence of hypotension, weakness aggravating in post-dialysis time, severe headache, paresthesia, lethargy, tearfulness, apathy, depression, and a lack of appetite). Considering the above symptoms, the patient was hospitalized to N.V.Sklifosovsky Research Institute for Emergency Medicine for therapy adjustment. Her body dry mass was 49 kg, her height was 175 cm. Meanwhile, given the severity of patient's condition and poor tolerability of renal replacement therapy, the patient was included in the "Urgent Waiting List" for repeated cadaveric kidney allotransplantation (CKAT).

The examination revealed: a controllable secondary hypertension, secondary anemia of mixed origin, peptic ulcer (in incomplete remission), erosive duodenitis, superficial gastritis, gastroesophageal reflux disease in the form of endoesophagitis, axial hiatal hernia, Grade I to II encephalopathy

of mixed origin, mixed anxiety and depression disorder (MADD). In addition, the patient was classified as being a high risk of developing acute rejection crisis due to identified high-titer Class I and II antibodies (4120 and 1459, respectively). Two months later, the patient underwent a left-side CKAT in the Institute Clinic. Moreover, considering her immunological status, the patient received an intraoperative PA session with a plasma replacement volume of 1500 ml. The patient was administered intravenous Simulect, 20 mg, twice, and a 4-component ummunosuppressive therapy (IST) (tacrolimus in combination with prednisolone, mycophenolate mofetil, and thymoglobulin, 50 mg/day for 10 days). Four PA sessions were also performed under close monitoring of immunological parameters (Immunogram).

A delayed graft function with the symptoms of acute tubular necrosis (ATN), grade II-III, was identified in the early postoperative period. Preventive antibiotic therapy, corrections of water-electrolyte balance and blood glucose levels, immunosuppressive therapy were started from the first post-CKAT day. In the first week, the daily urine output did not exceed 200 ml. Kidney allograft sonography performed in the 1st post-transplant day demonstrated no abnormalities; the kidney allotransplant size was 11.3 x 5.3 x 1.5 cm with a resistance index to 0.8-0.83, peri-renal area being without specific findings, pyelocaliceal system (PCS) not extended.

At the end of the 2nd postoperative day, the patient complained of cramping pain in the umbilical region, nausea, bile vomiting without giving a relief, false urge to defecate, and pain in the knee joints. The physical examination showed a slightly distended abdomen, soft, moderately tender to palpation in epi- and mesogastric areas, the tenderness being more pronounced on the left. Bowel sounds were hardly heard at auscultation, the

"splashing sound" was not identifiable. Peritoneal signs were negative; flatulence without gas passing. Moderately pronounced small foci of hemorrhagic rash on the legs were prominent and attracting attention. There was a single episode of the body temperature increase to 37.5° C the day before. Hematology study demonstrated a pronounced leukocytosis to $26x10^9$/L with the leftward shift in a WBC differential (stab neutrophils to 9%), decrease in hemoglobin from 133 g/L (on the first post-operative day) to 119 g/L, thrombocytosis to $442x10^9$/L. As no indications to emergency surgery were present, the decision was taken to make further examinations. The diagnosis was differentiated between the HV exacerbation (hemorrhagic impregnation of the intestinal wall or mesentery), acute surgical abdominal pathology (acute bowel obstruction, acute pancreatitis, acute mesenteric circulatory disorder), and other complications in early postoperative period. On the 3rd postoperative day, the diagnostic tests revealed hemoglobin reduction to 90 g/L, increased amylase activity to 478 U/L, C-reactive protein (CRP) of 102 mg/L; ultrasonography demonstrated the signs of acute macrofocal pancreatic necrosis, a localized fluid collection 6.5 x 3.4 cm in size of irregular shape with anechoic contents in the left paracolon, in the pancreas tail area, (Fig.1). The fluid collection was drained transcutaneously under an ultrasonographic guide; the volume of the drained hemorrhagic content was about 80-90 ml. The conservative therapy was started with regard to pathogenesis. On the 4th day, a washing and drainage system was placed using drainage tubes of Pigtail type N3 that was followed by a regular cleansing aspiration treatment of the destructed areas with antiseptic solutions. Dynamic monitoring of the cavity condition and the assessment of the evacuatory function of the drainage tubes was made using contrast radiographic examinations by the series of 7 fistulographies [3-7].

The fistulography performed after the drainage identified a cavity of irregular shape 92 x 64 x 49 mm in size, with uneven, somewhere indistinct contours localized in the retroperitoneal space; an upward ridge was passing from its upper edge (Fig. 1-2). Aspiration of contrast agent from the cavity was adequate (Fig.3). A series of subsequent fistulographies demonstrated positive dynamics in the form of cavity size reduction. A control fistulography identified the contrast agent collection at the end of the drainage tube (Fig.4-5).

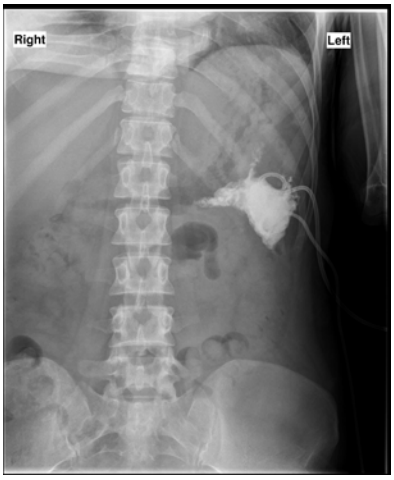

Fig. 1. Fistulography of the drained retroperitoneal cavity (antero-posterior view)

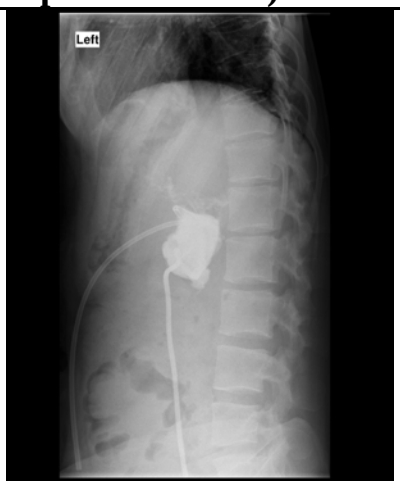

Fig. 2. Fistulography of the drained retroperitoneal cavity (lateral view)

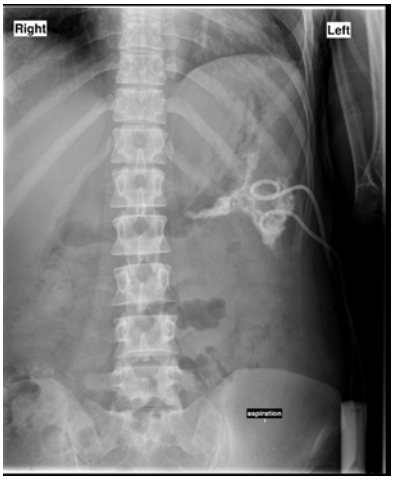

Fig. 3. Adequate aspiration of the contrast material from the retroperitoneal cavity

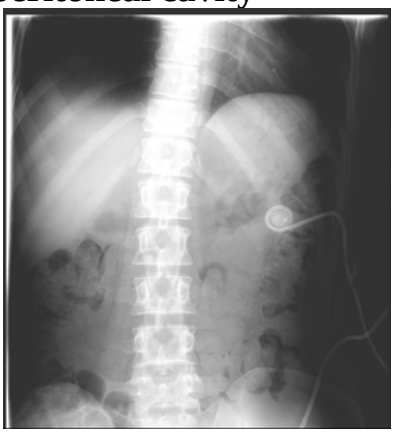

Fig. 4. A follow-up control fistulography of the drained retroperitoneal cavity (antero-posterior view)

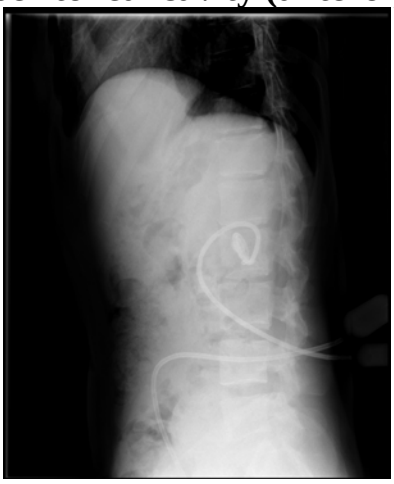

Fig. 5. A follow-up control fistulography of the drained retroperitoneal cavity (lateral view)

Definite improvements such as pain syndrome relief, diminished systemic inflammation, normalized blood laboratory parameters were noted in the course of treatment. Postoperative wound healed by primary intention. Diuresis amounted to 2500 ml without stimulation from the 17^{th} postoperative day. From the 24^{th} postoperative day, blood levels of nitrogenous waste products returned to normal: creatinine decreased to 88 mmol/L, and urea decreased to 8 mmol/L. Following 42^{nd} postoperative day, pancreatic amylase levels did not exceed 125 U, blood pressure not exceeding 130/85 mm Hg; a dry weight remained at 49.5 kg. All drainage tubes were consistently removed from the 42^{nd} to 48^{th} days. On the 52^{nd} postoperative day, the patient was discharged from hospital having a satisfactory kidney allograft function with glomerular filtration rate being 67 ml/min, the daily urine output 2000 ml; renal allograft at ultrasonographic examination was 11.2 x 5.3 x 1.7 cm in size, with clear-cut, even contours; PCS was not extended, kidney pelvis was to 1.0 cm, the resistivity index (RI) being 0.6-0.75. Echoic signs of subdiaphragmal fluid collection (5.6 x 1.8 cm) in the left paracolon persisted as did hematoma (4.6 x 1.5 cm) with the signs of localization in the kidney allograft area. The blood tests demonstrated mild symptoms of anemia with hemoglobin being 105 g/L, leukocytes 8.2 x 10^9/L, and platelets 144 x 10^9/L, ESR being 18 mm/h, creatinine 82 mol/L, urea 8.6 mmol/L, α-amylase 92 U. Urinalysis showed rel. density of 1014-1018, pH 6.0, was negative for protein and glucose, leucocytes being 0-1 per field of vision, erythrocytes 0-1 per field. Urine culture tests performed in dynamics were negative. CRP was 15 mg/L.

At a follow-up examination 3 month later, the patient's condition was satisfactory, the blood pressure normalized, she reported no complaints,

there were no MADD signs, blood parameters were within normal ranges (hemoglobin 114 g/L, α-amylase 48 U), the kidney allograft nitrogen-excretory function was satisfactory (creatinine being 97 mcmol/L, urea 4.6 mmol/L). The follow-up urinalysis showed no abnormalities.

Discussion

Patients with an end-stage chronic renal failure who have a history of hepatitis B belong to a group of highly-sensitized patients at a high risk of developing an acute rejection crisis (ARC), especially in the early postoperative period after organ transplantation [2, 8]. Our experience of renal transplantation in 12 patients with hepatitis B has shown that the ARC risk remains very high, despite current therapies with cytotoxic drugs, glucocorticoids, immunosuppressants, and the use of plasmapheresis (PA) [9, 10]. ARC was documented in 3 of the treated patients as early as on the 7^{th}, 9^{th}, and 16^{th} day after kidney transplantation, respectively. In 2 patients, ARC was seen after 1.5 and 4 years post-transplant after they had experienced a respiratory infection. Four of all the observed patients developed moderately pronounced signs of HV exacerbation on the 5-16^{th} days after kidney transplantation manifested as a cutaneous and articular syndrome that was controlled within several days. The use of a 4-component immunosuppressive therapy in those cases prevented the ARC development, despite the history of kidney retransplantation and a high titer of pre-existing antibodies during the 2 months preceding surgery. Possible risk factors for pancreatitis after kidney transplantation are known to be renal allograft dysfunction, hyperparathyroidism, a condition after parathyroidectomy, the presence of calculous cholecystitis, cytomegalovirus infection, and hypertriglyceridemia [11, 12]. All of these factors were excluded in this

clinical case in the pre- and postoperative periods. The patient most likely had an exacerbation of the underlying disease and the development of complications in the form of hemorrhagic macrofocal pancreatic necrosis with exudation into the retroperitoneal space that was revealed at day 2 after kidney retransplantation. The current diagnostic modalities ensuring a timely diagnosis, the use of puncture and drainage surgical techniques, extracorporeal ultrafiltration technique, plasmapheresis, and optimal antibiotic therapy, helped to avid a pancreatic peritonitis development in a patient on induction immunosuppressive therapy (IST).

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