Original Article

Nursing of acute graft-versus-host disease after simultaneous pancreas-kidney transplantation: a case series study

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Background: This paper aimed to summarize our experience in the nursing of acute graft-versus-host disease (aGVHD) after simultaneous pancreas-kidney transplantation (SPK).

Methods: We retrospectively collected and analyzed the demographic characteristics, preoperative evaluation, donor evaluation, screening, and surgical methods of patients with aGVHD after SPK in our center from September 2016 to September 2019.

Results: One patient developed intractable diarrhea with decline in platelet (PLT), white blood cell (WBC), and red blood cell (RBC) counts. Meanwhile, the other two patients experienced facial and trunk rashes, hepatic impairment, as well as decreased PLT, WBC, and RBC counts. We took the following nursing interventions: establishing an intensive care team and close monitoring of changes in the condition; protective isolation to minimize exogenous infections; nursing of pulmonary infections; and nutritional support. However, despite careful treatment and nursing, the conditions of the three patients subsequently worsened rapidly and became uncontrollable, and all died.

Conclusions: aGVHD is extremely rare after SPK, and no literature exists concerning nursing care or management related to this condition. Clinical manifestations and histopathology are helpful for diagnosis; however, treatment outcomes might be unsatisfactory and the prognosis is poor. Early detection, diagnosis, and intervention have a positive impact on the prognosis of aGVHD, and proper nursing can benefit patients.

Keywords: Simultaneous pancreas-kidney transplantation (SPK); acute graft versus host disease (aGVHD); nursing; case series

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Introduction

Simultaneous pancreas-kidney transplantation (SPK) is the preferred treatment option for diabetes mellitus accompanied by renal insufficiency, and is one of the most well-established multi-organ transplant procedures (1). As an effective treatment for type 1 diabetes mellitus and for some patients with type 2 diabetes mellitus accompanied by end-stage renal disease, it can restore long-term normoglycemia and prevent the development and progression of diabetes-related complications (2). However, as a complicated procedure, SPK is associated with a high incidence of postoperative complications (3-5). The main clinical complications include infections (e.g., pulmonary, urinary tract, and abdominal infections), acute rejection (e.g., acute rejection of the transplanted kidney, pancreas/duodenum, or pancreas and kidney), gastrointestinal bleeding, and intestinal obstruction. Meanwhile, the related surgical complications include poor incision healing, arteriovenous thrombosis of the transplanted pancreas, pancreatitis, intestinal leakage,

and pancreatic leakage. However, graft-versus-host disease (GVHD) has rarely been reported.

Acute GVHD (aGVHD) is a common complication that occurs after bone marrow transplantation, but its presence after solid organ transplantation is extremely rare. Indeed, the reported incidence of aGVHD after transplantation of solid organs such as the liver, pancreas, lung, or kidney is only 1–2%. However, once aGVHD occurs, it progresses rapidly, with a case fatality rate of up to 90% in liver transplant receipts (6-8). According to the time of onset, GVHD can be divided into aGVHD and chronic GVHD (cGVHD), and can affect multiple organ systems. Traditionally, 100 days is the line between acute and chronic GVHD. aGVHD is most likely an immune inflammatory reaction, and its clinical manifestations are typical lesions of the skin, gastrointestinal tract, and liver (9), with skin damage being the most common and earliest occurrence. Usually, skin maculopapular rash appears suddenly 2 to 5 weeks after surgery, which may be accompanied by itching. It is first seen on the palms, soles of feet, and behind the ears. In severe cases, the skin is peeled and vesicles appear. Digestive tract manifestations include varying degrees of diarrhea and liver damage, fever and weight loss.

cGVHD is a common late complication after allogeneic hematopoietic stem cell transplantation, and usually occurs 3 to 4 months after transplantation. The clinical manifestations include erythema, blisters, and even scleroderma-like changes on the cheeks and forehead. In addition, other manifestations including liver damage, keratitis, conjunctivitis. The early signs are not typical, and patients should be followed-up regularly and monitored closely. The diagnosis of cGVHD is primarily based on clinical signs, and biopsy can be ordered under the premise of difficult diagnosis and safety.

Since the introduction of SPK in our center in September 2016 to September 2021, a total of 212 patients received this procedure, among whom 3 (1.42%) developed aGVHD. In this paper, we describe our experience in the nursing care for these three cases. We present the following article in accordance with the AME Case Series reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-21-853/rc).

Methods

The demographic characteristics, preoperative assessment, and donor data of patients with aGVHD after SPK in our center from September 2016 to September 2019 were retrospectively collected and analyzed, and the patients' clinical data were also obtained and assessed. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Second Affiliated Hospital of Guangzhou Medical University (No. 2020-hg-ks-06). Written informed consent was obtained from the patients or their families for the publication of this study.

Donor information: the donated pancreases came from citizen organ donation led by the Organ Acquisition Organization. All the donors were clearly diagnosed as brain death, and the diagnosis was performed by senior physicians in the neurology, neurosurgery, and intensive care unit (ICU) departments, with qualifications for brain death identification according to relevant standards and technical specifications. All organ donation work had obtained the informed consent of the donor's relatives as well as the relevant approvals.

Recipient data: all recipients preoperatively met the diagnostic criteria for chronic kidney disease stage 5 with diabetes mellitus. We analyzed the demographic characteristics and preoperative assessment results of the three patients who developed aGVHD after SPK. All of these patients had received complete laboratory assessments (including routine blood and urine tests, blood biochemistry, coagulation function evaluation, bacterial and fungal cultures, drug sensitivity tests, and pathogen testing), medical imaging (of the heart, liver, lungs, kidneys, bladder, and other organs), and systematic assessment of the pancreas, kidneys, heart, blood vessels, bladder, and nervous system. The risk factors for aGVHD were also examined (*Table 1*), and no risk factors for aGVHD were found in any of the three patients.

Surgical method

The surgical procedure applied in our center was as follows: (I) the pancreas and kidney are placed in the ipsilateral iliac fossa; (II) external drainage: duodenal drainage; (III) internal drainage: portal vein drainage, preoperative injection of Basiliximab (Simulect) + Rabbit anti-human thymocyte immunoglobulin (i.e., Thymoglobuline) or anti-human T-cell rabbit immunoglobulin (antithymocyte globulin, ATG) and postoperative anti-rejection regimen using the classic triple immunosuppressive regimen: tacrolimus/cyclosporine + mycophenolate mofetil + methylprednisolone. Postoperatively, the trough concentration of tacrolimus was maintained at 5–10 ng/mL, and the trough concentration of cyclosporine was maintained at 100–200 ng/mL.

Table 1 Assessment of the risk factors of aGVHD in the three patients

Item	Case 1	Case 2	Case 3
HLA compatibility between donor and recipient	Yes	Yes	Yes
mHA compatibility between donor and recipient	Yes	Yes	Yes
Gender	Male	Female	Male
Age (years)	71	59	57
History of blood transfusion /pregnancy of the donor	None/none	Yes/none	None/none
Preoperative immune induction	No	No	No

aGVHD, acute graft-versus-host disease; HLA, major histocompatibility antigen; mHA, minor histocompatibility antigen.

Statistical analysis

The results were displayed as the mean ± standard deviation (SD). The data obtained in the study were expressed as number (n) for count data, while continuous data were expressed as mean ± SD.

Results

Case presentation

Case 1

A 71-year-old male patient was admitted to receive SPK. The perioperative induction treatment included rabbit anti-human thymocyte immunoglobulin and basiliximab, while the oral immunity-inducing regimen consisted of tacrolimus, mycophenolate mofetil, and prednisone. Postoperatively, the patient's urine output was normal, blood creatinine level gradually decreased to normal, and the blood glucose level was well controlled. The incision healed poorly, and negative-pressure wound therapy (NPWT) was applied until the wound was completely healed. The patient had nausea, vomiting, and intractable diarrhea after eating unclean food on the 26th postoperative day. He passed dark green watery stools 4–6 times a day in varying amounts, and experienced a progressive decline in white blood cell (WBC) count. Even after the dose of immunosuppressants was lowered, and WBC-increasing therapy, antimicrobials, anti-diarrhea agents, and immunity-enhancing drugs were administered, the symptoms did not improve. A diagnosis of aGVHD was made. The patient died of septic shock on the 35th postoperative day.

Case 2

A 59-year-old female patient underwent SPK. She was successfully discharged on the 30th postoperative day after the graft function returned to normal. On the 30th postoperative day, she was readmitted due to leucopenia. Upon admission, the patient exhibited repeatedly low WBC count; after a change and reduction of the immunosuppressant dose and application of WBC-increasing therapy, she developed a pulmonary infection, which improved after treatment with antimicrobials. However, the WBC, hemoglobin, and platelet (PLT) counts remained low. On the 34th postoperative day, the patient developed a rash with itching on the abdomen, forehead, and waist, which did not subside after pressure and could not be alleviated with anti-allergy treatment. A large number of rashes and partial desquamation then occurred on her face, neck, trunk, and thighs. As the patient also experienced a reduction in PLT, hemoglobin, and neutrophil count, a diagnosis of aGVHD was considered. Methylprednisolone pulse treatment was administered, and immunosuppressive agents and antimicrobials were withdrawn. The diagnosis of aGVHD was confirmed by skin biopsy, and the disease condition did not remarkably improve following application of the abovementioned treatments. On the 55th postoperative day, the patient experienced sudden acute left heart failure and was transferred to the ICU, where acute respiratory failure and liver dysfunction occurred, accompanied by consistently low WBC and PLT counts (0.06×10^9/L and 1×10^9/L, respectively). On the 63rd postoperative day, the patient fell into a coma and had an abdominal infection. On the 64th postoperative day, the patient was in critical condition, further treatment was abandoned, and the patient was discharged after signing the informed consent. The patient later died.

Case 3

A 57-year-old male patient was admitted to our center to receive allogeneic SPK. The perioperative induction

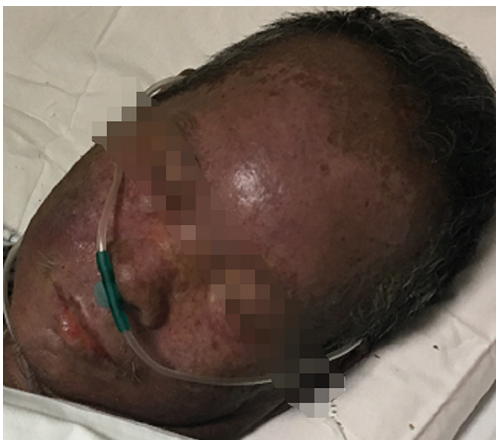

Figure 1 Facial skin of Case 3. This image is published with the patient's consent.

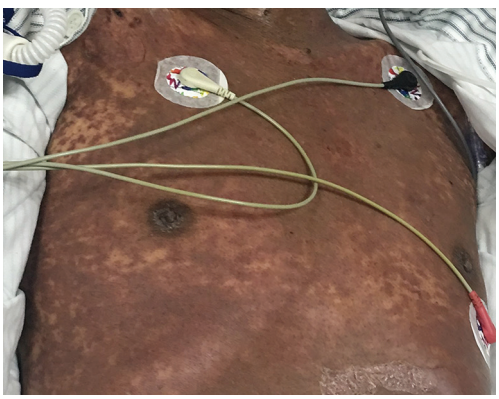

Figure 2 Skin of the anterior chest of Case 3.

treatment included rabbit anti-human thymocyte immunoglobulin and basiliximab, while the oral immunity-inhibiting regimen consisted of tacrolimus, mycophenolate mofetil, and prednisone. On day 19, the patient was scheduled to be discharged with good recovery. However, in the early morning of the day of discharge, the patient developed a fever, which did not improve after antimicrobial treatment. On day 24, the patient developed facial flushing, and anti-allergic treatment was ineffective. Subsequently, he experienced extensive rashes, corneal epithelial defect, liver function impairment, diarrhea, and leukopenia, thrombocytopenia, and other myelosuppressive manifestations. He became unconscious. Six biomarkers of GVHD were immediately detected, and skin biopsy was also performed. A diagnosis of aGVHD was confirmed based on the clinical symptoms, laboratory results, and pathological findings. The patient was treated with methylprednisolone and gamma globulin, and symptomatic treatment, including liver protection, WBC-increasing therapy, and PLT transfusion, were administered. However, the disease condition worsened, and exfoliated and dark facial skin (*Figure 1*) along with partially exfoliated and partially fused anterior chest rashes that were dark-red in color (*Figure 2*) appeared. Oxygen saturation decreased progressively on day 37, which did not improve with high-flow oxygen therapy with a respiratory humidifier. The patient was transferred to the ICU. On the same day, the patient's blood pressure and heart rate decreased, and he died despite active treatment.

Among the three patients, there were two men and one woman, and the ages ranged from 57 to 71 years. aGVHD occurred about 1 month after surgery in all three cases. One patient developed intractable diarrhea with a decline in PLT, WBC, and RBC counts, while the other two patients suffered from facial and trunk rashes, hepatic impairment, as well as decreased PLT, WBC, and RBC counts. All three patients died of multiple organ dysfunction syndrome (MODS). The skin rashes initially presented as diffuse erythema or papules, along with pruritus, which were quite similar to drug rash or measles, and could be easily misdiagnosed. In addition, along with the difficult-to-correct grade IV leukopenia ($<1\times10^9$/L) (10), severe thrombocytopenia ($<20\times10^9$/L) (11), and involvement of the lungs, heart, and other organs, aGVHD progresses rapidly and is difficult to manage, with an extremely poor prognosis. A definite diagnosis of aGVHD is typically made by skin biopsy.

Nursing protocol

Establishing an intensive care team after confirmation of aGVHD and close monitoring of changes in the condition

aGVHD progresses rapidly and is a highly critical condition. Upon diagnosis, an intensive nursing team was formed after discussions between the head nurse, nursing team leader, and senior charge nurses, and corresponding nursing measures were formulated. The dedicated team subsequently provided 24-hour nursing care. Changes of the patient's condition were closely observed, and all treatments were offered in an appropriate and timely manner. Essential nursing care was implemented, with the quality control being performed by the team leader. Continuous quality improvement was based on performance feedback.

Protective isolation to minimize exogenous infections

For patients with a WBC count of $\leq 2.0\times10^9$/L and a neutrophil count of $\leq 0.5\times10^9$/L, protective isolation measures should be undertaken to reduce the risk of infections caused by exogenous pathogens (12).

Ward requirements

The patient should be nursed in a single room, and no visitations should be permitted. Isolation signs stating "protective isolation" should be hung at the entrance to the ward. Appropriate temperature (18–22 ℃) and humidity (50–60%) should be maintained in the ward. Continuous air purification and disinfection are required, including regular ventilation for half an hour in the morning and evening. In the ward, bedside cabinets, bed units, and instruments and equipment should be wiped twice a day with 1,000 mg/L of chlorine-containing disinfection solution, and bed sheets, pillow cases, and quilt covers should be changed daily.

Requirements for items entering the ward

All items entering the ward must be disinfected, with appropriate methods being used depending on the type of material. Patients' clothes, bed sheets, quilt covers, and other bedding accessories should be packaged for disinfection with high-pressure steam in the supply room. Food should be disinfected with high heat in a microwave oven for 5 minutes. Household items should be wiped with 1,000 mg/L of chlorine-containing disinfection solution.

Requirements for medical staff entering the ward

Medical staff must wear sterile isolation clothing, shoe covers, masks, and headwear. Hands should be disinfected with a rapid-acting hand disinfectant. Only 1–2 staff members should be permitted entry into the ward at a time. All treatments should be delivered by dedicated staff members. Repeated entry and exit of the ward should be avoided. Aseptic techniques must be implemented to avoid infections.

Requirements for the support person

Only one support person should be allowed in the ward. The support person must wear protective clothing according to the standards of the medical staff. Nurses should supervise the support person in practicing hand hygiene. Individuals with respiratory infection or other infectious diseases should not be allowed to enter the ward.

Medications

Polyethylene glycol recombinant human granulocyte colony-stimulating factor, recombinant human granulocyte-stimulating factor, and recombinant human interleukin-11 should be administered as prescribed, and the use of antibacterials must be based on the results of bacterial culture and drug sensitivity.

Skin nursing to reduce irritation and maintain skin integrity

The skin is the most frequently involved organ system in aGVHD, and its lesions can be easily detected. Nursing should be focused on maintaining skin integrity and blocking contact between exogenous bacteria and patient wounds (13). Nurses should assess any changes to the rashes each shift to enable the early detection and treatment of the lesions and to avoid any aggravation of symptoms. The patient's body should be wiped daily with cooled boiled water (32–34 ℃) and then spot-wiped with soft washcloths, during which time blisters and broken skin should be avoided. Dexamethasone (5 mg) + saline (250 mL) should be applied to skin in the rash phase. Furthermore, moistened sterile gauze can be applied externally to any skin areas covered with a rash every 2 hours to keep the skin moist and avoid further spread and fusion of the rashes (14). No special treatment is required for small blisters (<1 cm in diameter).

In the case of blister rupture, the blister should first be cleaned with a cotton ball soaked in saline, disinfected with Anerdian (an iodine-containing skin disinfectant), and finally topically treated with mupirocin ointment. It is important that the blister epidermis cover the wound, as this helps to prevent wound infection. The daily maintenance of the indwelling midline catheters (MCs) after surgery should also be adjusted. The 75% alcohol and 2% chlorhexidine gluconate in the routine dressing should be changed to saline and Anerdian, which helps to reduce skin irritation and alleviate pain. When the MC is fixed, a sterile gauze block is placed between the catheter and the skin, and a multilayer sterile gauze block is applied around the arm and fixed with adhesive tape. The extended catheter is fixed with 3M elastic tape after C-shaped folding. Finally, the catheter is protected with an elastic bandage or a mesh sleeve, with appropriate elasticity. The tape should not be directly applied onto the skin. The dressing should be checked and maintained every other day and replaced at any time if it becomes loose or contaminated (15).

Nursing care for the eyes, oral cavity, and perineal area

Eyes

When there is excessive discharge in eyes, the eyes should be wiped daily with a cotton ball or swab soaked in a sterile saline solution. One of our patients had a corneal epithelial defect and was given levofloxacin eye drops,

recombinant bovine basic fibroblast growth factor, and erythromycin eye ointment alternately after consultation with ophthalmologists. Since the patient's eyes could not be closed under the patient's power, sterilized water gauze was applied to cover both eyes after the administration of eye drops.

Oral cavity

Patients who are conscious and able to cooperate should gargle with cetylpyridnium chloride in the morning, at bedtime, and within 30 minutes after each meal for >3 minutes (16). In comatose patients, cotton balls soaked in saline can be used to gently clean the oral wound, and this can be followed by cleaning of the oral cavity with cotton balls moistened with 2% sodium bicarbonate solution. To prevent the adhesion of cracked lips, the oral cavity may be coated with nysfungin and glycerin three times daily, and then a petroleum jelly gauze can be placed between the upper and lower lips (14).

Perineal area

When an indwelling urinary catheter is being used, the perineum should be wiped with saline to prevent irritation of the perineal skin by disinfectant solution. In addition, after each stool, the perineal area should be immediately cleaned. The perineal skin must be kept clean, dry, and intact. A 3M skin cleanser can be used to protect the perineal skin from breakage.

Preventing spontaneous bleeding in patients with severe thrombocytopenia

Spontaneous bleeding, especially visceral bleeding and even fatal intracranial bleeding, can occur when the PLT count is below 20×10^9/L. Bed rest is required, and vital signs must be monitored with electrocardiography (ECG). The patient can be gently turned from one side to another to prevent collision. The skin should be monitored for bruises and petechiae, puncture operations on the skin should be minimized, and tapping and rubbing should be avoided when a required puncture is being performed. An accurate and successful puncture needs to be made after only a single attempt, as subcutaneous bruises or hematomas due to repeated punctures must be avoided. The time of pressing the puncture point should be extended after puncture and injection. The color of urine and stool, along with abdominal signs should be observed, and constipation should be avoided. The vital signs, mental status, and pupils of the patient should be checked, with PLT-increasing drugs and PLT transfusions being applied as necessary. Two intravenous accesses should be maintained, and emergency items and drugs should be made available at the patient's bedside to facilitate timely active resuscitation when needed.

Preparing for cholestatic liver disease by observing the possible jaundice- and liver-related laboratory markers

The liver is another critical organ in aGVHD. The incidence of hepatic aGVHD after allogeneic hematopoietic stem cell transplantation has been reported to be 18.6% (17). Thus, hospital staff must be alert to the possibility of liver failure and hepatic encephalopathy during aGVHD. On a daily basis, the abdominal circumference should be measured, and yellow staining of the skin and sclera should also be checked for. Close attention should be paid to blood bilirubin, transaminase, albumin, and ammonia levels, and lactulose plus saline enema and liver protection drugs should be prescribed as needed.

Observing the gastrointestinal reaction and being alert to intestinal damage

After the skin and liver, the intestinal tract is one of the most affected organs by aGVHD. It has been reported that the incidence of intestinal aGVHD is about 20–30%, and intestinal aGVHD can be divided into four grades: grade I, diarrhea >500 mL/d; grade II, diarrhea >1,000 mL/d; grade III, diarrhea >1,500 mL/d; and grade IV, diarrhea >2,000 mL/d as well as abdominal pain and/or intestinal obstruction (18). Therefore, diarrhea is a particularly prominent symptom in intestinal aGVHD. For patients with only mild, transient diarrhea, the frequency, amount, color, and characteristics of the stools passed during diarrhea should be recorded, and specimens should be collected and analyzed to rule out the possibility of infections and bleeding. Additionally, patients should be instructed to eat easy-to-digest foods (such as white porridge and soft noodles) in small amounts and multiple times a day to prevent dehydration as well as internal environment, electrolyte, and microcirculatory disorders. The patients should be asked about possible nausea, vomiting, abdominal distension, and abdominal pain, and hospital staff should be alert to intestinal obstruction or bleeding.

Nursing of pulmonary infections

While the lungs are not recognized as an organ typically at risk from aGVHD in most of the related literature, some authors do believe that the lungs can be critically affected by aGVHD (19). Two of our patients experienced pulmonary infection, which was quite severe in one patient and was characterized by fever and impaired gas exchange.

The following appropriate nursing measures should be offered in such cases: (I) use of sensitive antibiotics based on blood, urine, and sputum cultures, and drug sensitivity results in a timely and accurate manner; (II) fever reduction using an ibuprofen suspension, compound aminophenazone and barbital injection, and subhypothermia therapy; (III) a timely change of clothes when excessive sweating occurs, so as to avoid the patient getting cold, with additional measures taken to keep the skin clean and dry; (IV) accurate documentation of intake and output, and the creation of appropriate rehydration plans according to the urine volume, sweating, central venous pressure, and other indicators; (V) monitoring of the oxygen saturation status and blood gases, and treatment of hypoxia (if detected) with high-flow oxygen therapy through use of a respiratory humidifier; and (VI) monitoring of sputum and breath sounds to assess the sputum. If a comatose patient cannot cough up his/her own sputum, the possibility of severe thrombocytopenia should be considered, and patting the patient's back should be avoided. The patient should be asked to inhale nebulized saline solution, followed by sputum aspiration. The patient's vital signs should be closely observed after aspiration, and medical staff should be alert to the risk of visceral bleeding.

Nutritional support

Nutritional support is crucial, and adequate nutritional support can promote the recovery of the body. However, patients with intestinal aGVHD can suffer from malnutrition due to a damaged and dysfunctional intestinal mucosal barrier, altered intestinal flora, imbalance between nutrient supply and demand, and psychological factors (20). The patient's condition should be comprehensively evaluated, and enteral nutrition (EN), parenteral nutrition (PN), or EN+PN may be selected as appropriate for the patient. When PN is chosen, the patient's skinfold thickness of triceps, Nutritional Risk Screening scale (NRS-2002) score, 24-hour intake and output, cardiopulmonary function, and laboratory test results must be comprehensively evaluated prior to the preparation to hang a PN bag. Nutrition should be supplemented by 24-hour intravenous infusion.

Blood glucose monitoring

Blood glucose is an important indicator of the endocrine secretion activity of the pancreas. Thus, close attention must be paid to the changes of blood glucose level in patients with aGVHD. In order to reduce the pain and enable the rapid, continuous, and dynamic observation of blood glucose, we used an instantaneous scanning glucose monitoring system to provide a daily glucose summary report, which enabled us to develop individualized treatment plans for these three patients, whose blood glucose levels were maintained at 6–12 mmol/L.

Discussion

During the process of allogeneic hematopoietic stem cell transplantation (Allo-HSCT), matched sibling donor (MSD) hematopoietic stem cell transplantation is the best option for Allo-HSCT, and the occurrence of GVHD is one of the major causes of death after transplantation. Therefore, the prevention of GVHD is very important in transplantation protocols. Currently, a major method of GVHD prevention in haploid transplantation is *in vivo* T-cell depleted bone marrow transplantation. There are two main protocols available; one is the Beijing protocol with antithymocyte globulin (ATG) as major therapy, and the other is the Baltimore protocol with cyclophosphamide (CTX) after stem cell transplantation as the major therapy. The research results published by Professor Huang Xiaojun's team in 2020 (T-MORE study) (21) confirmed that the use of low-dose ATG, combined with CsA + MTX + MMF during Human leukocyte antigen (HLA)—matched sibling donor transplantation (MSDT), can significantly reduce the incidence of acute/chronic GVHD in malignant blood cancer patients. Their study concluded that adding ATG to routine GVHD prophylaxis reduced the incidence of grade 2–4 aGVHD from 27.0% to 13.7%. Moreover, the addition of ATG also reduced the incidence of chronic GVHD without increasing the relapse and infection rates.

Histopathological examination results are an important basis for diagnosing aGVHD and evaluating its severity. Glucocorticoids are currently the standard first-line treatment for aGVHD. In the United States, the JAK1/2 inhibitor, ruxolitinib, is currently the standard of care for first-line glucocorticoid-resistant aGVHD. In China, the anti-interleukin-2 receptor antibody (IL-2RA) monoclonal antibody (basiliximab) is by far the most used second-line medication for aGVHD. Currently, there is no standard treatment regimen with good efficacy for cGVHD. Treatment methods include systemic immunosuppressive therapy, comprehensive adjuvant therapy, and comprehensive immunomodulatory therapy.

Previous studies have reported that aGVHD after combined is very rare. Asari *et al.* (22) observed that their patient presented with diarrhea on the 10th postoperative day, followed by fever and liver dysfunction. On the 40th day

postoperatively, their patient's body and extremities developed rash, pain, and itching. The patient had pancytopenia, and bone marrow biopsy showed severe bone marrow dysplasia. On postoperative day 69, comprehensive clinical manifestations and skin biopsy confirmed the diagnosis, and all symptoms were temporarily improved following administration of prednisolone treatment. However, on postoperative day 156, the patient died of infectious pneumonia. The patient's clinical manifestations, diagnosis, and prognosis were consistent with those reported by the author. In this study, the diagnosis of eight patients, aged between 14 and 58 years old, was confirmed between 18 days to 4.5 months postoperatively. The recovery of all patients was very poor, and all of them died between 22 days and 5.5 months after surgery. Among the three cases of GVHD after SPK reported by the author, the time from surgery to death was 35, 64, and 37 days, while that from diagnosis to death was 9, 29, and 13 days, respectively. In all cases, the outcome was death due to MODS, which was consistent with the findings of Asari *et al.* (22).

aGVHD is a common complication after bone marrow transplantation, but is relatively rare after solid organ transplantation. In our center, three of 212 SPK recipients (1.42%) developed aGVHD. Only a small number of articles in China and abroad have described the nursing management of aGVHD after SPK. When aGVHD occurs after solid organ transplantation, most of the transplanted organs function well. The lymphocytes of the donor are in an attack state, while the lymphocytes of the recipient are in a suppressed state; as a result, it is difficult to clear the lymphocytes of the donor (23) and achieve a satisfactory outcome. Thus, compared with aGVHD following bone marrow transplantation, aGVHD after solid organ transplantation is difficult to manage and has a high mortality rate. Even worse, the clinical presentation of this condition is non-specific, leading to a delayed diagnosis. When aGVHD occurs, it progresses rapidly and aggressively, involving multiple organs with serious complications that are difficult to control, and as a consequence, the prognosis is poor.

Since the early symptoms of aGVHD are usually non-specific, it is difficult to distinguish aGVHD-induced hepatitis, dermatitis, and colitis from those induced by drugs or infections, and therefore, the diagnosis can be easily delayed. In addition, aGVHD progresses rapidly and is difficult to control, and there is currently a lack of uniform and effective treatment. Therefore, early detection, diagnosis, and intervention are particularly important for the management and nursing of aGVHD. The clinical course of aGVHD is generally as follows: the patient presents with unexplained fever, diarrhea and hepatic impairment occur, and then characteristic rash with severe pain becomes apparent, with bone marrow suppression becoming evident later (22). In the cases described above, all three patients successively developed fever, diarrhea, liver function impairment, and bone marrow suppression, with two patients presenting with a typical characteristic rash.

Once 2–3 suspicious symptoms of aGVHD (e.g., fever, rash, diarrhea, and/or bone marrow suppression) appear after SPK, clinicians should be highly alert to the possibility of aGVHD. As the earliest and most frequently involved organ in aGVHD, skin lesions should be nursed according to the grade of rashes, so as to prevent the occurrence of exfoliative dermatitis. In contrast, intestinal aGVHD mostly manifests as diarrhea, which requires appropriate stool observation and dietary care according to the severity grade. Liver function should also be actively monitored. Protective isolation should be executed when bone marrow suppression occurs. Visceral and intracranial hemorrhage should be avoided, and infections should be prevented. Nursing of aGVHD after SPK is multi-faceted and highly challenging. We hope our experience will inform future nursing practice for this rare and fatal condition.

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Footnote

Reporting Checklist: The authors have completed the AME Case Series reporting checklist. Available at https://gs.amegroups.com/article/view/10.21037/gs-21-853/rc

Data Sharing Statement: Available at https://gs.amegroups.com/article/view/10.21037/gs-21-853/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-21-853/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are responsible for all aspects of the work to ensure that issues related to the accuracy or completeness of any part of the work are properly

investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the Ethics Committee of the Second Affiliated Hospital of Guangzhou Medical University (No. 2020-hg-ks-06). Written informed consent was obtained from the patients or their families for the publication of this study.

References

1. Redfield RR, Scalea JR, Odorico JS. Simultaneous pancreas and kidney transplantation: current trends and future directions. Curr Opin Organ Transplant 2015;20:94-102.
2. Gruessner AC, Gruessner RW. Long-term outcome after pancreas transplantation: a registry analysis. Curr Opin Organ Transplant 2016;21:377-85.
3. Fu Y, Wang H, Feng G, et al. Retrospective analysis of 145 cases of simultaneous pancreas and kidney transplantation in a Single center. Chinese Journal of Organ Transplantation 2019;40:260-5.
4. Fang JL, Guo YH, Ma JJ, et al. Clinical effect analysis of 146 cases of ipsilateral simultaneous pancreas and kidney transplantation. Zhonghua Yi Xue Za Zhi 2020;100:3853-8.
5. Wang Z, Fu Y, Wang H, et al. Management experience of perioperative surgical complications in 138 cases of simultaneous pancreas and kidney transplantation. Chinese Journal of Organ Transplantation 2020;41:526-9.
6. Au WY, Ma SK, Kwong YL, et al. Graft-versus-host disease after liver transplantation: documentation by fluorescent in situ hybridisation and human leucocyte antigen typing. Clin Transplant 2000;14:174-7.
7. Green T, Hind J. Graft-versus-host disease in paediatric solid organ transplantation: A review of the literature. Pediatr Transplant 2016;20:607-18.
8. Schrager JJ, Vnencak-Jones CL, Graber SE, et al. Use of short tandem repeats for DNA fingerprinting to rapidly diagnose graft-versus-host disease in solid organ transplant patients. Transplantation 2006;81:21-5.
9. Xu S, Xue X, Zhan S. Study on the care of cutaneous graft-versus-host disease after haematopoietic stem cell transplantation in children. Nursing of Integrated Traditional Chinese and Western Medicine 2019;5:228-31.
10. Li M, Liu Y, Zhang C, et al. Clinical effect of warm kidney separated moxibustion on leukopenia caused by chemotherapy. Chinese Contemporary Medicine 2020;27:144-6, 154.
11. Yang R, Wang W. Application of predictive intervention based on evidence-based concept in preventing bleeding from PICC catheterization in patients with thrombocytopenia. Nav Med J 2020;41:734-7.
12. Liao C, Liu Q. Nursing of bone marrow suppression in tumor patients after chemotherapy. Guangdong Trace Element Science 2005;12:67-9.
13. Xu L, Han T. Research progress of graft versus host disease after allogeneic hematopoietic stem cell transplantation. Journal of Clinical Internal Medicine 2011;28:725-8.
14. Zeng M, Li C. Nursing care of a patient with ventricular tumor complicated with intracranial infection and severe exfoliative dermatitis. Nursing of Integrated Traditional Chinese and Western Medicine 2020;6:168-70.
15. Tan C. Nursing care of a case of grade IV skin injury caused by acute graft-versus-host disease. Electronic Journal of Clinical Medical Literature 2020;7:174-5.
16. Zhang W. Oral care of mucor infection in a child with grade IV myelosuppression leukemia. General Nursing 2018;19:2428-9.
17. Xie M, Li M, Fan T, et al. Clinical characteristics, risk factors and prognosis of liver type acute graft-versus-host disease after allogeneic hematopoietic stem cell transplantation in patients with acute leukemia. Chinese Journal of Medical Frontier 2020;12:103-7.
18. Wang XN, Sun CH, Guo CL, et al. Risk Factors and Therapeutic Outcome of Intestinal Acute Graft Versus Host Disease in Acute Leukemia Patients after Haploidentical Peripheral Hematopoietic Stem Cell Transplantation. Zhongguo Shi Yan Xue Ye Xue Za Zhi 2017;25:880-4.
19. Liu QF, Luo XD, Fan ZP, et al. Association between acute graft versus host disease and lung injury after allogenic hematopoietic stem cell transplantation. Zhonghua Yi Xue Za Zhi 2009;89:538-42.
20. Song Y, Zhu X, Lu Y, et al. Research progress of nutritional support in patients with intestinal acute graft-versus-host disease. Journal of Nursing 2020;35:110-2.
21. Tang F, Xu Y, Chen H, et al. Comparison of the clinical

outcomes of hematologic malignancies after myeloablative haploidentical transplantation with G-CSF/ATG and posttransplant cyclophosphamide: results from the Chinese Bone Marrow Transplantation Registry Group (CBMTRG). Sci China Life Sci 2020;63:571-81.
22. Asari S, Matsumoto I, Toyama H, et al. Acute graft-versus-host disease following simultaneous pancreas-kidney transplantation: report of a case. Surg Today 2015;45:1567-71.
23. Du D, Zhou P, Guo H, et al. Diagnosis and treatment of a case of graft-versus-host disease after kidney transplantation. Chinese Journal of Organ Transplantation 2018;39:203-8.

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