Minimal change glomerulopathy after unrelated umbilical cord blood transplantation for the treatment of children：case report

Abstract: Umbilical cord blood allogeneic hematopoietic stem cell transplantation(UCBT) has been gradually applied in the treatment of patients with blood system diseases. This paper reports a case of a child patient with highly invasive T-cell lymphoma who underwent UCBT after chemotherapy and developed minimal change glomerulopathy after transplantation.

Key Words: Unrelated umbilical cord blood transplantation; Children; Minimal change glomerulopathy;

Due to the development of high-resolution of human leukocyte antigen (HLA) typing technology, more and more patients with blood system diseases choose hematopoietic stem cell transplantation(allo-HSCT) at the appropriate time[1]. HSCT is one of the most effective treatments for patients with hematological malignancies. However, graft-versus-host disease (GVHD) is the main cause of late morbidity and death in these patients, and impairs their quality of life (QOL)[2]. Transplantation using cryopreserved umbilical cord blood (UCB) can reduce the risk of GVHD and treatment-related mortality(TRM), thereby improving QOL[3]. Previously considered medical waste, cord blood is now considered a valuable cellular material[4]. Umbilical cord blood transplantation (UCBT) is gradually entering the public field of vision. Compared with allo-HSCT, it is still difficult to avoid related complications after transplantation. In 2019, a children with highly invasive T-cell lymphoma was admitted to the Oncology Department of the First Affiliated Hospital of Zhengzhou University. The patient was given UCBT after multiple chemotherapy, and minimal change glomerulopathy occurred after transplantation. The report is as follows.

1. Clinical datas

The patient, male, 8 years old, came to our hospital on June 9, 2019 due to cough, chest pain, and chest tightness. The all blood test results were normal. But the chest computerized tomography(CT)results showed that there was a huge soft tissue density mass shadow in the mediastinum,with the maximum cross section of about 111mm×87mm. Puncture was performed under CT localization, and the pathological findings of the puncture were as follows: First report: (2019.6.18) malignant tumors accompanied with necrosis, which required immunohistochemical

co-diagnosis. Second report:T-cell non-Hodgkin lymphoma, highly aggressive, with no specific expression in immunohistochemistry. Immunohistochemistry:AE1/AE3(-),CD3(+),CD20(focal+), CD21(-),CD7(+),PAX-5(-),TdT(-),MPO(-),Ki-67(80%+),SALL4(-),CD99(±),CD34(-),OCT-4(-),ALK(-),CD30(-),EMA(-),MUM-1(minority+),CD1a(-),CD10(-),CD56(-),TIA-1(-),GranzymeB(-).In situ hybridization ：EBER(-).

After signing the informed consent on June 27 in 2019 and excluding the contraindications of chemotherapy, the “VDLP scheme in BFM-90 regimen ” (prednisone 60mg d1-28+vindesine 3mg d8, 15, 22, 29+ doxorubicin 20mg d8, 15 ,22 ,29+peaspartase 2500IU d12)was administered.Re-examination of CT showed that the effect has reached PR (the huge soft tissue density mass is seen in the mediastinum, the largest cross-section is about 85mm×62mm).On July 26, “CAT scheme in BFM-90 regimen”(cyclophosphamide 1.0g, d1, 15 + cytarabine 75mg, d3-6, d17-20 + bleomycin 15mg, d10 +6-mercaptopurine 60mg, d1-28)”was given to the patient.After the treatment, the patient developed grade IV myelosuppression(low white blood cells and platelets). After given him relevent treatments,him symptoms were relieved.On September 08, the "VDLP" regimen was given again. The chemotherapy process went smoothly and bone marrow suppression occurred after chemotherapy. Myelosuppression had improved after active symptomatic treatment. Positron emission tomography-computed tomography(PET-CT) was performed on December 3, and the efficacy was evaluated by CRu (the huge soft tissue density mass was observed in the mediastinum, the largest cross section was about 80mm×14mm). On December 14, the "CAT" regimen was performed. Group IV degree myelosuppression occurred again after chemotherapy, and symptoms improved after symptomatic treatment.On January 9, 2020, the "Hyper-CVAD B regimen" chemotherapy was performed(methotrexate 0.5g d1 + cytarabine 0.8g Q12H d2-3, methylprednisolone 20mg Q12H d1-3). Group IV degree of bone marrow suppression was observed and the treatments were the same as before. On February 18, the “MA” regimen (methotrexate 1g d1+cytarabine 0.5g Q12H d2-3) was given 1 cycle.The blood test results (2020.01.29)showed that mycoplasma was weakly positive. Because the patient has no symptoms, no special treatment was done.But on March 1st , his blood test results showed: the titer of mycoplasma was 1:80. After 2 weeks of oral administration of azithromycin, the mycoplasma turned negative.

On March 16, the "FLU+Bu+Cy" regimen was performed, and on March 24, he was given unrelated UCBT. The matching results showed that the donor and the acceptor were not related, and HLA was completely compatible. The donor blood type was AB and Rh^+; The recipient blood type was O, Rh^+.In order to prevent GVHD, cyclosporine plus short-term methotrexate was given. Cyclosporine and mycophenloate mofetil tablets (MMF) were given orally continuously outside the hospital. During this period, the concentration of cyclosporine was monitored weekly to control it at 100-300ng/ml. Check blood routine every week. Liver and kidney function and electrolyte were tested every half month, the results were all within the normal range.

He went to our hospital for re-examination on July 27th, 2020. The blood test results showed:WBC: 10.73×10^9/L; RBC: 3.73×10^12/L; Hb: 112.9g/L; PLT: 180×10^9/L. Kidney function results showed: potassium 5.32mmol/L; sodium 139mmol/L; Calcium 2.11mmol/L; Urea 19.8mmol/L, creatinine 222μmol/L, uric acid 851μmol/L.The patient was actively given fluids, diuresis and other symptomatic treatments. The 24-hour urine output of the day was 380ml (2020.07.27-2020.07.28), which was in line with the characteristics of oliguria. The results of urgent examination of electrolytes, liver function and kidney function had showed(2020.07.28):potassium 5.99mmol/L; sodium 130mmol/L; Calcium 2.01mmol/L; Urea 126.36mmol/L, creatinine 258μmol/L, uric acid 1004μmol/L;The patient had a clear mind, poor spirit and obvious fatigue. Hemodialysis was given urgently, and the patient's oliguria and electrolyte imbalance improved significantly than before.The mental and fatigue symptoms were improved. Puncture of the patient's kidney was performed to confirm pathology, and the electron microscope diagnosis showed(2020-08-01):Minimal lesions glomerulonephritis; Electron microscopic observation showed: microvilli degeneration of the epithelial cells in the visceral layer of the glomerulus, diffuse fusion of the epithelial foot processes, shrinkage of the basement membrane segments, no electron dense deposits; vacuolar degeneration of the renal tubular epithelium, increased lysosomes, and partial luminal expansion ;the microvilli fall off; There were no obvious disease in the renal interstitium. The patient was actively treated with methylpredrone plus sirolimus for 15 days, and the patient's urine output, electrolytes and kidney function had gradually returned to normal. Prednisone plus sirolimus has been taken orally out of the hospital until now.

2. Disscussion:

In this case,this patient suffered severe myelosuppression several times after chemotherapy. Considering that the patient was relatively aggressive and young, chemotherapy drugs were not reduced in order to achieve better expected curative effect, and the patient's blood image was actively monitored and symptomatic treatment was conducted during chemotherapy.(The patient and his guardian signed informed consent form before chemotherapy every time.)

HSCT-related nephropathy is a rare event[5], and UCBT-related nephropathy is more rare.This patient developed abnormal kidney function about 3 months after UCBT. The reasons for this abnormality are considered as follows:(1)Because cyclosporine has kidney damage, renal toxicity may be caused by cyclosporin.The administration of cyclosporin was temporarily suspended.(2) Kirsten Brukamp[6] believes that glomerular lesions after HSCT may represent the renal manifestations of GVHD. Therefore, the kidney function of this child was abnormal, and GVHD was considered, manifested as renal damage, and the pathological type was minimal change glomerulopathy.The treatment principle of minimal change glomerulopathy is hormone plus immunosuppressive agent.

Because human cytomegalovirus (CMV) infection is very common after UCBT[7]. CMV were administered before and after transplantation but no CMV was found.An abnormal titer of mycoplasma was detected in the patient before transplantation, and macrolides were administered before transplantation until the mycoplasma in the blood turned negative considering that the immune system of the patient would be disordered after transplantation.

In addition to HLA matching, the total nucleated cell (TNC) dose also affects the results of UCBT[8]. Eliane Gluckman[9] believes that the cell dose is one of the important factors for UCB implantation and survival, which is positively correlated. In 2018, Xiao Lou[10] performed a meta-analysis of the efficacy for UCBT and allo-HSCT in acute leukemia, and recruited 6762 patients (UCBT: n = 2026; HSCT: n = 4736). It is concluded that there were no statistically significant differences in progression-free survival (PFS), overall survival (OS) and recurrence rate between UCBT and allo-HSCT in patients with acute leukemia. But patients in the UCBT group took longer to recover their neutrophils and platelets.

To conclude,the advantages and disadvantages of UCBT and allo -HSCT were summarized by reviewing the previous literature[11-20]. The advantages of UCBT are as follows: (1)Because of

the rich source of cord blood, convenient collection and long-term preservation, the matching time is greatly shortened; (2)Because of the role of placental barrier, umbilical cord blood reduces or even avoids the infection rate of CMV and Epstein-Barr virus; (3)There were relatively few T lymphocytes in umbilical cord blood, so the probability of GVHD in UCBT was relatively low, and the QOL of patients was higher than that of allo-HSCT. (4)Umbilical cord blood has a high tolerance against 1-2 human leukocyte antigen mismatch, and can tolerate the transplantation incompatible with HLA 1-2 sites. Of course, the shortcomings of UCBT are also obvious: (1)Because some children and adults with large surface areas, the dose of cells in umbilical cord blood maybe is smaller. (2) Delayed implantation or delayed immune reconstitution. (3) The infection rate is higher.

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Disclosure

The author reports no conflicts of interest in this work.

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