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Post-Transplant Lymphoproliferative Disorder Arising in Solid Organs (Lungs and Liver) After Hematopoietic Stem Cell Transplantation: A Case Report

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Abbreviations:

PTLD: Post-Transplant Lymphedema; Allo-HSCT: Allogeneic Hematopoietic Stem Cell Transplantation; SOT-Solid: Organ Transplantation; EBV-EB: Virus; CMV: Cytomegalovirus; GVHD: Graft Versus Hypopnea Syndrome; MTX: Methotrexate; MMF: Mycophenolate Mofetil; CSA: CyclocyclineA; ATG: Anti-Thymocyte Globulin; G-CSF: Recombinant Human Granulocyte Colony Stimulating Factor; CR: Complete Remission

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1. Abstract

1.1. Introduction

To explore the diagnosis and treatment of PTLD in solid organs after HSCT. We retrospectively analysed the clinical data of a patient who developed post-transplant lymphoproliferative disease (PTLD) in solid organs (lung and liver) after the second allogeneic hematopoietic stem cell transplantation (allo-HSCT) at Beijing Gao Bo Boren Hospital.

1.2. Case Presentation

A 26-year-old Chinese male, Han nationality, company employee, was diagnosed with T-ALL/LBL and received his first haploidentical hematopoietic stem cell transplant (father was the donor). He was diagnosed with CMV/EBV hyperaemia +2 months after the transplant, and the virus turned negative after symptomatic treatment. +3 months after transplantation, the tonsils became swollen and pathologically confirmed to be PTLD. The patient was cured by treatment with hormones combined with four doses of rituximab. +6 months after transplantation, painful lumps appeared in the right neck and right upper arm, and pathological results suggested recurrence of the original disease. He was admitted to Beijing Gao Boren Hospital and subsequently received a second allogeneic transplant from an unrelated donor (HLA 10/10 match). Six months after the second transplant, severe EBV-positive PTLD developed, initially manifesting as recurrent fever with pulmonary nodules, followed by rounded low-density lesions in the liver and subcutaneous tissue. There was no enlargement of lymph nodes throughout the body. After pathological diagnosis, chemotherapy was performed and the disease was cured.

1.3. Conclusion

PTLD, a complication of allo-HSCT, may occur alone in solid organs without involving lymph nodes. PTLD occurring in solid organs is easily misdiagnosed and requires precise treatment after pathological biopsy is confirmed.

2. Introduction

Post-transplant lymphoproliferative disorder (PTLD) is a severe complication involving lymphoid or plasma cell proliferation. It represents a rare but heterogeneous group of conditions occurring after solid organ or hematopoietic stem cell transplantation, with manifestations ranging from benign lymphoid hyperplasia to malignant lesions. The incidence of PTLD varies from 1% to 20%, while EBV-positive PTLD after allogeneic hematopoietic stem cell transplantation (allo-HSCT) occurs in 0.5% to 17% of cases [1-4]. Although PTLD may develop at any time post-transplant-sometimes as late as 10 years—most cases arise within the first year [5]. The disorder is notably associated with Epstein–Barr virus (EBV) reactivation and often follows an aggressive clinical course [6,7]. Common sites of PTLD involvement include the gastrointestinal tract (more frequently the jejunum than other segments), diaphragm, skin, tonsils, adenoids, liver, and lungs. The gastrointestinal tract is the most commonly affected extranodal site. Central nervous system involvement is uncommon, and primary solid organ PTLD is rare. One study of 288 adults who underwent umbilical cord blood transplantation reported EBV-PTLD sites as follows: liver (7 cases), spleen (6), central nervous system (4), Waldeyer's ring (3), and bone

marrow (3), underscoring the low incidence at these locations [8]. However, there are currently no relevant literature reports on PTLD occurring in solid organs after HSCT. This case report describes a rare instance of PTLD occurring in both the lungs and liver following HSCT, this case suggests that the possibility of PTLD should be considered in patients with recurrent fever and lesions in solid organs after hematopoietic stem cell transplantation. The specific case data is as follows:

3. Clinical Data

3.1. Clinical Data on Diagnosis and Treatment of T-ALL/LBL

The patient, Nong, male, 26 years old, Chinese, Han nationality, went to the hospital in July 2018 due to "high fever and fatigue". Past medical history: none; previous surgical history: none; family history: no genetic history; complete complete blood routine examination showed reduction of three lines (white blood cells 1.92*10^9/L, hemoglobin 68g/L, platelets 102*10^9/L); subsequent bone marrow puncture was performed to confirm the diagnosis: T-ALL/LBL. The disease went into remission after initial chemotherapy and subsequent haploidentical hematopoietic stem cell transplantation. Complications such as CMV, EB-Vemia, and PTLD occur after transplantation. All complications recovered after corresponding treatment. The patient's T-ALL/LBL relapsed extramedullary 7 months after haplo-HSCT. His condition remitted again after chemotherapy combined with immunotherapy, and then he underwent a second HSCT treatment (see Figure 1 for the specific treatment process).

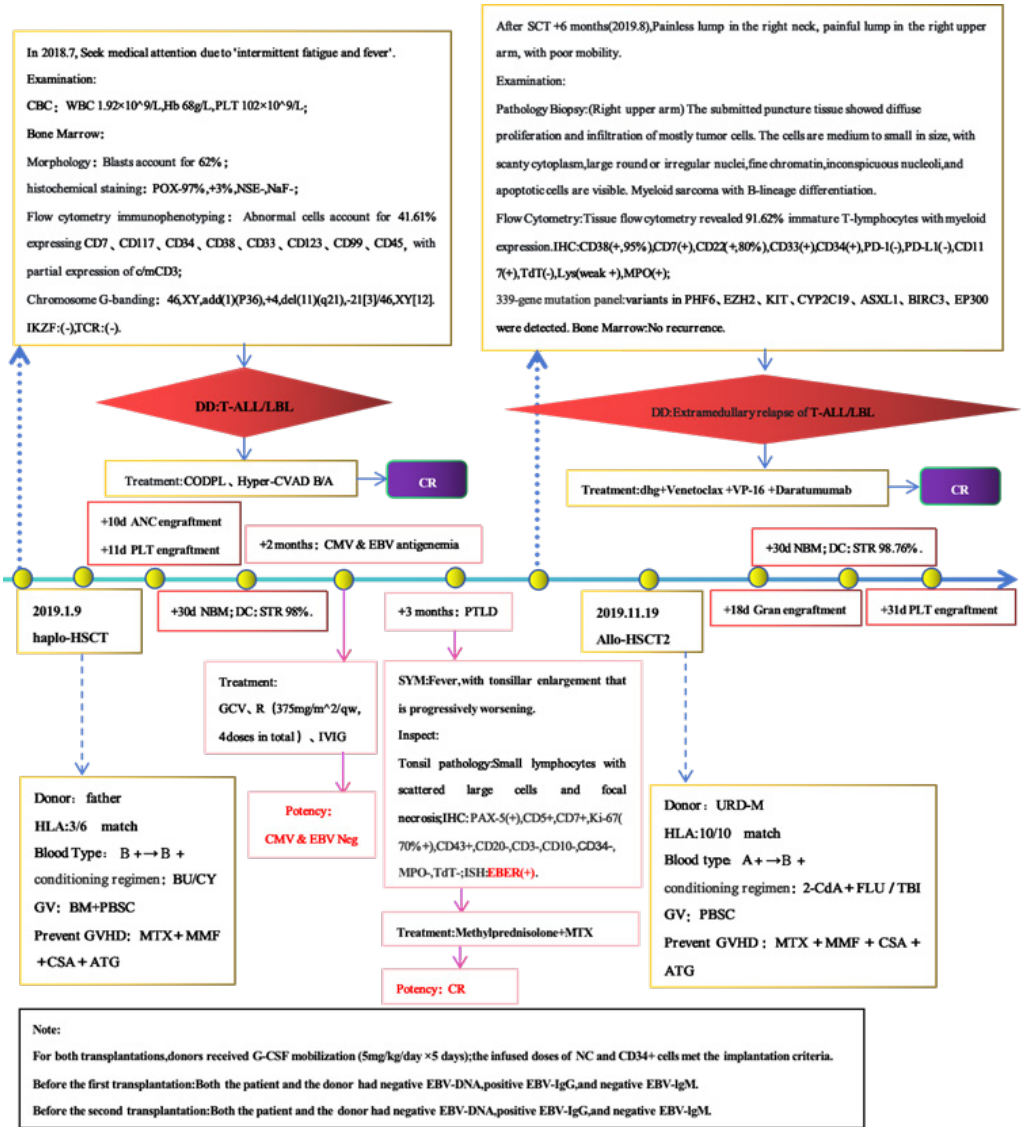

Figure 1: T-ALL/LBL diagnosis and treatment process.

3.2. Clinical Data on Pre- and Post-Diagnosis Examination and Treatment of PTLD

Fever occurred +128 days after transplantation (body temperature change: 37.8-38.3°C, irregular fever), accompanied by fatigue, night sweats, no cough, sputum production, and no other accompanying symptoms. Routine whole blood examination: WBC: 4.2×10^9/L, Hb: 82g/L, PLT: 34×10^9/L; chest CT showed: nodular shadow in the upper lobe of the left lung, confirming the diagnosis of EBVemia, excluding other infections. After corresponding treatment, the body temperature returned to normal and the EBV virus turned negative after 1 week. Considering that the treatment is effective, continue the original treatment plan. After 44 days of anti-infection, the body temperature rose again (temperature change: 38.0-39.3°C, irregular fever).

The entire body temperature changes during the course of the disease are shown in Figure 2. He was accompanied by fatigue and anorexia, no cough or sputum, pain in the flank areas on both sides, positive liver tenderness, and painful nodules on the inner thighs. Imaging examination showed that the lesions in the upper lobe of the left lung were enlarged compared with the previous ones, and at the same time, there were actual lesions in the liver. The pathological biopsy was completed to confirm the diagnosis of PTLD (lung and liver), and the PTLD was cured after 4 cycles of chemotherapy (see Figure 3 for the specific diagnosis and treatment process).

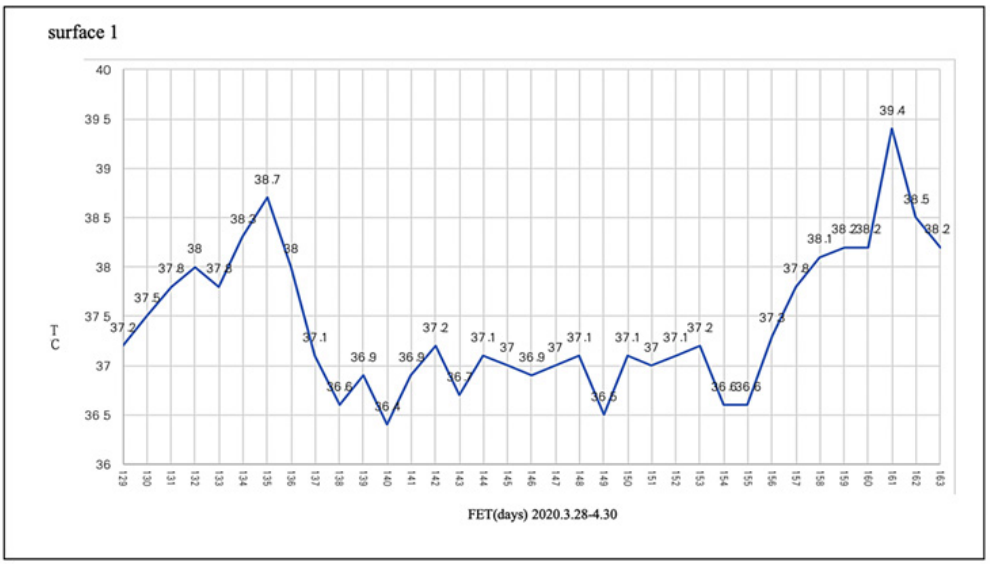

Figure 2: Change trend of body temperature during treatment before PTLD diagnosis.

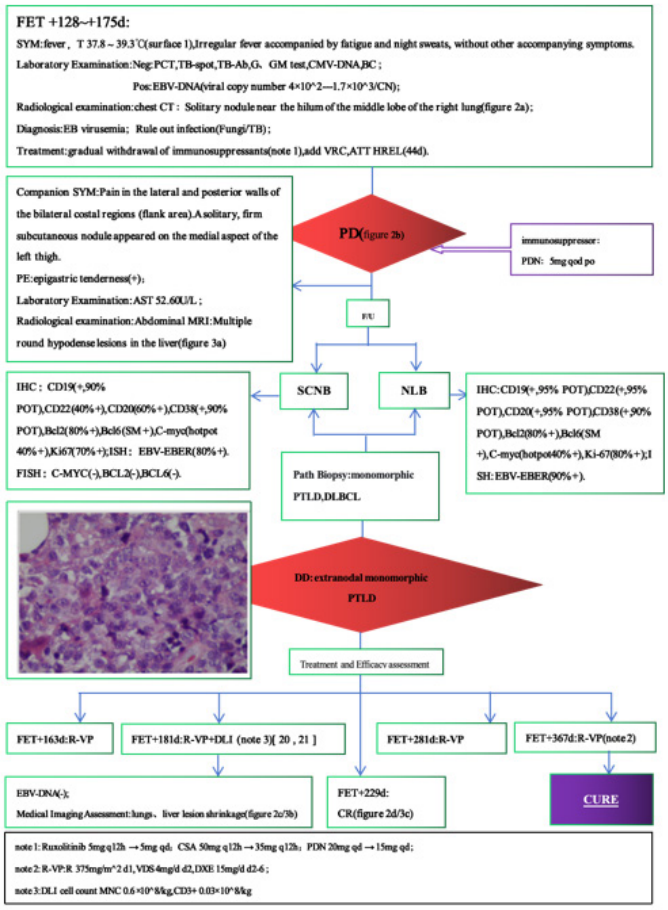

Figure 3: Diagnosis and treatment process before and after PTLD diagnosis.

3.3. Disease Outcome

The imaging changes before and after diagnosis and treatment of PTLD are shown (Figure 4). The patient has undergone a second transplant nearly 5 years ago, and a PET/CT scan of the bone marrow, lumbar region, and whole body has achieved complete remission (CR). The patient is currently living at home without disease.

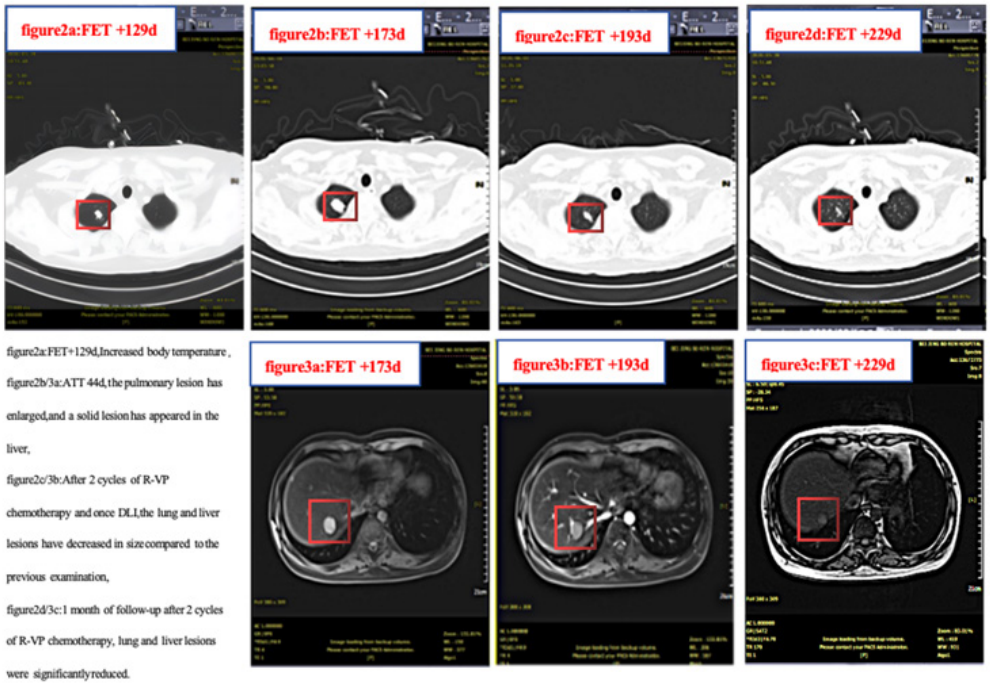

Figure 4: Imaging changes before and after diagnosis of PTLD.

4. Discussion

In the present case, PTLD involved solid organs after hematopoietic stem cell transplantation, as confirmed by pathological and immunohistochemical evaluation. The patient developed PTLD following both transplant procedures, likely due to intense conditioning regimens and post-transplant immunodeficiency leading to EBV reactivation [9-11]. A donor-related origin could not be excluded, and the use of an older male donor for the first transplant may have further increased the risk [12,13]. Notably, during the second transplant, PTLD manifested at uncommon sites, with very few reported cases primarily involving the lungs and liver. Such presentations are prone to misdiagnosis and may delay appropriate treatment. This patient presented with recurrent fever and multiple episodes of CMV/EBV reactivation post-transplant. Despite broad-spectrum anti-infective therapy, the fever persisted. Imaging eventually revealed nodal lesions in the lungs and liver, and pathological biopsy confirmed PTLD. Both PTLD episodes were managed with immunosuppression reduction and chemotherapy regimens based on meropenem [14-18], achieving complete remission on both occasions. During the second episode, anthracyclines were omitted due to poor hematologic recovery, yet the treatment response remained remarkable [19].

5. Conclusion

This patient developed fever and solid lung lesions early after transplantation. Conventional anti-infective treatment was not effective. The lung lesions were larger than before and solid lesions appeared in the liver. Later, pathological examination was completed to confirm the diagnosis of PTLD. Early empiric treatment misdiagnosis led to worsening of the condition. For patients who develop EBVemia and solid organ lesions (such as liver, lungs or other extranidal sites) after HSCT, we should be alert to the possibility of PTLD. For patients with recurrent fever and unresponsiveness to anti-infective treatment, it is recommended to perform pathological biopsy whenever possible to confirm the diagnosis. Rituximab-cantered treatments have shown effectiveness in such cases.

6. Advantages of this Article

The patient in this case has a clear diagnosis of T-ALL/LBL, a highly malignant disease, short-term disease recurrence after HSCT, disease remission after repeat HSCT, and a complicated treatment process. The patient developed PTLD after two HSCTs, and PTLD occurred in solid organs after second transplantation. The location of the disease is rare, and there are currently no relevant literature reports. Empirical anti-infective treatment in the early stage delayed the disease. Later, the possibility of secondary tumours was considered based on clinical experience, and pathological biopsy was improved to confirm the diagnosis. Timely discovery and diagnosis, and after precise treatment, the patient recovered.

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