Clinical imaging and pathology analysis of Epstein-Barr virus-associated monomorphic lymphoproliferative disease after liver transplantation in children—a retrospective case series

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Background: Post-transplant lymphoproliferative disease (PTLD) is a significant complication that can arise following solid organ transplantation or hematopoietic stem cell transplantation. It encompasses a spectrum of lymphoproliferative lesions, ranging from benign reactive hyperplasia to malignant tumors, and is among the most severe complications following liver transplantation in children. It is essential for clinicians to gain a comprehensive understanding of the prevention, clinical manifestations, early diagnosis, and treatment strategies for PTLD in order to reduce mortality rates.

Case Description: This study presents an analysis of six pediatric patients (three females and three males) diagnosed with monomorphic PTLD occurred at intervals of 1 month and 3 years post-transplantation. Five were localized in the gastrointestinal tract, while one was identified in the lymph nodes. The pathological diagnoses included diffuse large B-cell lymphoma (DLBCL) in three instances, Burkitt lymphoma in two, and peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) in one. Testing for Epstein-Barr virus-encoded RNA (EBER) yielded positive results in all cases. Following the reduction or cessation of immunosuppressive, antineoplastic, and anti-inflammatory medications, three patients succumbed within three months, while the remaining three patients were monitored for a duration of 6 to 13 months and remained in good condition.

Conclusions: The clinical manifestations of PTLD following liver transplantation are complex. Close monitoring of serum Epstein-Barr virus (EBV) levels after transplantation, along with early diagnosis of PTLD through imaging and pathological examinations, can assist clinicians in developing individualized treatment strategies to enhance patient prognosis.

Keywords: Post-transplant lymphoproliferative disease (PTLD); children; liver transplantation; Epstein-Barr virus (EBV); case series

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Introduction

Post-transplant lymphoproliferative disease (PTLD) is the most severe complication following liver transplantation in children. Its increased morbidity and mortality in pediatric patients are closely linked to Epstein-Barr virus (EBV) infection and the use of immunosuppressive medications. According to the 4th edition of the World Health Organization Classification of Lymphoid Neoplasms (WHO-HAEM4R) and the International Consensus Classification of Mature Lymphoid Neoplasms (ICC-2022), PTLD is classified into four subtypes: non-destructive PTLD, polymorphic PTLD, monomorphic PTLD, and classical Hodgkin's lymphoma PTLD (1,2).

The incidence of PTLD in children is approximately 5.1%, which is notably higher than the 3.8% rate observed in adults, and the time of occurrence is significantly earlier than that in adults, and the development of EBV-positive PTLD lesions occurs significantly earlier than EBV-negative lesions. In addition, nearly half of pediatric PTLDs (49%) occur within 1 year of liver transplantation (3). Compared to polymorphic PTLD, monomorphic PTLD has a poorer prognosis (4).

This research retrospectively examines six cases of EBV-associated monomorphic PTLD arising in the intestines and lymph nodes, delineates the clinical and pathological characteristics of these cases, discusses post-transplantation EBV infections, and proposes evidence-based therapeutic approaches based on existing literature to mitigate the morbidity and mortality associated with PTLD. We present this article in accordance with the AME Case Series reporting checklist (available at https://tp.amegroups.com/article/view/10.21037/tp-24-311/rc).

Case presentation

This study was a single-center, retrospective, and non-continuous investigation that included a total of six children diagnosed with PTLD. All cases were diagnosed and treated at Chongqing Medical University Affiliated Children's Hospital, a public institution, between 2018 and 2023. All procedures performed in this study were in accordance with the ethical standards of the Ethics Committee of Chongqing Medical University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from all families of the participating children for publication of this case series and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

The demographic information, including age, sex, primary disease, time of onset of PTLD, clinical presentation, imaging manifestations, therapeutic agents utilized, and follow-up results for the six pediatric patients are presented in *Table 1* and *Figure 1*. Additionally, the surveillance data for EBV infection and the results of laboratory liver function tests are detailed in *Table 2*. The pathological features are illustrated in *Table 3* and *Figure 2*.

Cases 1 to 5 of PTLD were all localized within the gastrointestinal tract, resulting in a relatively uniform clinical presentation. Each patient was admitted to the hospital due to gastrointestinal complications, which included symptoms such as anemia, hematochezia, abdominal distension, abdominal pain, or the presence of an abdominal mass. Imaging studies indicated that cases 1, 2, and 3 predominantly exhibited intestinal pneumoperitoneum, intestinal lumen dilation, abdominal effusion, and splenomegaly (see *Figure 1A*). In contrast, case 4 presented with a mass in close proximity to the bowel (see *Figure 1C*), while case 5 suggested bowel wall thickening and narrowing of the bowel lumen (see *Figure 1B*). Laboratory analyses revealed varying degrees of anemia and impaired liver function across all five cases. EBV testing indicated that all five children were negative for EBV prior to liver transplantation; however, at the time of PTLD

Highlight box

Key findings

• In pediatric patients following liver transplantation, it is essential to implement Epstein-Barr virus (EBV) surveillance, prevention, and early diagnosis of post-transplant lymphoproliferative disease (PTLD), as well as to develop personalized treatment strategies aimed at reducing mortality rates.

What is known and what is new?

• Surveillance for EBV during the initial postoperative year is crucial for the early detection of PTLD. Given the diverse clinical presentations and the nonspecific nature of imaging findings, pathological biopsy is indispensable for achieving an accurate diagnosis.

• The variability in clinical presentations has resulted in an absence of standardized treatment protocols, highlighting the necessity for the exploration of more individualized treatment strategies.

What is the implication, and what should change now?

• The early and definitive diagnosis of PTLD presents significant challenges. It is imperative for clinicians to enhance awareness of this condition, improve monitoring and diagnostic methodologies, and actively investigate personalized treatment strategies.

Table 1 Clinical data pertaining to pediatric patients following liver transplantation

Case	Sex/age (months)	Primary disease/surgical approach	Time to PTLD after transplantation	Clinical manifestations	Imaging findings	Immunosuppressive agents used and doses post-transplantation	Therapeutic drugs and programs after the occurrence of PTLD	Prognosis
1	M/16	Biliary atresia/DDLT	3 months	Anemia, gastrointestinal bleeding	Ultrasound: splenomegaly	Tacrolimus capsules: 6 mg, 3/24 h	Acyclovir, Tylenol, vancomycin, cyclosporine A	Died 2 months after diagnosis
					CT: fluid in the abdominal cavity, multiple pneumoperitonea, and dilatation of the colon and small intestine	Mycophenolate mofetil dispersible tablets: 125 mg, 2/24 h		
					PET-CT: NA			
2	M/95	Intrahepatic choledocholithiasis/LDLT	4 months	Fever, anemia, hematochezia, abdominal pain, abdominal distension	Ultrasound: splenomegaly, abdominal effusion	Tacrolimus capsules: 2.5 mg,1/12 h	Acyclovir, Tylenol, cyclosporine A	Died 1 month after diagnosis
					CT: dilatation of the small bowel with pneumoperitoneum is obvious	Mycophenolate mofetil dispersible tablets:250 mg, 1/12 h		
					PET-CT: NA			
3	M/53	Portal vein cavernous degeneration/LDLT	6 months	Blood in stool, anemia, depression	Ultrasound: splenomegaly	Tacrolimus capsules: 1.5 mg, 1/12 h	Acyclovir, Tylenol, rituximab	Good condition at 13 months follow-up
					CT: fluid and gas accumulation in the right middle and lower abdominal bowel with dilated bowel lumen	Mycophenolate mofetil dispersible tablets: 250 mg, 1/12 h		
					PET-CT: NA			
4	F/30	Biliary atresia/LDLT	2 years	Anemia, vomiting, abdominal mass	Ultrasound: splenomegaly	Tacrolimus capsules: 0.833 mg, 1/12 h	Acyclovir, rituximab + COPADM3/CVM	Good condition at 6 months follow-up
					CT: right abdominal space-occupying lesion with a close relationship to the bowel	Mycophenolate mofetil dispersible tablets: 125 mg, 1/12 h		
					PET-CT: intestinal lymphoma with multiple groups of enlarged lymph nodes in the mesentery and abdominal aorta			
5	F/41	Biliary atresia/LDLT	3 years	Anemia, vomiting, bloating, convulsions	Ultrasound: intestinal wall thickening and intestinal pneumatization	Tacrolimus capsules: 0.75 mg, 1/24 h	Acyclovir, BFM-95 regimen, V + Ar + BBr	Good condition at 6 months follow-up
					CT: thickening of intestinal wall with narrowing of intestinal lumen	Mycophenolate mofetil dispersible tablets: 125 mg, 1/12 h	Chemotherapy	
					PET-CT: NA			
6	F/62	Progressive familial intrahepatic cholestasis/LDLT	10 months	Anemia, abdominal pain, fever, generalized lymphadenopathy	Ultrasound: hepatosplenomegaly, pleural and abdominal effusion	Tacrolimus capsules: 1.5 mg, 1/12 h	Modified CHOP	Died 3 months after diagnosis
					CT: bilateral cervical and right axillary lymph node enlargement, Pleural effusion and hilar lymphadenopathy	Mycophenolate mofetil dispersible tablets: 250 mg, 1/12 h	Chemotherapy, acyclovir, Tylenol	
					PET-CT: diffuse lymphadenopathy with splenomegaly			

M, male; F, female; DDLT, deceased donor liver transplantation; LDLT, related living donor liver transplantation; PTLD, post-transplant lymphoproliferative disease; CT, computed tomography; PET, positron emission tomography; NA, not done; COPADM3/CVM, C, cyclophosphamide O, vincristine; P, dexamethasone; A, doxorubicin; D, cytarabine; M, methotrexate; C, cyclophosphamide; V, vincristine; M, methotrexate; BFM-95, Berlin-Frankfurt-Münster 95; V + Ar + BBr, vinorelbine + doxorubicin + bleomycin; CHOP, cyclophosphamide + doxorubicin hydrochloride + vincristine sulfate + prednisone.
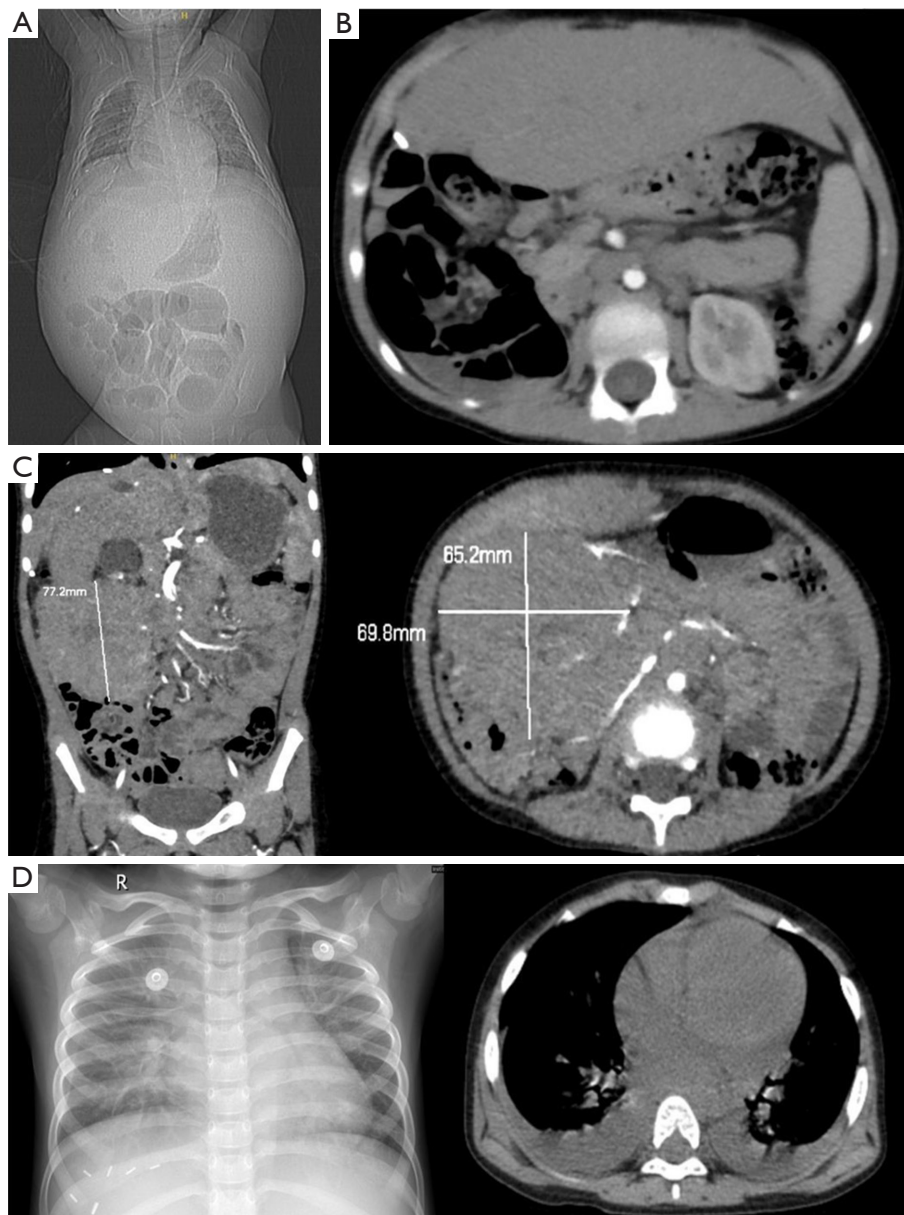
Figure 1 CT examination: imaging manifestations of pediatric patients with PTLD. (A) Cases 1, 2, and 3 exhibited similar clinical presentations, characterized by the presence of multiple colonic and small intestinal, fluid accumulation, and dilatation of the intestinal lumen. Additionally, splenomegaly with peritoneal effusion was observed. (B) Case 5 displayed uneven thickening of a section of the small intestinal wall, irregular narrowing of the intestinal lumen, and mild dilatation of specific intestinal segments. (C) Case 4 presented as a right abdominal mass measuring 7.7 cm × 7.0 cm × 6.5 cm, characterized by a well-developed vascular supply. The mass was closely associated with the intestinal wall and was accompanied by multiple enlarged lymph nodes. (D) Case 6 illustrates the presence of bilateral lung inflammation, pleural effusion and the enlargement of hilar lymph nodes. CT, computed tomography; PTLD, post-transplant lymphoproliferative disorder; R, right.

**Table 2** Laboratory test data of pediatric patients with PTLD

Case	Pre-transplant donor serum EBV status	Pre-transplant recipient serum EBV status	Serum EBV-PCR (copies/mL) post-transplantation	Receptor serum EBV status at PTLD	Serum EBV-PCR at PTLD (copies/mL)	HB (g/L)	ALB (g/L)	ALT (U/L)	AST (U/L)	PT (seconds)
1	NA	NA	NA	CA-IgG, NA-IgG	NA	66 ↓	25.5 ↓	69.2 ↑	42	17.6
2	NA	NA	NA	CA-IgG	NA	104 ↓	30.6 ↓	12.2	14.2	18.2
3	NA	EBV-PCR 7.25×10^3 copies/mL	<400	CA-IgG	2.68×10^4	107 ↓	32.2 ↓	12	54 ↑	22.5 ↑
4	NA	EBV-PCR <400 copies/mL	<400	CA-IgG, EA-IgG, NA-IgG	4.68×10^6	92 ↓	29.4 ↓	9	35	17.4
5	CA-IgG	EBV-PCR <400 copies/mL	<400	CA-IgG, EA-IgG, NA-IgG	4.31×10^4	48 ↓	51.4	29	20	22.6 ↑
6	NA	EBV-PCR <400 copies/mL	3.52×10^3	CA-IgG	9.8×10^4	79 ↓	35.7 ↓	13	29	16.9

↓: elevation; ↑: reduction. PTLD, post-transplant lymphoproliferative disorder; EBV, Epstein-Barr virus; PCR, polymerase chain reaction; NA, not done; CA-IgG, capsid antigen immunoglobulin G; NA-IgG, nuclear antigen immunoglobulin G; EA-IgG, early antigen immunoglobulin G; HB, hemoglobin; ALB, albumin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT, plasminogen time.

Table 3 Pathological characteristics of pediatric patients with PTLD

Case	Sites and biopsy modalities	Pathological type	EBERs ISH	EBNA2	CD20	CD3	BCL2	BCL6	CD10	C-MYC	CD30	PD-1	PD-L1	P53	Ki67	Detection of clonal gene rearrangements
1	Jejunum/surgical resection	DLBCL	+	+	+	10%+	_	_	_	_	+	_	+	20%	40%+	IgH, Igk
2	Ileum/surgical resection	DLBCL	+	+	+	10%+	_	_	_	_	+	_	+	20%	60%+	IgH,Igk,TCRγ
3	Jejunum/surgical resection	DLBCL	+	+	+	40%+	_	_	_	_	+	_	+	30%	30%+	IgH,Igk
4	Colonic hepatic area/puncture biopsy	Burkitt	20%+	_	+	_	_	+	+	+	_	_	40%+	40%	>95%+	NA
5	Jejunum/surgical resection	Burkitt	20%+	_	+	_	_	+	+	+	_	_	+	80%	>95%+	NA
6	Cervical lymph nodes/surgical removal	PTCL-NOS	40%+	_	_	+	_	_	_	_	_	10%+	50%+	10%	40%+	TCRγ

Note: The target of observation was the tumor cells. PTLD, post-transplant lymphoproliferative disorder; EBERs ISH, Epstein-Barr virus-encoded RNA in situ hybridization; DLBCL, diffuse large B-cell lymphoma; Burkitt, Burkitt lymphoma; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; NA, not done; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; Ig, immunoglobulin.
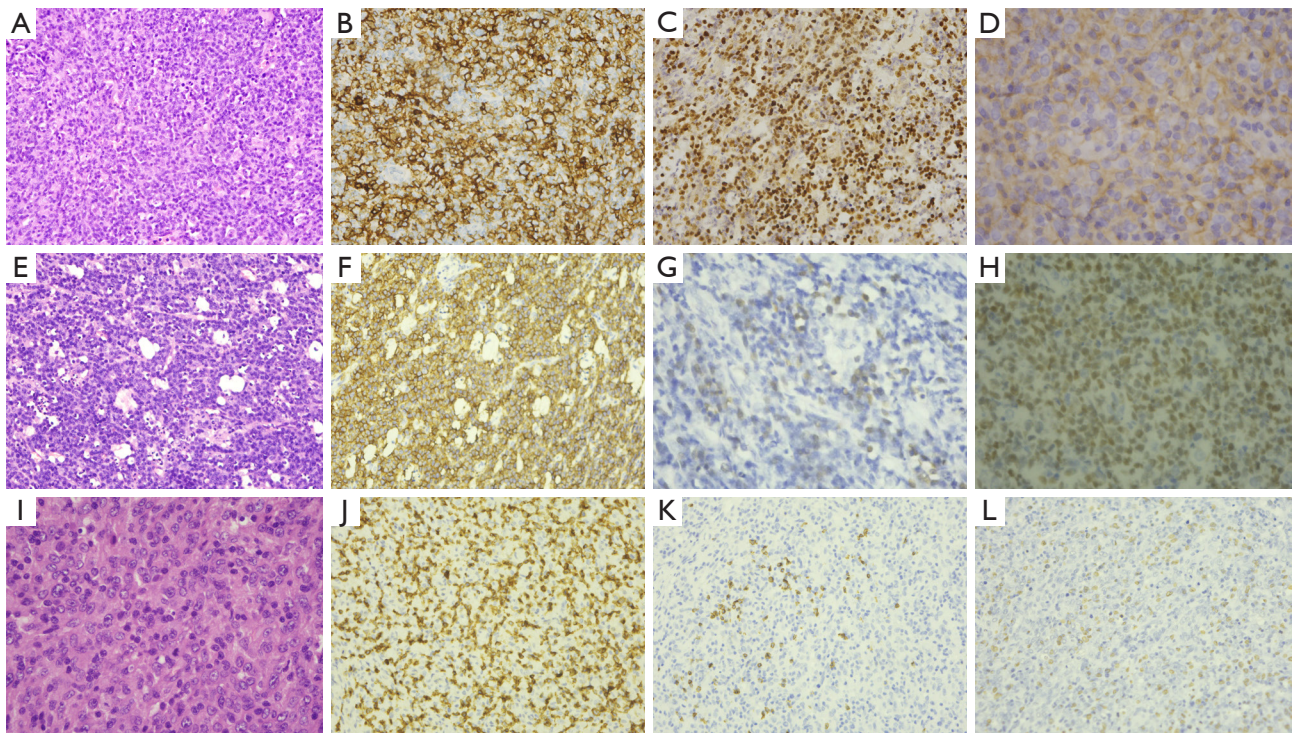
Figure 2 The pathological morphology, immunohistochemical features, and in situ hybridization characteristics of pediatric patients with PTLD. (A-D) DLBCL: (A) cases 1, 2, and 3 exhibit morphological similarities characterized by a diffuse proliferation of tumor cells that disrupts the structural integrity of the intestinal wall. The cytoplasm of the tumor cells is abundant and exhibits a pale staining pattern, with indistinct borders. The nuclei are large and display heterogeneity, accompanied by prominent nucleoli. Pathological nuclear divisions are readily observable (HE staining, ×200); (B) DLBCL tumor cells exhibit widespread and robust expression of CD20 (immunohistochemical staining, ×400); (C) DLBCL tumor cells are broadly positive for EBER (×200); (D) DLBCL tumor cells show diffuse positivity for PD-L1 (immunohistochemical staining, ×400). (E-H) Burkitt lymphoma: (E) cases 4 and 5 exhibited morphological similarities, characterized by medium-sized tumor cells with slightly basophilic cytoplasm, prominent pathological nuclear fission, and a focal "starburst" phenomenon (HE staining, ×200); (F) Burkitt lymphoma demonstrated diffuse expression of CD20 (immunohistochemical staining, ×400); (G) Burkitt lymphoma showed scattered positivity for EBER (×400); (H) diffuse positivity for C-MYC (immunohistochemical staining, ×400). (I-L) PTCL-NOS: (I) PTCL tumor cells exhibited a diffuse distribution characterized by medium-sized cells, pale cytoplasm, and distorted, irregular nuclei, pathologic karyorrhexis was readily observable (HE staining, ×400); (J) the majority of PTCL tumor cells demonstrated positivity for CD3, although some exhibited a deficiency in expression (immunohistochemical staining, ×200); (K) PTCL tumor cells did not express CD20 (immunohistochemical staining, ×200); (L) PTCL tumor cells showed positive staining for EBER (×200). PTLD, post-transplant lymphoproliferative disorder; DLBCL, diffuse large B-cell lymphoma; PTCL-NOS, peripheral T-cell lymphoma, not otherwise specified; EBER, Epstein-Barr virus-encoded RNA; HE, hematoxylin and eosin.

diagnosis, both serum antibody testing and EBV-DNA testing suggested the presence of EBV infection (refer to *Table 2*).

During the hospitalization and diagnostic process, cases 1 and 2 presented with severe conditions characterized by intestinal perforation, peritoneal effusion, and systemic infection. Both cases underwent partial intestinal resection, intestinal repair, intestinal mucosal laxation, and abdominal drainage. Following the clarification of their diagnoses,

immunosuppressive medications were discontinued, and the patients received anti-infective and supportive treatments. However, the infection could not be effectively controlled and subsequently progressed to pneumonia, ultimately resulting in death due to infectious shock and respiratory failure.

Cases 3, 4, and 5 exhibited improved baseline conditions following the surgical resection of the intestinal lesion. After the diagnosis of PTLD was established, the

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immunosuppressive therapy was reduced and subsequently discontinued. These patients received anti-inflammatory and anti-neoplastic treatments, including rituximab and combination chemotherapy, and demonstrated favorable outcomes at the follow-up visits conducted 6 to 13 months post-treatment. Pathological examinations of cases 1, 2, and 3 confirmed a diagnosis of diffuse large B-cell type PTLD (refer to *Figure 2A-2D*, *Table 3*), while cases 4 and 5 were diagnosed with Burkitt lymphoma type PTLD (refer to *Figure 2E-2H*, *Table 3*).

In contrast to the preceding five cases, the clinical presentation of case 6 was characterized primarily by generalized lymphadenopathy. Imaging studies indicated the presence of generalized lymph node enlargement, hilar lymphadenopathy, and pleural effusion (refer to *Figure 1D*). Additionally, ultrasound and positron emission tomography (PET)-computed tomography (CT) findings suggested splenomegaly and intestinal pneumoperitoneum. Pathological examination confirmed the diagnosis of T-cell type PTLD [peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)] (see *Figure 2I-2L*, *Table 3*). Following the diagnosis, the patient received antiviral and anti-infective therapy; however, they subsequently developed secondary hemophagocytic syndrome, bone marrow suppression, and severe infection, ultimately resulting in death three months after the diagnosis.

Discussion

The risk of PTLD occurrence is associated with various factors such as the recipient's age, location of the disease, EBV infection status of the donor and recipient pre- and post-transplantation, presence of concurrent viral infections, intensity and duration of immunosuppression, and time elapsed since the transplantation (5). Notably, EBV infection plays a crucial role in the pathogenesis of PTLD (6). In this investigation, the transplant cases had negative serum EBV antibody tests before the transplantation procedure. However, upon the onset of PTLD, all cases tested positive for the EBV test, indicating a strong correlation between EBV infection and PTLD.

Due to the decline in both the number and function of T cells in recipients as a result of immunosuppressive drug therapy, EBV-infected B cells cannot be effectively controlled by EBV-specific cytotoxic T cells. The unchecked proliferation of these cells may ultimately lead to the development of PTLD (7). EBV upregulates the programmed cell death protein 1 (PD-1) inhibitory receptor and its ligand programmed cell death ligand 1 (PD-L1) on the surface of T cells, resulting in the dysfunction of effector cells becoming unable to control infection (8).

Consequently, vigilant surveillance of EBV infection following transplantation can serve as a crucial indicator for clinicians regarding the potential development of PTLD, particularly in instances characterized by lymphadenopathy. This article presents four cases in which monthly postoperative EBV monitoring was conducted, with adjustments made to the immunosuppressant regimen based on the monitoring outcomes. However, in the initial cases (1 and 2), EBV monitoring was not performed postoperatively due to specific circumstances, resulting in the detection of EBV infection only upon the patients' readmission for PTLD, which had already progressed to a severe and poorly managed state.

The majority of the six cases examined in this study exhibited gastrointestinal lesions, which may be attributed to the substantial presence of lymphoid tissue in this anatomical region. Reiche (9) conducted a statistical analysis of nine studies on PTLD and found that the gastrointestinal tract was the organ most frequently affected, with specific involvement of the colorectum (18%), jejunum (12%), gastroduodenum (9%), and esophagus (3%), in that order (10). Among the cases of PTLD occurring in the gastrointestinal tract discussed in this paper, 4 out of 5 were located in the small intestine, while only one case was identified in the colon. Further statistical analysis of additional cases is warranted.

The clinical manifestations of patients with PTLD exhibit considerable variability depending on the cumulative sites involved and lack specificity. A definitive diagnosis necessitates a pathological examination. The fifth edition of the World Health Organization Classification of Lymphohaematopoietic Tumours (WHO-HAEM5) has introduced significant modifications to the classification of lymphomas associated with immunodeficiency or immunocompromise, notably the removal of the classification for post-transplant PTLD. The revised nomenclature comprises three primary components: histopathological diagnosis, the presence of oncogenic viral infection, and the clinical or immunodeficiency background. This underscores the necessity for a comprehensive diagnostic approach that integrates both pathological and clinical factors (11). However, the 2022 edition of the International Consensus Classification of Haemato-Oncology (ICC-2022) acknowledges that the clinical management of PTLD following organ transplantation is

distinctly different from that of immunodeficient PTLD arising from other etiologies. Consequently, its classification continues to rely on the criteria established in the WHO-HAEM4R.

According to the classification methodology employed in this study, all cases examined were identified as monomorphic PTLD. Among these, three cases were classified as diffuse large B-cell lymphoma [DLBCL, non-germinal center B-cell (non-GCB) type], two as Burkitt lymphoma, and one as peripheral T-cell lymphoma (PTCL-NOS). Monomorphic PTLD constitutes approximately 60–80% of all PTLD cases, with over 80% originating from B-cells. DLBCL is the most prevalent subtype, accounting for approximately 60% of cases, followed by Burkitt lymphoma and T-cell PTLD. Furthermore, EBV-positive B-cell PTLD is frequently associated with T-cell TCRγ rearrangements, which are typically oligoclonal or limited, indicating a potential impairment in immune surveillance due to T-cell attenuation (12,13).

Morphological subtypes play a crucial role in guiding the selection of specific treatments and assessing prognosis. In this study, case 6 was classified as T-cell PTLD. T-cell PTLD is regarded as a rare condition, representing approximately 10–15% of all cases, and is characterized by a significant degree of heterogeneity, with PTCL-NOS being the most prevalent histological subtype (14). Typically, T-cell PTLD exhibits a prolonged interval between engraftment and diagnosis, and is accompanied by EBV infection in approximately one-third of cases, which is linked to a poor prognosis (4,15).

The prognosis of Burkitt-type PTLD was more favorable compared to DLBCL-type PTLD, with the patient still alive at the 6-month follow-up. Notably, in the case of DLBCL-type PTLD, the presence of more T lymphocytes in the tumor tissue and morphological consistency with T-rich DLBCL features indicated a potentially better prognosis, as evidenced by the patient's good condition at the 13-month follow-up (16).

There exists a substantial correlation between the administration of immunosuppressive agents and the annual rise in the prevalence of monotypic PTLD. This phenomenon is likely attributable to the fact that tacrolimus extends the lifespan of transplanted patients while concurrently heightening their vulnerability to EBV (17,18). The primary therapeutic strategy involves either reducing or discontinuing the use of immunosuppressive medications; however, the optimal timing for the resumption of immunosuppression following PTLD remission, as well as the appropriate dosage, remains ambiguous. This uncertainty underscores the necessity for a more individualized treatment approach (19,20).

In pediatric patients, the recommended first-line chemotherapy regimen in combination with rituximab is rituximab plus cyclophosphamide, adriamycin, vincristine, and prednisone (21). Cases 1 and 2 did not undergo EBV surveillance due to familial circumstances, experienced rapid disease progression following the onset of their condition, lacked the necessary criteria to receive rituximab combination chemotherapy, and consequently exhibited a poor prognosis. In contrast, cases 3, 4, and 5 received both EBV surveillance and rituximab combination chemotherapy, resulting in a more favorable prognosis.

A variety of therapeutic approaches are currently under investigation, including EBV-specific cytotoxic T-lymphocyte (CTL) immunotherapy. This method involves the utilization of autologous or third-party-derived EBV-specific CTLs to target and eliminate aberrant B-cells, thereby reducing EBV DNA load and significantly enhancing remission rates as well as 3-year survival outcomes in refractory PTLD cases (22,23). Additionally, for patients with B-cell PTLD that express CD30, the anti-CD30 agent brentuximab vedotin (BV) is available and has demonstrated potential efficacy in individuals with PTLD who have not responded to initial therapies, as well as in cases of T-cell PTLD characterized by a poor prognosis (24).

PD-L1 expression is a prevalent characteristic of EBV-associated lymphoproliferative disorders (LPD) and indicates potential immune evasion. Monomorphic PTLD exhibits elevated PD-L1 expression and reduced PD-1 expression compared with polymorphic PTLD (25). Consistent with the existing literature, our case demonstrated heightened PD-L1 expression in tumor cells, particularly in cases of DLBCL with minimal PD-1 expression. Consequently, PD-L1 immunotherapy may hold promise for the treatment of monomorphic PTLD.

This is a single-center, retrospective study involving a small sample of pediatric patients. The postoperative observation period ranged from 6 to 13 months, and continued follow-up is necessary to determine long-term prognosis and recurrence rates. Clinical findings and therapeutic medications were extracted from medical records; however, there was no control group to evaluate potential biases in the results due to errors in exclusion documentation. Therefore, prospective or controlled studies with a larger, multicenter patient population are needed to gather more comprehensive clinical data.

Conclusions

Monomorphic PTLD is associated with a high mortality rate and presents with a complex clinicopathological profile. Consequently, it is imperative to conduct early monitoring of serum EBV levels, identify high-risk patients based on their clinical presentation, facilitate prompt diagnosis, and develop individualized treatment regimens. These measures are essential for enhancing the overall survival rates of pediatric patients.

Footnote

Reporting Checklist: The authors have completed the AME Case Series reporting checklist. Available at https://tp.amegroups.com/article/view/10.21037/tp-24-311/rc

Peer Review File: Available at https://tp.amegroups.com/article/view/10.21037/tp-24-311/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-24-311/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the Ethics Committee of Chongqing Medical University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from all families of the participating children for publication of this case series and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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