

Management of a Complex Orbital Post-transplantation Lymphoproliferative Disorder: A Case Report and Literature Review

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Abstract

Background/Aim: Post-transplantation lymphoproliferative disorder (PTLD) is an uncommon but serious complication of organ transplantation. Management often requires multiple treatment modalities and reduction in immunosuppressant treatment (RIT). Orbital involvement is rare, and optimal diagnostic and therapeutic approaches remain uncertain.

Case Report: Here, we report a case of localized orbital PTLD that was successfully treated with RIT alone. A 62-year-old man, who had undergone kidney transplantation 18 years prior, presented with left eye pain and proptosis. Imaging revealed an enhancing intraorbital mass extending to the optic nerve and adjacent intracranial structures. Transcranial biopsy confirmed B-cell-type PTLD. The lesion regressed with stepwise RIT alone without additional therapy. The patient showed clear clinical improvement and remained in remission for more than 13 months.

Conclusion: This case suggests the potential role of a conservative, individualized, stepwise approach in selected patients with localized orbital PTLD, and may inform management strategies for other localized forms of PTLD.

Keywords: Post-transplantation lymphoproliferative disorder, orbital lymphoma, reduction in immunosuppressant treatment, transcranial biopsy, kidney transplantation.



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Received January 29, 2026 | Revised February 26, 2026 | Accepted March 4, 2026



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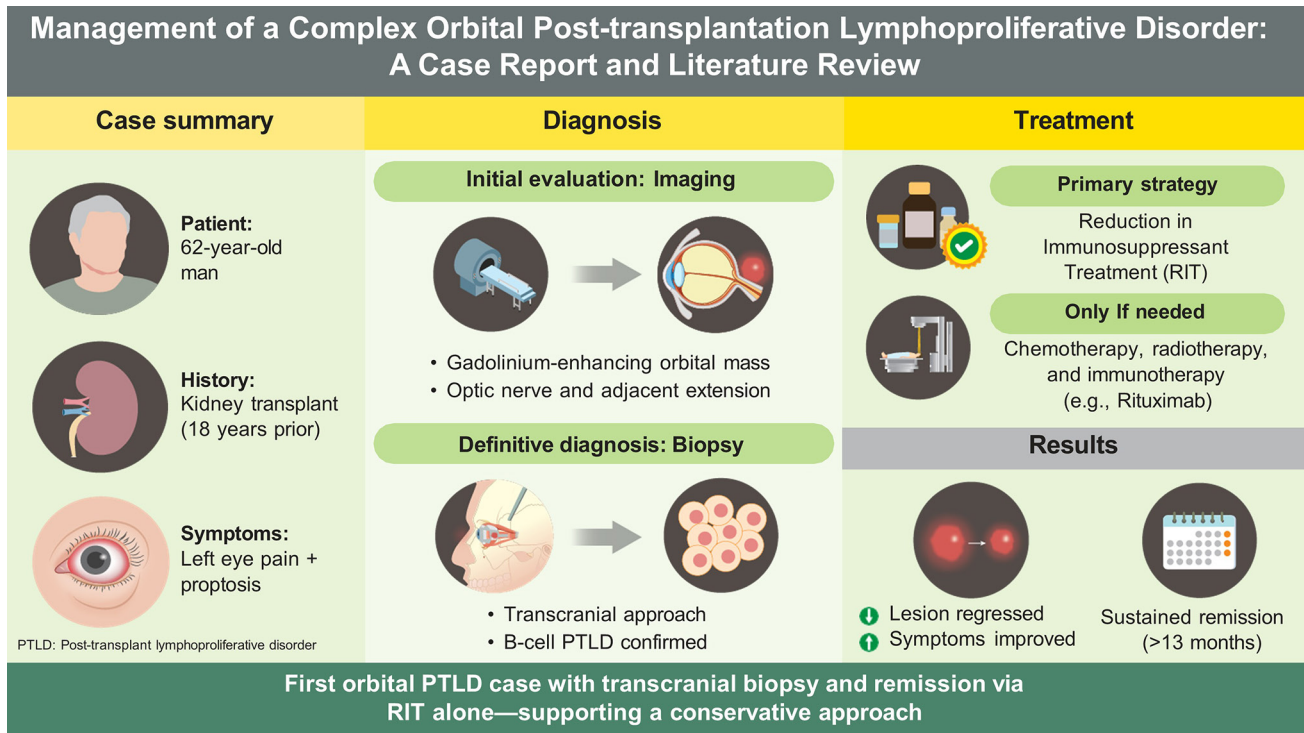


Figure 1. Overview of diagnosis, treatment, and outcome in a patient with orbital post-transplant lymphoproliferative disorder.

Introduction

Post-transplantation lymphoproliferative disorder (PTLD) is an uncommon complication of solid organ or hematopoietic stem cell transplantation (1). It represents a heterogeneous group of lymphoid proliferations related to Epstein–Barr virus (EBV) infection and prolonged immunosuppression, and may develop long after transplantation (2). PTLT can involve almost any organ; however, orbital involvement is extremely rare (3) and poses diagnostic and therapeutic difficulties because of its proximity to critical organs. Although a reduction in immunosuppressant treatment (RIT) is effective in select localized cases (1, 4), the optimal management of orbital PTLD remains uncertain. Herein, we describe a rare case of orbital PTLD that responded favorably to RIT alone. Figure 1 provides an overview of the diagnostic process, treatment strategy, and clinical outcome in this case.

Case Report

This case report was written in accordance with the ethical standards of the Declaration of Helsinki and prepared in compliance with the SCARE (Surgical Case Report) 2025 Guidelines. The patient was given the opportunity to withdraw consent to the publication of this report. The requirement for ethical approval was waived for this case report.

A 62-year-old man with chronic renal failure presented with pain in the left eye and proptosis 18 years after kidney transplantation. The patient had previously lost vision in the left eye due to retinal artery occlusion. The immunosuppressive regimen included mycophenolate mofetil (500 mg/day), tacrolimus (2.5 mg/day), and methylprednisolone (4 mg/day).

Magnetic resonance imaging revealed an enhancing intraorbital mass extending to the optic nerve, optic

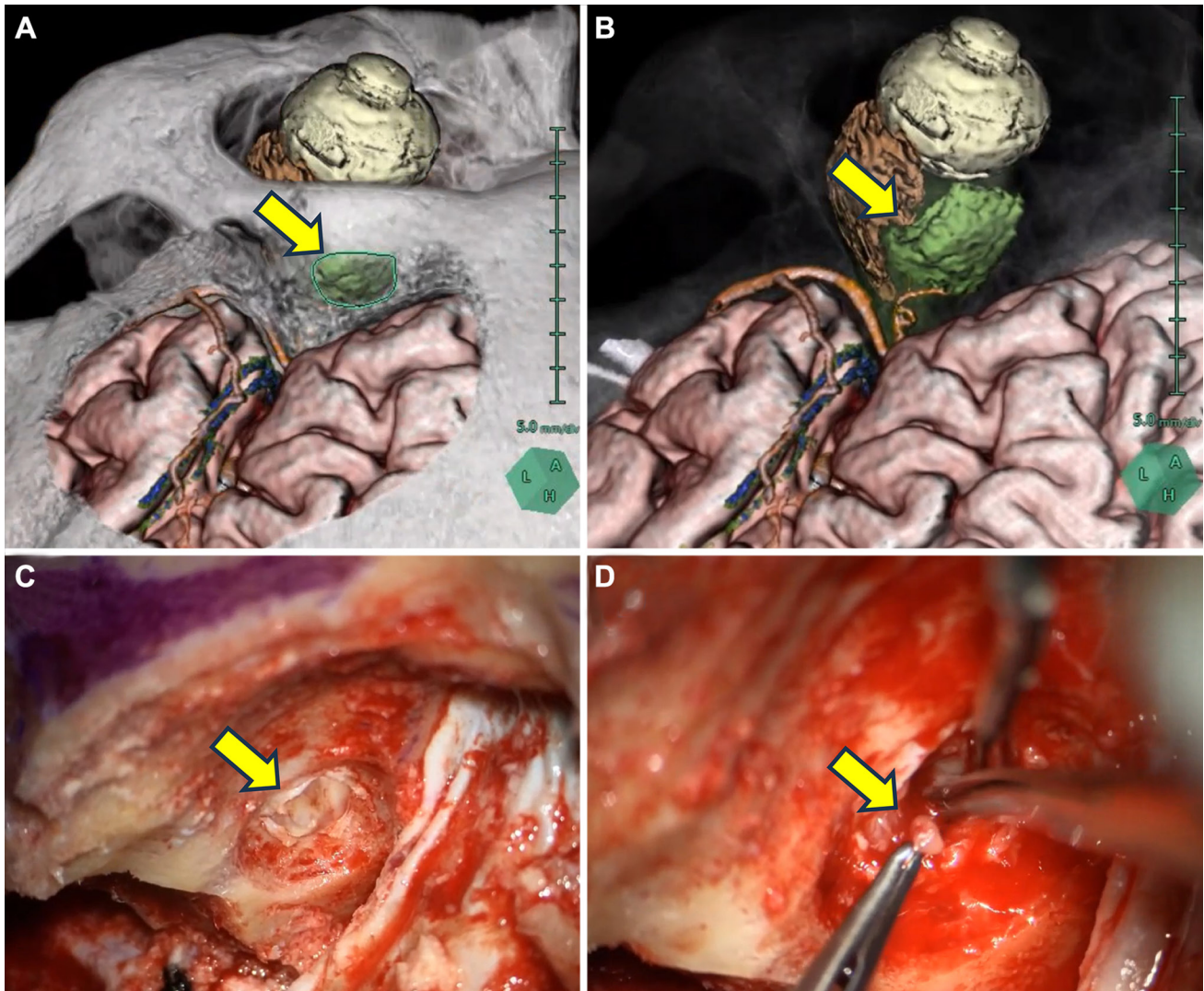


Figure 2. Transcranial biopsy guided by preoperative image simulation. (A, B) Image simulation showing the planned approach and the intraorbital mass. (C) Intraoperative view after creation of a burr hole. (D) Biopsy of the intraorbital mass.

chiasm, and straight and orbital gyri, without bone involvement on computed tomography. IgG4-related disease and optic nerve sheath meningioma were initially considered; however, laboratory tests and systemic imaging revealed no abnormalities.

To obtain adequate tissue, an open biopsy *via* the transcranial approach was performed with preoperative imaging simulation (Figure 2A and B). A transcranial biopsy was performed with cerebrospinal fluid drainage

and preoperative imaging guidance, allowing minimally invasive sampling of the hemorrhagic intraorbital mass without a dural opening (Figure 2C and D).

Histological examination revealed diffuse infiltration of lymphocytes without evident plasma cell differentiation (Figure 3A). On immunohistochemical examination, we observed scattered medium to large-sized clusters of differentiation (CD) 20-positive B cells (Figure 3B). In the background, we found numerous CD3-positive T

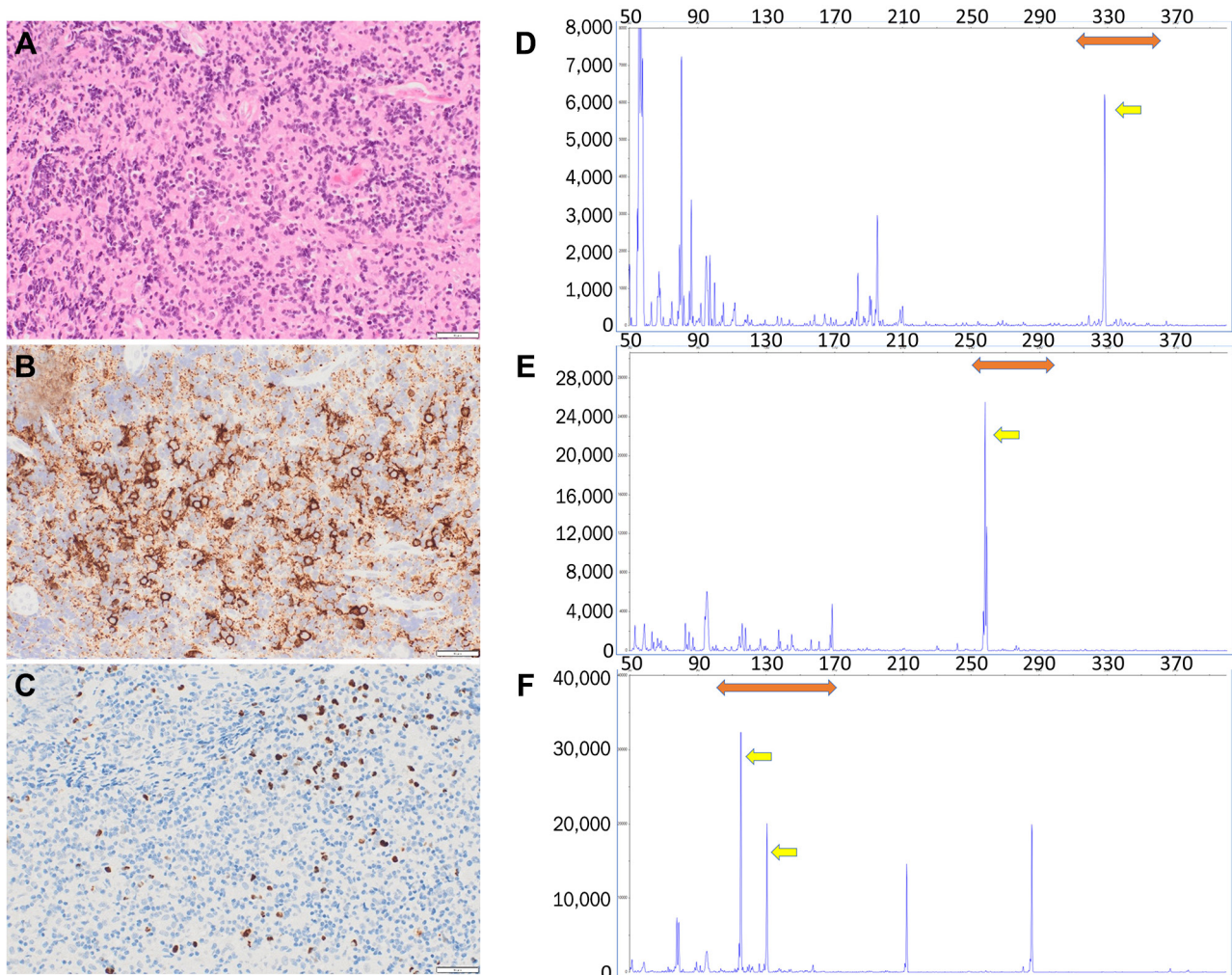


Figure 3. Pathological findings. (A) Hematoxylin and eosin staining reveals diffuse infiltration of lymphocytes without evident plasma cell differentiation (objective magnification, $\times 20$). (B) Immunohistochemical staining for cluster of differentiation 20 demonstrates scattered medium- to large-sized B cells (objective magnification, $\times 20$). (C) Epstein-Barr virus (EBV)-encoded small RNA in situ hybridization shows scattered EBV-positive cells (objective magnification, $\times 20$). Scale bar: 50 μm . (D-F) Immunoglobulin heavy-chain gene rearrangements were analyzed with GeneScan software and BIOMED-2 multiplex polymerase chain reaction (PCR). Fluorescently labeled PCR products targeting variable region–joining region recombination in framework regions FR1 (D), FR2 (E), and FR3 (F) were separated by capillary electrophoresis. The multiple clonal peaks (arrows) in the electropherograms indicate clonal immunoglobulin heavy-chain gene rearrangements, confirming oligoclonal B-cell proliferation. The double-headed arrow indicates the evaluation range. BIOMED-2: Biomedical and Health Research Programme - 2 (The BIOMED-2 network later evolved into the EuroClonality consortium).

cells; however, they were small. To assess the presence of clonal lymphoproliferation, we used the Gene Scan method (5) to perform a polymerase chain reaction-based analysis of immunoglobulin gene rearrangements. This analysis revealed oligoclonal growth patterns in the rearrangement of immunoglobulin heavy-chain genes, specifically in variable region–joining region recombination (Figure 3D-F).

EBV–encoded small RNAs in situ hybridization revealed scattered positive cells (Figure 3C). Based on these findings, we diagnosed orbital B-cell PTLD.

Because PTLD was strongly suspected, conservative RIT was initiated before pathological confirmation. Mycophenolate mofetil was discontinued, the tacrolimus dose was tapered from 2.5 to 1.2 mg/day, and

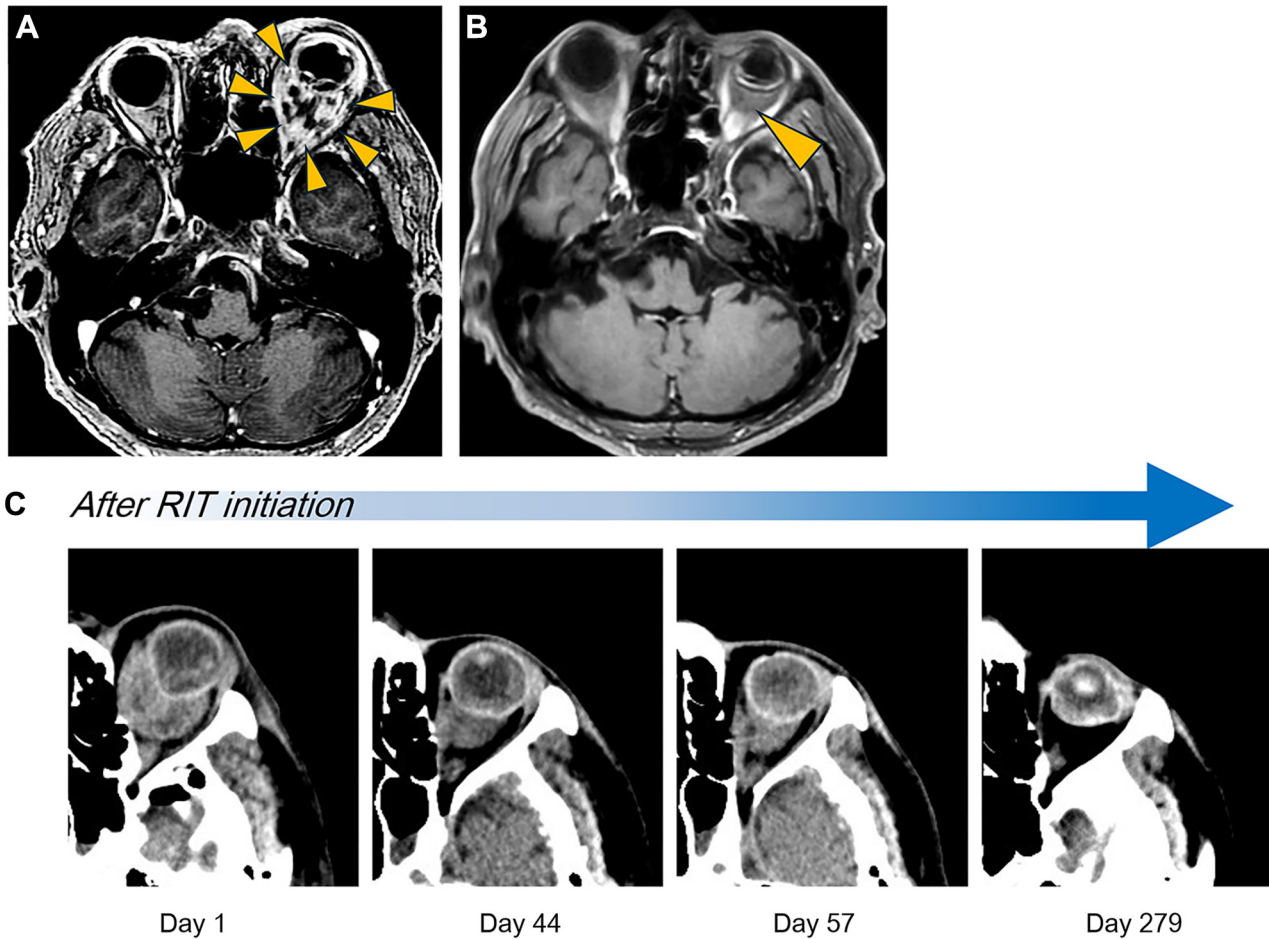


Figure 4. Serial magnetic resonance imaging (MRI) findings before and after reduction in immunosuppressant treatment (RIT). (A) MRI obtained 20 days before biopsy and initiation of RIT. (B) MRI obtained 65 days after biopsy, showing marked lesion regression. Day 0 indicates biopsy and initiation of RIT. (C) Serial computed tomography images showing changes in left orbital proptosis. From left to right, images were captured on days 1, 44, 57, and 279. Day 0 corresponds to the day biopsy was performed and RIT was initiated. Follow-up imaging showing gradual resolution of proptosis.

methylprednisolone was continued. The lesion regressed markedly without additional therapy (Figure 4A-C), and the patient remained clinically stable for more than 13 months without renal function deterioration.

Discussion

This case adds to the limited literature on orbital PTLD and suggests that RIT alone can achieve sustained remission even in diseases extending to critical orbital and intracranial structures.

To date, only 13 cases of orbital PTLD, including the present case, have been reported from 1984, when PTLD was first described (3, 6–14) (Table I). Many cases occur after kidney transplantation and often develop several years after transplantation, consistent with previous reports (15). EBV positivity is common, although EBV status does not appear to influence initial management. Clinical outcomes vary widely, ranging from remission to persistent visual impairment or death, illustrating that PTLD-directed therapies carry substantial risks in transplant recipients.

Table I. Reported cases of orbital post-transplantation lymphoproliferative disorder (PTLD).

Reference No. (Year)	Age/Sex	Transplanted organ (Years post-Tx)	Orbital site	EBER	Initial treatment	Outcome
(6) (1996)	4/F	Liver (3)	Superior orbit	NA	RIT+CHOP*	Remission
(3) (2002)	53/M	Lung (7)	Orbit–apex	+	Rituximab+RT	Remission**
(3) (2002)	61/M	Heart (3.5)	Bilateral orbit	NA	Rituximab+RT+RIT	Death
(3) (2002)	4/F	Heart and lung (2)	Anterior orbit	+	RIT+Rituximab	Remission
(7) (2006)	49/M	Kidney (10)	Bilateral lacrimal glands	+	RIT+Rituximab	Remission***
(8) (2007)	8/M	Bone marrow (0.25)	Conjunctiva	+	RIT+EBV-specific CTL	Death
(9) (2008)	45/F	Kidney (>2)	Lacrimal gland	+	Excision+RIT	Remission
(10) (2011)	50/M	Kidney (19)	Superior orbit+ optic nerve	-	Excision+CHOP+RIT	Death
(11) (2018)	37/F	Kidney (3.7)	Conjunctiva	-	RT+RIT	Remission
(12) (2020)	72/M	Kidney (10)	Bilateral lacrimal glands	+	RIT	Lost to follow-up (although Rituximab+CHOP was scheduled)
(13) (2021)	13/F	Cord blood (0.6)	Conjunctiva	+	RIT+Rituximab+ Curettag	Remission
(14) (2024)	11/F	Kidney (5)	Bilateral lacrimal glands	+	Cyclophosphamide+ Rituximab+RIT	Remission
Current case	62/M	Kidney (18)	Orbit+apex/ optic pathway	+	RIT alone	Remission (>13 months)

*CHOP regimen without cyclophosphamide. **Persistent visual impairment. ***Graft rejection requiring hemodialysis. CHOP: Cyclophosphamide, doxorubicin, vincristine, and prednisone; CTL: Cytotoxic T lymphocyte; EBER: Epstein-Barr virus-encoded small RNAs; EBV: Epstein-Barr virus; F: female; M: male; NA: not applicable; RIT: reduction in immunosuppressant treatment; RT: radiotherapy; Tx: transplantation.

Among the previously reported 12 cases, eight patients achieved remission, although visual symptoms often persisted, and three patients died. These fatal outcomes underscore the fact that PTLD treatment is not without risk in transplant recipients, and may be associated with considerable morbidity and mortality.

As the number of transplant recipients continues to increase and long-term survival improves (16, 17), the incidence of PTLD is also expected to increase. Late-onset orbital PTLD has been associated with poor prognosis (3), making early diagnosis and treatment particularly important. However, as orbital PTLD is extremely rare, no standard treatment strategy has been established. RIT is widely used as first-line therapy for PTLD (18) and may be sufficient in selected localized cases with careful follow-up. In the present case, RIT alone resulted in a durable response, avoiding the need for additional therapies and their associated toxicities.

These findings support a conservative, individualized, and stepwise approach, particularly for vulnerable transplant recipients.

Another important aspect of the present case was the diagnostic approach. To the best of our knowledge, this is the first report of orbital PTLD diagnosed using a transcranial biopsy. This approach allows safe and accurate tissue sampling while minimizing the risk of injury to critical orbital structures (19). Therefore, careful selection of diagnostic and therapeutic strategies is essential for managing this rare condition.

Conclusion

Further accumulation of similar cases may help to clarify which subsets of patients with localized PTLD can be effectively managed using a conservative, stepwise approach, while minimizing treatment-related toxicity.

Conflicts of Interest

The Authors declare no conflicts of interest, such as financial, personal, or institutional relationships that could be perceived as influencing the work reported in this manuscript.

Authors' Contributions

Conceptualization: TM, YH, TH. Methodology: TM, YH, TH. Investigation: TM, YH, KK, Hirofumi Miyahira, FK, MT, NW. Data curation: TM, YH, KK, Hirofumi Miyahira, FK, MT, NW. Writing – original draft: TM, TH. Writing – review & editing: All authors. Supervision: TH. Project administration: TM, TH. All authors contributed to the critical revision of the manuscript. All authors have approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Acknowledgements

The Authors would like to express our sincere gratitude to all the hospital staff involved in the care of our patient. We thank Mr. Kaito Koki, a member of the technical staff in the Department of Pathology and Oncology, Graduate School of Medicine, University of the Ryukyus, for his valuable technical assistance. The Authors are also grateful to Enago (www.enago.jp) for the English language editing and to Editage (www.editage.jp) for their assistance in creating the Figure 1 for this paper.

Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

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