Clinicopathological Findings and Treatment Outcomes of Primary Vitreoretinal Large B-cell Lymphoma: A Case Series.

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Abstract

Objective: To report the clinicopathological findings, treatment modalities, and outcomes of primary vitreoretinal large B-cell lymphoma (PVR-LBCL).

Methods: This retrospective study recruited newly diagnosed PVR-LBCL between January 1, 2013, and December 31, 2022 at Thammasat University Hospital. We reviewed clinical presentations, diagnostic findings, treatment approaches, and outcomes.

Results: Nine PVR-LBCL cases (16 eyes) were elderly (median age 73 years, range 59-78 years), female predominant (n = 6, 67%), and bilateral involvement (n = 7, 78%). All cases presented with blurry vision, while only 3 (33%) reported floaters. Fundus examination revealed vitreous haze (n = 9, 100%), vitreous cells formed sheets (n = 8, 89%) and sub-retinal lesions (n = 5, 56%). The median time from symptom onset to pathologic diagnosis was 8 months (range 1-15 months). One patient transferred after diagnosis and did not have staging. The central nervous system (CNS) involvement was concurrent at diagnosis in 2 cases. The oldest patient did not receive treatment. The initial treatment modalities included ocular radiation (RT), intravitreal (IVT) methotrexate (MTX) or rituximab, whole brain RT, and systemic chemotherapy. The treatment complications were radiation-related cataract and maculopathy (n = 2), and keratopathy (n = 1). The outcomes were refractory disease with CNS progression (n = 1), complete remission (CR) then CNS relapse (n = 3), CR then ocular relapse (n = 1), and CR without event (n = 2).

Conclusion: PVR-LBCL presents a significant challenge in diagnosis and its management. Various modes of treatment were effective, but nearly half relapsed and died.

Keywords: Primary vitreoretinal large B-cell lymphoma, Intravitreal Rituximab, Intravitreal Methotrexate, Ocular radiation

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Introduction

Primary vitreoretinal large B-cell lymphoma (PVR-LBCL) is a rare but aggressive intraocular malignancy. Its non-specific symptoms often lead to delayed diagnosis, frequently disseminating to the central nervous system (CNS), resulting in poor prognosis.[1] The incidence of PVR-LBCL reported to be 2% of all uveitis patients.[2] PVR-LBCL predominantly affects individuals over 40, with a peak incidence between 50-70 years. No significant gender difference has been established.[3,4] No apparent differences in incidence have been reported across racial or geographic populations.

The clinical presentation of PVR-LBCL is often insidious and non-specific. Common symptoms include blurry vision and floaters.

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The average time from symptom onset to diagnosis ranges from 6 to 8 months.[1,3,4] As the disease progresses, cases may present with vitritis and/or retinitis.[1,3-6]

Clinical features of PVR-LBCL include (1) steroid-resistant uveitis, (2) vitritis with vitreous clump, (3) creamy yellow sub-RPE lesions, and (4) retinal vasculitis or haemorrhages. These features are particularly indicative when bilateral or accompanied by neurological symptoms such as headaches, weakness, seizures, or memory impairment.[1,3,4,7] A significant proportion of cases (60-90%) develop CNS involvement, which may occur at initial diagnosis or within months to 2-3 years after ocular presentation.[1,3-6]

The mean time between first ocular symptoms and diagnosis was 7 ± 7 months (range 1-24).[8] Factors associated with delayed diagnosis were low clinical suspicion of PVR-LBCL, low incidence of lymphoma, masquerading as chronic uveitis, and prior use of corticosteroids.[9,10] In cases of uveitis masquerade syndrome, the use of steroid therapy delays the correct diagnosis of lymphoma and result in vitritis resistant to corticosteroids.[10]

Definite diagnosis of PVR-LBCL requires vitrectomy and/or retinal biopsy for cytology (morphology) and flow cytometry (immunophenotype) or immunohistochemistry in identifying neoplastic large B-cells.[11] The pathological diagnosis of PVR-LBCL is difficult because limited amount of vitreous sample, neoplastic cell fragility, and demanding laboratory techniques.[12,13] Moreover, prior steroid use causes apoptosis of the lymphoma cells leading to poor morphology and decrease the number of viable cells.[12] Intraocular lymphoma cells are fragile and require prompt processing. Delay in transfer of samples to the laboratory and the use of fixative materials can negatively affect cell structure, morphology and immunoreactivity.[12,13]

PVR-LBCL management requires a multidisciplinary team involving ophthalmologists, oncologists, neurologists, and radiologists. The disease's poor prognosis and high recurrence rate necessitate aggressive treatment strategies.[1,3,4,14] The primary treatment modalities include intravitreal chemotherapy, systemic chemotherapy, and radiation therapy.

Given the complexities surrounding PVR-LBCL, questions arise regarding its clinical characteristics, difficulty in diagnosis, the clinical outcomes of various treatment modalities, and the associated treatment side effects. This study aims to address these questions to enhance our understanding of the disease in resource-challenged settings such as Thailand.

Methods

This retrospective observational study consecutively recruited patients diagnosed with PVR-LBCL at Thammasat University Hospital, Thailand, between January 1, 2013 and December 31, 2022. The diagnosis was based on diagnostic criteria from WHO Classification of Tumours Editorial Board 2023: (1) large B-cell lymphoma primarily confined to the vitreous or retina at presentation and (2) the exclusion of secondary involvement by systemic lymphoma. The Ethics Committee of Thammasat University (Faculty of Medicine) approved the study protocol.

We collected data from medical records, including patient demographics (age, gender, underlying diseases, immune status), clinical presentation (symptoms, affected eye, date), ocular signs (visual acuity, keratic precipitates, anterior chamber cells, vitreous cells/haze, retinal lesions, date), pathological examination (vitreous cytology, histopathology, flow cytometry, immunohistochemistry, date), and ocular imaging (i.e., fundus photography, optical coherence tomography, date). We gathered results from brain MRI/CT and/or cerebrospinal fluid analysis for CNS involvement, and chest CT, whole abdomen CT, and bone marrow biopsy for staging.

Treatment modalities included IVT MTX or rituximab, ocular/brain radiation, and high dose MTX and Ara-C. Disease monitoring post treatment based on any of ocular examination, imaging, and pathologic examination, and categorized outcomes into complete remission (disappearance of tumor for at least 1 month), relapse (new ocular or CNS lesion following remission), and refractory (no response). Time to diagnosis was the duration between date of symptoms and date of diagnostic vitrectomy. Remission duration was between last date of initial treatment to date of last fundus examination without lesion. Time to event was the duration between last date of initial treatment to date of the earliest occurrence of refractory disease or progressive disease. We also recorded

treatment-related side effects, events, and duration of follow-up.

Statistical Analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Continuous variables were expressed as means and medians with interquartile ranges. Categorical variables were reported as frequencies and percentages.

Results

Nine cases (16 eyes), six females (67%) and three males (33%), had a median age of 73 years (range: 59-78 years). All cases were immunocompetent and HIV-negative. Bilateral involvement presented in 7 cases (78%).

Symptoms and signs

All cases complained of blurry vision, but only 3 cases (33%) reported floaters. Non-specific signs included anterior chamber cells observed in 4 cases (44%), keratic precipitates observed in 6 cases (67%), and retinal vasculitis observed in 2 cases (22%). Suggestive signs for PVR-LBCL included vitreous cells and subretinal lesions. Vitreous haze were found in all cases and vitreous cells organizing into sheets was the most common ocular finding, present in 8 cases (89%) (Figure 1). Subretinal lesions were observed in 5 cases (56%) (Figure 2). Optical Coherence Tomography (OCT) revealed subretinal infiltrates in 5 cases (56%), appearing as hyperreflective material between the retinal pigment epithelium (RPE) and Bruch's membrane (Figure 3).

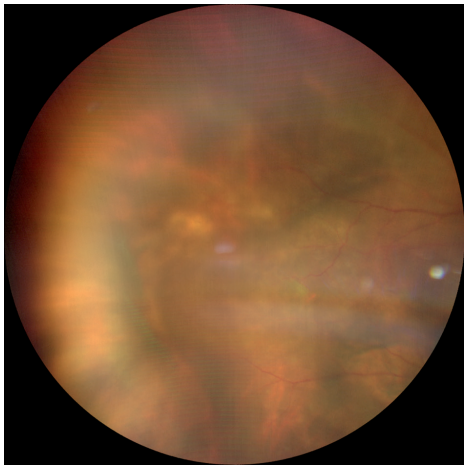

Figure 1: Vitreous haze with cells organizing into sheets and subretinal lesions.

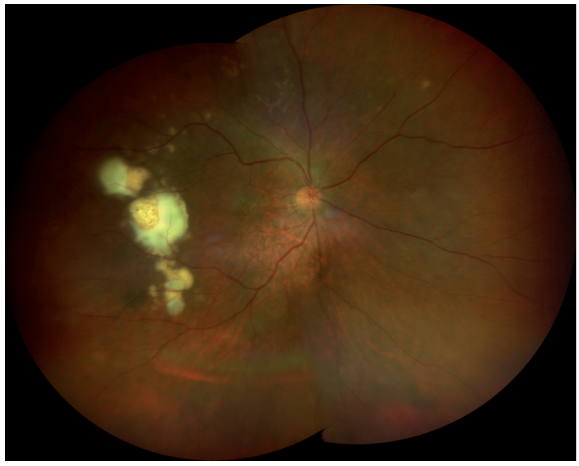

Figure 2: Multiple subretinal lesions (Leopard spots) and subretinal fibrosis.

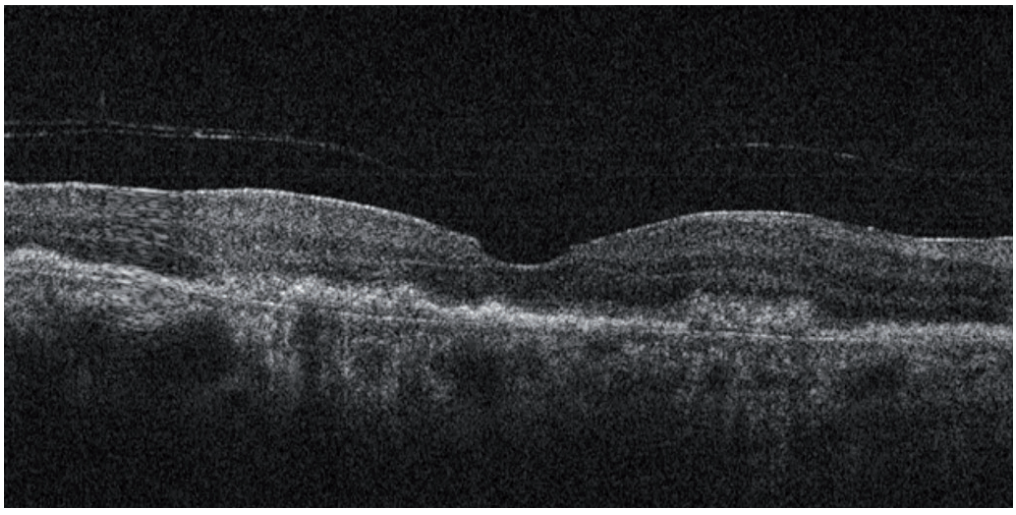

Figure 3: Optical Coherence Tomography revealed hyperreflective material between the retinal pigment epithelium and Bruch's membrane from subretinal tumor.

Diagnosis

The median time to diagnosis from symptom onset was 8 months (range: 1-15 months). Diagnostic vitreous biopsy via pars plana vitrectomy (PPV) was performed in all cases. The initial diagnostic yield from the first PPV was limited, with 5 cases (56%) showing positive cytology for malignant large atypical cells from the first procedure. The tumor cells were scant and fragile. A second PPV was required in 4 cases (44%), including 2 cases (22%) who needed additional retinal biopsy for definitive diagnosis.

Flow cytometry in 8 diagnostic specimens reported aberrant B-cell populations in 5 cases, negative in 2 cases, and insufficient cellularity in 1 case. Immunohistochemistry on 5 diagnostic specimens revealed tumor expressing B-cell marker (CD20) in 5/5 cases.

CNS involvement

One patient transferred before staging. Brain involvement was detected in 6 from 8 cases (75%), with 2 cases (25%) showing CNS involvement at initial diagnosis, 1 case as progression in refractory disease, and 3 cases (37.5%) as relapse. The median time to CNS involvement after diagnosis in 4 patients was 27 months (range: 12-54 months) (Table 1).

Treatment Approaches

Seven patients started treatment within median timeframe after diagnosis. One patient transferred to another hospital right after diagnosis. Another patient decided not to treat due to old age (78 years old) who showed no disease progression and died after colonic adenocarcinoma with brain metastasis.

Treatment strategies were individualized based on disease extent and patient factors:

1. **Concurrent CNS involvement** (cases 4, 5): Received whole brain radiation therapy
2. **Refractory disease** (case 3): Initially treated with intravitreal therapy and ocular radiation, later developed CNS progression
3. **Complete remission then CNS relapse** (cases 1, 8, 9): Various initial treatments followed by CNS progression
4. **Complete remission without events** (case 6): Maintained sustained response

Local Treatment

Intravitreal chemotherapy was administered in 5 cases (56%), with rituximab used in 3 cases (33%) and methotrexate in 3 cases (33%). One case (11%) received intravitreal rituximab and developed granulomatous panuveitis after injection which spontaneously resolved. After that, treatment switched to intravitreal injection of methotrexate.

The regimen for intravitreal methotrexate was administered methotrexate (400 mcg/0.1 ml) twice weekly injections for 4 weeks, followed by weekly injections for 8 weeks, and then monthly injections for one year. The regimen for intravitreal rituximab was rituximab (1 mg/0.1 ml) every week injection for 4 times. While rituximab exhibits lower ocular tissue toxicity,[19] we considered intravitreal injection of rituximab for the first option of intravitreal chemotherapy. However, if the patients cannot afford rituximab due to financial issue or had side effects, then we gave intravitreal injection of methotrexate. Ocular remission after intravitreal chemotherapy was found in 5 cases (83%). One case was refractory to intravitreal injection of methotrexate and subsequently developed CNS involvement.

Radiation therapy was utilized in 5 cases (56%). Ocular radiation (30-35 Gy in 15 fractions) was administered in 4 cases (44%), and 3 cases (33%) received whole brain radiation. Two cases (22%) received both ocular and whole brain radiation. All cases with radiation achieved remission.

Case number 3 had bilateral involvement, received ocular radiation in more severe eye and intravitreal chemotherapy in less severe eye. She developed granulomatous panuveitis in eye treated with intravitreal rituximab. We decided to discontinuation of rituximab and then switch to intravitreal methotrexate. The more severe eye treated with ocular radiotherapy showed complete resolution but developed maculopathy while the less severe eye treated with intravitreal therapy showed refractoriness.

Systemic Treatment

One case (11%) received intrathecal chemotherapy, consisting of high-dose methotrexate and cytarabine.

Treatment Outcomes

From 7 patients who received treatment, six cases (67%) achieved remission, with 3 cases (33%) maintaining remission without relapse throughout the follow-up period. Three cases (33%) experienced disease relapse after remission, with a median time to relapse of 17 months (range: 5.5-52.8 months). One case (17%) was refractory with subsequent CNS relapse. One case (17%) denied any treatment and had no ocular/CNS progression in 84.9 months follow-up. One case (17%) elected to continue treatment at another hospital after diagnosis.

Treatment-related complications included radiation-related brown cataract formation in 2 cases (22%, 2 eyes), radiation-related maculopathy (VA: no pl) in 2 cases (22%, 2 eyes) and methotrexate-related keratopathy in 1 case (11%). All eyes with radiation-related maculopathy had tumors in the macula before radiation treatment. One case (11%) developed granulomatous panuveitis following rituximab injection.

The median follow-up time was 26.8 months (range: 6.2-96.1 months). At the final follow-up, 5 cases (56%) remained alive, 3 cases (33%) had died from CNS lymphoma.

Table 1: Summary of demographics, clinical information, laboratory findings, treatment approaches, and outcomes.

Case	Gender	Age (year)	Blurry vision duration	VA	Suggestive ocular signs & Laterality	Ocular surgery	Cytology	Flow cytometry	Time to diagnosis (month)	CNS involvement at staging	Initial treatment	Outcome & management	Side effect	Challenge
1	Female	77	1 month	HM OD HM OS	Vitreous haze **OU**, subretinal lesion OD	1st PPV OS	Negative	Negative	10	Negative	-Ocular RT OD at 3-4 months after diagnosis -IVT-MTX OS (4 doses) at 3-4 months after diagnosis	Complete remission CNS Relapse (brain MRI) at 12 mo post diagnosis then loss to follow-up	OD - Brown cataract and maculopathy	PPV *2 Retinal biopsy CNS relapse
						2nd PPV with retinal biopsy OD	Vitreous – Negative	Negative						
							Retina – Few large cells	CD20+, CD19+, no surface κλ						
2	Female	59	2 months	20/40 OD 20/40 OS	Vitreous haze **OU** (cells organized into sheets)	1st PPV OS	Negative	N/A	8	N/A	N/A	NA	N/A	PPV *2 times
						2nd PPV OD	Rare large cells	CD20+ (dim), CD19+, κ+						
3	Female	73	3 months	20/70-1 OD 20/100 OS	Vitreous haze **OU** (cells organized into sheets OD), subretinal lesion OU	PPV OD	Rare medium to large cells	CD20+, CD19+, κ+	6	Negative	Ocular RT OD at 4-5 months after diagnosis	OD – Resolved OS – Progression (fundus -diffuse retinal yellow lesion) at 7 mo from diagnosis – Rx IVT-Rituximab 4 doses and IVT-MTX 8 doses OS – Progression (fundus – active lesion) at 9 mo post last IVT-Rituximab CNS involvement (brain MRI) at 18 mo post diagnosis - Rx WB RT Death at 23 mo post diagnosis	OD – Dense cataract and maculopathy OS - Granulomatous panuveitis	Progression to OS and CNS Death
4	Female	75	1 week	FC 1 ft OD 20/50 OS	Vitreous haze **OU** (cells organized into sheets), subretinal lesion OD	1st PPV OS	Few small to medium B cells CD20+	Negative	2	Positive (brain MRI)	-IVT-Rituximab (4 doses) -Ocular RT OU -Whole brain RT	Complete remission 29 mo Alive at 32 months post diagnosis	None	PPV *2 times Retinal biopsy
						2nd PPV & retinal biopsy OD	Vitreous – Negative	Negative						
							Retina – Some large B cells CD20+	N/A						

Table 1: Summary of demographics, clinical information, laboratory findings, treatment approaches, and outcomes. (Cont.)

Case	Gender	Age (year)	Blurry vision duration	VA	Suggestive ocular signs & Laterality	Ocular surgery	Cytology	Flow cytometry	Time to diagnosis (month)	CNS involvement at staging	Initial treatment	Outcome & management	Side effect	Challenge
5	Female	61	3 months	5/200 OD	Vitreous haze **OD** (cells organized into sheets)	PPV OD	Rare large cells CD20+	Insufficient cellularity	12	Positive (brain MRI)	- IT MTX-cytarabine - Systemic HD-MTX-AraC - Whole brain RT include orbits	Remission 7 mo OD - Ocular relapse (Vitreous OD cytology at 9 mo from post end of RT Last status - loss to follow-up	None	Ocular relapse
6	Male	59	1 week	20/40 OD	Vitreous haze **OD** (cells organized into sheets)	PPV OD	Rare large cells CD20+	N/A	1	Negative	IVT-Rituximab OD (4 doses)	Remission 105 mo	None	None
7	Male	78	2 weeks	20/40 OD 20/70 OS	Vitreous haze **OU** (cells organized into sheets)	1st PPV OD	Degeneration	Negative	4	Negative	No treatment	No progression for 88 mo after diagnosis	N/A	No Rx – No progression
						2nd PPV OS	Some large cells CD20+	Increased B cells (CD20+/CD19+)						
8	Male	66	1 year	20/30 OD 20/30 OS	Vitreous haze **OU** (cells organized into sheet)	PPV OS	Few large cells	CD20+/CD19+	13	Negative	IVT-Rituximab OS (4 doses)	Remission 61 mo CNS relapse (brain MRI) at 54 mo post IVT-Rituximab Rx - Palliative Death at 67 mo post diagnosis	None	CNS relapse & death
9	Female	77	2 months	20/50+2 OD 20/70+1 OS	Vitreous haze **OU** (cells organized into sheets), white subretinal lesion OS	PPV OS	Some large B cells CD20+	Negative	15	Negative	Ocular RT OU	Remission 12 mo OD - Ocular relapse at 12 mo post end of RT - Rx: IVT-Rituximab OD 7 doses CNS relapse (brain MRI) at 35 mo post diagnosis Death 60 mo post diag	Keratopathy OD	CNS relapse & death

Note: Case 2 decided to establish care in another institution.

Abbreviations:

HM Hand motion, FC Counting finger, CMT Chemotherapy, IT Intrathecal, IVT Intravitreous, MTX Methotrexate, N/A Not available, OD Oculus Dexter (right eye), OS Oculus Sinister (left eye), OU Oculus Uterque (both eyes), PPV Par Plana Vitrectomy, RT radiation

Outcome duration: time between initial treatment to event

Follow-up time: time between last date of FU to 1st OPD eye visit

Discussion

Our study revealed a demographic profile with median age of 73 years and female predominance (67%), consistent with previous reports.[1,3] High bilateral involvement (78%) underscores the importance of thorough examination in both eyes.[3] Suggestive clues for PVR-LBCL include older age with new-onset uveitis, vitreous cells organized into sheets, or sub-RPE lesions, which were observed in all cases. The "aurora borealis" sign, characterized by vitreous cells organizing into sheets or clumps that create a swirling, luminescent appearance reminiscent of the northern lights, was present in 89% of cases, providing the most common valuable diagnostic clue.[7] Sub-RPE lesions were present in 56% of cases.

Diagnostic Challenges

PVR-LBCL presents substantial diagnostic challenges. The diagnostic yield of first vitreous biopsy in our series was limited (56% positive from first procedure), highlighting the need for repeated sampling in some cases. Four cases (44%) required a second vitreous biopsy, and 2 cases (22%) needed additional retinal biopsy for definitive diagnosis.

Diagnostic challenges in our cases arose from several factors affecting sample quality. First, the fragile nature of tumor cells, which degenerated rapidly after collection,[15,16] compromised cytological evaluation. Second, sampling techniques, particularly the cutting speed during vitrectomy, may have caused mechanical destruction of these delicate cells.[17] Third, the heterogeneous distribution of malignant cells within the vitreous cavity likely contributed to sampling variability, with some areas containing few or no diagnostic cells.[18] Fourth, the small sample volume obtainable during vitreous biopsy limited cellular yield.

It's noteworthy that all cases in our study had not received any steroid treatment prior to diagnostic sampling, eliminating steroid-induced lympholysis as a potential cause of false-negative results, which has been reported in previous studies.[19] This underscores the inherent challenges in PVR-LBCL diagnosis even under optimal conditions without the confounding effect of prior treatment.

Recommendations for Specimen Collection and Processing

Based on our experience and the challenges encountered, we recommend the following protocol for specimen collection and preservation:

1. **Vitrectomy technique:** Use lower cutting speeds (≤ 1,500 cuts per minute) to minimize mechanical trauma to fragile lymphoma cells[16,17]
2. **Immediate processing:** Transport specimens to the pathology laboratory immediately, ideally within 30 minutes of collection
3. **Fixation:** For cytology, use cytospin preparation with air-dried slides for Giemsa staining and 95% alcohol-fixed slides for immunocytochemistry. For tissue specimens, use formalin fixation for histopathology
4. **Sample allocation:** Divide the vitreous specimen for multiple diagnostic modalities: cytomorphology, flow cytometry, and if sufficient, molecular studies
5. **Communication:** Coordinate with the pathology team prior to surgery to ensure proper handling and processing protocols

Limitations in Diagnostic Approach

Several limitations in diagnostic PPV were identified in our setting:

- The small sample volume obtained during vitrectomy, particularly in cases with minimal vitreous involvement
- Limited availability of immediate flow cytometry, which occasionally resulted in inadequate cell preservation

The median time to diagnosis in our study was 8 months.

Treatment Approaches and Outcomes

There is no standard treatment protocol for PVR-LBCL. Intravitreal chemotherapy was used in 56% of our cases, with rituximab (44%) being utilized more frequently than methotrexate (22%), consistent with current trends.[19] Intravitreal agents offer the advantage of avoiding systemic side effects, though refractoriness was observed in one case (11%).

The number of intravitreal injections varied by agent and response: intravitreal rituximab was administered as 4 weekly doses in most cases (with one patient receiving 7 doses for ocular relapse), while intravitreal methotrexate followed a protocol of twice-weekly injections for 4 weeks, then weekly for 8 weeks, and monthly maintenance.

In severe ocular infiltration, ocular radiation proved highly effective, as observed in 44% of our cases. Case number 3 provides particular insight into treatment efficacy. This 73-year-old female with bilateral involvement received intravitreal rituximab combined with methotrexate in one eye and ocular radiation in the other. The eye treated with ocular radiotherapy showed complete resolution, while the eye treated with intravitreal therapy showed refractoriness and the patient later developed CNS involvement, suggesting that ocular radiotherapy provided better local control in this case.

Case number 7 had vitreous haze (cells organizing into sheets) in both eyes and underwent diagnostic PPV in both eyes. Ocular examination showed neither vitreous haze nor subretinal lesions after the operation. This case did not receive any treatment. The disease outcome was no progression after 84.9 months of follow-up, suggesting this might have been a more indolent form of the disease.

Treatment-Related Complications

Treatment-related complications in our series included radiation-related brown cataract formation (22%), radiation-related maculopathy (22%), and methotrexate-related keratopathy (11%). Radiation-related maculopathy and blindness can occur when the tumor involves the macular area. Therefore, ophthalmologists should be aware of this potentially vision-threatening complication, especially when the lesion involves the macula.

One case (case 3) developed granulomatous panuveitis following intravitreal injection of rituximab, which spontaneously resolved. This represents an uncommon but important complication to recognize. After this reaction, treatment was switched to intravitreal methotrexate for that eye.

CNS Involvement and Surveillance

CNS involvement was common (67% of cases), highlighting the need for comprehensive neurological evaluation.[6] In our series, CNS involvement was diagnosed using brain MRI in all cases, with enhancement patterns typical of CNS lymphoma. Two cases (22%) had CNS involvement at initial diagnosis, and 4 developed CNS relapse during follow-up.

Based on our experience and current literature, we recommend the following surveillance protocol for CNS involvement:

- Brain MRI at initial diagnosis for all PVR-LBCL patients
- Regular follow-up brain MRI every 6-12 months for the first 3 years, then annually
- Prompt neurological evaluation and brain imaging if any neurological symptoms develop (headaches, seizures, weakness, cognitive changes, or personality changes)
- Consider cerebrospinal fluid analysis in selected cases with high suspicion for CNS involvement but negative MRI

The high relapse rate with a median time to relapse of 27 months (range 12-54 months for CNS relapse) emphasizes the need for vigilant monitoring. Patients who experienced CNS relapse typically presented with changes detected on brain MRI during routine surveillance, though some developed neurological symptoms. The median time from ocular diagnosis to CNS relapse was 27 months, underscoring the importance of long-term follow-up.

Survival outcomes considerably varied, with 29% of cases in complete remission and alive at the end of follow-up, while 33% died from CNS lymphoma progression. The development of CNS involvement, either at diagnosis or as relapse, was associated with poor prognosis.

Despite the limitations of this retrospective study with a small sample size, our findings contribute to the emerging literature on PVR-LBCL, especially in Thai populations. Our demographic and clinical findings are consistent with another recent Thai study from the Northern region, which also reported similar patterns of

disease presentation and diagnostic challenges.[20] The multiple surgeries required for challenging issues in diagnosis, prevention of relapse and the management of refractory disease highlight ongoing clinical challenges. Future research should explore less invasive diagnostic techniques and novel targeted therapies.

In conclusion, PVR-LBCL is the diagnosis challenge and management requires individualized treatment approaches, multidisciplinary collaboration, and vigilant monitoring for both ocular and CNS disease progression. The diagnostic yield of first vitreous biopsy is limited, and multiple sampling procedures may be necessary. Treatment efficacy varies, with ocular radiation providing good local control but potential vision-threatening side effects. The high rate of CNS involvement and disease relapse underscores the aggressive nature of this malignancy.

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