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Case Report

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A Case of Bilateral Sequential Central Retinal Vein Occlusion Secondary to Chronic Myeloid Leukemia

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Abstract: This article reports a complex case where bilateral central retinal vein occlusion (CRVO) occurred successively in both eyes due to multiple factors including chronic myeloid leukemia, underlying diseases, and drug treatment. The article analyzes the ocular manifestations, treatment process, and prognosis of this case, aiming to emphasize that clinicians should break away from the single-etiology thinking and attach importance to the integrated assessment of hematological abnormalities, underlying diseases, and drug effects. By leveraging multimodal imaging techniques and strengthening multidisciplinary collaboration, precise intervention for the disease can be achieved.

Keywords: Central Retinal Vein Occlusion; Leukemic Retinopathy; Multimodal Ocular Imaging; Multidisciplinary Clinical Collaboration; Chronic Myeloid Leukemia; Case report

1 Introduction

Chronic myeloid leukemia (CML) is a three-phase tumor characterized by the BCR-ABL fusion gene and abnormal proliferation of myeloid cells [1], accounting for approximately 15% of adult leukemias [2]. Most cases of CML have an insidious onset, but up to 90% of patients may present with ocular manifestations[3]. In CML patients, the presence of fundus changes not only indicates hematological abnormalities, but may also foreshadow the development of venous occlusion-related lesions such as retinal hemorrhage; among these, CRVO is one of the major causes of vision loss in patients[4-5].

Currently, case reports of CML-associated RVO remain relatively rare. This report describes a case of CML complicated by bilateral CRVO occurring sequentially due to the superimposition of multiple factors. The aim is to elucidate the multifactorial synergistic pathogenesis of retinal vascular lesions in the context of complex systemic diseases, and to emphasize the need to move beyond a single-cause mindset in clinical practice. This involves strengthening integrated multifactorial assessment and multidisciplinary collaboration to achieve dual interventions targeting both the underlying cause and symptomatic treatment.

2 A case report

A 44-year-old man presented to our hospital's outpatient clinic on July 1, 2024, complaining of "blurred vision in the right eye accompanied by a sensation of obstruction for one week." One week prior to admission, the patient noticed blurred vision in his right eye accompanied by a sensation of obstruction in his field of vision; however, he did not take it seriously. During this period, the sensation of obstruction gradually worsened, prompting him to seek medical attention. Ophthalmological

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examination: Right eye: VOD: 0.02, Corrected visual acuity: +3.00DS/-0.25DC*42° → 0.02, NCT: 19 mmHg; Left eye: VOS: 0.8, Corrected visual acuity: 0.25DS/-0.25DC*122° → 0.8, NCT: 27 mmHg. No significant abnormalities were observed in the anterior segments of both eyes. Right eye fundus: clear optic disc margin, pale red color, C/D ≈ 0.53, tortuous arteriovenous course, A/V ≈ 1:3; flame-shaped hemorrhages throughout the retina, flat retina, and marked elevation and edema in the macular area; left eye fundus showed no significant abnormalities (Fig. 1, 2). Right eye OCT showed: disappearance of the fovea, marked elevation and edema in the macular area, and numerous moderate-to-low-intensity patchy reflective signals between the neuroepithelial layer and the pigment epithelium (Fig. 3). Fundus Fluorescein Angiography (FFA) examination of both eyes revealed: extensive patchy hyperfluorescence and areas of non-perfusion in both eyes (Fig. 4). The patient was previously diagnosed with CML during a visit to the hematology department of another hospital in September 2023. The results of molecular pathology testing at that hospital, specifically quantitative detection of the BCR::ABL1(p210) fusion gene (using PCR-fluorescent probe method), showed: BCR::ABL1(p210) fusion; gene (+); BCR::ABL1(p210): 4.36×10˜1; BCR::ABL1(p210)/ABL (IS): 0.0178. Currently taking “Olverembatinib 10 mg, 4 tablets every other day” regularly. History of “Type 2 diabetes” for over 3 years; currently taking “Sitagliptin and metformin tablets 50 mg, once daily,” and “ History of “hypertension” for over 6 months; currently taking “Sakarbatril and Valsartan Sodium Tablets 100 mg once daily, Nifedipine Extended-Release Tablets 30 mg once daily.” Blood glucose and blood pressure are usually well-controlled; blood glucose measured on admission: 9.0 mmol/L; blood pressure: 121/87 mmHg. No significant abnormalities were observed in infection or immune markers. No history of surgery, trauma, or hereditary eye diseases. Considered diagnoses:(1) Central retinal vein occlusion of the right eye (2) Macular edema of the right eye (3) Chronic myeloid leukemia (4) Hypertension(5) Type 2 diabetes. Treated with intravitreal injection of ranibizumab 0.5 mg/0.10 mL in the right eye. One month postoperatively, the patient received an intravitreal injection of dexamethasone implants (Odis, 0.7 mg/0.7 mg) in the right eye for anti-inflammatory treatment, followed by regular monthly injections of ranibizumab. The patient’s overall ocular condition remained stable, with visual acuity maintained at 0.15 logMAR, and no significant increase in retinal hemorrhage was observed. After five regular injections, during the follow-up visit at 8 months, the right eye was found to have tortuous and distorted arterial and venous vessels, with distal vessels exhibiting white sheaths. Scattered punctate and patchy hemorrhages were observed on the retinal surface, and uncorrected visual acuity had decreased to 0.1. To prevent further worsening of ischemia and avoid secondary visual impairment, panretinal photocoagulation was performed (Figure 5). One month later, a single maintenance dose of ranibizumab was administered, and the patient responded well. Subsequently, the patient was managed on a PRN (as needed) basis, with the next dose administered 4 months later. The right eye has cumulatively received 10 intravitreal anti-VEGF injections. The use of ranibizumab in this patient’s eye yielded ideal results, with a sustained and stable effect. At 2 months, the central macular thickness (CMT) recorded by OCT in the right eye

decreased from 1147 ± 243 μm to 372 ± 138 μm. CMT was 307 ± 27 μm at 4 months, 516 ± 139 μm at 6 months, and 260 ± 55 μm at 1 year; by this time, the patient had regained 0.15 logMAR visual acuity in the right eye. However, one month after the last injection (September 4, 2025), the patient reported worsening blurred vision in the right eye. After admission and further evaluation, the patient was diagnosed with neovascular glaucoma (NVG) in the right eye and underwent pars plana vitrectomy (PPV), ultrasound cycloplasty (UCP), among other treatments; however, postoperative follow-up revealed poor visual recovery and inadequate control of intraocular pressure.

On November 27, 2024, the patient was admitted with a chief complaint of "blurred vision in the left eye for 1 week, worsening over the past day." The patient's uncorrected visual acuity in the left eye was 0.2, and intraocular pressure (IOP) was 13.5 mmHg. Fundus examination revealed tortuous and distorted retinal vessels in the left eye, with flame-shaped hemorrhages in the retinal vessels and punctate and patchy hemorrhages throughout the retina, as well as macular edema (Figure 6), OCT (Figure 7) and OCTA (Figure 8) results supported the diagnosis. The patient was treated with an intravitreal injection of ranibizumab 0.5 mg/0.10 mL. In the second month, the right eye also received an intravitreal injection of dexamethasone implant (Aodisi) 0.7 mg/0.7 mg for anti-inflammatory therapy. Subsequently, the patient received monthly injections of ranibizumab for a total of five sessions. During this period, the patient's fundus condition remained stable with no significant worsening. Treatment was subsequently switched to a PRN regimen, and the left eye also received a cumulative total of 10 intravitreal anti-VEGF injections. The patient's visual acuity in the left eye ultimately improved to 0.25 logMAR.

Fig.1

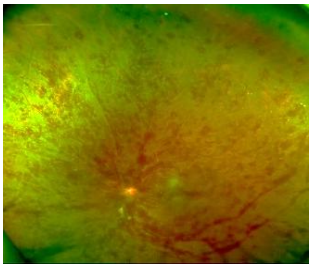


Fig.1: The fundus of the right eye shows tortuous and distorted arterial and venous patterns, flame-shaped hemorrhages throughout the retina, a flattened retina, and marked elevation and edema in the macular region;

Fig.2

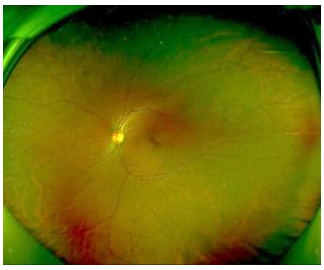


Fig.2: The fundus of the left eye is largely normal.

Fig.3

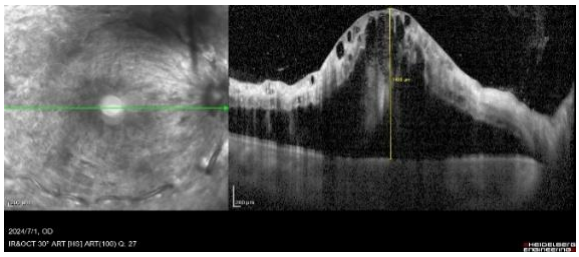


Fig.3: OCT: The fovea of the right eye is absent, with marked elevation and edema in the macular region; extensive patchy low-to-moderate reflectivity signals are observed between the neuroepithelial layer and the pigment epithelium.

Fig.4

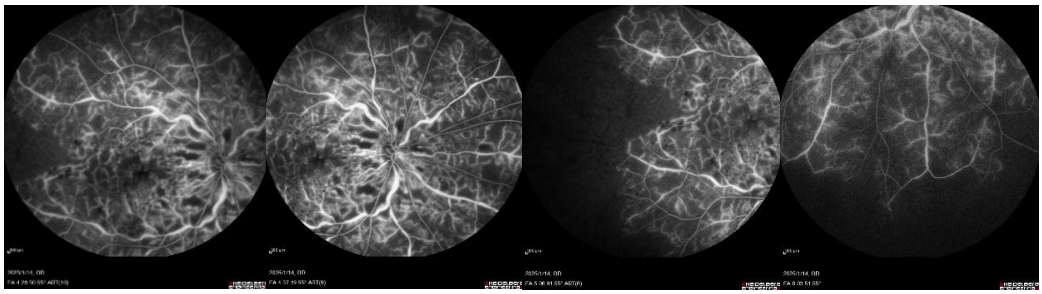


Fig.4: Right eye FFA: Widespread tortuous dilation of retinal vessels, accompanied by varying degrees of fluorescein leakage and large areas of ischemia in the peripheral retina; Left eye FFA: Tortuous dilation of retinal veins, widespread punctate and patchy fluorescein leakage, accompanied by the formation of capillary ischemic areas, and late-phase vascular wall staining.

Fig.5

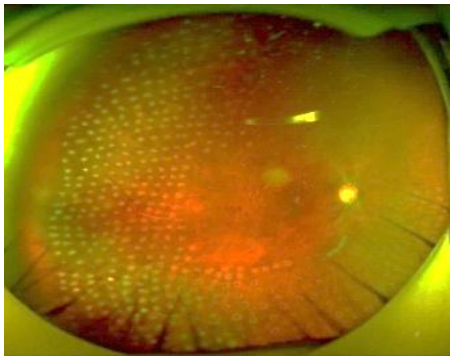


Fig.5: Fresh laser spots are visible across the entire retina of the right eye.

Fig.6

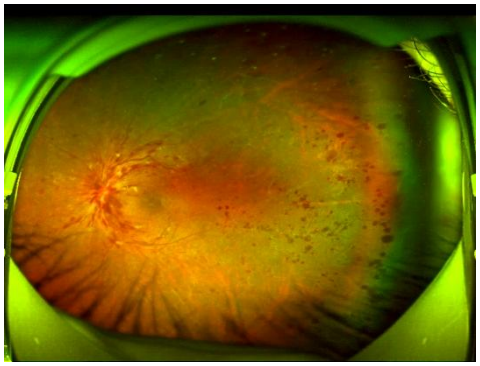


Fig.6: Retinal vessels are tortuous and distorted; flame-shaped hemorrhages are visible in the retinal vessels; the reflex in the fovea is absent.

Fig.7

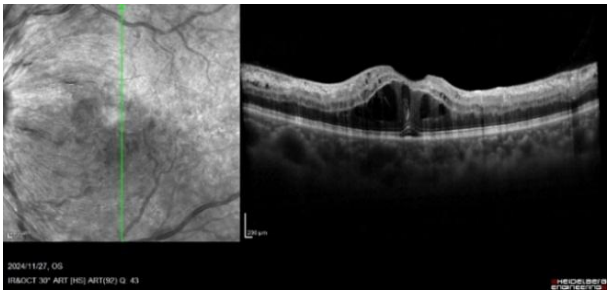


Fig.7: Left eye OCT: The foveal structure in the macular region is absent; extensive cystic edema is observed in the neuroepithelial layer.

Fig.8

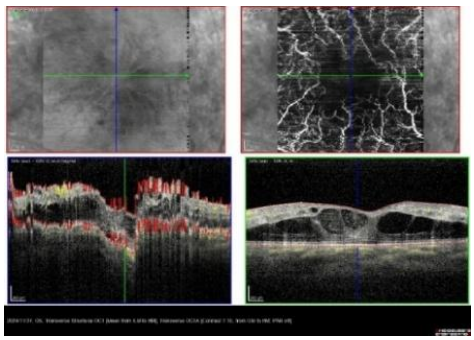


Fig.8: Left eye OCTA: The arch-ring structure in the macular region is absent; blood flow distribution is uneven.

3 Discussion

Leukemia is a group of malignant blood disorders originating from white blood cells, caused by acquired clonal abnormalities in hematopoietic stem cells that replace normal bone marrow. Ocular manifestations can serve as clues for initial diagnosis and may also be observed in patients with an established diagnosis [6]. Ocular involvement in leukemia primarily manifests in two forms: first, tumor cells directly infiltrate multiple sites such as the anterior uvea, orbit, and optic nerve; simultaneously, due to the blood-ocular barrier makes it difficult to completely clear the lesions with chemotherapy drugs, turning the eye into a “refuge” for the tumor and making ocular symptoms prone to recurrence[7]; second, complications arising from hematological abnormalities, including: abnormal blood composition (e.g., decreased hemoglobin levels associated with retinal hemorrhage, elevated white blood cell counts associated with Roth’s spots [8]), changes in blood rheology, and leukocytosis leading to vascular stasis and hyperviscosity can cause peripheral retinal hypoperfusion and venous ischemia, thereby inducing retinal neovascularization; these new vessels not only rupture easily but also bleed further, exacerbating venous outflow obstruction [9]), as well as ischemic damage and its chain reaction (particularly in CML, worsening retinal ischemia can lead to capillary occlusion, progressing to proliferative lesions [10]).

Leukemic retinopathy is the most common characteristic finding, including Roth spots, cotton-wool spots, leukemic infiltrates, pre-retinal hemorrhage, intraretinal hemorrhage, subretinal hemorrhage, vascular dilation and tortuosity, optic disc congestion, and retinal vascular sheath formation, with virtually all ocular structures potentially affected[11]. The occurrence of CRVO can be partially attributed to the same

pathogenic mechanisms as leukemic retinopathy: blood flow abnormalities such as high blood viscosity and leukocyte stasis easily induce thrombus formation; post-occlusive vascular stasis and exudation trigger inflammatory responses; and ischemia and hypoxia exacerbate oxidative stress, primarily manifesting as papilledema, flame-shaped hemorrhages, and tortuous dilated veins [12-13]. Studies have shown that when leukemia patients present with concomitant retinopathy, this often indicates the presence of more severe systemic complications and a poorer prognosis[14].

CML is caused by the t(9;22)(q34;q11.2) chromosomal translocation, which results in the formation of the BCR-ABL1 fusion gene[15]. This, in turn, produces the BCR-ABL1 fusion protein, which possesses abnormal tyrosine kinase activity and plays a key role in the proliferation and survival of CML cells [16]. In this case, following a diagnosis of CML, the patient was regularly treated with olverembatinib, a novel oral formulation that targets the BCR-ABL1 fusion protein. It exhibits significant antileukemic activity in CML patients, particularly those with BCR-ABL1 T315I mutations who have developed resistance to first- and second-generation tyrosine kinase inhibitors (TKIs). kinase inhibitors (TKIs), and demonstrates significant antileukemic activity. As a third-generation novel TKI with a unique molecular structure, this drug specifically inhibits the BCR-ABL1 protein while simultaneously inhibiting fibroblast growth factor receptor (FGFR1), FMS-like tyrosine kinase (FLT3), c-KIT/KIT, and other kinases associated with multiple signaling pathways[17-18]. Studies have shown that this drug exhibits good antitumor activity against CML, acute myeloid leukemia, Ph+ acute lymphoblastic leukemia, and various gastrointestinal, and offers a new treatment option for patients with relapsed or drug-resistant disease[19]. However, attention must be paid to the hematological adverse reactions caused by this drug, such as thrombocytopenia, anemia, and neutropenia [20]; among these, thrombocytopenia may further increase the risk of retinal hemorrhage and venous occlusion in this CML patient, which were already present.

In addition, the patient has a history of both type 2 diabetes and hypertension, and fundus changes associated with both of these underlying conditions are evident. Diabetic retinopathy primarily manifests as retinal microvascular changes, with fundus findings including tortuous and dilated retinal veins, microaneurysms, retinal hemorrhages, and exudates, as well as neovascularization in the proliferative stage and secondary retinal detachment due to fibrous neovascular membranes. In contrast, hypertensive retinopathy presents with arterial narrowing and the “triad of ischemia” (flame-shaped hemorrhages, cotton-wool spots, and star-shaped exudates). These lesions, combined with the hemodynamic abnormalities caused by CML, collectively exacerbated the damage to the retinal vasculature.

4 Conclusion

In summary, the sequential occurrence of retinal vein occlusion (RVO) in both eyes in this case was due to the combined effects of multiple factors: ① Direct infiltration by tumor cells and incomplete local clearance due to the blo od-retinal barrier; ②Hematological complications of CML (vascular stasis cause d by leukocytosis, hyperviscosity syndrome, and ischemic damage) inducing ne ovascularization; ③Thrombocytopenia induced by olverembatinib, increasing th

e tendency to bleed; ④Long-term progression of microvascular lesions caused by diabetes and hypertension. The combination of these factors ultimately led to abnormalities in the structure and function of the retinal vasculature in both eyes. Retinal vein occlusion (RVO) is the second most common retinal vascular disease, including central retinal vein occlusion(CRVO) and branch retinal vein occlusion(BRVO). It is characterized by retinal vein obstruction leading to macular edema (ME) and retinal and subretinal hemorrhage, and is one of the leading causes of vision loss[21]. With widespread recognition of the role of elevated vascular endothelial growth factor (VEGF) in the pathogenesis of macular edema, anti-VEGF agents have gradually become the first-line treatment for various types of RVO-ME[22]. Among these, ranibizumab was the first anti-VEGF drug used worldwide for the treatment of ME. It primarily targets VEGF-A, has a smaller molecular weight (48 kDa), and exhibits better tissue penetration. Treatment regimens should be individually tailored to the patient's specific condition to achieve optimal therapeutic outcomes. In this case, ranibizumab also demonstrated definite efficacy. However, due to the poor initial condition of the right eye at the time of diagnosis, despite receiving aggressive systemic anti-VEGF intervention and maintaining stable disease control for 1 year, the patient ultimately experienced a poor prognosis due to the prolonged course of the disease. In contrast, the left eye successfully regained good visual acuity due to early and timely intervention.

This case highlights that retinal lesions associated with hematological and systemic diseases progress rapidly and have a poor prognosis; therefore, systemic treatment should be initiated as early as possible to reduce the risk of contralateral retinal vein occlusion and delay disease progression. Early retinal laser photocoagulation, anti-VEGF therapy, and surgical intervention play a positive role in controlling the ocular condition. When hematologists or oncologists treat patients with chronic myeloid leukemia, in addition to actively managing the primary disease, they should be vigilant for potential ocular complications and refer patients to ophthalmologists at an early stage. Similarly, endocrinologists managing patients with hypertension or diabetes should incorporate ocular assessments into their long-term follow-up protocols. Concurrently, when diagnosing and treating retinal ischemic diseases such as CRVO and ME, ophthalmologists must take a detailed medical history, including systemic conditions and medication use, and conduct a comprehensive evaluation using multimodal imaging techniques. All specialties should transcend the limitations of single-specialty care, adhere to long-term follow-up and multidisciplinary team (MDT) collaboration, prioritize the patient's overall health, and ultimately achieve systematic, precision-oriented comprehensive management.

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Authors' contributions

Tian Zhao and Wenze Du conceived the idea for the work and wrote the original manuscript, revised, edited the manuscript and delivered it. Yanli Zhang and Cong He modified and edited the manuscript. Zilu Zhong participated in the design and revision of the picture and table in attachment. All authors agreed to be accountable for the content of the work and approved the final version for publication.

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Availability of data and materials

All data files are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethics approval and consent to participate

The publication of this case report has been reviewed and approved by the Medical Ethics Committee of Zhongshan Aier Eye Hospital, Guangdong Province. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participant.

Disclosure statement

No potential conflict of interest was reported by the author(s). Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare no competing interests.

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