BILATERAL CENTRAL RETINAL VEIN OCCLUSION IN PLASMA CELL DYSCRASIAS IMPLICATIONS FOR HYPERVISCOSITY IN MULTIPLE MYELOMA

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INTRODUCTION

Bilateral central retinal vein occlusion (CRVO) is a rare but severe ocular complication associated with hyperviscosity (HVS) in plasma cell dyscrasias (PCD), particularly multiple myeloma (MM) and Waldenström macroglobulinemia (WM). No clinical trials address HVS-related CRVO in MM. Early multidisciplinary management involving hematology and ophthalmology may help reduce vision impairment and improve patient care.

AIM

To evaluate the available evidence on CRVO as a manifestation of hyperviscosity syndrome in plasma cell dyscrasias and to highlight the importance of early multidisciplinary recognition and management.

METHOD

We conducted a PubMed search (2015–April 2026) to capture contemporary reports of retinal manifestations of HVS in PCD. Publications describing non-occlusive HVS retinopathy and bilateral CRVO were included to reflect the spectrum of microvascular involvement. Macular detachment was included only when associated with confirmed CRVO. Studies lacking characterization of MM or WM were excluded. Extracted data included underlying PCD diagnosis, treatment, and correlations with fundoscopic, optical coherence tomography (OCT), and OCT angiography (OCTA) findings (e.g., vessel density, microvascular abnormalities), as well as ocular phenotype. Systemic disease control, local therapies, and visual outcomes were also assessed.

CONCLUSIONS

Retinal findings in relapsed MM and WM reflect a spectrum of hyperviscosity-driven microvascular injury, with bilateral CRVO as the most severe form. The retina may serve as a clinically visible clue of hyperviscosity, highlighting the value of prompt multidisciplinary management to potentially improve outcomes.

RESULTS

Table 1: Retinal Manifestations of Hyperviscosity in Plasma Cell Dyscrasias: A Spectrum from Microvascular Changes to Bilateral CRVO

Author (Year)	Disease	N (Eyes/Patients)	Ocular Phenotype	Imaging Modality	Key Retinal Findings	PCD-related Disease Characteristics	Treatment Response
Czakó (2023)	MG (incl MM)	44 eyes (27 pts)	Non-CRVO	OCTA	Reduced vessel density, impaired microvascular perfusion	Presence of monoclonal gammopathy	Subclinical microvascular dysfunction study, no treatment reported, reduced superficial retinal vessel density on OCTA
Dursun (2022)	MM	31 pts	Non-CRVO	OCTA	Reduced retinal vessel density (SCP/DCP/RPC/ONH) and enlarged FAZ (OCTA), consistent with microvascular ischemia	Known MM	Subclinical ischemia / microvascular dysfunction study, no treatment reported, reduced retinal vessel density on OCTA
Watson (2021)	WM	1 pt	Non-CRVO	Fundus, FA, OCT, OCTA	HVS retinopathy, serous macular detachment (angiographically silent)	Elevated IgM	Intravitreal anti-VEGF, mild response with limited visual recovery
Li (2020)	WM	1 pt	Non-CRVO	Fundus, FA, OCT, OCTA	Retinal hemorrhages, venous dilation, macular edema, serous detachment; OCTA: microvascular impairment and choroidal dilation	Markedly elevated IgM, Bone marrow lymphoplasmacytic infiltration, anemia	Systemic therapy and intravitreal anti-VEGF, very good partial response with partial visual recovery
Kim (2016)	WM	1 pt	Non-CRVO	Fundus	Retinal hemorrhages, venous dilation	Elevated IgM	Not reported
Lee (2023)	WM	1 pt	Non-CRVO	Fundus, OCT, OCTA	HVS retinopathy, retinal hemorrhages, venous congestion, macular edema; OCTA: capillary plexus damage and choroidal dilation	Elevated IgM with hyperviscosity	Intravitreal anti-VEGF and steroid; systemic chemotherapy, improvement after systemic therapy with partial visual recovery
Cruz (2021)	MM (initial presentation)	1 pt	Mixed (HVS retinopathy with CRVO-like features and macular involvement)	Fundus, OCT	Retinal hemorrhages, macular edema, serous detachment	Elevated monoclonal immunoglobulin (kappa), bone marrow plasma cell infiltration, hyperviscosity features	Systemic therapy; intravitreal steroid (no response), partial response with limited visual recovery
Tandlich (2022)	MM (initial presentation)	1 pt	CRVO (bilateral)	Fundus	Bilateral retinal hemorrhages, venous dilation/tortuosity	Elevated monoclonal immunoglobulin, anemia, renal dysfunction, hyperviscosity	Supportive ocular therapy (e.g., anti-VEGF, steroids) and systemic management, improvement after therapy but not specified
Shrestha (2023)	WM	1 pt	CRVO (bilateral)	Fundus, OCT	Bilateral CRVO, macular edema	Elevated IgM (kappa), supporting monoclonal protein spike, bone marrow lymphoplasmacytic infiltration	Plasmapheresis, systemic therapy (bortezomib-based), intravitreal anti-VEGF, improvement after therapy, partial visual recovery
Plante (2023)	therapy-resistant WM	1 pt	Mixed (HVS retinopathy with CRVO features)	Fundus, OCT	Retinal hemorrhages, macular edema, CRVO-like changes	Elevated IgM (MYD88, CXCR4 mutation), hyperviscosity	Plasmapheresis, systemic therapy (zanubrutinib), intravitreal anti-VEGF, partial response with limited visual recovery
Golesic (2015)	MM (initial presentation)	1 pt	CRVO (bilateral)	Fundus	Bilateral retinal hemorrhages, venous dilation/tortuosity	Elevated monoclonal immunoglobulin, hyperproteinemia, hyperviscosity	Plasmapheresis followed by systemic therapy, with visual recovery
Lee (2016)	WM	1 pt	CRVO (bilateral)	Fundus	Bilateral retinal hemorrhages, venous dilation/tortuosity, macular edema	Elevated IgM, hyperproteinemia, anemia, clinical hyperviscosity features	Systemic chemotherapy without documented plasmapheresis, leading to partial visual recovery and improvement in retinal findings
Neroev (2020)	WM	1 pt	Mixed (HVS retinopathy with CRVO features)	Fundus	Bilateral retinal vascular occlusion, hemorrhages	Elevated IgM, hyperproteinemia clinical hyperviscosity features	Systemic therapy (plasmapheresis not reported), partial visual recovery
Finn (2024)	MM	1 pt	CRVO (atypical)	Fundus, OCT	Retinal hemorrhages, venous dilation, atypical CRVO features	Elevated monoclonal immunoglobulin	Intravitreal anti-VEGF (systemic MM therapy not specified), partial visual recovery

Abbreviations: AE, adverse event; BCVA, best-corrected visual acuity; BRVO, branch retinal vein occlusion; CRVO, central retinal vein occlusion; DCP, deep capillary plexus; FA, fluorescein angiography; FAZ, foveal avascular zone; HRVO, hemiretinal vein occlusion; HVS, hyperviscosity syndrome; Ig, immunoglobulin; IgM, immunoglobulin M; incl, including; IOP, intraocular pressure; IVT, intravitreal; ME, macular edema; MG, monoclonal gammopathy; MM, multiple myeloma; OCT, optical coherence tomography; OCTA, optical coherence tomography angiography; ONH, optic nerve head; pt, patient; pts, patients; RCT, randomized controlled trial; RPC, radial peripapillary capillaries; RVO, retinal vein occlusion; SCP, superficial capillary plexus; VD, vessel density; WM, Waldenström macroglobulinemia.

Table 2: FDA-Approved and Commonly Used Therapies for Central Retinal Vein Occlusion (Macular Edema)

Agent / Route of Administration	FDA Approved Indication (Year)	Mechanism	Pivotal Trial (NCT) *	Study Design / N	Imaging Modality	Key Safety Findings	Key Efficacy Findings
Ranibizumab / intravitreal injection	Macular edema following CRVO (2010)	Anti-VEGF	CRUISE (NCT00485836)[1]	Phase III RCT; n=392	Fundus, OCT	Ocular AEs including conjunctival hemorrhage; generally well tolerated	Significant BCVA improvement (~+14–15 letters at 6 months) vs sham
Aflibercept / intravitreal injection	Macular edema following CRVO (2012)	Anti-VEGF	COPERNICUS (NCT00943072); GALILEO (NCT01012973)[2,3]	Phase III RCTs; n=189, n=177	Fundus, OCT	Favorable safety profile; no new safety signals	Significant visual gains (~+17 letters) and rapid edema reduction
Faricimab / intravitreal injection	Macular edema following CRVO/BRVO (2023)	Dual Ang-2 + VEGF-A inhibitor	COMINO (NCT04740931)[4]	Phase III RCT; n=729 (CRVO/HRVO)	Fundus, OCT, FA	Comparable safety to aflibercept; no new safety signals	Noninferior to aflibercept with improved leakage resolution
Dexamethasone / intravitreal implant	Macular edema following CRVO/BRVO (2009)	Corticosteroid	GENEVA (Pivotal trial)[5]	Phase III RCT; n=1267 mixed RVO population (CRVO + BRVO)	Fundus, OCT	Increased IOP and cataract risk; steroid-related AEs	Modest short-term visual improvement; effect declines over time
Bevacizumab / intravitreal injection	Used beyond the approved label for CRVO	Anti-VEGF	SCORE2 (NCT01969708)[6]	Phase III RCT; n=362 (CRVO/HRVO)	Fundus, OCT	Comparable safety; rare endophthalmitis and IOP elevation	Noninferior to aflibercept for visual acuity at 6 months

* No PCD-specific data were reported; patients with plasma cell dyscrasias (WM/MM) were not specifically evaluated

References: 1. Campochiaro et al. Ophthalmology. 2011; 2. Scott et al. JAMA. 2017; 3. Korobelnik et al. Am J Ophthalmol. 2021; 4. Heier et al. Ophthalmology. 2024; 5. Haller et al. Ophthalmology. 2010; 6. Park et al. phthalmol Sci. 2025.

Table 3: Published Prospective Clinical Trials in CRVO (2015 to March 2026)

Study Drug (NCT number)	Study Design / N (Eyes/Patients)	Disease	Imaging Modality	Key Safety Findings	Key Efficacy Findings
Ranibizumab vs dexamethasone implant (NCT01396083)[1]	Phase IIIb RCT; n=243 pts	CRVO with macular edema	Fundus, OCT	Higher ocular adverse events with dexamethasone vs ranibizumab; safety consistent with known profiles	Ranibizumab superior to dexamethasone at months 3–6 with greater BCVA gain
Bevacizumab vs aflibercept (NCT01969708)[2]	Phase III randomized trial; n=362 pts	CRVO/HRVO with macular edema	Fundus, OCT	Similar safety profiles; ocular AEs included IOP elevation and rare endophthalmitis (bevacizumab)	Bevacizumab noninferior to aflibercept for visual acuity at 6 months
Aflibercept (NCT01870427)[3]	Phase IV; n=20 pts	Chronic non-ischemic CRVO with macular edema (previously treated)	Fundus, OCT	Well tolerated with no new safety concerns reported	Significant extension of macular edema–free interval, with improved visual acuity (+8 letters) and reduced retinal thickness
Aflibercept (NCT02800642)[4]	Phase IV; n=162 pts	CRVO with macular edema	Fundus, OCT	Safety profile consistent with prior studies; no new safety signals	Significant visual acuity improvement (+20 letters) and marked reduction in retinal thickness with treat-and-extend aflibercept
Ranibizumab (NCT01318941)[5]	prospective observational; n=327 pts	CRVO (treatment-naïve) with visual impairment in real-world practice	Fundus, OCT	Favorable long-term safety with low incidence of serious ocular adverse events and no new safety signals over 5 years	Favorable long-term safety with low incidence of serious ocular adverse events and no new safety signals over 5 years
Faricimab vs aflibercept (NCT04740905/ NCT04740931)[6]	Phase III RCT; n=553, NCT04740905; n=729, NCT04740931;	treatment-naïve CRVO/HRVO with macular edema	Fundus, OCT, FA	Well tolerated with safety comparable to aflibercept; similar rates of ocular adverse events	Faricimab noninferior to aflibercept for visual acuity gains with comparable retinal thickness reduction and greater resolution of FA-based macular leakage
Autologous CD34+ stem cells (NCT03981549)[7]	Phase I/II RCT; n=16	Chronic CRVO with vision loss	Fundus, FA, OCT, OCTA	Well, tolerated with no serious treatment-related ocular adverse events; most common AE was floaters; no persistent ≥15-letter vision loss	Feasible with stable or improved vision

References: 1. Hoerauf et al. Am J Ophthalmol. 2016; 2. Scott et al. JAMA. 2017; 3. Khurana et al. Int J Retina Vitreous. 2019; 4. Korobelnik et al. Am J Ophthalmol. 2021; 5.Lotery et al. Eye (Lond). 2022; 6. Heier et al. Ophthalmology. 2024; 7. Park et al. Ophthalmol Sci. 2025.

REFERENCES

- Golesic, Sheidow. Retin Cases Brief Rep. 2015.
- Lee et al. J Korean Ophthalmol Soc. 2016.
- Li et al. World J Clin Cases. 2020.
- Watson et al. J Vitreoretin Dis. 2021.
- Kim, Kweon. N Engl J Med. 2016.
- Cruz et al. Case Rep Ophthalmol. 2021.
- Dursun et al. Curr Eye Res. 2022.
- Tandlich, Williamson. Clin Pract Cases Emerg Med. 2022.
- Czakó et al. J Clin Med. 2023.
- Shrestha et al. J Med Case Rep. 2023.
- Plante et al. J Blood Med. 2023.
- Neroev et al. Vestn Oftalmol. 2020.
- Finn, Miller. Ophthalmic Surg Lasers Imaging Retina. 2024.
- Lee et al. J Korean Ophthalmol Soc. 2023.

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