

Retinal Arteriovenous Malformation in Wyburn-Mason Syndrome: A Rare Diagnostic Challenge Mimicking Central Retinal Vein Occlusion

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ABSTRACT

Wyburn-Mason syndrome (WMS) is a rare congenital disorder characterized by retinal and intracranial arteriovenous malformations (AVMs). These vascular anomalies can resemble central retinal vein occlusion (CRVO), potentially leading to misdiagnosis and inappropriate treatment. A 50-year-old female was initially misdiagnosed with CRVO and received intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections. Despite partial regression of macular edema, persistent vascular anomalies prompted multimodal imaging, confirming the diagnosis of WMS. Fundus examination revealed dilated, tortuous arteriovenous vessels extending from the optic disc, with macular exudation and a localized vitreous hemorrhage. Fluorescein angiography demonstrated early arteriovenous shunting without capillary nonperfusion, distinguishing it from CRVO. Optical coherence tomography (OCT) showed persistent cystoid macular edema without subretinal fluid. Systemic evaluation ruled out additional intracranial AVMs, apart from the patient's known primary sclerosing cholangitis. Despite anti-VEGF therapy, macular edema only partially improved, and vision remained stable. This case underscores the importance of distinguishing WMS from CRVO through multimodal imaging and highlights the limited efficacy of anti-VEGF therapy in WMS-associated macular edema. Accurate differentiation between these conditions is essential for optimizing management and preventing unnecessary interventions.

Keywords: Wyburn-Mason syndrome, Retinal arteriovenous malformation, Central retinal vein occlusion, Fluorescein angiography

INTRODUCTION

Wyburn-Mason syndrome (WMS), also known as Bonnet-Dechaume-Blanc syndrome, is a rare congenital neuro-oculocutaneous disorder characterized by nonprogressive arteriovenous malformations (AVMs) affecting the retina, brain, and, less frequently, other organ systems.¹ These vascular anomalies result from embryological defects in blood vessels' mesodermal and ectodermal development, leading to direct arterio-venous communications without an intervening capillary network.¹ Retinal involvement in WMS is typically unilateral, with tortuous, dilated vessels extending from the optic disc. While the condition is often asymptomatic, complications such as vitreous hemorrhage,

macular edema, and secondary vascular occlusions can contribute to progressive visual impairment.^{2,3}

The clinical presentation of WMS is highly variable and largely depends on the extent of vascular anomalies. Neurological manifestations such as headaches, dizziness, and focal neurological deficits may arise due to the presence of associated intracranial AVMs.⁴ The retinal vascular abnormalities in WMS can closely mimic central retinal vein occlusion (CRVO), particularly in cases where macular edema and venous engorgement are prominent.⁵ This resemblance frequently leads to misdiagnosis, which may result in unnecessary interventions or delayed recognition of the underlying congenital condition.³

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The differentiation between WMS and CRVO is critical, as their pathophysiological mechanisms and management strategies differ significantly. Fluorescein angiography (FA) is a key diagnostic modality, as it reveals direct arteriovenous shunting in WMS, whereas CRVO is characterized by capillary nonperfusion, delayed venous filling, and extensive leakage. Optical coherence tomography (OCT) further aids in distinguishing these conditions by identifying macular edema patterns and structural retinal changes.⁶ While anti-vascular endothelial growth factor (anti-VEGF) therapy is commonly used in CRVO, its role in WMS remains controversial, with limited evidence suggesting only partial efficacy in managing macular edema.³

In this case report, we present a patient initially diagnosed with CRVO but later identified as having Wyburn-Mason syndrome. The patient exhibited persistent vascular anomalies and macular edema, with partial improvement following anti-VEGF therapy. This case underscores the importance of differentiating WMS from CRVO and highlights key imaging features that aid in accurately diagnosing this rare condition.

CASE DESCRIPTION

A 50-year-old female patient presented to our clinic with complaints of progressive vision loss in her left eye (OS). She had a previously diagnosed primary sclerosing cholangitis (PSC) but no other systemic diseases. Additionally, she reported intermittent dizziness and headaches. There was no history of prior ocular trauma, intraocular surgery, or systemic vascular anomalies.

On ophthalmologic examination, best-corrected visual acuity (BCVA) was 1.0 in the right eye (OD) and 0.05 in the left eye (OS). The patient reported that visual blurring in the left eye had first appeared approximately six months prior to presentation and had gradually worsened, leading to significant visual impairment. Despite receiving anti-VEGF therapy during this period, BCVA in the left eye remained stable at 0.05 on the Snellen chart, although the patient subjectively reported mild improvement in visual clarity.

Intraocular pressure was within normal limits in both eyes. Anterior segment examination revealed no pathological findings bilaterally. Posterior segment evaluation of

the right eye showed a normal optic disc, macula, and retinal vasculature (Figure 1a). In contrast, fundus examination of the left eye revealed markedly dilated, tortuous, and engorged arteriovenous vessels extending from the optic disc. These findings were accompanied by macular exudation, cystoid macular edema (CME), scattered intraretinal hemorrhages, and a localized vitreous hemorrhage overlying the abnormal vasculature (Figure 1b).

Multimodal imaging further characterized the retinal findings (Figure 1). Fluorescein angiography (FA) revealed early, rapid filling of dilated venous structures via direct arteriovenous shunts without an intervening capillary bed. There was no evidence of capillary dropout, a hallmark of central retinal vein occlusion (CRVO). Diffuse hyperfluorescence and vascular leakage were observed in the late phases, particularly in the macular region, corresponding to the clinically detected macular edema (Figure 2). Optical coherence tomography (OCT) demonstrated significant CME with intraretinal cystic spaces and pronounced retinal thickening but no evidence of subretinal fluid (Figure 3a). These findings led to the diagnosis of Wyburn-Mason syndrome (WMS).

Following the diagnosis, the patient was referred for a comprehensive systemic evaluation to investigate the presence of extracranial or intracranial vascular malformations. Contrast-enhanced brain and orbital magnetic resonance angiography (MRA) showed no additional arteriovenous malformations (AVMs). However, magnetic resonance cholangiopancreatography (MRCP) confirmed intrahepatic bile duct irregularities consistent with the previously known PSC.

Given the presence of persistent CME and progressive visual symptoms, the patient underwent a series of three intravitreal injections of bevacizumab (Avastin, Genentech, USA), followed by a single dose of aflibercept (Eylea, Regeneron, USA). The patient did not adhere to regular follow-ups and returned approximately one year after the final injection. BCVA remained unchanged at 0.05 on the Snellen chart at follow-up, although the patient subjectively reported improved visual clarity. Fundus examination showed that the retinal AVMs remained stable, with resolution of the previously observed vitreous hemorrhage. OCT imaging demonstrated persistent CME, with partial

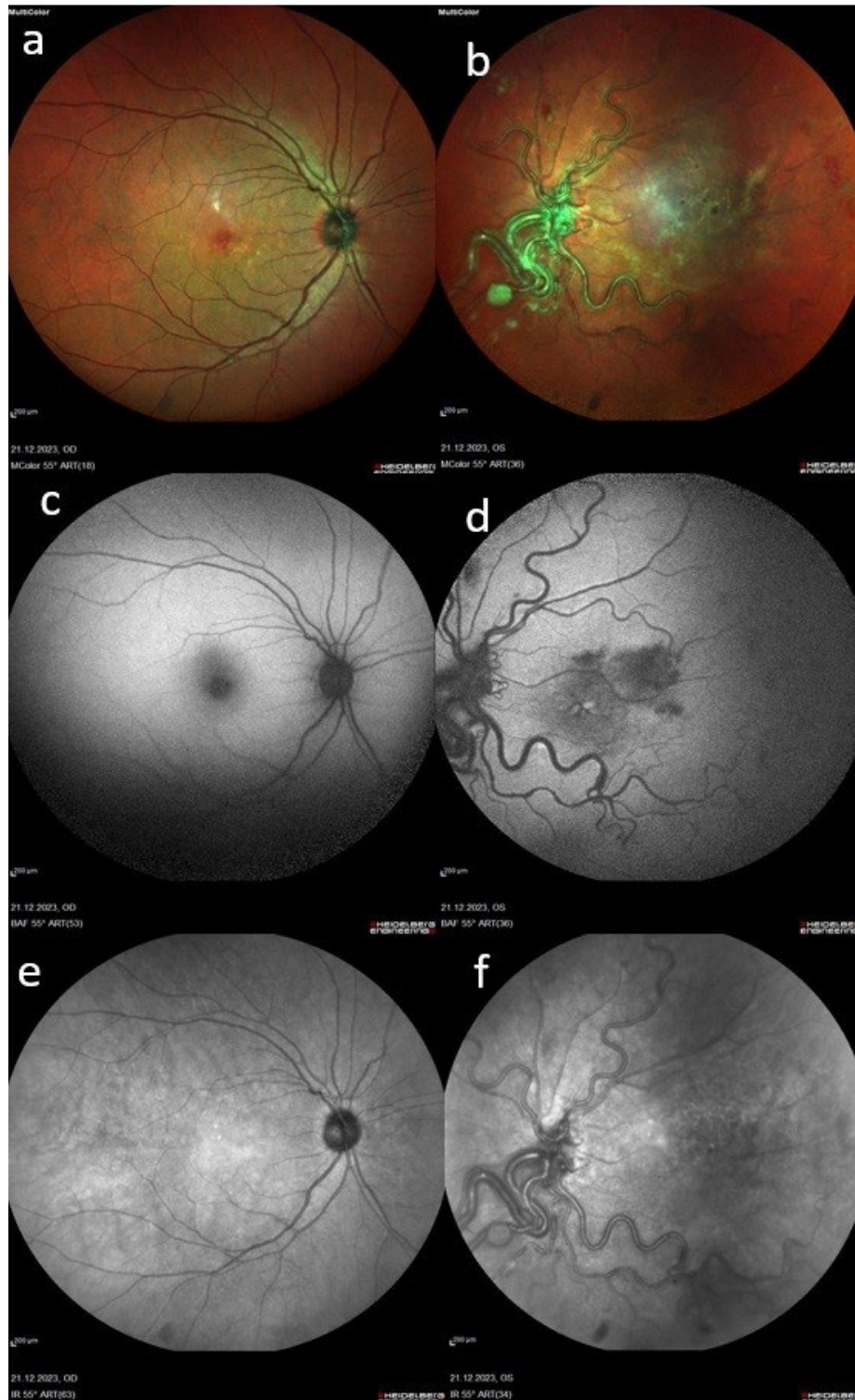


Figure 1. Multimodal Imaging of the Left Eye with Wyburn-Mason Syndrome

- (a) Color fundus photograph of the right eye (OD) showing a normal posterior pole.
- (b) Multicolor imaging of the left eye (OS) at initial presentation, demonstrating tortuous, dilated, and anomalous retinal vessels extending from the optic disc, consistent with retinal arteriovenous malformation (AVM). Exudative changes and macular edema are also observed.
- (c) Blue autofluorescence (BAF) image of the right eye, appearing normal.
- (d) BAF image of the left eye, showing hypofluorescent areas corresponding to hemorrhages and exudative changes.
- (e) Infrared reflectance (IR) image of the right eye, appearing normal.
- (f) IR image of the left eye, illustrating the vascular anomalies more clearly, with areas of hyperreflectivity corresponding to hemorrhages and vascular malformations.

regression of cystic spaces compared to baseline (Figure 3b). Despite the recommendation for further treatment, the patient declined additional intravitreal therapy.

This case highlights the importance of differentiating Wyburn-Mason syndrome from CRVO, emphasizing

the crucial role of multimodal imaging in establishing an accurate diagnosis. Additionally, it underscores that anti-VEGF therapy may lead to only partial anatomical improvement in WMS-associated macular edema, necessitating individualized treatment approaches.

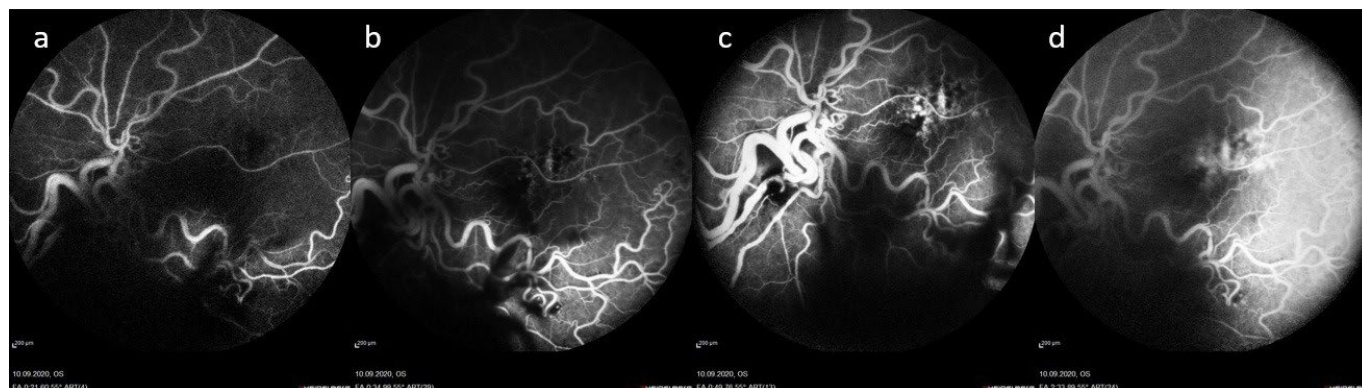


Figure 2. Fluorescein Angiography (FA) Findings at Initial Presentation

(a) Early-phase FA of the left eye, revealing large, tortuous retinal arteriovenous anastomoses without an intervening capillary bed, characteristic of Wyburn-Mason Syndrome.

(b) Mid-phase FA showing extensive leakage from the abnormal vessels and masking effects from vitreous hemorrhage (noted as shadowing in the superior quadrant).

(c) Late-phase FA demonstrating persistent vascular leakage and exudative changes, consistent with macular edema.

(d) Even later phase FA showing increased hyperfluorescence and diffuse leakage, confirming persistent macular edema despite retinal perfusion.



Figure 3. Optical Coherence Tomography (OCT) Analysis Before and After Treatment

(a) Baseline OCT at initial presentation showing severe cystoid macular edema (CME) with large intraretinal cystic spaces.

(b) Follow-up OCT after three intravitreal bevacizumab (Avastin) injections and one aflibercept (Eylea) injection, revealing partial resolution of macular edema with residual cystic spaces.

DISCUSSION

Wyburn-Mason syndrome (WMS) is a rare congenital nonhereditary disorder characterized by arteriovenous malformations (AVMs) primarily involving the retina and central nervous system.⁷ The condition arises from embryological disruptions in vascular development, leading to direct arteriovenous communications without an intervening capillary network. While retinal AVMs in WMS are typically asymptomatic, complications such as macular edema, vitreous hemorrhage, and secondary vascular occlusions can significantly impact vision.^{5, 8} In clinical practice, WMS is frequently misdiagnosed as central retinal vein occlusion (CRVO), mainly when retinal venous engorgement and macular edema are prominent.² ⁸ This diagnostic confusion may result in unnecessary interventions and suboptimal management.

The primary challenge in differentiating WMS from CRVO is their overlapping clinical presentations, including retinal vascular dilation, hemorrhages, and macular edema.⁹ However, the pathophysiological mechanisms of these conditions are distinct. Thrombotic obstruction of the central retinal vein leads to capillary nonperfusion, intraretinal hemorrhages, and widespread vascular leakage.⁵ In contrast, WMS exhibits direct arteriovenous shunting, with arterialized venous flow and the absence of capillary dropout or ischemia. This key distinction is best appreciated through fluorescein angiography (FA), which reveals early, rapid venous filling in WMS due to high-flow arteriovenous connections. In contrast, CRVO is characterized by delayed venous filling, capillary dropout, and extensive late-phase leakage.⁶ In our case, FA findings were highly suggestive of WMS, demonstrating rapid, direct arteriovenous filling without capillary nonperfusion, which effectively excluded a diagnosis of CRVO.

Optical coherence tomography (OCT) is also critical in distinguishing these conditions. In CRVO, macular edema is primarily driven by capillary endothelial dysfunction and ischemic damage, resulting in disorganization of the inner retinal layers (DRIL), intraretinal cystic spaces, and, in some cases, subretinal fluid.⁶ In contrast, WMS-associated macular edema is believed to arise from chronic hemodynamic alterations and venous hypertension, leading to retinal thickening with persistent cystoid changes.³ Notably, our patient's OCT revealed pronounced cystoid

macular edema (CME) without subretinal fluid, further supporting the diagnosis of WMS rather than CRVO.

Another crucial aspect of our case was the partial anatomical response to anti-VEGF therapy.⁹ While anti-VEGF agents, such as bevacizumab and aflibercept, are standard treatments for CRVO-related macular edema, their efficacy in WMS remains controversial and largely unestablished.⁹ The underlying pathophysiology of macular edema in WMS differs from CRVO in that there is no primary ischemic insult or VEGF-driven neovascularization.⁹ Instead, chronic arteriovenous shunting leads to long-standing hemodynamic stress and venous stasis, which may not fully respond to VEGF inhibition.

In contrast to previous reports where triamcinolone led to resolution of CME in Wyburn-Mason syndrome, such as the case described by Onder et al.¹, our patient showed only partial anatomical response despite multiple anti-VEGF injections. This discrepancy may reflect the variability in underlying hemodynamics and inflammatory response among individual cases. Additionally, Tanrıverdi et al.¹⁰ reported a Turkish pediatric patient with retinal and cerebral AVMs who died of subarachnoid hemorrhage, underscoring the life-threatening potential of WMS and the need for timely diagnosis and systemic surveillance. These findings collectively emphasize that although WMS may present with overlapping retinal findings such as CME, the underlying disease course and treatment response may differ significantly. Multimodal imaging and individualized management strategies remain essential.

Beyond the ophthalmologic features, systemic evaluation is paramount in cases of WMS, given the risk of concurrent cerebral AVMs, which can lead to life-threatening hemorrhagic events. Previous studies have reported a significant association between WMS and neurological complications such as seizures, intracranial hemorrhages, and focal neurological deficits.⁴ Our patient exhibited dizziness and headaches but had no additional intracranial vascular anomalies detected on magnetic resonance angiography (MRA). This highlights the importance of comprehensive systemic screening in WMS patients to identify and monitor potential cerebrovascular involvement.

CONCLUSION

This case highlights the importance of multimodal imaging in distinguishing Wyburn-Mason syndrome from central retinal vein occlusion, particularly in patients presenting with macular edema and dilated retinal vasculature. Fluorescein angiography remains a key diagnostic modality, with early arteriovenous shunting serving as a critical differentiator from CRVO. Our findings support the notion that anti-VEGF therapy may offer only limited anatomical improvement in WMS-associated macular edema, with minimal functional gain. In contrast to prior reports showing favorable response to corticosteroids, our patient demonstrated persistent CME despite intravitreal anti-VEGF therapy, suggesting variability in therapeutic response depending on the underlying hemodynamics.

Moreover, this report adds to the existing literature by emphasizing the need for a multidisciplinary approach and long-term follow-up, especially given the potential for serious systemic complications such as cerebral AVMs. The inclusion of both international and national case reports supports the clinical diversity of WMS and underlines the value of early and accurate diagnosis in optimizing outcomes.

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