

From blindness to light: A clinical conundrum - central retinal vein occlusion as an initial manifestation of inflammatory bowel disease

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ABSTRACT

This case report emphasizes central retinal vein occlusion (CRVO) as the primary cause of blindness, typically linked to impaired retinal venous drainage from critical vein obstruction. While conditions like diabetes and hypertension are known risk factors for CRVO, rare instances associate it with inflammatory bowel disease (IBD). Here, a 19-year-old male initially presented with painless vision loss, revealing ocular ischemia secondary to panuveitis and moderate CRVO. Genetic testing indicated HLA-B51/B52, suggesting Behcet's disease initially, treated with immunosuppressants and steroids. Despite initial recovery, severe gastrointestinal symptoms later led to ulcerative colitis diagnosis. This sequence highlights CRVO preceding IBD symptoms in a high-risk individual, prompting caution in its differential diagnosis, especially in younger patients without typical risk factors. Prompt recognition and a collaborative approach between gastroenterologists and ophthalmologists are crucial for improving patient outcomes.

Keywords: central retinal vein occlusion, ulcerative colitis, inflammatory bowel disease, retinal vasculitis, systemic vasculitis, colonoscopy

INTRODUCTION

Central Retinal Vein Occlusion (CRVO) is a serious condition characterized by the obstruction of the central retinal vein, the primary vessel responsible for draining blood from the retina. When blood flow is impeded, it leads to ischemia, edema, and hemorrhages within the retina, potentially causing significant visual impairment or blindness. CRVO is commonly associated with systemic conditions such as hypertension, diabetes, hyperlipidemia, and thrombogenic disorders [1].

In some cases, CRVO has been identified as an initial manifestation of Inflammatory Bowel Disease (IBD), a group of chronic inflammatory conditions affecting the digestive system and classified as autoimmune disorders [2]. IBD includes two main types: ulcerative colitis and Crohn's disease. It is widely accepted that IBD results from an interaction between genetic predisposition, environmental factors, and an abnormal immune response to gut microbiota, though its precise molecular mechanisms remain undetermined [3].

Several potential mechanisms have been proposed to explain the link between CRVO and IBD. These include vascular changes due to endothelial dysfunction, retinal vasculitis, systemic inflammation leading to hypercoagulability, and pathological autoimmune processes targeting large blood vessels [4].

This case report involved a young male patient with no prior comorbidities who presented with CRVO and was subsequently diagnosed with ulcerative colitis, a subset of IBD. This case underscores the importance of considering IBD as an underlying cause of CRVO, particularly in young patients without traditional risk factors.

CASE REPORT

Salient clinical observations

The question arises as to why a healthy 19-year-old male, with no prior health issues, suddenly experi-

enced painless blindness in his right eye. Upon examination, an ophthalmologist diagnosed Central Retinal Vein Occlusion (CRVO), a rare condition in such a young individual without known risk factors. In view of suspicion of autoimmune aetiology, autoimmune panel was sent and was positive for HLA-B51 and HLA-B52, which confirmed the diagnosis of Behçet's disease [5].

To manage the condition, the patient was initially treated with high-dose parenteral steroids, oral steroids and azathioprine. However, his clinical situation changed unpredictably as he began experiencing gastrointestinal symptoms, including high fever, bloody stools, and abdominal pain. Colonoscopy with tissue diagnosis and contrast-enhanced CT scan of the abdomen identified the underlying cause as ulcerative colitis, a form of inflammatory bowel disease (IBD).

Interestingly, the ocular manifestation of CRVO appeared before the onset of gastrointestinal symptoms, which is atypical for IBD. This case underscores the importance of a multidisciplinary approach in diagnosing complex medical conditions. It also underscores the importance of expanding the diagnostic framework even in cases where initial clinical data may seem discordant and incomplete.

CASE PRESENTATION

Patient presentation

A 19-year-old male with no prior medical history experienced sudden, painless vision loss in his right eye, lasting for one day.

Clinical findings

Extensive general and detailed tests revealed no abnormalities. Ophthalmological examination revealed intraretinal vein occlusion detected in the right eye, leading to a diagnosis of Central Retinal Vein Occlusion (CRVO).

Diagnostic evaluation

A comprehensive rheumatological workup was performed, including measurements of complement levels (C3 and C4), ANA immunoblot panel, antinuclear antibodies (ANAs), HLA panels and hypercoagulability work up. The results showed positive HLA-B51 and HLA-B52 markers, negative ANCA, negative ANA immunoblot panel, and normal ANA levels. C3 blood levels were normal, while C4 levels were decreased. A hypercoagulability workup, encompassing tests for protein C, protein S, antiphospholipid antibodies (APLA), Factor V Leiden mutation, and serum homocysteine levels, was conducted and yielded negative results. These findings narrowed the diagnostic consideration to Behçet's disease, leading to pulse therapy with intravenous methylprednisolone (500 mg in 200 ml of normal saline, once daily) for three days.

Additional assessment

Patient developed sudden onset abdominal pain, multiple episodes of loose stools.

Ultrasound imaging revealed a segmented bowel loop thickening in the lower right abdomen and the presence of ascites.

This prompted further imaging with CT abdomen with contrast.

CT scan of the abdomen showed segmental bowel wall thickening with submucosal edema (maximum thickness of 6.8 mm) from the sigmoid colon to the rectum, with associated engorged mesenteric vasculature and few subcentimetric lymph nodes. Features suggestive of inflammatory bowel disease.

The patient was referred to a gastroenterologist for further evaluation. Gastroenterology planned to do colonoscopy and advised to start intravenous metronidazole and piperacillin/tazobactam for seven days, alongside mesalamine suppositories.

Histopathological examination and colonoscopy

Colonoscopy revealed severe hemorrhagic pancolitis with exudates in proximal and distal colon.

Histopathological analysis showed cryptitis and abscesses, lamina propria edema, and lymphoplasmacytic inflammatory infiltrate, consistent with moderate active colitis. No granulomas were observed.

Fecal calprotectin was >800 ug/g.

Diagnosis

Based on colonoscopic, histopathological and biochemical findings, the patient was diagnosed with ulcerative colitis, a type of inflammatory bowel disease.

Monitoring and results

Following treatment with mesalamine, steroids, and antibiotics, the patient's gastrointestinal symptoms improved and vision slightly improved. For ongoing care, the patient continues to be monitored by a multidisciplinary team including rheumatology and gastroenterology specialists.

TABLE 1. Appropriate laboratory investigations
[Source: Saveetha Medical College and Hospital]

Investigation	Result	Reference range
Hemoglobin (Hb)	15 g/dL	13-18 g/dL (males), 12-16 g/dL (females)
Total white blood cells count	16,359 cells/mm ³	4,500-11,000 cells/mm ³
Platelet count	2.56 lakhs/mm ³	150,000-450,000 cells/mm ³

Investigation	Result	Reference range
ESR	51 mm/hr	0-20 mm/hr (females), 0-15 mm/hr (males)
CRP	16.7 mg/L	<3.0 mg/L
BUN	16 mg/dL	7-20 mg/dL
Serum creatinine	0.6 mg/dL	0.7-1.3 mg/dL (males), 0.6-1.1 mg/dL (females)
SGOT	16 U/L	10-40 U/L
SGPT	15 U/L	7-56 U/L
Total bilirubin	1.05 mg/dL	0.2-1.2 mg/dL
Direct bilirubin	0.45 mg/dL	<0.3 mg/dL
Mantoux test	8 mm induration	-
HIV	Negative	-
HBsAg	Negative	-
HCV	Negative	-
Prothrombin time (PT)	16.4 seconds	-
Activated partial thromboplastin time (aPTT)	29.7 seconds	-
International normalized ratio (INR)	1.46	-
Antinuclear antibody (ANA)	Negative	-
Immunological workup	Negative	-
Hypercoagulability workup	Negative	-
HLA-B51	Positive	-
HLA-B52	Positive	-
Complement C3	Normal	-
Complement C4	Low	-
Anti-neutrophil cytoplasmic antibody (ANCA)	Negative	-
Fecal calprotectin	> 800 µg/g	< 50 µg/g

Key results from the CECT abdominal imaging (Figure 1) are as follows:

- Segmental thickening of at least 6.8 mm of the bowel wall, involving mainly the rectum and sigmoid colon. The submucosa is identified as pallor.
- Loose free fluid is detected in the pelvis;
- Engorged mesenteries and a few subcentimetric lymph nodes are associated findings;
- A target pattern of intestinal wall enhancement is detected.

TABLE 2. Appropriate laboratory investigations
[Source: Saveetha Medical College and Hospital]

Assessment	Outcomes
Colonoscopy	Severe hemorrhagic pancolitis characterized by extensive mucosal erythema, edema, ulceration, and thick exudates in both proximal and distal colon.
Colonic biopsy	The colonic mucosa has extensive superficial ulceration, there are cryptitis and abscesses, mixed inflammation in the lamina propria, lymphoplasmacytic infiltration in the edematous lamina propria, and no granulomas are seen.

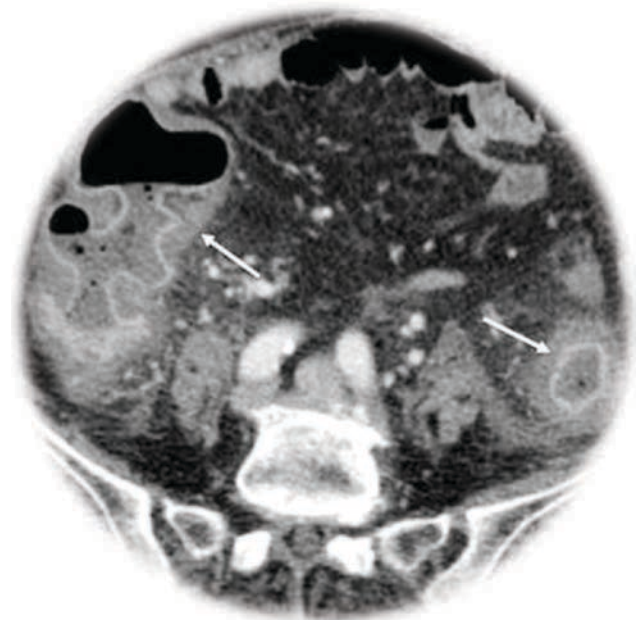


FIGURE 1. CECT abdomen showing target pattern of intestinal wall enhancement

SUMMARY

In this case, the main conclusions were:

- A 19-year-old male experienced sudden, sharp, and painless vision loss in his right eye. Initial examination revealed a diagnosis of central retinal vein occlusion.
- Positive findings in an autoimmune workup, including HLA-B51 and HLA-B52, led to a suspected diagnosis of Behcet's disease, which prompted treatment with steroids.
- During the course of treatment, the patient experienced symptoms of abdominal pain, hematochezia, and fever.
- Colonoscopy with biopsy, contrast CT of the abdomen and elevated fecal calprotectin levels confirmed the diagnosis of ulcerative colitis, a type of inflammatory bowel disease (IBD).

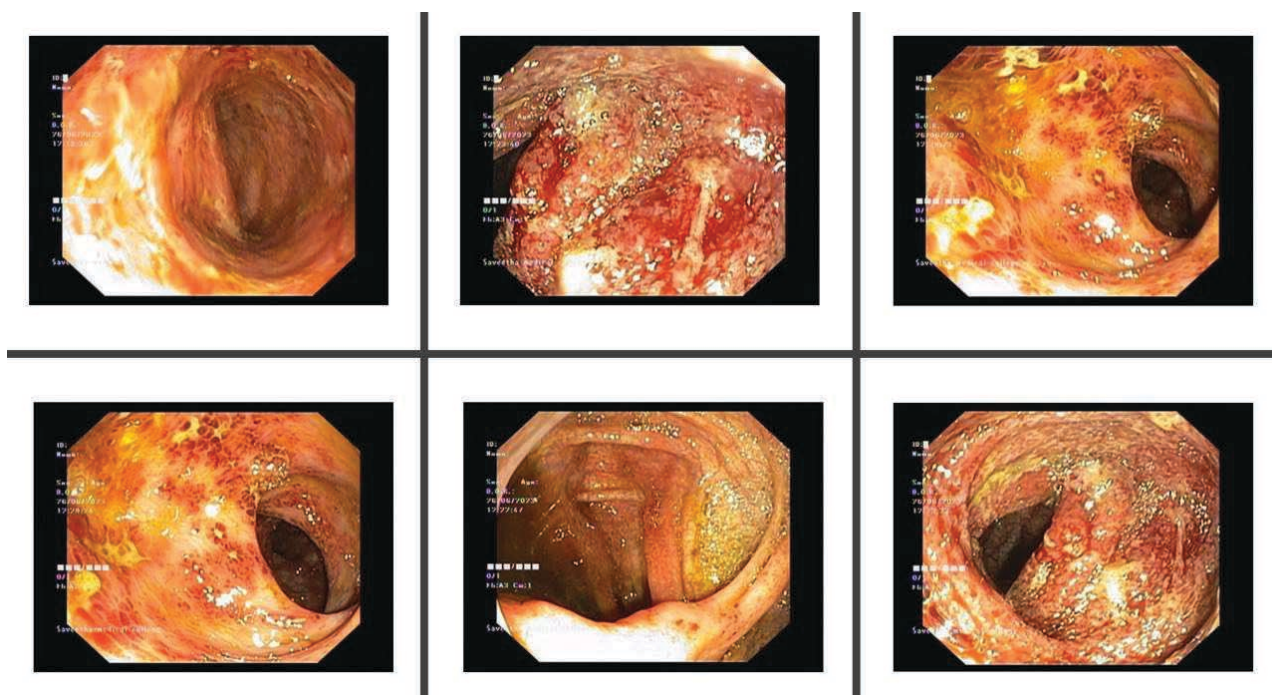


FIGURE 2. Colonoscopic images displaying severe hemorrhagic pancolitis in a patient, characterized by extensive mucosal erythema, edema, ulceration, and thick exudates in both proximal and distal colon

- Central Retinal Vein Occlusion (CRVO) was the initial symptom, presenting before gastrointestinal symptoms, indicating the onset of inflammatory bowel disease.
- A multidisciplinary approach was adopted for treatment, involving gastroenterologists, rheumatologists, and ophthalmologists. The treatment regimen included steroids, immunosuppressants, antibiotics, and mesalamine.

DISCUSSION

Central Retinal Vein Occlusion (CRVO) is a rare but significant ocular complication in patients with Inflammatory Bowel Disease (IBD). This discussion examines various presentations of CRVO in IBD patients, comparing them to our case involving an 19-year-old male with no prior health issues who presented with unilateral, painless vision loss, subsequently diagnosed as CRVO and initially suspected of having Behçet's disease. This case later revealed ulcerative colitis upon the emergence of gastrointestinal symptoms during steroid treatment, and the patient recovered after using mesalamine.

A case series by Choi et al. highlighted CRVO as a rare ocular complication in IBD documenting several cases with diverse presentations. The case series emphasized that CRVO in IBD can present with or without concurrent gastrointestinal symptoms [1].

A review by Mintz et al. emphasized that ocular manifestations of IBD can either coincide or occasionally precede gastrointestinal presentations of IBD [2].

Case reports by Larrson and Hansson-Lunblad et al. and Tien et al. presented cases of CRVO in patients with established inflammatory bowel disease suggesting a correlation between disease activity and CRVO onset [3,5].

These case report illustrate the fact that CRVO has a varying temporal relationship with the course of inflammatory bowel disease.

The study by Zhang et al. focuses on the recommendation to look for systemic causes when young patient present with CRVO [5].

Hypertension, diabetes, and hypercoagulable states are traditional risk factors, frequently leading to age-related vision-threatening conditions such as Central Retinal Vein Occlusion (CRVO). However, in this case, our patient presented with no prior co-morbidities and had none of the traditional risk factors.

This reiterates our main focus point to always evaluate for other systemic causes such as autoimmune disease when patient with no traditional risk factors present with CRVO.

A review by Licona Vera et al. underscores that inflammatory bowel disease (IBD) is a systemic condition with potential involvement across various organ systems. Ophthalmic manifestations may manifest as initial symptoms of the disease, and in patients with established IBD, new ocular complaints may serve as markers of disease severity. The review also highlights the necessity of a multidisciplinary approach for comprehensive management of these patients [6].

Elhag et al. reviewed treatment protocols of IBD and predictive biomarkers of therapeutic response.

The study discussed the role of various treatments including mesalamine in managing IBD and its associated complications [7].

Although the exact mechanism linking IBD and CRVO remains unclear, several hypotheses provide partial explanations:

Pathogenetic mechanisms

The exact mechanisms linking CRVO and UC remain unclear, but several hypotheses offer insight into potential pathogenetic pathways:

- **Systemic inflammation and hypercoagulability:**
 - **Inflammatory state:** UC is characterized by chronic systemic inflammation, which can induce a hypercoagulable state. Elevated levels of inflammatory cytokines, such as TNF-alpha and interleukins, play a crucial role in this process.
 - **Endothelial dysfunction:** Chronic inflammation can damage the endothelium, leading to endothelial dysfunction. This dysfunction increases the risk of thrombus formation by promoting platelet aggregation and disrupting normal anticoagulant mechanisms.
 - **Coagulation cascade disruption:** Inflammatory mediators can alter the balance of pro-coagulant and anticoagulant factors, enhancing the propensity for thrombosis. This disruption can contribute to the development of CRVO by obstructing the retinal vein.
- **Vasculitis:**
 - **Vascular inflammation:** UC-associated vasculitis can involve various vascular territories, including the retinal vessels. Inflammation of the retinal vessels can lead to endothelial damage, reduced oxygenation, and subsequent thrombus formation.
 - **Immune complex deposition:** The deposition of immune complexes in the vascular

walls can incite local inflammation, further exacerbating the risk of vascular occlusion.

- **Autoimmune mechanisms:**
 - **Autoantibodies:** Autoantibodies associated with UC may target vascular tissues, contributing to endothelial damage and increasing the likelihood of thrombotic events.
 - **Systemic inflammatory response:** The interplay between autoimmune activity and systemic inflammation may exacerbate vascular damage, predisposing the patient to CRVO.

- **Genetic factors:**

HLA Associations: The presence of HLA-B51 and HLA-B52 in this patient suggests a genetic predisposition that could influence the immune response and inflammatory processes, thereby increasing the risk of thrombotic complications such as CRVO.

CONCLUSION

This case report underscores the critical importance of considering Inflammatory Bowel Disease (IBD), particularly ulcerative colitis, in the diagnosis of Central Retinal Vein Occlusion (CRVO) in young patients without typical risk factors. The various presentations of CRVO in IBD patients highlight the complexity and variability of this association. While CRVO is a rare ocular complication, it can serve as an early indicator of underlying IBD, especially in young patients without traditional risk factors. Our case underscores the importance of considering IBD in the differential diagnosis of CRVO and demonstrates the effectiveness of a multidisciplinary approach in managing such complex cases. Further research is needed to elucidate the precise pathogenetic mechanisms and optimize treatment strategies for CRVO in IBD patients.

Patient consent: Patient consent obtained

Conflict of interest: none to declare

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