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

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

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ABSTRACT

Background. The primary etiology for the discussed condition leading to blindness is central retinal vein occlusion (CRVO). CRVO occurs due to impaired retinal venous drainage resulting from the obstruction of a critical retinal vein. Better control of underlying conditions such as diabetes and hypertension is known to reduce the risk of CRVO. However, in rare cases, inflammatory bowel disease (IBD) may precede the syndrome. This case report highlights a patient with ulcerative colitis, a subtype of IBD, identified through the presentation of CRVO.

Results. The subject is a 19-year-old male who experienced painless vision loss as his initial symptom, despite having no prior health issues. Extensive imaging revealed ocular ischemia secondary to panuveitis, an HLA-B51/B52 genotype, and moderate-grade CRVO. The preliminary diagnosis of Behcet's disease was considered based on the patient's medical history and clinical examination findings. The treatment regimen included immunosuppressive agents and steroids. Initially, all test results were normal, but the patient soon developed severe gastrointestinal symptoms. Further testing subsequently revealed ulcerative colitis. Notably, the sudden onset of CRVO in this high-risk patient occurred prior to the development of gastrointestinal symptoms associated with IBD.

Conclusion. This case underscores the importance of considering IBD in the differential diagnosis of CRVO, particularly in young patients who do not present with typical risk factors. Prompt recognition and a collaborative approach between gastroenterologists and ophthalmologists are crucial for improving patient outcomes. A comprehensive understanding of the mechanisms underlying the IBD-CRVO connection is necessary, rather than limiting it to specific aspects. This knowledge will better equip physicians for diagnosis and treatment, enhancing their clinical expertise. Early detection and multidisciplinary teamwork are vital for the effective management of such cases, ultimately leading to significant preservation of vision.

Keywords: retinal vein occlusion, ulcerative colitis, Behcet's disease, differential diagnosis, multidisciplinary teamwork and prompt management

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 thrombophilic 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 subtypes: 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 experienced 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 steroids, oral steroids, and the immunosuppressant azathioprine. However, his clinical situation changed unpredictably as he began experiencing gastrointestinal symptoms, including high fever, bloody stools, and abdominal pain. A colonoscopy with biopsies and a contrast-enhanced CT scan of the abdomen identified the underlying cause: 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 highlights the necessity of broadening the diagnostic scope even when initial clinical information appears nonsensical and fragmented.

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), and HLA panels. 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. These findings narrowed the diagnostic consideration to Behcet's disease, leading to pulse therapy with intravenous methylprednisolone (500 mg in 200 ml of normal saline, once daily) for three days.

Additional assessment

Ultrasound imaging revealed a segmented bowel loop thickening in the lower right abdomen and the presence of ascites.
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. He was treated with intravenous metronidazole and piperacillin/tazobactam for seven days, alongside mesalamine suppositories.

Histopathological examination and colonoscopy

Colonoscopy revealed severe hemorrhagic colitis in 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 Cell Count	16,359 cells/mm³	4,500-11,000 cells/mm³
Platelet Count	2.56 lakhs/mm³	150,000-450,000 cells/mm³
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	-
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

Table 2: Colonoscopy and Histopathological Findings [Source: Department of medical Gastroenterology, Saveetha Medical College and hospital]

Assessment	Outcomes
Colonoscopy	Distal colon exudates associated with hemorrhagic pancolitis
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.

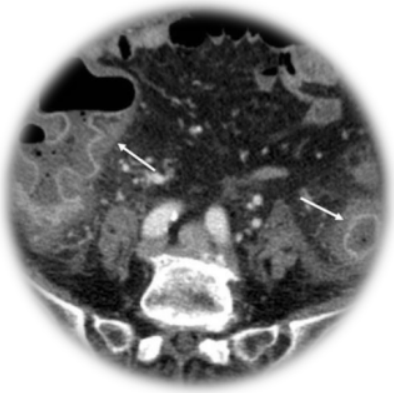

Fig 1: CECT Abdomen

Key results from the CECT abdominal imaging (Fig. 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.

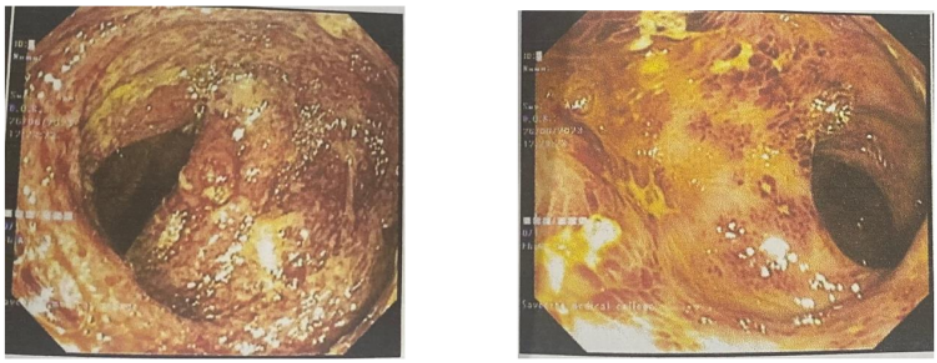

Fig 2: Colonoscopy images showing hemorrhagic colitis

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 and imaging scans (Contrast CT of the abdomen) confirmed the diagnosis of ulcerative colitis, a subtype of inflammatory bowel disease (IBD).
- 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 18-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].

Form et al detailed a case report similar to our case, a young patient with no prior IBD diagnosis presenting with CRVO as initial manifestation of IBD [7].

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

Patil et al provided a comprehensive perspective on ocular manifestations in IBD and describes CRVO as a rare but dangerous complication of inflammatory bowel disease and reinforces the need for a multidisciplinary approach [6].

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

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 [5].

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 [10].

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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TABLES

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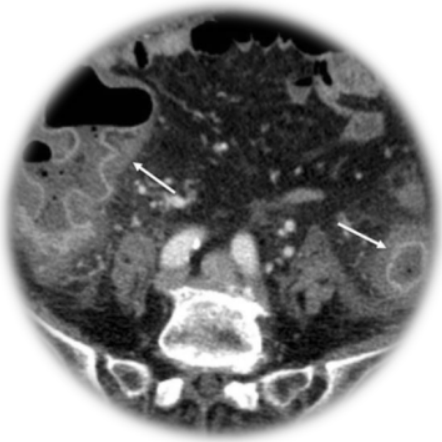
FIGURES



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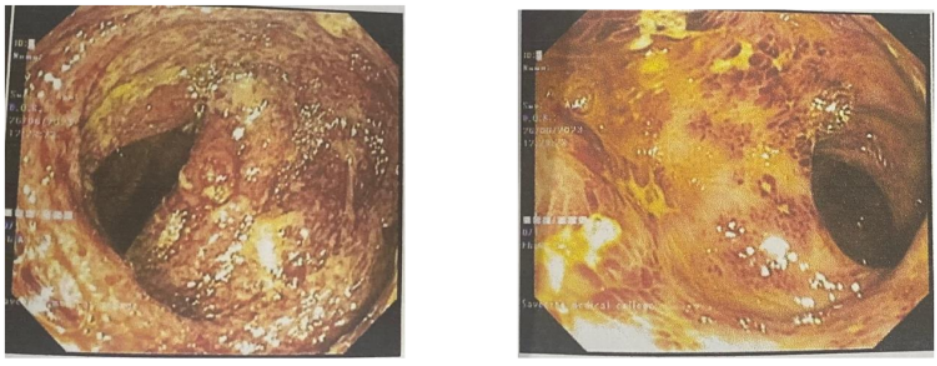

Fig 2: Colonoscopy images showing hemorrhagic colitis