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Central retinal artery occlusion as the initial manifestation of mixed connective tissue disease in a young woman: a case report

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Abstract

Background Retinal artery occlusions are rare amongst young adults, and relevant risk factors and etiology remain unclear. In this report, we present a case of central retinal artery occlusion (CRAO) as the initial manifestation of mixed connective tissue disease (MCTD) in a young woman.

Case presentation A 22-year-old female presented to the emergency department with a sudden decrease in visual acuity in her right eye for 1 hour. She reported a similar episode in her left eye five years prior, which resolved spontaneously after 2 hours. Initially misdiagnosed with optic neuritis in the right eye at another hospital, she was referred to our institution the following day. Clinical examination revealed a CRAO in her right eye. A detailed medical history revealed that she had developed livedo reticularis (LR) on both lower limbs five years ago, which had been overlooked and untreated. Further rheumatologic history, hematologic tests, and an autoimmune work-up confirmed a diagnosis of mixed connective tissue disease (MCTD).

Conclusion In young patients presenting with CRAO, further examinations should be conducted to investigate systemic disease or an embolic source to prevent future sequelae.

Keywords Central retinal artery occlusion, Mixed connective tissue disease, Livedo Reticularis, Young adults

Introduction

Central retinal artery occlusion (CRAO) is an acute ischemic event in the eye that can lead to severe vision loss. It predominantly affects elderly individuals with conditions such as hypertension, coronary atherosclerosis, diabetes, carotid artery dissection, internal carotid artery aneurysm, and vasculitis, particularly giant cell arteritis. CRAO is also associated with tuberculosis and syphilis, often serving as an early indicator of cardiovascular and cerebrovascular disease progression [1]. However, CRAO is extremely rare in children and young adults, with an incidence rate estimated at less than 1 in 50,000 among individuals under 30 years of age [2]. While atherosclerosis is a common cause in older patients, younger patients may present with a variety of underlying disorders,

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ranging from localized ocular issues to systemic diseases [3]. The etiologies of CRAO in younger individuals are diverse and may include conditions predisposing to embolic events, congenital anatomical abnormalities, hypercoagulable states, trauma, autoimmune diseases, and tumors [4].

Mixed connective tissue disease (MCTD) is an autoimmune disorder characterized by overlapping features of systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and polymyositis [5]. MCTD is serologically identified by elevated titers of anti-U1-RNP antibodies. MCTD-associated retinal has been reported on sparsly, and its underlying mechanism remains poorly understood. Here, we present a unique case of MCTD-associated CRAO in a young adult.

Case presentation

A 22-year-old female presented to the emergency department with a sudden loss of vision in her right eye, lasting for 1 hour. Five years prior, she experienced a similar episode in her left eye, which spontaneously resolved within 2 hours without treatment. At presentation, her best-corrected visual acuity (BCVA) was no light perception in the right eye and 0.8 (Snellen decimal) in the left eye. A relative afferent pupillary defect (RAPD) was positive in the right eye. Initially, she was misdiagnosed with optic neuritis in the right eye and received medical treatment. She was referred to our institution the following day, with no improvement in her vision.

Standard ophthalmic examination revealed normal ocular motility and external appearances across both eyes. Her bilateral intraocular pressure was 12 mmHg. The right eye displayed a white ischemic retina with a prominent cherry-red spot at the fovea, while the left eye appeared normal (Fig. 1A1 and B1). Optical coherence tomography (OCT) revealed increased reflectivity and thickening of the inner retinal layers of the right eye, with atrophy and decreased thickness of the inner retina layers in the left eye (Fig. 1A2 and B2). Fluorescein angiogram confirmed right CRAO, with a markedly delayed arteriovenous filling time (Fig. 1A3 and B3). The patient was diagnosed with right CRAO and was immediately treated with sublingual isosorbide dinitrate, systemic pentoxifylline to increase blood oxygen content and dilate retinal arteries, methylcobalamin to support nerve health, and anterior chamber paracentesis to reduce intraocular pressure and improve retinal artery perfusion [1]. However, these treatments did not result in significant improvement in visual acuity compared to observation alone [6]. Nevertheless, they may play a role in preventing CRAO in the contralateral eye and providing psychological comfort to the patient.

This patient was in an extremely low risk group for CRAO, given her young age and absence of known risk factors such as diabetes, hypertension, ischemic heart disease, cerebrovascular accidents, smoking, oral contraceptive use, pregnancy, recent dental work, or facial cosmetic procedures [4].

After a thorough examination and a detailed medical history review, we discovered that the patient had developed livedo reticularis (LR) on both lower extremities 5 years prior (Fig. 2A), which had not been diagnosed or treated. Comprehensive systemic and autoimmune-related examinations were conducted, revealing elevated anti-U1 RNP antibodies, anti-nuclear antibodies at a titer of 1:1000, positive anti-dsDNA antibodies, and weakly positive anti-nucleosome antibodies. Anti-phospholipid antibodies, rheumatoid factor, and lupus anticoagulant were negative. Homocysteine levels were 13.5 μmol/L. Erythrocyte sedimentation rate (ESR) was 32 mm/hour, and C-reactive protein (CRP) was 3.5 mg/L. Coagulation studies showed an activated partial thromboplastin time

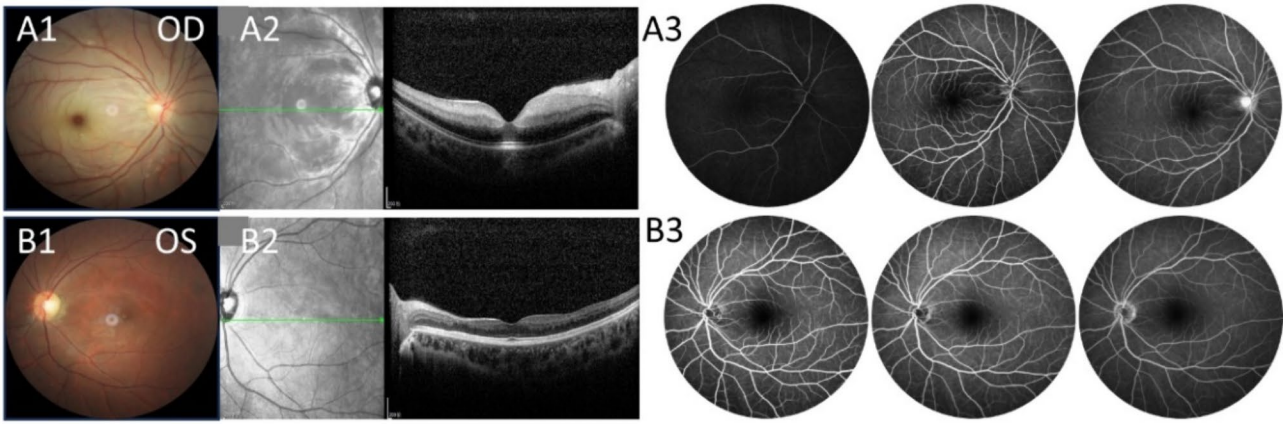

Fig. 1 Fundus photography, OCT, and fluorescein angiogram at initial presentation in our hospital. **A1**: Fundus photography of the right eye showing a white retina with a cherry-red spot. **A2**: OCT of the right eye showing edema and increased reflectivity in the inner retinal layers. **A3**: Fluorescein angiogram of the right eye showing delayed arteriovenous filling. **B1**: Fundus photography of the left eye appears normal. **B2**: OCT of the left eye showing atrophy and reduced thickness of the inner retinal layers. **B3**: Fluorescein angiogram of the left eye showing delayed arteriovenous filling

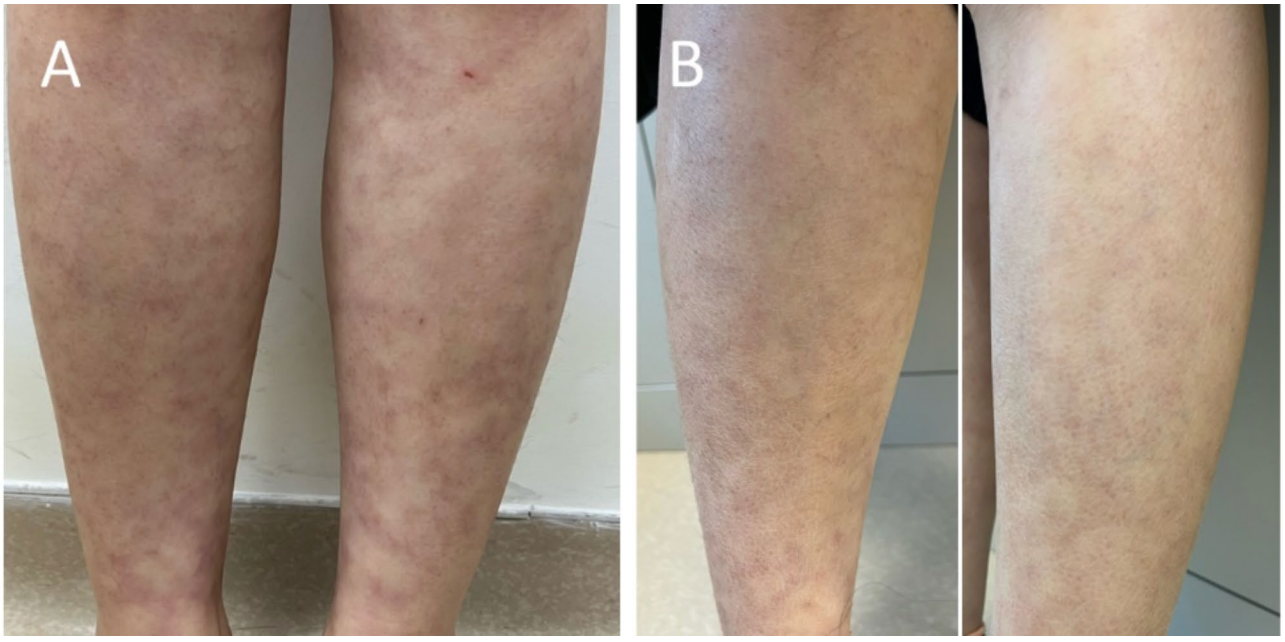

Fig. 2 Local lower limb photos of the patient before and after treatment. **A**: The legs are covered with livedo reticularis. **B**: 3 months later, the livedo reticularis on both lower limbs had improved

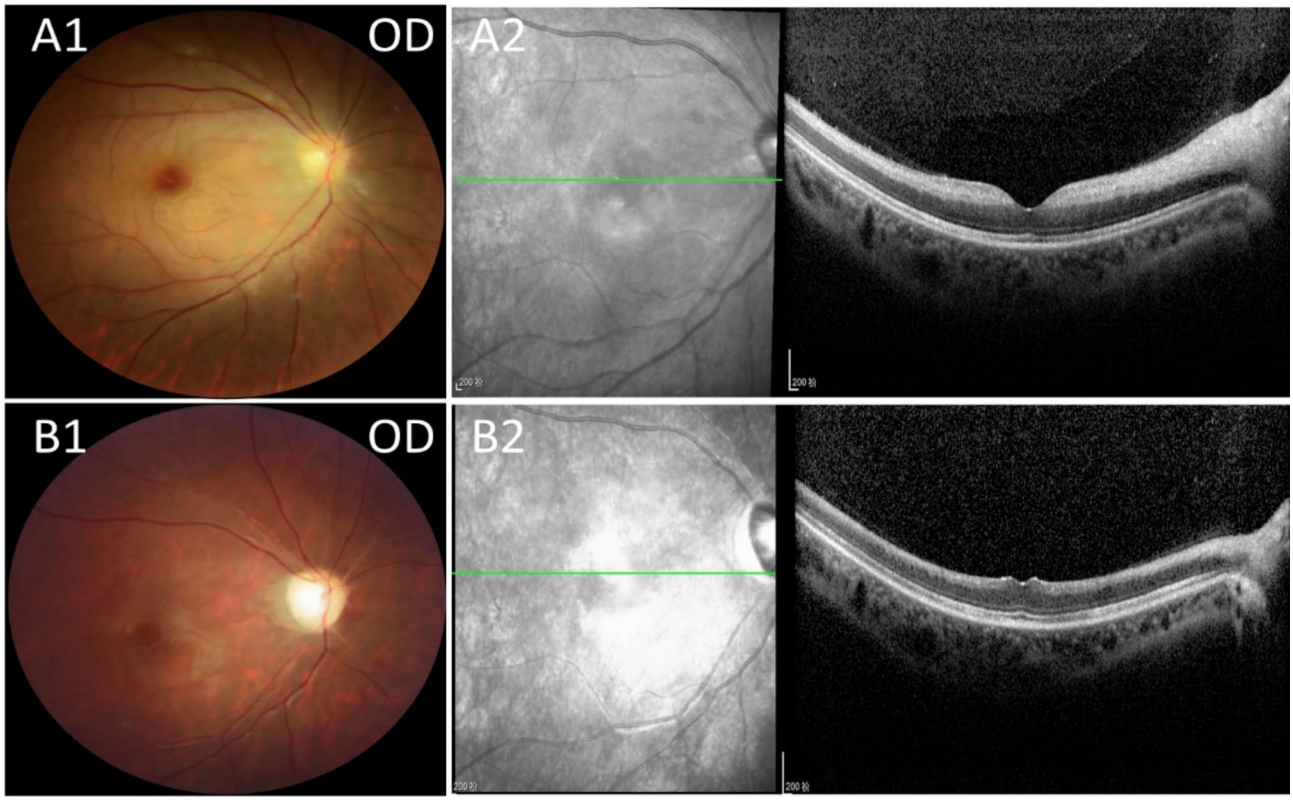

Fig. 3 Fundus photography and OCT after treatment. **A1**-**A2**: 2 weeks following treatment, retinal edema had resolved remarkably in right eye. **B1**-**B2**: 3 months later, optic nerve atrophy and retinal artery stenosis were observed in the right eye

(APTT) of 28.9 seconds (reference range 22.7–31.8 seconds) and a prothrombin time (PT) of 11.3 seconds (reference range 10.5–15 seconds). Tests for HIV, Hepatitis B, Hepatitis C, herpesvirus, toxoplasmosis, Epstein-Barr virus, and syphilis were negative. MRI and MRA of the brain, as well as electrocardiogram and echocardiograph, were normal.

The patient was diagnosed with MCTD by rheumatologists and started on prednisone acetate tablets 60 mg and hydroxychloroquine sulfate 400 mg daily. At the first evaluation, two weeks after presentation, her right eye visual acuity had improved to hand motion, and the retinal edema had resolved remarkably in the right eye (Fig. 3A1 and A2). However, 3 months later, optic nerve atrophy and retinal artery stenosis were observed in the right eye (Fig. 3B1 and B2). The LR on both lower limbs improved significantly after treatment (Fig. 2B).

Discussion

Central retinal artery occlusion (CRAO) is a common retinal vascular disease that significantly impairs patients' visual function and quality of life. CRAO is typically caused by emboli related to atherosclerosis and thrombosis resulting from atherosclerotic disease, hypercoagulable states, or inflammatory disease. CRAO can be categorized into four distinct clinical entities: non-arteritic permanent CRAO, non-arteritic transient CRAO, non-arteritic CRAO with cilioretinal artery sparing, and arteritic CRAO [5]. By age, CRAO is classified as occurring in the elderly, young adults, or children. CRAO is extremely rare in young people, where the etiologies and risk factors are multifactorial. These include hypercoagulable states (such as hyperhomocysteinemia and coagulation abnormalities), congenital anatomical variations, trauma, tumors, and autoimmune diseases like mixed connective tissue disease (MCTD), systemic lupus erythematosus (SLE), and antiphospholipid antibody syndrome (APS) [4, 7].

Livedo reticularis (LR) is a violaceous, blue, or red net-like or mottled pattern on the skin, typically seen on the trunk, arms, or legs. The pattern may consist of regular, unbroken circles or irregular, broken circles and reflects an underlying change in cutaneous blood flow [8]. Physiological LR, a normal vasospasm response in healthy individuals under cold conditions, disappears after rewarming. Pathological LR, however, is associated with conditions such as vasculitis, hypercoagulability, and autoimmune diseases. In young women, common causes of pathological LR include MCTD, SLE, APS, and Sneddon syndrome. The underlying pathology in LR often involves obstruction or inflammation of arterioles [9].

Eye complications of MCTD include dry eye syndrome, conjunctival dryness, scleritis, and other anterior segment lesions [10]. Previous studies have shown that MCTD can also lead to retinal vascular disease. Postlethwaite et al. reported an 18-year-old woman diagnosed with MCTD presenting with retinal vasculitis and choroidopathy [11]. Similarly, Pete et al. described a 31-year-old woman with MCTD complicated by frosted branch angiitis [12]. Another study reported a 31-year-old female with MCTD who experienced central retinal vein occlusion in both eyes [13]. MCTD can be serious, leading to pulmonary, kidney, cardiovascular, gastrointestinal, and central nervous system manifestations, such as pulmonary arterial hypertension, glomerulonephritis, pericarditis, myocarditis, conduction disturbances, and esophageal dysfunction [14–16]. Some patients with anti-U1-RNP antibodies may satisfy the criteria for systemic lupus erythematosus (SLE) or systemic sclerosis (SSc) during the clinical course and may experience a shift from MCTD to the true features of SLE [17]. Additionally, studies have found that patients with SLE can experience unilateral or bilateral CRAO [18–20]. However, the exact mechanism remains unclear. It is speculated that the pathogenesis may involve immune complex-mediated vasculitis and vascular occlusion [21]. A study indicated that 30% of MCTD patients experience vascular leakage, which is more frequent than in primary Sjögren's syndrome and SLE [22].

The patient in this case is a young woman who experienced sudden loss of vision and a positive relative afferent pupillary defect (RAPD+). Retinal changes on OCT were not recognized by the initial treating physician, leading to a misdiagnosis of optic neuritis. It is important to note that RAPD+can occur in cases of optic neuritis, CRAO, central retinal vein occlusion, traumatic optic neuropathy, and other conditions. In the early stages of ischemia, the retina may not show obvious morphological changes. An experimental study showed that rhesus monkeys' retinas did not exhibit detectable damage after 97 minutes of CRAO, but progressive ischemic damage occurred later, with CRAO lasting about 4 hours leading to irreversible retinal damage [23]. Based on the patient's early symptoms, CRAO should have been considered. For young patients with sudden vision loss, in addition to optic neuritis, careful examination of retinal layers and arteriovenous vessel changes on OCT is crucial. Reviewing the patient's initial OCT at another hospital, paracentral acute middle maculopathy (PAMM) was evident, characterized by thinning of the inner retinal layers [24]. PAMM is an early OCT finding suggestive of retinal vascular ischemia, and OCT angiography, a non-invasive tool, would have been helpful. The patient's transient visual loss in the left eye five years ago, which resolved spontaneously, may have been due to partial retinal obstruction or PAMM at that time. Before progressing to CRAO, PAMM may be the first sign requiring attention. When the patient presented to our hospital the next

day, the right eye's fundus showed typical symptoms of CRAO.

Previous study has reported that patients with Susac syndrome complicated by CRAO [25]. Susac syndrome, characterized by the triad of encephalopathy with or without focal neurological signs, branch retinal artery occlusions, and hearing loss, was considered but excluded based on normal brain MRI and MRA findings and the absence of hearing loss [26, 27]. Susac syndrome also typically involves repeated occlusion of branch arteries, which were not present in this case. Previous study has shown that patients with Sneddon syndrome also suffer from CRAO [28]. Sneddon syndrome, also known as idiopathic LR with cerebrovascular accidents, is another condition reported to involve persistent LR and cerebrovascular disease [29]. It is characterized by persistent LR and cerebrovascular disease and involves noninflammatory thrombotic vasculopathy affecting small arteries and arterioles in the brain and skin, potentially leading to transient ischemic attacks, strokes, and dementia [28–30]. However, the patient's brain imaging was normal, and serological testing revealed anti-U1-RNP antibodies, a 1:1000 titer of anti-nuclear antibodies, positive anti-dsDNA antibodies, and weakly positive anti-nucleosome antibodies, with negative results for anti-phospholipid antibodies, rheumatoid factor, homocysteine, and lupus anticoagulant. The patient was ultimately diagnosed with CRAO in the right eye and MCTD. In young patients with CRAO, comprehensive examinations of the heart, blood, and autoimmune systems are as important as ophthalmic evaluations.

Conclusion

This case is the first to report a young patient with CRAO associated with MCTD. CRAO is extremely rare in young individuals, who often present with a variety of underlying conditions, ranging from localized ocular issues to systemic diseases. In cases of obstructive vasculopathy in young patients without an obvious cause, we recommend comprehensive systemic evaluations to identify the underlying cause of CRAO. Early diagnosis, active treatment, and prevention strategies are crucial to minimize the risk of CRAO in the other eye and to reduce the potential for additional morbidity and mortality in these patients.

Abbreviations

CRAO	Central retinal artery occlusion
MCTD	Mixed connective tissue disease
LR	Livedo reticularis
BCVA	Best corrected visual acuity
RAPD	Relative afferent pupillary defect
OCT	Optical coherence tomography
SLE	Systemic lupus erythematosus
PAMM	Paracentral acute middle maculopathy

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Author contributions

CLC contributed to the conception and design of the case report. KL and YZL collected the patients' medical records. KL wrote the main manuscript text. CLC, XHY, LC revised the manuscript.

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Data availability

Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate

Ethics approval and consent to participate this study was approved by the ethics committee of Beijing Tongren Eye Center.

Consent for publication

Written informed consent for publication of clinical evidence and images was obtained from patient's parents.

Competing interests

The authors declare no competing interests.

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