



ANCA-Negative Churg-Strauss Syndrome Presenting as Bilateral Central Retinal Artery Occlusion: A Case Report

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Abstract

A 42-year-old man with undiagnosed Churg-Strauss syndrome (CSS) developed bilateral central retinal artery occlusion (CRAO). His medical history included bronchial asthma and irregular prednisolone usage but no atherosclerotic risk factors. At presentation, visual acuity (VA) was hand motion in the right eye and counting fingers in left eye. On fundoscopy, retinal whitening and a cherry red spot were observed in the right eye, while the fundus was normal in the left eye. After eyeball massage and systemic intraocular pressure lowering agents, his VA improved. On day 5 of treatment, he experienced right limb weakness and purpura on his right foot, and electromyography revealed mononeuritis multiplex. Laboratory tests indicated eosinophilia (52%). Based on the presence of hypereosinophilia, bronchial asthma, mononeuritis multiplex, vasculitis purpura, and sinusitis that was detected during etiological investigations, the patient was diagnosed as having CSS according to the American College of Rheumatology diagnostic criteria. Intravenous methylprednisolone 1 g/day was administered for 3 consecutive days and 1 g cyclophosphamide was started and continued monthly for 6 months. Foot drop and vasculitic purpura improved after 7 days, but there was no further improvement in visual acuity. In conclusion, in the presence of bilateral CRAO and lack of atherosclerotic risk factors, CSS should be considered as a predisposing factor and investigations should be conducted accordingly.

Keywords: Central retinal artery occlusion, anti-neutrophil cytoplasmic antibodies, Churg-Strauss syndrome

Introduction

Central retinal artery occlusion (CRAO) is a devastating ocular emergency that usually occurs secondary to one or more serious systemic diseases such as carotid artery or cardiac valvular disease, hypercoagulability, atrial fibrillation, and autoimmune diseases.¹ According to pathophysiology, CRAO can be divided into two groups, arteritic and non-arteritic. The arteritic category comprises less than 5% of CRAO cases and is related to a vasculitic etiology.² Eosinophilic granulomatosis with polyangiitis (EGPA), also called Churg-Strauss syndrome (CSS), is known as a form of vasculitis characterized by inflammation of the blood vessels that can restrict blood flow and damage vital organs and tissues. Individuals diagnosed with EGPA

usually have a history of asthma or allergies. Despite the presence of clear diagnostic criteria, the diagnosis of CSS can be delayed in the clinical setting. This is partly related to the sheer variety of clinical presentations of the disease.³ Regarding anti-neutrophil cytoplasmic antibody (ANCA) status, CSS can be divided into two major subsets: the ANCA-positive patients, who demonstrate clinical and histopathologic features of vasculitis, and the ANCA-negative patients, who exhibit tissue eosinophilic infiltration.⁴ Eosinophilic myocarditis⁵, neuroendocrine carcinoma⁶, eosinophilic vasculitic neuropathy⁷, multiple oral ulcerations⁸, and inflammatory pseudotumor of the anterior orbit⁹ have been reported as initial presentations of CSS in the literature. Herein, we describe a patient with undiagnosed

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CSS who developed simultaneous bilateral CRAO. To the best of our knowledge, this is a rare case of CSS with this clinical presentation, which we recognized during CRAO workup. This case report is of great importance, as the first presentation of CSS might be purely ocular.

Case Report

A 42-year-old man presented to the hospital due to acute painless loss of vision in the right eye 12 hours before and in the left eye immediately before admission. He had a 6-month history of bronchial asthma and irregularly took prednisolone 10 mg/day. Ocular examination revealed that his visual acuity (VA) was hand motion in the right eye and counting fingers (CF) in the left eye. Slit-lamp examination showed bilateral posterior subcapsular cataract that was more severe in the right eye. Fundus photograph showed a significant retinal whitening and cherry red spot in the right eye (Figure 1A), and varying degrees of retinal whitening and soft exudates in the left eye at the presentation (Figure 1B).

Eyeball massage was performed as the initial treatment for both eyes, followed by systemic intraocular pressure lowering medication. The patient refused fluorescein angiography in the acute phase of CRAO. Therefore, the diagnosis of CRAO was made according to fundus appearance. Two hours after the initial treatment, retinal perfusion improved in both eyes, and VA was CF in the right eye and 3/10 in the left eye. The patient underwent a thorough systemic work-up including assessment for diabetes, hypertension, hyperlipidemia, carotid stenosis, and cardiovascular diseases in an effort to identify undiagnosed risk factors, but the results were negative.

Neurologic, respiratory, and dermatologic examinations were unremarkable on the day of admission. Laboratory data showed leukocytosis ($11,900/\text{mm}^3$) and eosinophilia (8%). C-reactive protein (CRP) level was 21 mg/dL (normal range: <5 mg/dL) and erythrocyte sedimentation rate (ESR) was 43 mm/h. Hepatic and renal laboratory tests were normal. Lupus anti-coagulant, anti-cardiolipin, and anti-B2 glycoprotein levels were within normal ranges. Transthoracic echocardiography was normal and there were no abnormal findings in chest X-ray or brain computed tomography (CT). Because of the elevated ESR and CRP and lack of atherosclerotic risk factors, there was a high suspicion of vasculitis as the etiology and oral prednisolone 60 mg/day was administered. However, there was no further improvement in his vision.

On day 5 of treatment, the patient experienced right limb weakness and purpura on his right foot. Neurologic examination showed L5 neuropathy and foot drop. Electromyography and nerve conduction velocity were performed and mononeuritis multiplex was reported. Skin examination revealed palpable, non-blanchable purpuric rash on his right foot (Figure 2). Repeat complete blood count showed significant leukocytosis ($17,400/\text{mm}^3$) with 52% eosinophils. Perinuclear and cytoplasmic ANCA (p-ANCA and c-ANCA) were negative.

ESR was 51 mm/h and CRP level was 32 mg/dL. Brain magnetic resonance imaging was normal (Figure 3A, B) but coronal and axial slices revealed paranasal sinusitis (Figure 3C, D). Therefore, CT scans were not performed to prevent radiation. Based on the presence of hypereosinophilia, bronchial asthma, mononeuritis multiplex, vasculitic purpura, and sinusitis, the patient met the classification criteria of the American College of Rheumatology (Table 1) and was diagnosed as having CSS.

Intravenous methylprednisolone 1 g/day for 3 consecutive days and 1 g cyclophosphamide was started and continued monthly for 6 months. Thereafter, oral prednisolone 50 mg/day was prescribed and tapered to 25 mg/day at 6 weeks. Foot drop and vasculitic purpura improved 7 days later; however, there was no further improvement in his visual acuity. Fundus photograph showed retinal exudate in the posterior pole and macular retinal pigment epithelial changes as well as pale disc due to optic atrophy in the right eye (Figure 4A) and normal fundus in the left eye (Figure 4B) at 2-month follow-up. As expected, CRAO led to optic atrophy in the right eye.

The patient provided written informed consent for publishing the images and details of the disease. Based on our university

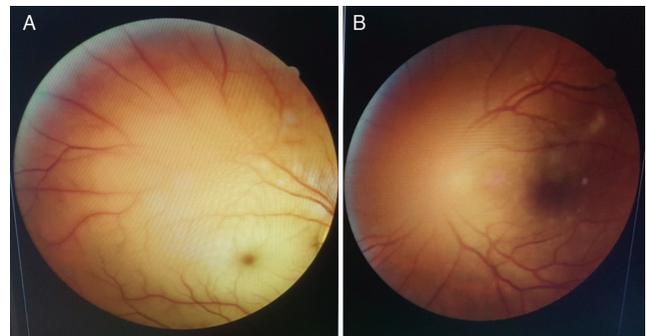


Figure 1. A) Color fundus photograph of the right eye showing a classical cherry-red spot in the macula. B) Retinal whitening and soft exudates in the left eye



Figure 2. Palpable, non-blanchable purpuric rash on the patient's right foot

Table 1. Churg-Strauss syndrome: American College of Rheumatology classification criteria (4 of the 6 criteria should be present)¹²

Asthma
Eosinophilia >10%
Mononeuropathy or polyneuropathy
Non-fixed pulmonary infiltration
Paranasal sinus abnormalities
Extravascular eosinophils infiltration on biopsy finding

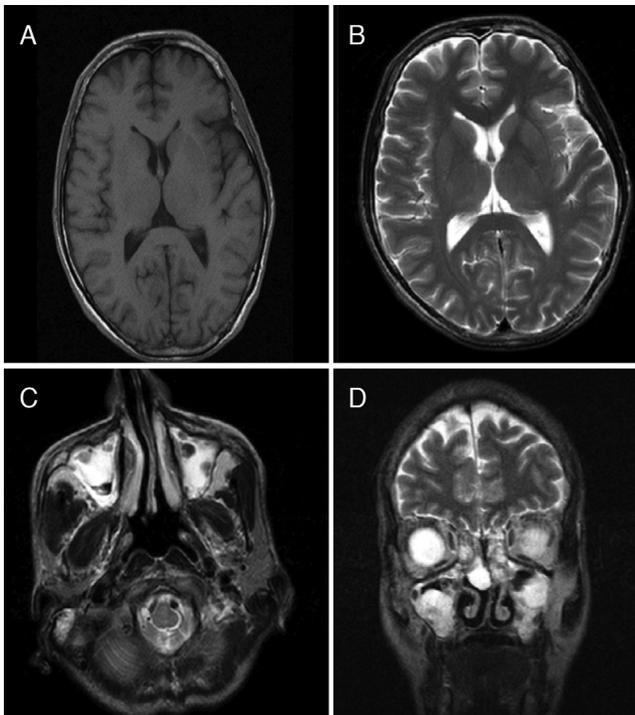


Figure 3. Magnetic resonance imaging (MRI) of the brain is normal (A, B). Coronal (C) and axial (D) slices show paranasal sinusitis

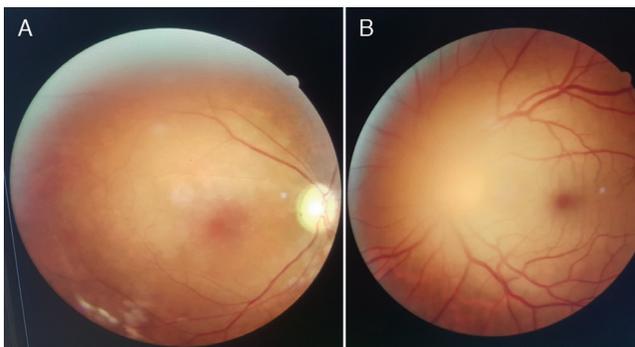


Figure 4. Color fundus photograph at 2-month follow-up: A) Retinal exudates in the posterior pole and macular retinal pigment epithelial changes as well as pale disc in the right eye. B) Normal fundus in the left eye

policy, institutional review board approval is not required for case reports.

Discussion

CSS is a rare disease with small vessel vasculitis characterized by eosinophilia and occurs almost exclusively in patients with asthma. The syndrome can vary in presentation and there is no pathognomonic ocular finding. Ocular presentations can be categorized into 2 groups, largely for prognostic explanations, as idiopathic orbital inflammation-type and ischemic vasculitis-type. Patients with ischemic vasculitis tend to be older than those with idiopathic orbital inflammation.¹⁰ According to a report by Takanashi¹¹, ANCA-positive patients are more likely to present clinically with classical small-vessel vasculitis, which affects the disease progression and outcomes. However, this was not confirmed in a study by Akella et al.¹⁰ that showed no statistically significant difference in ANCA positivity between the ischemic and inflammatory groups. In the literature, ischemic vasculitis presentations including retinal artery and vein occlusions have been reported in 12 patients. These presentations were mostly accrued in the known cases of CSS and were not the first presentations, and in two cases they were bilateral.¹⁰ However, our patient was ANCA-negative with bilateral CRAO as the first presenting clinical sign, and steroid pulse therapy resulted in no improvement in visual acuity. This result is consistent with the Akella¹⁰ study showing that ischemic vasculitis-type ophthalmic presentations have a less dramatic response to steroids. However, early diagnosis and timely treatment of CSS can prevent systemic life-threatening complications.

In the presence of bilateral CRAO and lack of atherosclerotic risk factors, it is important to rule out systemic vasculitis like CSS. Early diagnosis of the disease can be life-saving. However, the effect of systemic treatment on improving the patient’s vision is still unclear.

Ethics

Acknowledgment: Special thanks to the patient for granting us permission to report his illness.

Informed Consent: Written informed consent was obtained from the patient for publishing the images and details of the disease.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: M.N., Z.S, Design: M.N., Z.S, Data Collection or Processing: M.N., Z.S, Analysis or Interpretation: M.N., Z.S, Literature Search: M.N., Z.S, Writing: M.N., Z.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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