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Central Retinal Artery Occlusion: Acute Management and Treatment

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Abstract

Purpose of Review—This review will seek to answer if advances in ophthalmic imaging and evolution of treatment modalities have shed further light on the epidemiology, pathophysiology, diagnosis, and acute management of acute CRAO.

Recent Findings—Imaging characteristics of acute CRAO have been further characterized with the use of fluorescein angiography, optical coherence tomography (OCT), OCT-angiography, and indocyanine-green angiography. Layer segmentation of OCT imaging has found inner retinal layer hyper-reflectivity to be a common finding in acute CRAO. Non-invasive therapies, fibrinolytic delivery, and surgical interventions for acute CRAO have been further evaluated as potential management tools.

Summary—A large body of literature reports very inconsistent treatment success with a wide variety of modalities. Currently, there is no clear evidence supporting the use of fibrinolytics in acute CRAO. Large, multicenter, randomized control trials are necessary to elucidate the role of the various acute treatment options in the management of CRAO.

Keywords

retina; central retinal artery occlusion; intra-arterial tPA; optical coherence tomography angiography

Introduction

Central retinal artery occlusion is a devastating ocular emergency with no accepted treatment and a poor visual prognosis. This review will survey epidemiology, pathophysiology, diagnosis, and acute management.

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Epidemiology, Risk Factors, and Prognosis

Central retinal artery occlusion (CRAO) is a rare event with an age and sex adjusted incidence of 1.9 per 100,000 people in the United States.[1] An analysis of claims data from the Korean National Health Insurance Service demonstrated a similar incidence rate for CRAO of 1.8 per 100,000 person-years. The authors noted an increasing rate of CRAO with increasing age and a 1.47 times greater incidence rate in men relative to women.[2] They reported a doubling of the incident rate of CRAO with increasing 10-year age brackets (2.44, 5.85, and 8.56 per 100,000 person-years in the 50–59, 60–69, and 70–79 age brackets, respectively).[2]

A diagnosis of CRAO in the absence of cilioretinal sparing carries a poor prognosis with vision ranging from count fingers to hand motion in a majority of patients. A prospective study of 260 patients with CRAO reported best corrected visual acuity (BCVA) of 20/400 or worse vision in 80% of eyes.[3] Ten percent of patients with CRAO maintain good central vision.[3] Risk factors include systemic hypertension (seen in 2/3 of patients)[1], diabetes, carotid and coronary artery disease, and smoking tobacco.[4]

Development of CRAO carries prognostic significance for the development of further systemic pathology. Analysis from the Korean National Health Insurance claims data indicated that patients with CRAO carry a 1.78 fold increased risk (95% confidence interval, 1.32 – 2.41) of development of cerebral stroke within 4 years when compared to a cohort of age-matched controls.[5] A 2016 review of retrospective cohort-control comparison studies (324,518 total cases) indicated that patients presenting with retinal artery occlusion had a higher lifetime development of cerebrovascular disease including myocardial infarction and stroke (odds ratio of 2.01; 95% confidence interval: 1.21–3.34).[6] In fact, 23–24% of patients with acute retinal ischemia have MRI evidence of concurrent silent cerebral infarctions, as seen in three retrospective studies of a combined 375 patients who were imaged with diffusion-weighted MRI at time of visual loss.[7–9]

Pathophysiology

The central retinal artery is terminal branch of the ophthalmic artery and provides circulation to the inner thirds of the neurosensory retina. CRAO is believed to occur due to an embolic or thrombotic occlusion of the central retinal artery with resultant retinal ischemia. Patients with retinal artery occlusion present with acute painless loss of vision of a varying degree depending on absence or presence of a cilioretinal artery and duration of blood flow cessation.

CRAO can be divided into four distinct clinical entities. Non-arteritic permanent CRAO accounts for two thirds of all cases and is the result of thrombosis or emboli inducing severe vision loss. The exact location of the occlusion is unclear but is believed to occur at the narrowest part of the retinal artery lumen as it traverses the optic nerve.[10] Irreversible damage from ischemia has been noted to occur at 240 minutes in experimental animal models.[11] The primary sources for emboli are believed to be carotid plaques and plaques emanating from the heart.[12] Histologic studies reveal that 74% of central retinal artery

emboli are composed of cholesterol, 10.5% composed of calcific material, and 15.5% of platelet-fibrin complexes.[13]

While the overwhelming majority of CRAOs presents with permanent vision loss, a subset of non-arteritic CRAOs may manifest as *amaurosis fugax* (Latin for “fleeting darkening”) and accounts for 15% of cases. Not surprisingly, this carries the best prognosis for vision but portends a grave prognosis for ocular recurrence and cerebrovascular recurrence.[12] The North American Symptomatic Carotid Endarterectomy Trial (NASCET) study demonstrated that patients with *amaurosis fugax* and ipsilateral carotid stenosis have a 14.9–22.2% rate of ipsilateral stroke in 5 years depending on degree of stenosis and therapy (medical management versus carotid endarterectomy).[14]

The third entity, non-arteric CRAO with cilioretinal sparing is associated with less severe central vision loss as the cilioretinal artery may spare perfusion to the fovea. Approximately 30% of eyes are believed to possess a patent cilioretinal artery which arises proximal to the central retinal artery and nourishes the papillomacular bundle.[15]

Finally, arteritic CRAO comprises less than 5% of CRAO cases and is attributed to a vasculitic etiology, the most common being giant cell arteritis (GCA). GCA is an idiopathic vasculitis that primarily affects an elderly population with granulomatous inflammation of the intima of the small to medium-sized arteries of the upper body and head resulting in stenosis and occlusion of flow. Patients over the age of 50 years presenting with retinal artery occlusion and symptoms of scalp tenderness, jaw claudication, nodular temporal arteries, fever, malaise, and upper or lower body muscle tenderness or weakness should be evaluated with a complete blood count, erythrocyte sedimentation rate, and C-Reactive Protein.[3] Other less common vasculitic etiologies of CRAO include polyarteritis nodosa, granulomatosis with polyangiitis (formerly Wegener’s), Churg-Strauss syndrome, and Behcet’s disease. Given the rarity of these conditions in CRAO, hematologic work-up should be guided by a careful review of systems including, but not limited to, hemoptysis, epistaxis, joint pains, malaise, back pain, oral or genital ulcers, shortness of breath and dysuria.[12]

Ophthalmic Investigation

Visual acuity testing, evaluation for an afferent pupillary defect, funduscopic examination, and fluorescein angiography (FA) remain the mainstay tools for diagnosing central retinal artery occlusion. Funduscopic findings performed within 7 days of CRAO development include retinal whitening, a cherry-red spot (due to axoplasmic stasis and swelling of the ganglion cells accentuating the foveal center devoid of ganglion cells), “cattle trucking” or box-carring (due to sludging and segmentation of the blood column in the retinal vessels), retinal arterial attenuation, and optic disc edema (Figure 1 and 2). Findings in chronic CRAO include optic nerve atrophy, retinal arterial attenuation, cilioretinal collaterals, and macular retinal pigment epithelial changes.[16]

Certain groups have further sub-classified CRAO based on clinical and imaging findings. Schmidt and colleagues categorized CRAO into incomplete (reperfused), subtotal (partially

reperfused), or total depending on the degree of vision loss, retinal edema seen by ophthalmoscopy, and delay in arterial blood flow seen on FA (Figure 3 and 4). Diminished visual acuity, mild retinal edema and thickening, and delayed but not completely interrupted blood flow on FA indicated incomplete CRAO. Severe reduction in visual acuity, distinct retinal edema with a cherry-red spot, and distinct delay in arteriolar blood flow on FA indicated subtotal CRAO. No light perception, massive retinal edema, occluded arterioles (predominantly perimacular) with occasionally interrupted choroidal blood flow on FA indicated total CRAO.[17]

A recent study from Tianjin Medical University in China categorized fluorescein angiography studies of 63 patients with CRAO into ‘poor perfusion type’ (demonstrating >23 second arm to retina time), ‘exudative type’ (demonstrating normal circulation time but with prominent fluorescein leakage), and ‘mixed type.’ They noted that patients with ‘exudative type’ fluorescein angiography studies presented with less severe initial visual loss suggesting presence of perfusion correlates better with visual acuity than the degree of retinal edema.[18]

Few studies document indocyanine green (ICG) angiographic features in CRAO[4,19–21]. These are limited to case reports rather than large retrospective series. Yilmaz and colleagues detailed the ICG angiographic appearance of a single patient with a CRAO and cilioretinal artery sparing. The presumed etiology was believed to be thrombotic occlusion from uncontrolled systemic hypertension given an otherwise negative work-up. They noted decreased choroidal ICG fluorescence in the peripheral retina and normal strength and timing of choroidal fluorescence under the region of the well-perfused cilioretinal artery. The authors suspected the decreased peripheral choroidal fluorescence was due to blockage of signal by inner retinal edema and axoplasmic stasis in the peripheral non-perfused retina.[19] In another case of embolic CRAO, the ICG demonstrated normal choroidal perfusion. The role of ICG, however, remains useful for identifying cases of vasculitic etiologies as GCA may be accompanied by choroidal hypoperfusion.[21] A recent case report highlighted the superiority of ultra-wide field ICG angiography versus fluorescein angiography in identifying delayed choroidal perfusion in cases of GCA-associated central retinal artery occlusion.[20] In clinical practice, we advocate the use of ICG as an adjunctive imaging tool if the clinical suspicion for GCA is high.

Optical coherence tomography (OCT) is a non-invasive, non-contact imaging technology that allows in vivo evaluation of the inner and outer retinal architecture.[22] Ahn and colleagues were able to correlate distinct OCT characteristics with the CRAO stages provided by Schmidt and colleagues. Incomplete CRAO demonstrated minimal disruption of the retinal architecture and inner layer hyper-reflectivity without retinal edema. Subtotal CRAO demonstrated inner macular thickening and loss of organization of the inner retina, and total CRAO demonstrated marked inner retinal thickening and subfoveal choroidal thinning. The authors suspected the greater rate of subfoveal choroidal thinning, which would indicate decreased choroidal blood flow in total CRAO, may be due to potential ophthalmic artery occlusion, which is difficult to distinguish from total CRAO without fluorescein angiography. Their retrospective analysis of 134 eyes with CRAO demonstrated

that eyes that presented with subtotal and total CRAO and increased central macular thickness (CMT) were associated with severe final vision loss (BCVA <20/200).

Similarly, Ahn et al. demonstrated a correlation between increasing parafoveal macular thickness in acute CRAO with worse final BCVA.[23]

At one month, patients in all groups demonstrated inner retinal layer thinning, patients with subtotal and total CRAO demonstrated significant outer retinal layer thinning, and a portion of patients with total CRAO demonstrated concurrent choroidal thinning.[23] OCT derived quantitative characteristics can alone differentiate ocular ischemic disease. A recent report argued OCT might be used to differentiate chronic CRAO from non-arteritic anterior ischemic neuropathy (NAION) as CRAO eyes (n=12) demonstrated significantly greater macular thinning compared to NAION eyes (n=12).[24] Segmented layer analysis can also be valuable in differentiating acute NAION from acute CRAO.[25,26] For example, recent literature identifies an early decrease in macular ganglion cell-inner plexiform layer (mGCIPL) measurement by spectral domain-OCT in NAION.[27–29] For CRAO, a study of 35 eyes with acute retinal artery occlusion reported thickening and hyper-reflectivity of the inner retinal layers.[30] Chen, et al applied the Iowa Reference Algorithm to segment and measure layer-specific OCT signal intensity for 29 CRAO patients and 33 normal controls and found increased signal intensity in the inner retinal layers and lower signal intensity in the outer retinal layers in eyes with CRAO. The authors found highest association with increased intensity of the inner nuclear layer (INL) with CRAO, and speculated that outer retinal signal reduction was secondary to shadowing effect given no noted signal decrease in the outer retina of the fovea (which is devoid of overlying inner retina).[31] In a later study of 15 patients with CRAO, the same group identified a strong association by Spearman correlation with final BCVA to the optical intensity ratio, a parameter derived by dividing the optical intensity of inner retina by the optical intensity of photoreceptor/RPE layer ($r = 0.825$, $p < 0.001$).[32]

OCT-Angiography (OCT-A) is a novel technology used to generate *en face* vascular maps of the retina by correlating optical intensities of repeated OCT scans to differentiate between static and dynamic (vascular) tissue.[33] This technology has the potential to quantify the degree of nonperfusion in the superficial, middle, and deep capillary beds with greater detail than FA. A 2015 series of three patients with CRAO imaged with OCT-A demonstrated attenuation of vascular flow in both the superficial and deep capillary plexus in an acute case of CRAO, restoration of deep capillary plexus flow in a patient with chronic CRAO with cilioretinal sparing, and decreased flow in the radial peripapillary plexus in a patient with chronic CRAO.[34] Leng, et al presented a case report in which the diagnosis of CRAO was obtained via OCT-A alone.[35] Some limitations of this technology include the inability to understand patterns of vascular leakage and delays in perfusion time that we currently gain from FA. Additionally, OCT-A requires a longer image acquisition time relative to standard OCT. In CRAO patients that may have poor fixation, OCT-A imaging is further susceptible to motion artifact, amongst other artifacts inherent to this imaging modality.[36]

Systemic Testing

All patient who present with CRAO must undergo a thorough systemic work-up including assessment for hypertension, hyperlipidemia, diabetes, carotid stenosis, and cardiovascular disease in an effort to reveal previously undiagnosed risk factors and initiate secondary prevention.[4] The European Assessment Group for Lysis in the Eye (EAGLE) study revealed a previously undiagnosed risk factor in 78% of patients who presented with CRAO. The most frequent finding was ipsilateral clinically significant (>70%) carotid stenosis in 40% of patients. Only 3% of the cohort had previously been identified to have significant carotid stenosis, suggesting a strong role for carotid duplex in the complete medical work-up of patients who present with CRAO.[37,38] Adults without atherosclerotic risk factors and children that present with CRAO require evaluation for other predisposing factors such as vasculitis, myeloproliferative disorders, hypercoagulable states, and the use of oral contraceptive pills and intravenous drugs.[39] Elderly patients presenting with CRAO and endorsing symptoms of giant cell arteritis including headache, scalp or temporal artery tenderness, jaw claudication, ear pain, malaise, fevers, or weight loss require further laboratory evaluation with erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and platelet count.[40] Clinicians must keep a high suspicion for this disease and initiate steroids immediately followed by temporal artery biopsy with histologic evaluation. While the classic presentation is of “waxy optic nerve” pallor, this typically indicates an arteritic NAION and may not be the presenting finding in a GCA patient with a CRAO.

Treatment and Management of Acute Embolic Central Retinal Artery Occlusion

Spontaneous resolution of the offending occlusion is believed to occur in less than 1% of cases.[41] Therefore, a number of treatments for acute embolic CRAO have been attempted throughout the years. Acute management can be subdivided into non-invasive or invasive therapies to dislodge or lyse emboli with thrombolytics or surgery. While multiple treatments have been proposed, none has demonstrated consistent efficacy in the management of CRAO. All patients should be counseled on diet and lifestyle modification as a secondary preventative measure to reduce the risk or reduce the burden of hypertension and diabetes to ultimately reduce the risk of future ischemic disease.[42,43]

Non-invasive therapies to alter retinal vascular perfusion

Non-invasive therapies are predicated on altering retinal vascular perfusion pressure to theoretically dislodge the offending embolus and restore retinal blood flow.[44] Therapies to dilate the central retinal artery include sublingual isorbide nitrite[41], rebreathing of expired carbon dioxide[45], hyperbaric oxygen treatment[46], and breathing a fixed mixture of 95% oxygen and 5% carbon dioxide (known as Carbogen)[47]. Ocular massage with direct digital pressure or three-mirror contact lens application has been reported to physically remove an embolus.[41] Use of topical antiglaucoma drops, intravenous acetazolamide, and intravenous mannitol to reduce intraocular pressure and increase retinal perfusion pressure has also been reported to dislodge the embolus.[41,48] The body of evidence supporting the former therapies is a combination of case reports and series that report varying levels of effectiveness, with a

mean visual improvement rate of 15–21%.[38,44] Anterior chamber paracentesis to reduce intraocular pressure was compared to conservative treatment in a 2014 retrospective analysis of 74 patients (59 of whom received paracentesis) with no significant difference in BCVA at day 3 noted.[49]

Two non-invasive therapies have been studied with randomized control trials. Werner and colleagues performed a randomized, non-masked trial that treated ten patients with hemodilution and ten patients with hemodilution and enhanced external counter-pulsation (ECCP), a non-invasive method to increase cardiac output. Hemodilution was performed in all patients for a total 4 days with 500mL of hydroxyethyl starch or electrolyte solution. On day 1, the ECCP group received one 2-hour session of pressure application by three air-filled cuffs to the lower extremities during diastole. They reported an increase in retinal blood flow by scanner laser Doppler flowmetry but no difference in visual outcome.[50] Incandela and colleagues randomized ten patients to 4 weeks of oral pentoxifylline (a nonselective phosphodiesterase inhibitor thought to increase erythrocyte flexibility and increase microvascular flow) or placebo treatment and also reported an increase in retinal blood flow velocity in the pentoxifylline group.[51] There were no visual acuity outcomes reported in this paper, however, limiting the applicability of this conclusion.

Surgical methods to remove/dislodge emboli

A small body of literature focused on the use of novel surgical techniques directed at embolus removal. A 2006 prospective, interventional case series on the utilization of surgical removal of embolus within 36 hours of symptom onset by means of pars plana vitrectomy, longitudinal incision of the blocked arteriole, and manual retrieval of the embolus reported improvement of visual acuity from a median of 20/400 to 20/40 in seven out of seven patients.[52] In 2009, Lu et al reported a case series of 10 patients with CRAO treated within an average of 72 hours after initial symptomatology with pars plana vitrectomy and manual central retinal artery massage with improvement of vision of three lines from CF in six out of ten cases.[53] Complications included cataract formation in two patients and vitreous hemorrhage in two patients in the embolectomy case series and localized intraoperative disc hemorrhage in 9 patients and central retinal vein occlusion in one patient in the manual central retinal artery massage case series. A 2015 case report by Nadal, et al. presented a 65 year-old man diagnosed with CRAO 1 hour after development of count fingers vision who was taken for pars plana vitrectomy to create surgically managed hypotony. The patient’s vision was reported to be 20/20 five days after the procedure.[54] Photodisruption of intraluminal emboli with Nd:YAG laser therapy has been reported as a therapy for CRAO in a case series of 19 patients by Opremcak, et al.[55] BCVA visual acuity improved by a mean of 4.7 lines from a median initial acuity of 20/200 in 17 patients. Complications included vitreous hemorrhage in seven patients requiring vitrectomy in five patients and subhyaloid hemorrhage in one patient. Valid critiques of the aforementioned studies include technical challenges of the procedures, significant delay in symptoms onset to therapy, and results perhaps mimicking the natural history of the disease.[56]

Intravenous and intra-arterial thrombolysis

The 2013 American Heart Association/American Stroke Association (AHA/ASA) guidelines for the treatment of acute ischemic stroke supports the use of intravenous tissue plasminogen activator (tPA) (0.9 mg/kg, maximum dose 90 mg) for selected patients within 3 hours of onset of ischemic stroke (Class I; Level of Evidence A), and attempts have been made to extrapolate this method to CRAO.[57] Study of intravenous tPA use in CRAO is confounded by the often delayed presentation of patients. Varma et al a found an average time from symptom onset to emergency department evaluation of 13.1 hours with a 5.2 hour delay associated with initial presentation to an outside provider.[4] Intravenous tPA for CRAO was studied in a 2011 randomized controlled trial by Chen et al. which demonstrated improved visual acuity of three lines or greater only in a subgroup of patients treated with intravenous tPA within 6 hours of symptomatology.[58] One patient out of the eight patients in the tPA group developed intracranial hemorrhage requiring intubation and was ultimately discharged with residual pyramidal deficits and a modified Rankin score of two. Hattenbach and colleagues reported a case series in which seven of 17 eyes that received intravenous thrombolytic treatment within the first 6.5 hours of symptomatology achieved a final BCVA greater than or equal to 20/50 from a presenting vision worse than or greater to 20/100. None of the patients treated greater than 6.5 hours from onset achieved greater than 20/50 vision.[59]

The 2015 AHA/ASA updated guidelines for treatment of acute ischemic stroke states intra-arterial fibrinolysis may be considered over intravenous fibrinolysis only in select cases of ischemic stroke within 6 hours of symptoms (Class IIb; Level of Evidence C) and recommended use of endovascular therapy with stent retrievers over intra-arterial fibrinolysis (Class I; Level of Evidence E).[60–63] Intra-arterial fibrinolysis with recombinant tissue plasminogen activator (tPA) has been evaluated in embolic CRAO in the previously mentioned EAGLE study.[38] This included 84 patients: 44 were treated with local intra-arterial thrombolysis (LIF) with “superselective” catheterization of the ophthalmic artery versus 40 patients receiving ‘conservative standard treatment’ (CST) including 3–5 minutes of ocular massage, one drop of topical b-blocker, 500mg of acetazolamide, and isovolemic hemodilution within 20 hours of presentation with a mean treatment time of 13 hours (range 4.75 to 23.43 hours). No significant difference in visual acuity was noted between the two study arms. Minor adverse events were noted in 12 patients (34.3%) in the intervention arm and included headache, vessel puncture site hematoma, eyelid edema, epistaxis, and facial hyperesthesia versus 1 (2.1%) adverse event in the CST arm that presented with a corneal abrasion. Severe complications including 1 case of cerebral and 1 case of cerebellar hemorrhage were noted in the thrombolysis group. One patient in the CST arm developed a right hemiparesis and reduced consciousness 1 day after treatment with incomplete recovery. The study was terminated early due to patient safety concerns. Additionally, the study has been criticized for including 5 days of IV heparin in the treatment protocol for both arms of the study; the latest American Heart Association/American Stroke Association guidelines do not recommend any use of IV heparin for the treatment of acute ischemic stroke.[57,64]

A non-randomized study of 42 patients with CRAO treated with LIF within 15 hours of presentation (via selective cannulation of the ophthalmic artery and release of small aliquots

of intra-arterial tPA until patency of the central retinal artery) versus CST (various combinations of ocular paracentesis, carbogen inhalation, and topical intraocular pressure-lowering agents) demonstrated an improvement of vision of 1 line or more in 72% of patients treated with LIF versus 33% of patients treated with CST.[65] However, it should be noted that mean time to presentation differed between the two groups (3.4 hrs +−2 hrs in the thrombolysis group and 25.8 +−20 hours in the conservative group), and that final visual acuity was not stratified to time of presentation.

Further literature for thrombolysis in CRAO has taken the form of small case series. In 2007, Biousse et al. summarized twelve IV tPA studies for CRAO (from 1965–2007) and twenty-four ophthalmic artery-tPA studies (from 1984–2006), reporting 50 (48.5%) of 103 patients with acute CRAO treated with IV thrombolysis and 87 (34.9%) of 249 patients treated with IA thrombolysis had obvious improvement of visual acuity (at least 4 Snellen lines or “full recovery”).[66]

Although this level of visual recovery is greater than the natural history of the disease, the authors did not support the routine use of fibrinolytic given heterogeneous treatment protocols and outcome measurements in the literature, publication biases, and lack of controlled trials in the literature to date.

Finally, when considering thrombolysis and visual acuity outcomes, few studies have stratified CRAO as incomplete, subtotal, total, or having cilioretinal artery sparing. Ahn and colleagues retrospectively compared 57 cases of CRAO treated with LIF (with selective cannulation of the proximal ophthalmic artery and one-time release of up to 500,000 units of urokinase) to 44 cases treated with CST (ocular massage and intraocular pressure-lowering agents) and found significant visual improvement only in the incomplete subtype of CRAO (1.08 +/− 0.53 vs. 0.08 +/− 0.57 logMAR, $P < 0.001$).[67]

In summary, the historical review from Biousse and colleagues; the EAGLE study; the recent case series from Hattenbach, Ahn, and Aldirch; and the randomized trial from Chen fail to provide clear evidence supporting the use of fibrinolytics in acute CRAO and provide important information on adverse events after thrombolysis.[38,58,59,65–67]

Treatment and Management of Arteritic Central Retinal Artery Occlusion

CRAO due to giant cell arteritis is a distinct clinical entity that requires immediate and specific treatment.[68] Goals of therapy include resolution of GCA symptoms, prevention of further vision loss in the presenting eye, and prevention of loss of vision in the fellow eye (20–50% risk of bilateral vision loss with delay or stoppage of steroid treatment).[69] High-dose glucocorticoids (80–120 mg per day oral prednisone) should be initiated in all patients with suspected GCA.[70] Although not accepted as standard of care, a three-day course of IV pulse methylprednisolone at a dose of 500–1000 mg daily followed by high-dose prednisone may be considered.[71] The British Society of Rheumatology recommends concurrent treatment with 75mg of oral aspirin daily.[72,73] Temporal artery biopsy (TAB) should be performed within the following 14 days. Steroid initiation should not be delayed for biopsy. Patients with positive TAB should be treated for at least four weeks with high-dose

prednisone or until resolution of symptoms and laboratory abnormalities and then tapered gradually over 6–24 months. There is no protocol or recommend guidelines on how to taper these patients, however.

The TAB may be negative due to the presence of skip lesions or a short biopsy specimen. Patients with high clinical and laboratory suspicion of GCA should be managed as suspected GCA regardless of biopsy results.[74] For patients with a high clinical suspicion for GCA who are not surgical candidates, temporal artery ultrasound and evaluation for the "halo sign" may obviate the need for a biopsy.[75] Patients with negative biopsy results and low GCA suspicion should be tapered off steroids within 2 weeks and treated for alternative causes of vision loss. During taper, patients with relapse of headache should be returned to the previous step-off dosing, and patients with relapse of eye symptoms should be reinitiated on full dose therapy.[71]

The table summarizes the classification, clinical and imaging findings, systemic evaluation and management of patients with CRAO.

Conclusion

CRAO is an ophthalmic emergency with poor visual outcome that requires urgent systemic investigation to reduce the risk of further patient morbidity and mortality. A large body of literature reports very inconsistent treatment success with a wide variety of modalities. Further large, multicenter, randomized control trials are necessary to elucidate the role of the various acute treatment options in the management of CRAO.

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•Of importance

••Of major importance

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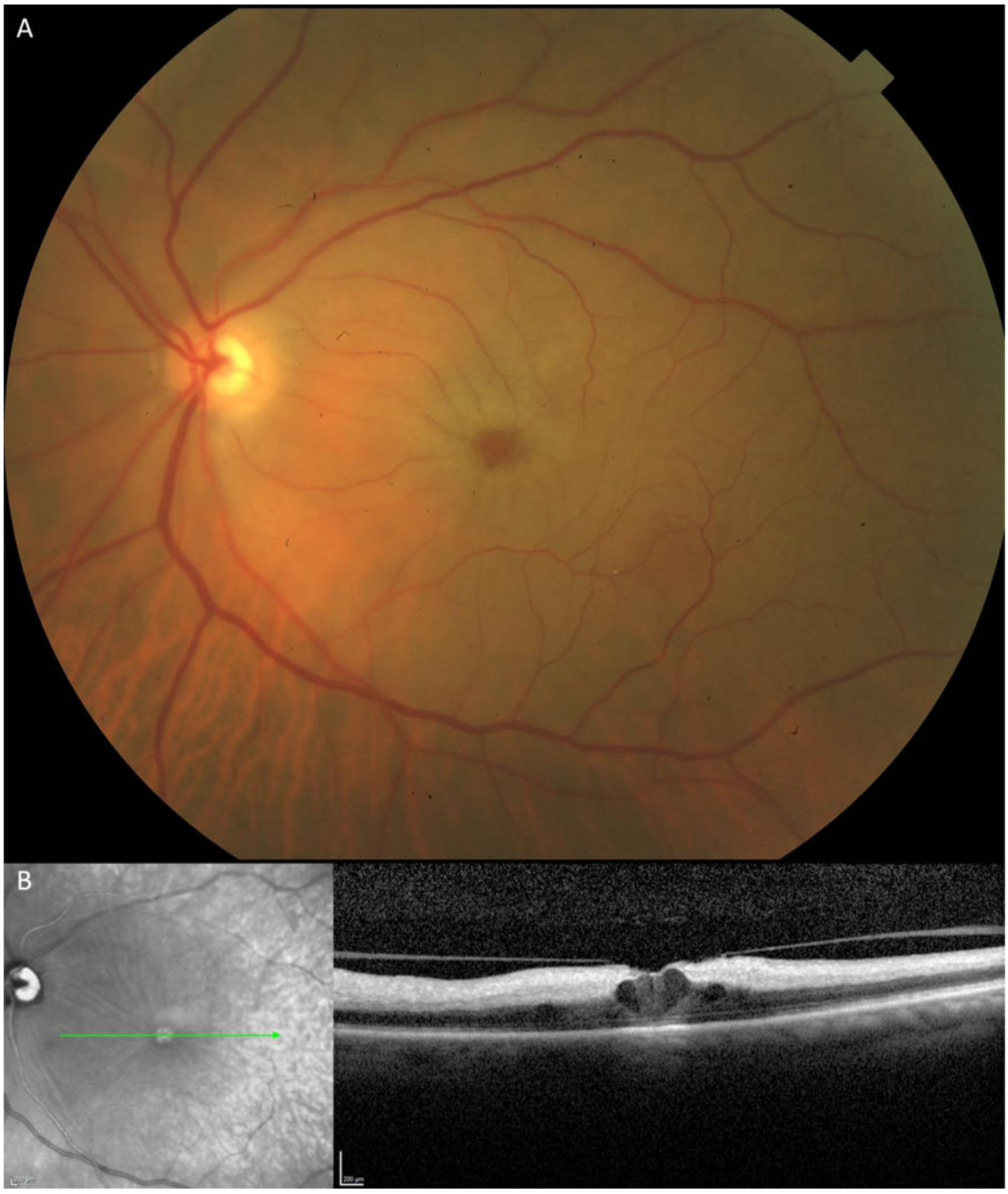

Figure 1.

72-year-old female was diagnosed with central retinal artery occlusion in her left eye. A. Color fundus photograph demonstrates whitening of the retina with the classical appearance of the cherry-red spot. B. Optical coherence tomography scans shows thickening and hyperreflectivity of the inner and middle retinal layers with posterior shadowing. Cystoid foveal changes are also observed.

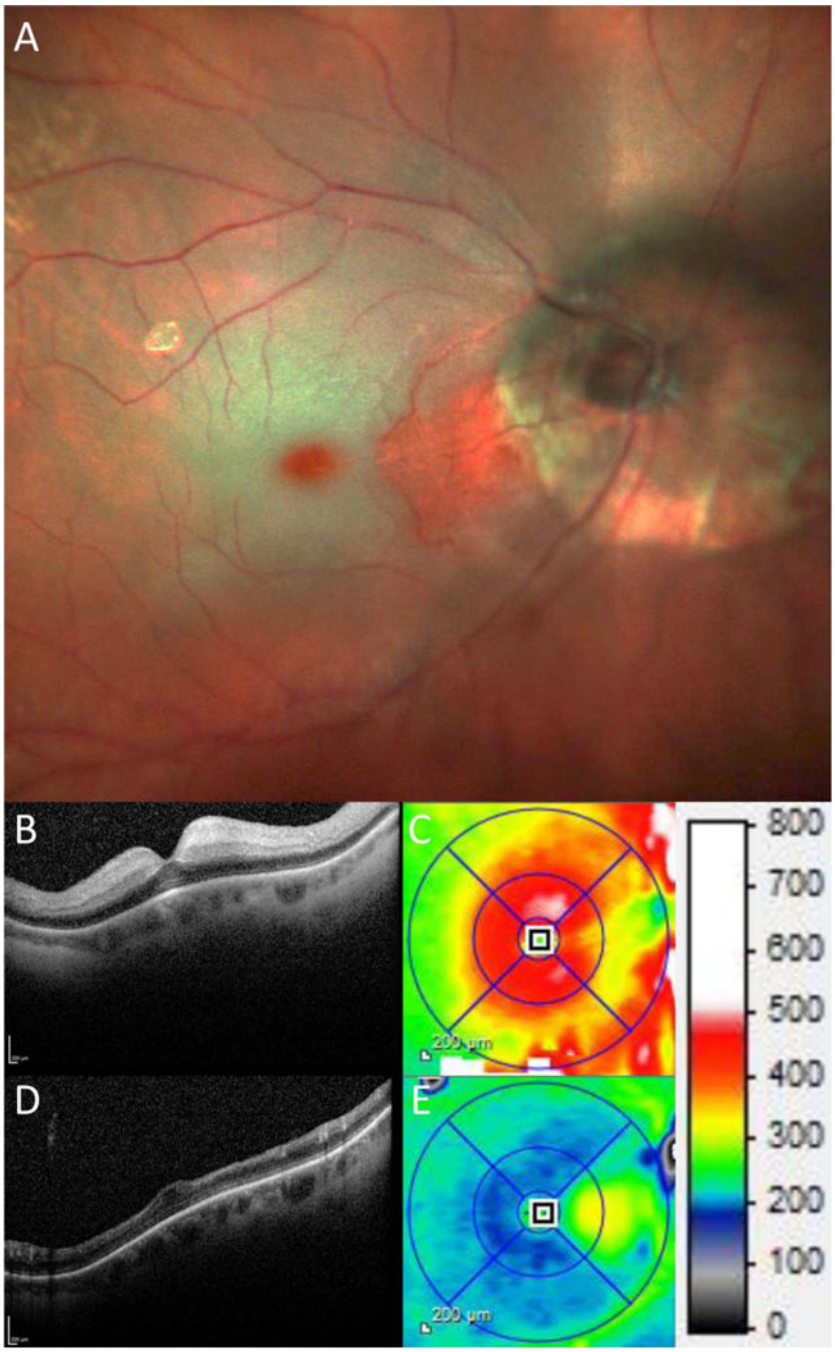

Figure 2.

78-year old female diagnosed with central retinal artery occlusion in her right eye with presence of cilioretinal artery. A. Multicolor imaging reflectance shows whitening of the retina with a cherry-red spot and a peripapillary area of sparing in the area of perfusion of the cilioretinal artery. B, D. Optical coherence tomography scans at baseline and 1 year, respectively, demonstrate early hyper-reflectivity and thickening of the inner retinal layers at baseline and diffuse thinning of the inner retinal layers at 1 year. Color thickness maps demonstrate changes in the retinal thickness values at baseline (C) and 1-year follow-up (E).

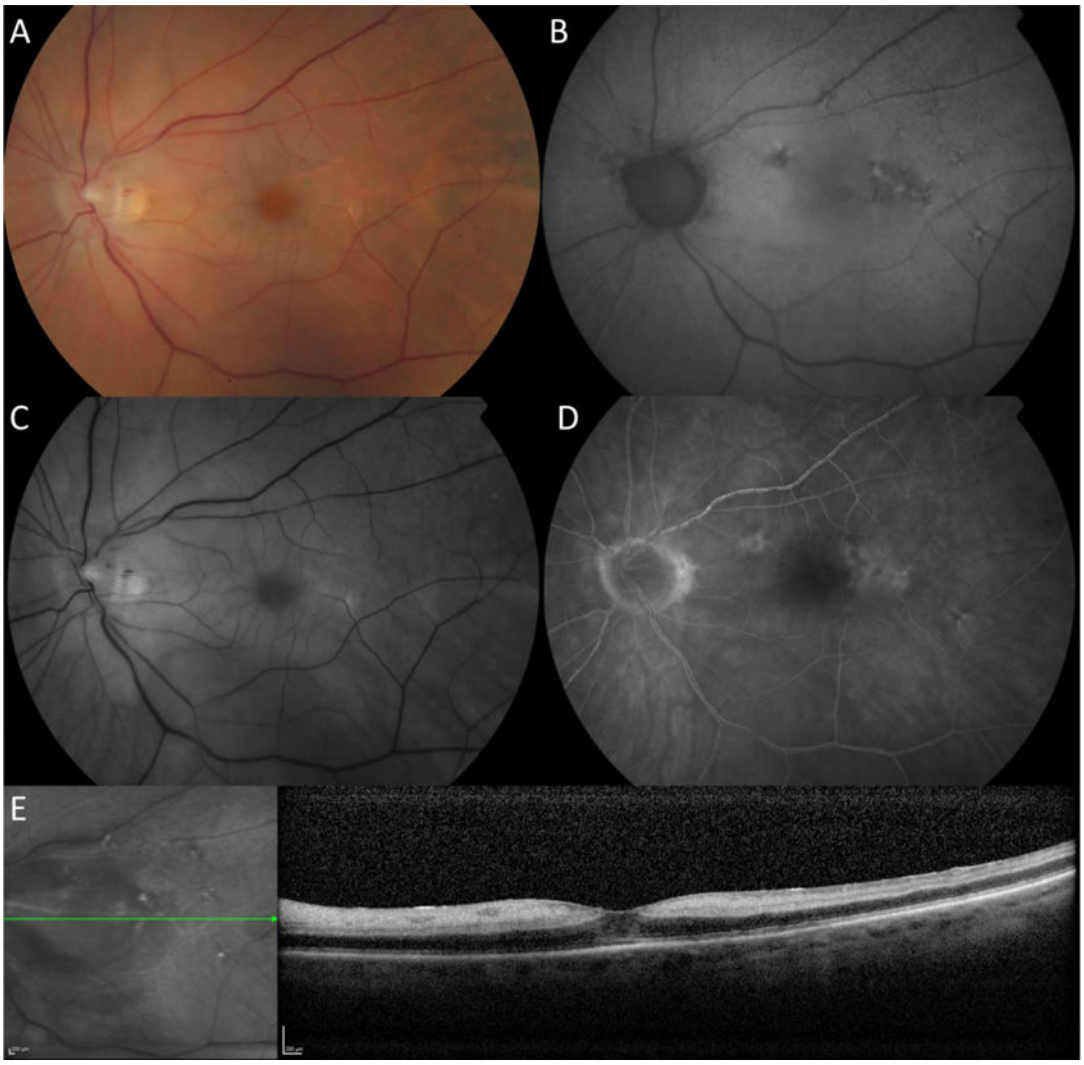

Figure 3.

98-year-old female presenting with reperfused central retinal artery occlusion. A. Color fundus photograph shows the classic cherry–red spot. B. Fundus autofluorescence show diffuse pigment alterations and obscuration of the macular details due to retinal edema. C. Red-free imaging highlights the whitening of the retina. D. Fluorescein angiography demonstrates reperfusion of arterial flow with staining of the arterial wall. E. Optical coherence tomography demonstrates thickening of the inner retinal layer with marked hyperreflectivity and posterior shadowing in the entire macular area with sparing of the fovea.

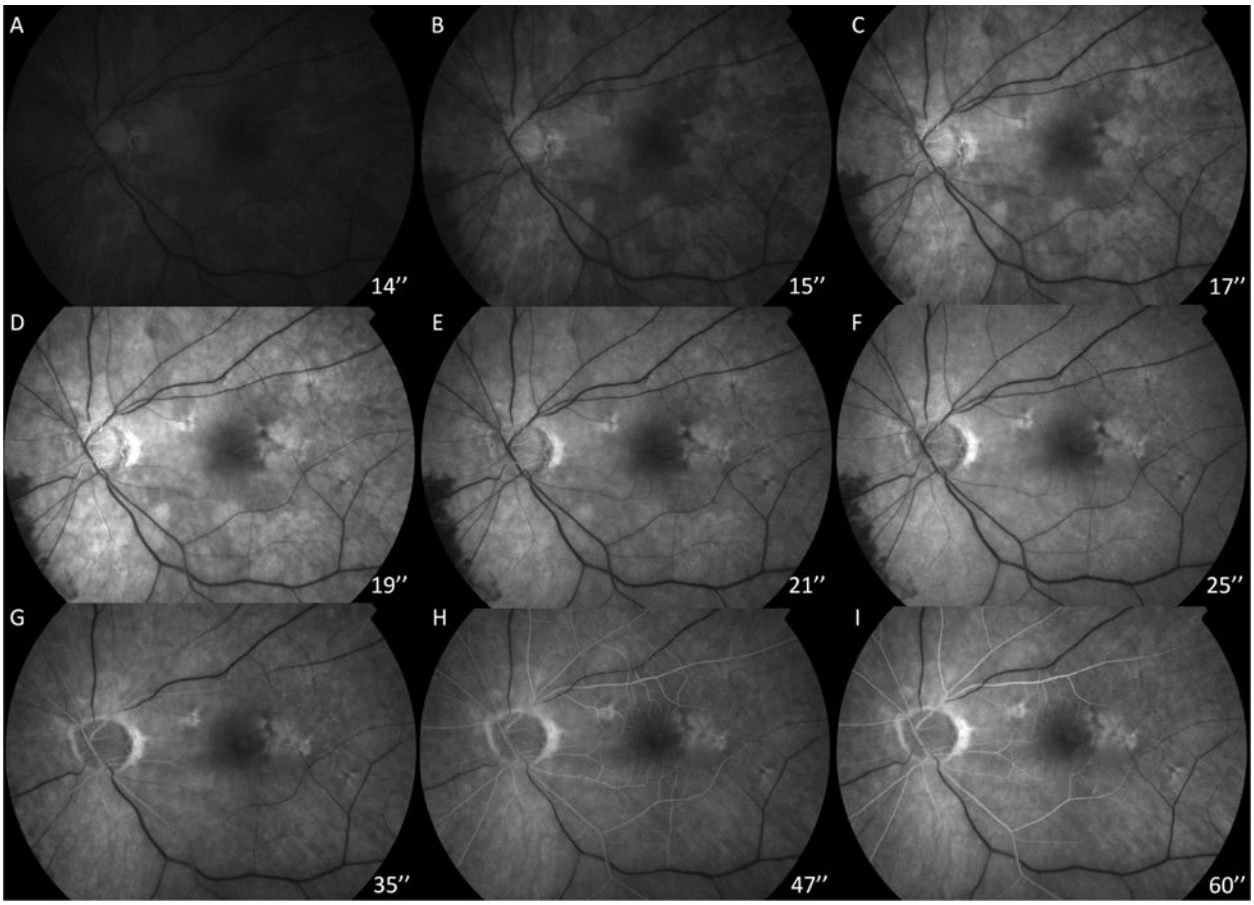

Figure 4.

First minute fluorescein angiography sequence on a 98-year-old female diagnosed with partially reperfused central retinal artery occlusion (same case in Figure 3). A–I. Angiography shows a marked delay on the arterial filling.

Table 1

Classification, Characteristics, and Management of CRAO

	Reperfused CRAO	*Nonperfused CRAO*	*CRAO with Cilioretinal Sparing*	*Arteritic CRAO*
Degree of Vision Loss	Transient	Severe	Variable	Severe
FA Characteristics	Mild perifoveal leakage, delayed arteriolar flow	Occluded arterioles; possible perifoveal leakage	Occluded retinal arterioles with filling of macular cilioretinal artery	Delayed choroidal and retinal arteriolar filling
OCT Characteristics	Minimal disruption of the retinal architecture and inner layer hyper-reflectivity without retinal thickening	Marked inner retinal thickening and edema	Variable, sharp demarcation of inner retinal thickening and hyper-reflectivity between the perfused nasal macula (from the cilioretinal artery) and nonperfused retina	Variable hyper-reflectivity within the inner retinal layers
Ophthalmic Characteristics	Mild retinal edema, no cherry red spot	Cherry red spot, pale fundus	Variable, pale fundus with normal macular color	Variable retinal and choroidal findings, with optic nerve edema
Systemic Work-up	Hematologic and imaging work-up for embolic/thrombotic etiologies	Hematologic and imaging work-up for embolic/thrombotic etiologies	Hematologic and imaging work-up for embolic/thrombotic etiologies	Urgent ESR, CBC, and CRP followed by TAB.
Treatment	Identification of risk factors and initiation of secondary prevention.	**1** Identification of risk factors and initiation of secondary prevention. **2** Ocular combined standard therapy vs. observation	**1** Identification of risk factors and initiation of secondary prevention. **2** Ocular combined standard therapy vs. observation	Immediate high-dose steroid therapy followed by temporal artery biopsy

CRAO: Central retinal artery occlusion, FA: fluorescein angiogram, OCT: optical coherence tomography, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, CBC: complete blood count, TAB: temporal artery biopsy