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INVITED REVIEW

Ocular Involvement in Giant Cell Arteritis

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Note:
This manuscript was reviewed by Özlem Dikmetaş.

Introduction

Giant cell arteritis (GCA) is a granulomatous vasculitis that affects large and medium-sized arteries [1]. GCA is the most feared ophthalmological emergency as it may cause irreversible profound vision loss [2]. Horton and Magath in 1937 and Jennings in 1938 were the first to report a visual loss in one or both eyes as an ocular complication in GCA [3,4]. GCA-associated vasculitis particularly involves the temporal, ophthalmic, and posterior ciliary arteries (PCA). The PCA are branches of the ophthalmic artery, supplying the choroid, optic nerve head, and cilioretinal artery when present. The retinal layers are supplied mainly by the central retinal artery, another branch of the ophthalmic artery [5]. The ophthalmic artery also provides blood to the extraocular muscles via its other branches. The ocular involvement reported 20-70% in GCA is primarily ischemic in nature due to thrombosis by granulomatous inflammation of one or more of the PCAs, and rarely of the ophthalmic or central retinal artery [2].

GCA - Ocular Symptoms

The most dreadful aspect of GCA is the progressive reduction and permanent loss of visual acuity. In a series of 170 consecutive predominantly Caucasian patients with temporal artery biopsy-proven GCA, the incidence of ocular involvement was 50% and visual loss 49%. Patients with ocular findings were older than the others. In the 85 patients with ocular involvement, diplopia was the leading complaint in 6% and eye pain in 8%. Amaurosis fugax - painless transient visual loss lasting for seconds to minutes - was reported in 31% [2]. Lower incidences have been reported in other series [6-9]. Bilateral visual loss in GCA, reported at differing rates in the literature (26.9-36%), was present at the initial visit in 32% in this series [2,6,8,10]. Half of the cases became aware of the visual loss when the second eye was involved. In the others, the time interval varied from 1 day to more than six months [2]. Recognition of visual symptoms due to GCA and initiation of appropriate treatment in a short time may prevent second eye involvement and thus bilateral visual loss [11]. Recognition of visual symptoms due to GCA by physicians in a short time is very valuable.

Systemic signs of GCA generally accompany the ocular symptoms, i.e., headache, jaw claudication, neck pain, scalp tenderness, fever, weight loss, increased inflammatory response parameters, and visual symptoms accompanied by systemic symptoms or present only. However, it should be kept in mind that *the absence of systemic symptoms and normal erythrocyte sedimentation rate do not rule out GCA*. GCA may be occult in up to 21.2% of the cases [12].

GCA Ocular Findings

Ocular ischemia due to GCA may manifest as amaurosis fugax, arteritic anterior ischemic optic neuropathy (A-AION) and arteritic posterior ischemic optic neuropathy (A-PION) at the optic nerve; central retinal artery occlusion, cilioretinal artery occlusion and cotton wool spots at the retina; choroidal ischemic lesions, anterior segment ischemia, pupillary disorders, ischemia and motility disorders of extraocular muscles, ocular ischemic syndrome, and inflammatory orbital syndrome.

Arteritic- anterior ischemic optic neuropathy (A-AION)

A-AION is the most common manifestation of GCA, the main reason for permanent vision loss. Most cases of A-AION occur within a few weeks after the onset of GCA. Optic disc ischemia develops after partial or total involvement of short PCAs, which provide the main blood supply of the optic disc. Although medial short PCA is frequently involved, lateral or bilateral PCA may be affected by GCA [13]. A-AION is reported in 81.2 % of patients in Hayreh's series [2]. The mean age of patients presenting with A-AION was 76.2 ±7.0 (range 57– 93 years), and it was more common in women and Caucasians [2].

Patients with A-AION present with a sudden, painless, severe visual loss [8]. This may be preceded by amaurosis fugax in 39% of the cases [2]. At ophthalmoscopy in the acute phase, the optic disc is pale, edematous, and has a chalky-white appearance with no superficial congestion of capillaries (Figure 1) [11]. Edema regresses within 6-8 weeks, optic atrophy develops, and cupping may occur. This cupping can be confused with glaucomatous optic cupping, but in glaucoma, the optic rim appears normal, whereas, in A-AION, the optic rim is pale [14]. A-AION is accompanied by occlusion of the cilioretinal artery if present.

Differentiation from nonarteritic AION depends on clinical appearance (optic disc is more hyperemic in NAION), associated systemic symptoms, and laboratory evaluation [15].

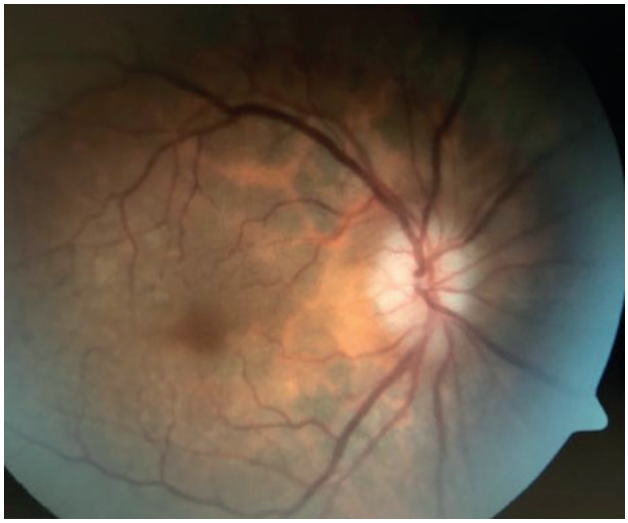

Figure 1. Chalky white optic disc edema in a patient with GCA

Arteritic- posterior ischemic optic neuropathy (A- PION)

PION is not as common as AION in GCA. It is due to occlusion of pial branches of the ophthalmic artery, which supply the retrolaminar portion of the optic nerve. In Hayreh's study, PION was reported in only 6 of 85 patients with ocular involvement [2]. A-PION presents with sudden painless loss of vision. Visual acuity is 20/200 or worse in 50% of cases. Fundus and optic disc are normal at ophthalmoscopy. Optic disc pallor appears within 6-8 weeks, especially temporally. The treatment is the same as A-AION, but there is no adequate response [14].

Central retinal artery occlusion (CRAO)

CRAO is due to GCA in 4.5% of cases. GCA should be ruled out in CRAO patients, especially in those over 50 years of age. CRAO was reported at different rates in patients with GCA; Singh et al.[16] reported 4%, while Hayreh et al. [2] reported 12%. CRAO patients usually present with sudden vision loss. It is due to the occlusion of the central retinal artery along with PCA. At ophthalmoscopy, the retina is edematous with a cherry-red spot appearance in the macula (Figure 2) [17]. But if the choroidal blood supply is significantly impaired, a cherry red appearance may not be seen. Optic disc edema may accompany. At later stages, optic atrophy, retinal attenuation, and pigmentary changes at the macula can be seen [18]. Fundus fluorescein angiography (FFA) is vital to detect whether concomitant PCA involvement could be detected. CRAO and PCA involvement are nearly almost diagnostic for GCA [1].

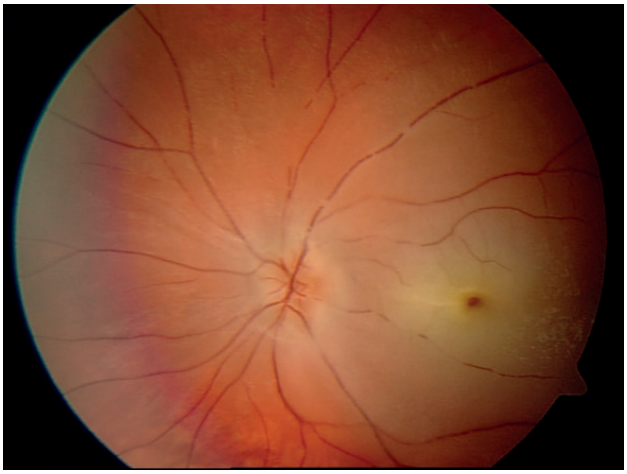

Figure 2. Central retinal artery occlusion with retinal edema and cherry red spot appearance at the macula

Cilioretinal artery occlusion (CLRAO)

The cilioretinal artery (CLRA), with a prevalence of 6.9 to 49%, is an important anatomic variation [19]. It may arise directly from the peripapillary circulation or PCA and supply the papillomacular area, where photoreceptors are concentrated. CLRA may play a role in maintaining visual acuity in CRAO [20]. In GCA patients, CLRA may also be affected along with PCA. CLRAO may accompany A-AION and CRAO in these patients or present alone [21]. In Hayreh's series, CLRAO was detected in 14 of 85 GCA patients with visual symptoms; twelve were with AION, one was accompanied by PION, and one was pure CLRAO [2]. Sudden painless vision loss is the main symptom, but transient vision loss may proceed [21]. In patients with only CLRAO, the visual prognosis may remain above 20/40 even if they do not receive any treatment. Conversely, visual acuity remains low in cases of accompanying CRAO or AION [22]. At ophthalmoscopy, the retinal area fed by the CLRA appears white and edematous. The definitive diagnosis needs FFA. It is very important to rule out GCA in a patient with CLRAO [1].

Cotton wool spots

Cotton wool spots (CWS) are focal inner retinal ischemic lesions. They are due to the axonal infarcts of the retinal nerve fiber layer, seen at an acute stage in one-third of patients with visual loss. At ophthalmoscopy, they appear as soft, fluffy white patches (Figure 3). Cotton wool spots probably develop after platelet microembolization from thrombosed arteries [1].

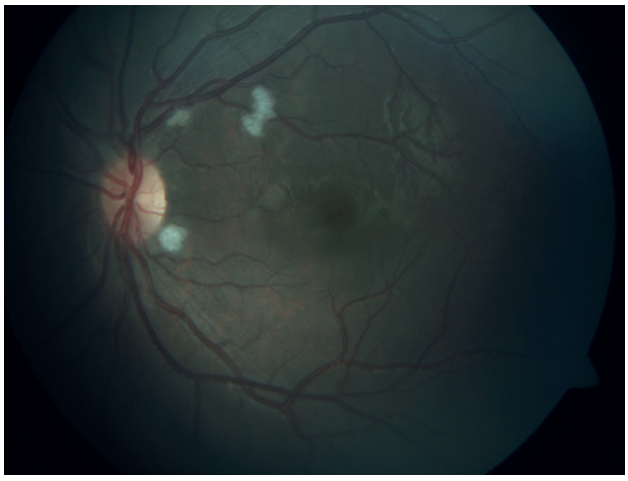

Figure 3. Cotton wool spots

Choroidal ischemic lesions

Occlusion of PCAs may create choroidal infarct areas, usually in addition to A-AION [1], but choroidal infarct alone has also been reported. Ophthalmoscopy during the acute period of visual loss may reveal white, yellow, and deep retinal lesions [23]. Approximately 2-3 weeks later, pigmented chorioretinal degeneration areas are usually seen in the midperiphery, with the apex towards the posterior pole [1].

Anterior segment ischemia

Anterior segment ischemia is rare and may develop after general ocular ischemia. Ocular hypotonia, decreased corneal sensitivity, corneal edema, iris ischemia, and scleritis may develop [24]. It may be mistaken for anterior uveitis.

Pupillary abnormalities

GCA-related tonic pupils and Horner's syndrome have been reported [25,26]. The most common pupillary defect is a relative afferent pupillary defect due to vision loss in the eye [2].

Extraocular motility disorders

Extraocular muscle involvement in GCA may be neurogenic or myogenic and presents with diplopia which is often a temporary finding [17]. Diplopia has been reported in GCA at varying rates, though not common [7,8,16]. GCA should be ruled out in patients over 50 presenting with diplopia.

Visual Prognosis

In GCA patients with ocular involvement, visual acuity often decreases to 20/200 or less, even to no light perception. Unfortunately, it may not recover [27]. Danesh-Meyer et al. reported that despite a high dose of methylprednisolone in the first six days, visual deterioration occurred in 27% of the patients. Visual acuity increased in 15% of eyes, but few had corresponding visual field improvement [28]. In another study, permanent vision loss was observed in 15.75% of patients, and 30.4% were bilateral [6]. Salvarani et al. [8] reported that 63.4% of patients with visual symptoms developed permanent vision loss, and 26.9% were bilateral. In GCA, which can result in blindness in both eyes, initiation of appropriate treatment in a short time may result in a reduction in permanent vision loss [11].

Conclusion

GCA is a potentially blinding disease. Quick recognition of visual symptoms due to GCA by physicians is essential to prevent bilateral permanent visual loss by the prompt institution of therapy.

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