Giant Cell Arteritis: A Formidable Opponent

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Abstract:

Giant cell arteritis is an ophthalmological emergency due to the potential for permanent vision loss. Presented is a case of devastating bilateral vision loss secondary to temporal arteritis, despite prompt diagnosis and maximum medical treatment.

I. Case History

An 85 year old Caucasian male presented to the emergency room complaining of blurry vision in the left eye upon awakening the previous day. He thought it would clear up but says the vision got worse. He reported “thunder-like” flashes the day before but no new floaters. Patient denied preceding transient monocular vision loss or diplopia. Upon questioning, patient admitted to mild bilateral neck pain extending from his ears down the sides of his neck that started the previous day, and bilateral jaw ache for the past two to three days. He denied headache, loss of weight, malaise, fever and symptoms suggestive of polymyalgia rheumatica.

Ocular history was positive for cataract extraction with posterior chamber intraocular implants OU and subsequent YAG capsulotomy OS. Patient also had an iridectomy OD and basal cell carcinoma which was excised from his right lateral canthus.

Patient’s medical history was significant for hypertension, that was well controlled, and prostate cancer in remission status post radiation treatment two years previous. The patient reported he quit smoking 40 years ago. Patient’s medications included HCTZ, Lisinopril, and 81 mg Aspirin. He received the shingles vaccine six months prior.

II. Pertinent Findings

On examination the patient’s corrected visual acuity was 20/20-1 OD and 20/400 which improved to 20/150 with pinhole OS. His left pupil was surgical and displaced inferior temporal, the right pupil was round and both were reactive to light. There was a 3+ afferent papillary defect OS. Ocular motilities were full with an exotropia present on upgaze. Confrontation visual fields were full without defect OD,
and constricted 360 degrees OS. Temporal arteries were prominent, non-tender, and pulsatile bilaterally.

Biomicroscopy revealed well-positioned posterior chamber intraocular lenses with a deep anterior chamber OU. The cornea had trace endothelial pigment, OD greater than OS, and there was a patent PI superior nasal OD. There was a mild anterior chamber reaction OS with trace flare and 1+ cells. Goldman applanation tonometry was 9 mm Hg OU.

Dilated fundus exam of the right eye revealed a posterior vitreous detachment. The optic nerve was pink and healthy with distinct margins and a .20 cup to disc ratio. There was one nerve fiber layer hemorrhage along the inferior temporal arcade and the retinal veins were dilated and irregular in caliber. Periphery was unremarkable.

Dilated evaluation of the left eye revealed a pallid, edematous nerve with indistinct borders and no cup. Retinal veins were dilated and no cilioretinal artery was present. There was also a PVD and mild RPE changes superior to the fovea. Peripheral exam was unremarkable.

Laboratory studies were remarkable for a significantly elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The ESR was 87 (reference range 0-20) and C-reactive protein was 238 (reference range 0-7.43). Patient’s platelets were 387 and his white blood cell count 12.3.

Radiologic studies, including a head CT without contrast, brain and orbit MRI, and brain MRA were non-contributory and showed no acute findings. A carotid duplex was also performed and revealed less than 50% stenosis bilaterally.

III. Differential diagnosis

Differential diagnosis in this case included nonarteritic anterior ischemic optic neuropathy and arteritic ischemic optic neuropathy. Both are associated with sudden, painless vision loss and an afferent papillary defect. There is a similar clinical picture with pale, swollen discs; however nonarteritic tends to be to a lesser degree.

Nonarteritic ischemic optic neuropathy is more common and the patient’s risk factors included hypertension, his low blood pressure (105/64) at admission, and a disc at risk in the fellow right eye. It
is common to notice vision loss upon awakening due to nocturnal hypotension, which was the scenario in this case.

Concern for arteritic anterior ischemic optic neuropathy, which is associated with giant cell arteritis, was heightened for several reasons including the extent of his vision loss, complaint of bilateral neck and jaw pain and the elevated inflammatory biomarkers.

IV. Diagnosis and Discussion

Our patient was diagnosed with arteritic ischemic optic neuropathy OS, presumed due to giant cell arteritis. Giant cell arteritis (GCA), also known as temporal arteritis, is a chronic vasculitis that targets large and medium sized blood vessels. Although the event that triggers the immune attack on vascular walls is unknown, the process is T cell dependent (1). GCA almost exclusively occurs in patients older than 50 and in Caucasian individuals, and is more common in women than men (2).

Giant cell arteritis is important to eye care providers due to the varying ocular presentations and its potential for devastating, permanent vision loss.

In one study of patients with a positive temporal artery biopsy, 50% had ocular symptoms at presentation (3). Of patients with ocular symptoms, vision loss was the complaint in 97.7% of patients (4). Amaurosis fugax is another common symptom reported in GCA, and is an ominous sign for impending vision loss. In a Mayo Clinic report more than 46% patients with GCA experienced amaurosis fugax, and 50% of them went on develop vision loss (5). Hayreh proposed that this phenomenon is likely caused by transient ischemia to the optic nerve, as opposed to the retina (Hayreh1). Interestingly, when fluorescein angiography was performed on patients with a history of amaurosis fugax, there was evidence of significantly slowed and impaired choroidal filling (6). It is believed this is due to decreased perfusion pressure in the choroid from partial occlusion to the posterior ciliary arteries (6).

Transient diplopia is also a symptom that is reported by 2-14% patients with temporal arteritis (7). It has been proposed that diplopia may be one of the earliest signs of GCA and may be caused by ischemia to the cranial nerves or brainstem (4). Because the oculomotor nerves are supplied by fine blood vessels and GCA has a predilection for medium to large arteries, Hayreh proposed the double vision is more likely due to ischemia of the extraocular muscles (4).

A variety of ocular complications have been associated with temporal arteritis and they are all ischemic in nature. Optic nerve ischemia can involve either the anterior or posterior portion of the optic nerve,
though anterior ischemic events are more common. Anterior ischemic optic neuropathy (AION) is the major cause of vision loss in giant cell arteritis (3). The incidence of AION caused by giant cell arteritis had been documented to be from 18-88% (8) and in Hayreh’s study on ocular complications of GCA, the incidence was 81% (3). Early, extensive vision loss is characteristic of AION, and one study found 54% GCA patients with AION had vision from counting fingers to no light perception (4). Posterior ischemic optic neuropathy is much less common, only occurring in 5.6% patients in Hayreh’s report (3). The fundus exam will appear unremarkable at the time of vision loss, but optic atrophy will be present 6-8 weeks after the event (3).

Temporal arteritis can also lead to ischemic events in the retina, causing cotton wool spots and occlusions of both the central retinal artery and cilioretinal artery. The incidence of central retinal artery occlusions (CRAO) in GCA has been documented to be 2-18% (8). Interestingly, fluorescein angiographies done on these patients show that both the central retinal artery and one or more of the posterior ciliary arteries were occluded (3). This finding is due to the fact that the central retinal artery and posterior ciliary arteries originate from a common trunk in 60% patients (9). Hayreh therefore suggests patients over the age of 50 with a new onset CRAO should have a fluorescein angiography performed and, if both arteries are involved, it is indicative of GCA and needs to be treated accordingly (3). Although the fluorescein shows evidence of combined CRAO and AION, the disc does not appear edematous because the ischemic retinal ganglion cells are no longer forming axoplasm (10).

Since the cilioretinal artery derives from the posterior ciliary artery, giant cell arteritis can also cause cilioretinal artery occlusions, as it did in almost 22% of patients in Hayreh’s study (3). Although cilioretinal artery occlusions were present in 22% patients, it occurred as an isolated finding in only one case (3).

Choroidal ischemic lesions have been described as white, triangular areas with the apex pointing to the posterior pole, and are usually located in the midperiphery (11). On fundus examination 2-3 weeks after the insult, these areas will appear as patches of chorioretinal degeneration (3).

Anterior segment ischemia is rare in GCA, and is thought to be due to involvement of the ophthalmic artery. Neovascular glaucoma, hypotony, anterior uveitis and marginal corneal ulcers have been described (3). Ischemia in the anterior segment can also lead to pupil abnormalities such as bilateral tonic pupils and Horner’s syndrome (12-13).
Since there is such a risk for vision loss in giant cell arteritis, it is important to understand the criteria and tests used to diagnose this disease.

Erythrocyte sedimentation rate is a non-specific test for inflammation and can be affected by age and gender. Miller and colleagues developed a formula to determine normal ESR: age in years divided by 2 for men and age + 10 divided by 2 for women (14). Because this is a non-specific test, it is important to realize that an elevated ESR may support a diagnosis of GCA, but a normal ESR cannot be used to rule out GCA.

C-reactive protein is an acute-phase protein found in the blood that increases in response to inflammation and is another non-specific test used in the diagnosis of GCA. CRP has some advantages over ESR because it is not affected by age and gender and responds more rapidly to disease. In Hayreh’s study it was shown to be 100% sensitive and around 80% specific in the detection of GCA (15).

In addition to the two well known tests previously mentioned, other hematologic tests have provided useful information. Patients with GCA had significantly higher platelet counts than controls (16). Also GCA patient showed higher WBC and lower hemoglobin and hematocrit levels compared to those without GCA (16).

All of these tests can provide useful information and aid in the diagnosis of GCA, but it has been shown that ESR and CRP used together have a specificity of 97% percent, and should guide the diagnosis and management of GCA (15).

Temporal artery biopsies (TAB) are considered the gold standard for diagnosis of GCA. This disease is well known to show skip lesions, which can lead to false-negative biopsies if an inadequate specimen size is obtained. The current recommendation is to take a minimum length of 2 cm. Hayreh used one inch sections and found 100% yield of positive temporal artery biopsies (15). Whether or not to do bilateral TAB has been the area of some debate. Some have suggested that simultaneous bilateral biopsies improved the diagnostic yield (17), while others did not concur (18). With that being said, temporal artery biopsies are not without complications, and unilateral biopsy is usually sufficient to establish a diagnosis. If the temporal artery on one side seems abnormal on clinical examination or clinical signs are unilateral, the biopsy should be taken from the suspicious side. A biopsy on the contralateral side is usually only performed if the first was negative, yet there is still high suspicion for GCA. It is important to note that corticosteroid treatment does not affect the results of temporal artery biopsies (5, 19) and one study found positives results even after four weeks of steroid treatment (20).
Steroids should never be held in order to obtain a biopsy in patients with a strong suspicion for giant cell arteritis.

Noninvasive imaging has been looked at to aid the diagnosis of GCA. In a study of patients suspected of having giant cell arteritis, contrast enhanced MRI found abnormal enhancement in all patients with positive TAB (21). On ultrasound, it has been reported that patients with GCA show a “halo sign”, which is a hypoechoic area around involved arteries, but is only 40% sensitive (22). These tests may provide some useful information, but are unreliable as the sole means of detection.

The American College of Rheumatologists (ACR) developed criteria to diagnose giant cell arteritis which includes: age greater than or equal to 50 at onset, new localized headache, temporal artery tenderness or decreased temporal artery pulse, elevated erythrocyte sedimentation rate greater than 50 mm/h and positive temporal artery biopsy. They found that having three of these five criteria was 93% sensitive and 91% specific for giant cell arteritis (23).

Hayreh and colleagues conducted a study to define the most reliable criteria for diagnosing giant cell arteritis and found several differences from ACR guidelines (15). One important finding was that 21.2% of patients with biopsy proven GCA and vision loss had occult giant cell arteritis, meaning they had no systemic symptoms (15). Therefore, if only systemic criteria only were used for diagnosis, this important group of patients would be missed. This study also found jaw claudication, neck pain and C-reactive protein greater than 2.45 mg/dl greatly increased the odds of having a positive temporal artery biopsy (15). Although new onset headache is one of the ACR’s 5 criteria, Hayreh found this to be unreliable, with almost the same number reporting headaches in the positive biopsy group as the negative biopsy groups (15). Although physical examination of temporal arteries can provide helpful information, Hayreh found abnormal temporal arteries in only 19.8% patients with a positive temporal biopsy (15). It is also important to note that a normal ESR cannot rule out GCA. In Hayreh’s study ESR ranged anywhere from 4 to 140 mm/hr at initial presentation in patients who had biopsy confirmed GCA (15).

Treatment:

It is well known that systemic corticosteroids are effective in treating temporal arteritis, yet there has been some controversy whether to use intravenous steroids followed by oral treatment or oral steroids alone. Although it is uncertain whether IV treatment is more advantageous in preventing vision loss, the consensus is to start patients on intravenous steroids if there is vision loss at presentation, a history of amaurosis fugax, or early signs on involvement in both eyes (4). In addition to more effectively
preventing vision loss, one study found that a three day course of IV steroids allowed patients to be tapered off steroids more quickly, have a lower frequency of relapse and a lower cumulative dose (24).

The proper dosing of steroids has also been the area of some controversy. It is generally accepted that the higher the risk for vision loss, the more aggressively the disease needs to be treated. Currently the accepted starting dose is 1000 mg intravenous steroids a day for three days if vision is already affected or there is a high risk of becoming affected and 40 to 60 mg of prednisone a day for all other patients with giant cell arteritis (25). Some have suggested an alternate day therapy, but it has been shown that this is not successful in controlling patient’s symptoms (26).

The tapering schedule needs to be individualized for each patient and the steroids need to be reduced gradually. Using improvement in systemic symptoms as a guide is often unreliable, especially considering 21% patients with vision loss never experienced any systemic symptoms at all (27). Hayreh and Zimmerman found observing the CRP and ESR is the most sensitive and reliable way to monitor disease progression (4). They suggested starting to taper only once the ESR and CRP reach the lowest stable level, which usually takes 2-3 weeks (4). The maintenance dose is then the lowest dose of prednisone that keeps the ESR and CRP at their lowest achieved level (4).

There have been several reports that steroid treatment needs to be maintained for periods longer than two years, and the data in Hayreh’s study showed that in some cases treatment is needed indefinitely (4, 28). Some doctors worry that long-term steroid use puts the patient at higher risk serious illness and death, however there have been studies that showed patients on steroids were not at a higher risk for either morbidity or mortality when compared to the general population (29-30).

Some adverse affects of steroids include bone fracture, diabetes mellitus, infection and gastrointestinal bleeding (31) and the importance of adding prophylactic treatments is often overlooked. Calcium, vitamin D, stomach protection, as well as updating vaccinations are important adjunctive therapies.

It has been suggested that adding aspirin may reduce the risk of thrombotic complications in patients with giant cell arteritis, either due to its anti-platelet effect or by its anti-inflammatory role. Two recent retrospective studies reported patients who were on aspirin prior to their diagnosis of GCA developed less cranial ischemic events than those patients not treated with aspirin (32-33). Though a prospective study is needed before aspirin’s role is defined, a recently published guideline for managing GCA suggests that as long as there is no contraindication, a low-dose aspirin should be recommended to patients diagnosed with temporal arteritis (34).
Due to the potential for systemic side effects with long-term steroid use, several glucocorticoid-sparing agents have been investigated. Methotrexate, Azathioprine and tumor necrosis factor-alpha inhibitors have been considered, but studies have shown discordant results and their role in treating giant cell arteritis has yet to be established (35).

V. Treatment and Management

The plan in this case was to administer intravenous methylprednisolone 250 mg every 6 hours for three days, followed by oral steroids and rheumatology was consulted to guide the dosing. The case was also reviewed with neurology and the patient was admitted to their service. Omeprazole was initiated for gastric protection and calcium and vitamin D were started for bone prophylaxis. Insulin on a sliding scale was given for reactive hyperglycemia. Patient’s aspirin dose was increased from 81 mg to 325 mg a day. The patient was educated to avoid systemic hypotension and avoid taking blood pressure medications before bed to limit the risk of poor perfusion to the fellow eye. Vascular was consulted to perform a left temporal artery biopsy.

The IV steroids were initiated the day of presentation in the emergency room to avoid treatment delay. He was followed in the eye clinic on the following day. His visual acuity was found to be stable at 20/20-1 OD, but reduced to 20/400 with no improvement on pinhole OS. Confrontation fields showed an inferior nasal constriction OD, and stable 360 degree constriction OS. A Humphrey visual field was performed on the right eye, which revealed an absolute inferior arcuate defect and an early superior arcuate defect. The anterior segment and posterior segment findings were stable to the initial presentation OU. It was presumed that the right eye had developed posterior ischemic optic neuropathy, in addition to the anterior ischemic optic neuropathy OS. At this point, patient was to stay the course with the IV steroids 250 mg every six hours. Patient advised to go on bed rest in supine position to avoid reducing ocular perfusion with postural changes.

When the patient was seen on day four, both ESR and CRP were responding to the steroids. The ESR was now 42 and CRP was 36.3. The vision OD remained stable, but OS further deteriorated to no light perception. Confrontation fields OD showed inferior constriction and a new superior nasal constriction and were still constricted 360 OS. Dilated fundus exam OD showed global pallor of the disc, segmental disc swelling, and a decrease in cup to disc ratio to .10. Patient was diagnosed with arteritic ischemic optic neuropathy OD. Due to continuing decline in visual and ocular parameters, rheumatology decided
to continue IV methylprednisolone for five days. Left temporal artery biopsy was performed and results returned consistent with giant cell arteritis.

After five days of IV treatment, patient was transitioned to 60 mg oral prednisone a day. When the patient was seen next, five days since initial presentation, vision in the right eye was reduced to 20/200 on the Feinbloom low vision chart at 2 feet and only 5 degrees of visual field remained in the superior temporal quadrant. Vision OS was still no light perception. Pupils now showed only a 1+ afferent pupillary defect OS. Dilated fundus examination revealed diffuse disc pallor and edema OU. Over the course of the next week vision OD continued to decline and acuity stabilized at light perception OD and bare light perception OS.

The patient was discharged on prednisone 60 mg a day and medical prophylaxis including omeprazole, calcium and vitamin D. Bactrim was also initiated for Pneumocystis pneumonia protection and vaccinations, such as the Pneumococcal vaccine, were updated. The patient was registered with the Massachusetts Commission for the Blind and met with the Vision Impairment Service Team. Polycarbonate glasses were ordered for the patient. Rheumatology has since tapered patient’s prednisone to 40 mg a day, and his most recent ESR and CPR were back within normal limits, at 10 and 5.84 respectively. He is scheduled to begin a blind rehabilitation program in September.

Visual deterioration despite steroid treatment, such as in this case, has been described in the literature. One of the reasons for a further decrease in vision is that the steroid dose is inadequate, and this can occur at any time in the course of the disease. Progression of vision loss despite proper steroid treatment may be due to the lag in arresting the inflammatory process (6). Hayreh and Zimmerman found that in patients who experienced vision deterioration while on adequate steroid treatment, it consistently occurred within five days of the initiation of treatment, and the vision usually stabilized over 1-3 days (6). With that being said, they recommended a guarded prognosis for further vision loss during the first week of steroid treatment. Provided that the patient is on adequate maintenance doses of steroid, it is unlikely that the vision will continue to decline after the first week of treatment (6). In patients that did experience further vision loss, 81% of them had final acuities of light perception or no light perception (36). It is very rare for an uninvolved eye to become affected after the initiation of proper treatment (6, 36).
VI. Conclusion

Giant cell arteritis is an ophthalmological emergency carrying a risk of profound, permanent vision loss if treatment is delayed. Although maximum and expeditious treatment was initiated in this case, our patient sustained progressive, bilateral vision loss over five days.
References:


