ACADEMIC: CASE STUDY

Risk factors and treatment window in arteritic anterior ischaemic optic neuropathy: a case study

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Case

A 76-year-old NZ European male presented to the emergency department with sudden onset vision loss in the left eye for two days. He reported sudden loss of vision while watching television, with no flashes or floaters. He had experienced a mild left-sided temporal throbbing pain for three months, lasting ten seconds per episode and occurring several times a day. In addition, he suffered from one month of blurry vision and dizziness on bending forward. There was no jaw claudication, no constitutional symptoms, and the systems review was unremarkable.

The patient was initially screened on admission for a cerebrovascular accident, thyrotoxicosis, and cardiac causes using head computed tomography (CT), thyroid function tests, and an electrocardiogram (ECG), respectively. The results of these tests were all negative.

The patient had a past history of stroke, anxiety and hypertension and was on aspirin, atorvastatin, clonazepam and amlodipine. He was a retired accountant and a non-smoker with minimal alcohol intake (three standard drinks per week).

There was no family history of note.

Physical examination revealed no perception of light in the left eye (0/6 visual acuity), with Ishihara results of 14/15 in the right eye and 0/15 in the left eye. Severe left relative afferent pupillary defect was also present. Fundoscopy showed a pale left optic disc with a normal cup-to-disc ratio. Temporal artery pulsations were normal bilaterally.

INVESTIGATIONS

1. C-reactive protein (CRP): 61 mg/L (normal range: <5), erythrocyte sedimentation rate (ESR): 44mm/hr (normal range: 2–25)
2. Normal complete blood count, urea and electrolytes, thyroid function tests, renal function tests, glucose, and haemoglobin A1C
3. Normal head computed tomography (CT), ECG, carotid Doppler ultrasound
4. Temporal artery biopsy after treatment commenced – consistent with giant cell arteritis

PROBLEM LIST:

1. Acute arteritic anterior ischaemic optic neuropathy likely secondary to giant cell arteritis
   - › Most likely diagnosis due to history of temporal ache, inflammatory markers and fundoscopy findings
   - › Differentials: retinal detachment, retinal artery or vein occlusion, acute glaucoma, stroke
2. Hypertension and previous stroke
   - › Vascular risk factors

MANAGEMENT

1. Intravenous (IV) methylprednisolone 1g daily for three days, initiated on the day of presentation

SUMMARY

A 76-year-old NZ European man presented with sudden onset visual loss in his left eye after experiencing intermittent temporal aches and blurry vision for over a month. He had a history of stroke and hypertension but no past ophthalmological history. A pale optic disc, raised inflammatory markers, and temporal artery biopsy confirmed a diagnosis of acute arteritic anterior ischaemic optic neuropathy secondary to giant cell arteritis. High-dose intravenous methylprednisolone was administered within 24 hours of presentation, but the likelihood of vision loss reversal was unlikely.

Discussion

Giant cell arteritis (GCA) is a significant condition with potentially threatening consequences to vision. According to the American College of Rheumatology Criteria for Giant Cell Arteritis, a total weighting score of six points or higher can be classified as having GCA.[1] The diagnostic criteria includes: positive temporal artery biopsy or temporal artery halo sign on ultrasound (+5 points); erythrocyte sedimentation rate ≥50mm/hr or C reactive protein ≥10 mg/L (+3 points); sudden visual loss (+3 points); morning stiffness in shoulders or neck, jaw or tongue claudication, new temporal headache, scalp tenderness, temporal artery abnormality on vascular examination, bilateral axillary involvement on imaging and fluorodeoxyglucose-positron emission tomography activity throughout the aorta (+2 points each).[1] This discussion covers the pathophysiology, the major complications of GCA, risk factors for GCA and vision loss, treatment timing, and dose. In addition, new treatment options were briefly explored.

PATHOPHYSIOLOGY AND MAJOR COMPLICATIONS

GCA is a type of systemic vasculitis that involves medium to large arteries around the head and neck, causing the temporal ache experienced by the patient. In GCA, the optic nerve is typically considered in two parts: the optic nerve head (anterior), and the rest of the optic nerve (posterior). Anterior ischaemic optic neuropathy is usually more common than posterior ischaemic optic neuropathy.[2] Anterior ischaemic optic neuropathy can be further subdivided into arteritic and non-arteritic classifications. Arteritic anterior ischaemic optic neuropathy (AAION) relates to inflammation of arteries supplying blood to the optic nerve, whereas non-arteritic anterior ischaemic optic neuropathy describes reduced blood supply secondary to other causes, such as profound hypotension, increased intraocular pressure, and artery narrowing. In the patient's case, inflammation from GCA likely resulted in thrombotic occlusion of the posterior ciliary artery, the main arterial supply of the optic nerve originating from the ophthalmic artery, precipitating optic nerve ischaemia and sudden vision loss.[3] Therefore, this case specifically relates to AAION.

AAION is one of the most feared complications of GCA due to

the risk of permanent vision loss. The proportion of GCA cases that resulted in permanent vision loss was estimated to be approximately 8%, with AAION occurring in 7% of GCA patients but attributable in 85% of patients who suffered permanent vision loss.[4]

RISK FACTORS

Significant risk factors for developing GCA includes smoking, hypertension, vascular disease, low body mass index, and advancing age, with a peak incidence 70–79 years and age being the strongest risk factor.[5] The patient's past history of stroke and hypertension increased his risk of GCA compared to the general population. Additionally, his age of 76 years fell within the peak incidence range for GCA.

Studies have also investigated specific risk factors for permanent vision loss in GCA. One prospective study of 174 patients with temporal arteritis identified the strongest risk factor for permanent vision loss as prior transient visual ischaemic symptoms (odds ratio = 6.3, 95% confidence interval 1.4 – 29; P = 0.02). Note that the wide confidence interval was due to the small subset of total patients who had prior visual symptoms (n=35). Thus, the patient's blurry vision and sudden vision loss in his left eye significantly increased his likelihood of suffering permanent vision loss. Current literature has also demonstrated that markedly elevated inflammatory markers (ESR, CRP) at the time of diagnosis reduced the probability of vision loss, but in contrast, moderate elevation (ESR < 100mm/hr) was a predictor of irreversible vision loss.[7] The patient had moderately increased inflammatory markers, which may have worsened his prognosis, further compounding the risk of permanent vision loss in the affected eye.

TREATMENT TIMING

The literature shows that the timing of treatment may be more critical than the dose of treatment prescribed. Studies have not demonstrated a discernible difference between intravenous pulse therapy versus oral prednisone and their impact on visual outcomes.[7, 8] Early treatment initiation was shown as the only significant predictor of visual improvement (odds ratio = 17.7, 95% confidence interval 1.6 – 197.6).[7] Treatment was initiated within 24 hours of the patient's presentation to the hospital. However, considering he had experienced vision loss for two days prior to his presentation, high-dose glucocorticoid treatment was only initiated between 48 to 72 hours after symptom onset. Based on the literature, he only had a 4% to 34% chance of visual acuity improvement in his affected eye with his timing of treatment.[7]

TREATMENT DOSE

Due to AAION being a significant complication of GCA, its treatment primarily involves managing GCA to prevent vision loss in the unaffected eye and further deterioration in the affected eye. Treatment for patients with visual symptoms involves early administration of high-dose IV glucocorticoid therapy (methylprednisolone 1g IV daily for three days) before receiving the result of a temporary artery biopsy (gold standard diagnostic test for GCA). This approach is due to the risk of vision deterioration while awaiting biopsy results.[9] For patients without visual symptoms, oral prednisone 40mg to 60mg daily may be appropriate as a prophylactic measure (compared to pulse therapy), although the exact dosing remains debated.[9, 10] Early treatment is generally defined as the initiation of treatment within 24 hours of vision loss. The mechanism of action of glucocorticoid therapy is immunosuppression. This dampens inflammation, which disrupts thrombotic events that precipitate ischaemia and vision loss.

As per the 2018 European Alliance of Associations for Rheumatology (EULAR) guidelines on the management of large vessel vasculitis, 0.25g to 1g IV methylprednisolone for three days should be considered for patients with acute visual loss or amaurosis fugax.[10] The patient, who presented with complete vision loss in his left eye, a visual symptom of GCA, was treated appropriately with high-dose pulse glucocorticoid therapy, consistent with EULAR guidelines.[10]

OUTCOMES OF TREATMENT

The patient's prognosis was complicated by his unilateral vision loss at the time of presentation. Despite the initiation of glucocorticoid therapy, pre-existing vision loss could still progress within the first week of treatment in close to 10% of patients.[11] Typically, the prognosis of AAION following GCA is poor, and this was further compounded by the severity of vision loss in his left eye. At the time of presentation, the patient had no light perception in his left eye for two days, which reduced the likelihood of successful reversal of the ischaemic processes with glucocorticoid therapy. A recent review of 27 large retrospective studies found that despite timely glucocorticoid therapy, the visual acuity of most patients with pre-existing vision loss remained unchanged and may even worsen.[12] This follows logically, as the primary function of early treatment in GCA is to prevent catastrophic vision loss. It is important to note that although high-dose glucocorticoids have a role in preventing further ischaemic episodes, it is unable to reverse any vision loss that has already occurred. Furthermore, there are potentially significant side effects of long-term steroid use. In the patient's case, glucocorticoid therapy may prevent AAION of his unaffected eye but provides limited benefit to the eye that already experienced severe vision loss.

The patient's prognosis following left AAION is guarded. Despite the administration of IV glucocorticoid pulse therapy on the day of presentation, the duration of his visual symptoms, moderately elevated inflammatory markers, and initiation of treatment outside of the optimal treatment window (within 24 hours of symptom onset) all undermine his long-term prognosis.

NEW TREATMENTS

To prevent further vision loss in the unaffected eye and developing other complications of GCA, the patient likely requires long-term glucocorticoid therapy. However, the literature highlights a 53% to 86% increased risk of developing major adverse events from prolonged glucocorticoid use, such as diabetes and cataracts. Recent research has targeted adjunctive treatments or alternative therapies.[13] A recent randomised control trial on 251 patients compared the effects of tocilizumab (an interleukin-6 receptor alpha inhibitor) in combination with a 26-week prednisone taper versus a 26-week prednisone taper alone for long-term GCA remission. Interleukin-6 induces the synthesis of acute phase proteins and plays a role in both local and systemic inflammatory processes, so inhibition of interleukin-6 is thought to reduce inflammation. Tocilizumab monotherapy was not trialled in this study as its efficacy in treating giant cell arteritis remains uncertain. However, this study demonstrated a superior safety profile for patients receiving tocilizumab fortnightly.[14] This suggested that tocilizumab combination therapy showed efficacy in achieving sustained glucocorticoid-free remission in patients with GCA, which significantly reduces the risk of side effects with long-term steroid therapy. The patient could be a candidate for tocilizumab therapy to maintain GCA remission. However, the efficacy of tocilizumab in preventing AAION, as well as its long-term durability and safety, still require extensive research.

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About the author

› Reuben is a final year medical student at the University of Auckland.

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Ethical approval/patient consent

Written patient consent was obtained to publish this case report.

Declarations

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