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BAOJ Ophthalmology

Clare M Wilson and Penny J D'Ath, BAOJ Ophthalmol 2017 2: 1
2: 007

Case Report

A Case of Sixth Cranial Nerve Palsy and Suspected Giant Cell Arteritis

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Summary

Sudden onset of horizontal diplopia in an elderly patient can be due to giant cell arteritis. Although the patient reported was a vasculopath, a concurrent headache, mild reduction in visual acuity, scalp tenderness and raised inflammatory markers lead to a diagnosis of giant cell arteritis (GCA) and commencement of steroids. After an inconclusive temporal artery biopsy and resolution of visual acuity, the steroids were stopped, but within this time her hypertensive and diabetic treatment had been markedly disturbed. The rationale for treatment is discussed.

Case Report

A 70 year old lady presented to her routine diabetic retinopathy clinic appointment complaining of recent onset diplopia and mild headache. As well as having poorly controlled diabetes, she also suffered a myriad of other related illnesses including hypertension, renal failure and peripheral vascular disease which had resulted in a left below knee amputation. She had endured a prolonged hospital stay of over eight months duration the previous year due to infected leg ulcers.

On direct questioning, her mild headache was globally distributed, although she reported some tenderness on combing her hair in the left temporal region. The diplopia was horizontal and had started that morning. She had no recent weight loss, anorexia, malaise, fever or joint pains. She had no jaw claudication or myalgia.

On examination, her best corrected visual acuity was 6/6 in the right eye and 6/12 in the left eye. The left eye vision had decreased slightly from 6/9+1 at the previous visit four months earlier. There was no relative afferent pupillary defect and Ishihara colour plate testing revealed full colour vision bilaterally. Ocular motility testing revealed a left esotropia and decreased left lateral gaze. Anterior segments were healthy and intraocular pressures were within the normal range. Dilated examination revealed bilateral non proliferative diabetic retinopathy, no clinically significant macular oedema and healthy pink optic discs. There was mild temporal artery tenderness on the left hand side. Neither temporal artery was pulsatile. Humphrey automated visual field testing was unremarkable. A diagnosis of sixth nerve palsy possibly secondary to GCA was made.

On presentation, her blood pressure and blood glucose were well controlled, urinalysis was unremarkable, ESR was 54 and CRP was 18. Platelets were within normal range. She was commenced on oral prednisolone, adcal and lansoprazole and arrangements were made for a temporal artery biopsy to be performed. She was already taking aspirin. She was given a Fresnel prism to alleviate the diplopia.

Temporal artery biopsy (TAB) was challenging and histopathology revealed a venular structure had been excised. The diagnosis was therefore still not clear two weeks following presentation. Her visual acuity had improved to 6/9 in the left eye within this time. The high dose oral steroids were disrupting her blood pressure and blood sugar control significantly and a decision to gradually reduce the prednisolone dose was made after discussions with the rheumatology team. Her hypertension and diabetes reverted to improved control and the headaches subsided. The sixth nerve palsy was almost completely resolved six weeks following the onset of the condition. A retrospective diagnosis of microvascular sixth nerve palsy was assigned to this vasculopathic patient.

Discussion

The American College of Rheumatology 1990 Criteria classifies GCA as follows [1]:

1. Age of onset ≥50 years of age
2. New headache
3. Temporal artery tender/reduced pulsation
4. Elevated ESR, defined as 50mm/h (Westergren method)

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Sub Date: 16 January, 2017, **Acc Date:** 18 January, 2017, **Pub Date:** 26 January, 2017.

Citation: Clare M Wilson and Penny J D'Ath (2017) A Case of Sixth Cranial Nerve Palsy and Suspected Giant Cell Arteritis. BAOJ Ophthalmol 2: 007.

5. Abnormal arterial biopsy – showing necrotising vasculitis with predominant mononuclear cell infiltration or granulomatous inflammation

This patient was 70 years old, had a new onset headache, temporal artery tenderness and absent temporal artery pulsation. Her ESR and CRP were raised. The upper limit for normal ESR has also been described to increase with age and has been defined as age divided by 2 for men and age plus 10 divided by 2 for women. As this lady was 70 years old, her upper limit according to this method was 40mm/h. ESR is traditionally the most important laboratory test for GCA. However, there are many reports of patients with a normal ESR yet positive temporal artery biopsy. There are also many other reasons for this lady who had been recently hospitalised with leg ulcers, to have a raised ESR. CRP is an acute phase protein released by liver hepatocytes in response to inflammation. It has been found that CRP is more specific for GCA, and that a combination of raised ESR and raised CRP is the most specific [2].

GCA predominantly affects Caucasians over 50 years, with women affected at least twice as often as men. Monozygotic twin concordance and familial clustering suggests an inherited component. The HLA-DR4 haplotype has been associated with GCA, as have the intercellular adhesion molecule-1 (ICAM-1) genes [3].

TAB is the gold standard for diagnosing GCA, yet has limited sensitivity, and can be challenging particularly when the artery is non-pulsatile due to extensive disease. It is suggested that a second biopsy on the opposite side should be performed following an unsuccessful first biopsy, although second attempts only give a low positive yield, for example 9% of cases in one study [4]. Ultrasonography aids artery detection prior to biopsy, and it has been suggested that duplex ultrasonography should be the first-line investigation for diagnosing GCA, with biopsy being reserved for patients with a negative scan [5]. Although TAB has a low complication rate of 0.5%, there is a potential risk of facial nerve damage or stroke [6-8]. Halo sign of oedema is a hypoechoic halo in the artery wall, and is probably caused by oedema.

Oral prednisolone is first-line acute therapy for GCA, but the initial starting dose varies widely. Fraser et al recommend a 3-day induction dose of IV methylprednisolone at 15mg/kg/d followed by oral prednisolone maintenance therapy at 1mg/kg/d initially for GCA with visual loss [9]. This is echoed by the Royal College of Physicians [10]. Despite treatment with IV corticosteroids, visual acuity will reduce in 27% of patients with GCA (mostly within the first six days), however the treatment is effective at reducing the likelihood of fellow eye involvement. Without treatment, the risk of fellow eye involvement is 54% to 95% [10].

The Royal College of Physicians guideline entitled "Diagnosis and management of GCA" includes features to aid early recognition of GCA [10]:

1. Abrupt onset headache
2. Scalp tenderness
3. Jaw and tongue claudication
4. Visual symptoms
5. Constitutional symptoms
6. Polymyalgia symptoms
7. Limb claudication

Of these features, the reported patient had only scalp tenderness; her presenting features being horizontal diplopia. Extraocular motility disorders in GCA are thought to be due to extraocular muscle ischaemia caused by thrombotic occlusion of the respective muscular arteries [2].

GCA is a systemic vasculitis, preferentially involving medium and large sized arteries, particularly those of the extracranial branches of the carotid artery. It can cause arteritic anterior ischaemic optic neuropathy (AAION). Other causes of AAION are rare and include polyateritis nodosa, systemic lupus erythematosis and herpes zoster.

The histopathological hallmark of GCA is granulomatous inflammation surrounding the internal elastic lamina in medium and large vessels. The arterial media is most commonly involved, but all three layers may be affected. Macrophages, lymphocytes and fibroblasts make up the inflammatory infiltrate. Multinucleated giant cells may or may not be present, and are pathognomic of disease, fragmenting the internal elastic lamina. Visual loss has been associated with presence of giant cells [11]. "Skip lesions" may occur due to varied temporal and spatial disease. Inflammation leads to local vascular damage and intimal hyperplasia which may result in stenosis or occlusion. There is also thought to be an angiogenic role in GCA. The multinucleated giant cells produce platelet derived growth factor (PDGF) and vascular endothelial growth factor (VEGF). Normal arteries have avascular media and intima with a capillary network (vasa vasorum) in the adventitia only. In GCA, new capillaries appear in the media and intima and are more numerous in arteries with luminal stenosis secondary to advanced intimal hyperplasia [12].

It could be argued that this patient had only minimal visual loss and was at low risk of GCA. Visual acuity can be normal in GCA. In a study of 123 eyes with visual acuity loss due to GCA, 21% had a visual acuity of 6/12 or better. but 62% had a visual acuity of 6/60 or worse [13]. Conversely, 21% of patients with GCA have occult GCA – that is visual loss and a positive temporal artery biopsy without any of the systemic features of GCA.

A fluorescein angiogram may have aided diagnosis. The main lesion in GCA causing visual loss is thrombosis and occlusion of the posterior cerebral arteries giving choroidal filling defects. However, this must be done in the early stages as collateral circulation resolves the filling defects in time.

Evidence concerning possible increased mortality rate in patients with GCA over the normal population is limited and contradictory. It seems that death due to cardiovascular disease is increased in patients with GCA [14].

Conclusions

The treatment of the reported lady with steroids based on new

onset diplopia with a headache with marginally raised ESR and CRP is controversial. However, the devastating consequences of untreated GCA may warrant a lower threshold for intervention in these cases.

Important points to note:

1. GCA is a challenging diagnosis
2. ESR is a non specific indicator of inflammation – increases in malignancy, infection, CT disorders, trauma, anaemia, hypercholesterolaemia
3. CRP and platelet count can help with diagnosing GCA
4. USS for guided biopsy, and potentially for optical biopsy
5. The possible side effects of steroids should not be underestimated.

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