A 65-year-old lady with long-standing hypertension, presented with history of headache and odynophagia for 2½ months, sudden painless loss of vision of right eye for 20 days prior to admission and blurring of vision in the left eye. She also had multiple episodes of amaurosis fugax for 2 days. Permanent visual loss in the right eye followed an episode of amaurosis fugax. There was history of anorexia and weight loss. There was no history of diabetes mellitus, tuberculosis and the patient’s father and brother had similar complaints but their detailed records were not available.

On examination the elderly lady was conscious, oriented, of average build and nourishment. Her pulse rate was 86/min, BP was 130/80mmHg and the temperature was 37°C. She had pallor, oral thrush and palpable, thickened and tender superficial temporal arteries (the right being thicker than the left). On examination the right fundus showed a cherry red spot at the macula suggestive of central retinal artery occlusion while left fundoscopy showed pallid disc oedema with peridiscal haemorrhage suggestive of anterior ischaemic optic neuropathy (AION).

What is the possible aetiological diagnosis in this patient at this stage?

Given the history of hypertension, headache, multiple episodes of amaurosis fugax, fundal changes consistent with central retinal artery occlusion (CRAO) in the right eye and with AION in the left eye, possible differential diagnoses include arteritic and non-arteritic conditions involving the retinal blood vessels. The non-arteritic causes include emboli composed of either cholesterol, calcium or platelet fibrin debris. The most common source is an atherosclerotic plaque in the carotid artery, aorta or heart. The important arteritic causes include giant cell arteritis and various collagen vascular disorders like systemic lupus erythematosus.

How would you investigate this patient to reach a diagnosis?

The investigations to be done should include:

(i) To rule out the non-arteritic causes leading to the headache and visual symptoms: Echocardiography, CT Scan of the head, Lipid and coagulation profile.

(ii) To look for possible arteritic aetiological causes: Chest X-ray, ANA, c-ANCA, p-ANCA, temporal artery biopsy once there is suspicion of Giant Cell Arteritis.

What other investigations are required for the complete work-up of this patient?

Complete blood count, renal and liver function tests, estimation of blood glucose level and MRI angiography of the cranial vessels.

The results of the investigations done revealed leukocytosis (total leucocyte count 16500/cumm, Neutrophils 89%, Lymphocytes 10%, Monocytes 1%, Eosinophils 1%), elevated ESR 110 mm at the end of 1 hr and thrombocytosis (platelets 6,20,000/cumm). p-ANCA, c-ANCA and ANA were negative. CT scan of the brain showed a well-defined meningoia in relation to the right occipital bone under the tentorium. This was an incidental finding and was not contributing to her present problem. The liver and renal function tests were normal. Her coagulation and lipid profiles were also normal. Her fasting blood glucose was 98mg/dl. Chest radiograph and echocardiography did not reveal any abnormality. MRI angiography of the cranial vessels showed diffuse narrowing of the blood vessels. The right temporal artery biopsy showed mixed cell inflammatory infiltrates associated with disruption of internal elastic lamina and was suggestive of giant cell arteritis.

What are the clinical manifestations of Giant Cell Arteritis?

Giant cell arteritis (GCA), a chronic vasculitis of large and medium-sized vessels, is a disease that primarily affects patients over 50 years of age. It has been described in all races but is more common in whites. The onset of GCA tends to be gradual, but can be abrupt in a minority of subjects. Systemic symptoms are present in about half of the patients. Headache is probably the most frequent symptom and occurs in two-thirds of patients and may be associated with tenderness over the temporal artery. Headache is frequently marked and tends to be located over the temporal or occipital areas. Nearly half of the patients suffer from claudications of jaw muscles. Occasionally, intermittent claudications may occur in the muscles of the tongue or in those involved in swallowing.
Visual loss is the most dreaded complication of GCA and it usually results from AION or CRAO. Partial or complete loss of vision in one or both eyes occurs in up to 20% of patients. Affected patients typically report partially obscured vision, which may progress to total blindness. If untreated, the other eye is likely to become affected within one to two weeks. Amaurosis fugax is an important visual symptom that precedes permanent visual loss in 44% of patients.³

What is the prognosis in this condition?
Visual loss in GCA is often irreversible even with appropriate treatment. The main factor influencing the therapeutic response is the delay in diagnosing the condition and instituting appropriate therapy. In a retrospective study, 7 of 12 patients treated within the first 24 hours after the onset of the visual loss showed improvement. But when the treatment was delayed for more than one day, only 1 of 17 patients had some recovery of vision. Several case reports have suggested that intravenous pulse steroid therapy may be the treatment of choice for patients with recent visual loss due to GCA. Although its efficacy seems to be comparable to that of high-dose oral prednisolone, immediate treatment is of great importance.

What are the predictors of ischaemic manifestations of GCA?
Some investigators have tried to assess the best predictors of visual ischemic manifestations and permanent visual loss in GCA.⁵ Anaemia was found to be a negative predictor for visual ischemic manifestations. In contrast, as described in the present case, amaurosis fugax was a predictor of irreversible visual loss.⁴ In approximately 10-15% patients, the branches of the aortic arch, particularly the subclavian and axillary arteries become narrowed and result in the claudication of the arms. Thoracic aortic aneurysm is 17 times as likely in patients with GCA in comparison to those without the disease.⁷

The American College of Rheumatology in 1990 (Table 1) formulated ARA Criteria for the classification of giant cell arteritis.⁸ These criteria were designed for use in investigative studies to help distinguish GCA from other types of vasculitides. They are not useful for making the diagnosis in an individual patient.

Our patient had all the features of GCA. She had bilateral vision loss with two different eye lesions with progressive visual loss despite treatment with high-dose steroids. She had CRAO in the right eye with AION in the left eye, which is a distinctly unusual occurrence; only two such cases have been reported in the literature.⁹ It may, however, be conceded that it is not uncommon for cases with GCA to have two different lesions in the same eye due to the involvement of the ophthalmic artery in the arteritic process.

| What are the various mechanisms of blindness in a case of GCA? |
| Visual loss is the most dreaded complication of GCA and various possible aetiologies include AION, CRAO and PION. The basic mechanism leading to visual loss in a case of GCA is arteritis. |

What is the gold standard for diagnosing Giant Cell Arteritis?
Temporal artery biopsy is recommended in all patients who are suspected of having Giant cell arteritis. The inflammatory involvement of affected arteries is often intermittent rather than continuous. When possible, temporal artery biopsy should be performed before treatment is initiated but treatment should not be delayed just to obtain a histopathological diagnosis. Examination of temporal artery biopsy specimens may reveal evidence of arteritis even after more than two weeks of corticosteroid therapy.¹⁰ Concern about failing to establish the diagnosis (histopathologically) because of previous treatment should never interfere with the institution of appropriate treatment.

In GCA, arteries are usually affected by an inflammatory infiltrate associated with marked disruption of internal elastic lamina. This infiltrate is usually focal and segmental. The classical histological picture of GCA, observed in 50% of the cases, is of granulomatous inflammation in which giant cells are usually located at the junction between the intima and media. The other 50% have panarteritis with a mixed cell inflammatory infiltrate that is predominantly composed of lymphomononucleated cells with occasional neutrophils and eosinophils but without giant cells.

How would you manage this patient?
The patient was started on intravenous methylprednisolone 1 gm for 5 days on high index of suspicion followed by oral prednisolone at 1.5 mg/kg. Steroid therapy should be continued initially for one month and then slowly tapered off to a maintenance dose of 7.5 to 10 mg/day. The therapy should be continued for 1-2 years to prevent relapse. The side effects of steroids should be regularly monitored and patients who can tolerate it may be started on alternate day regimen. The use of steroid sparing agents like Methotrexate or other immunosuppressive agents still warrant large randomised control trials. Subsequently, right temporal artery biopsy that was done

Table 1: Traditional criteria for the classification of Giant Cell (Temporal) Arteritis

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<th>Criterion</th>
<th>Definition</th>
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<td>Age at onset of disease ≥ 50 years</td>
<td>Development of symptoms or findings beginning at the age of 50 or older</td>
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<td>Recent onset of headache</td>
<td>New onset of or new type of localized pain in the head</td>
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<td>Temporal artery abnormality</td>
<td>Tenderness of temporal artery to palpation or decreased pulsation unrelated to arteriosclerosis of cervical arteries</td>
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<tr>
<td>Elevated erythrocyte sedimentation rate</td>
<td>Erythrocyte sedimentation rate ≥ 50 mm per hour according to the Westergren method</td>
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<tr>
<td>Abnormal findings on biopsy of temporal artery</td>
<td>Artery-biopsy specimen shows vasculitis characterized by a predominance of mononuclear-cell infiltrates or granulomatous inflammation, usually with multinucleated giant cells</td>
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on the third day confirmed the diagnosis of GCA. She was also started on aspirin and low molecular weight heparin. Her headache and odynophagia settled in two days but impairment of vision in the left eye could not be halted.

GCA causes visual dysfunction from involvement of a variety of different structures. Although early treatment may occasionally result in the resolution of visual deficit, most patients who lose vision from GCA do not improve. It is imperative that clinicians diagnose the condition before visual loss occurs by combining a careful history and examination with appropriate laboratory studies.

Patients in whom GCA is suspected should be treated immediately with systemic corticosteroids, after which a unilateral or bilateral temporal biopsy should be performed for confirmation. Although thromboembolic occlusion is not a mechanism in GCA, therapeutic benefit has been reported with the use of low-dose aspirin. Prevention of platelet aggregation is potentially effective even in patients with partial luminal occlusion. Progression of visual loss from GCA, despite intravenous methylprednisolone therapy, may benefit by the addition of heparin therapy.

What are the futuristic treatment modalities available for the management of GCA?

Large, multi-centre, randomised, double-blind, placebo-controlled studies are required to define the role of methotrexate and the immunosuppressants as corticosteroid-sparing drugs in GCA. A recent pilot study found that infliximab was efficacious in patients with corticosteroid-resistant GCA.

References