

REVIEW

Giant cell arteritis

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Giant cell arteritis has been considered an enigmatic disease. It is characterised by chronic granulomatous inflammation of the walls of large and medium-sized arteries. The process has a predilection for the extradural cranial arteries, which include the ophthalmic and the posterior ciliary arteries. It is a multi-symptom disease of older individuals and patients often present with challenging issues and diagnostic dilemmas. We review the literature and latest protocols for the diagnosis and management of giant cell arteritis.
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Glaser¹ and Jacobs and Foster,² along with others^{3,6} define giant cell arteritis (GCA) and its specific manifestation temporal arteritis as a systemic vasculitis, which predominantly affects medium-sized extracranial arteries of the carotid circulation. Poorly understood in the eye, it may lead to arteritic ischaemic optic neuropathy (ION), precipitating blindness, while in the body, it may lead to stroke or death.^{1,20} Although it is primarily a disease of older individuals (more than 70 years of age) and because of its potentially significant and irreversible visual consequences, GCA should not be overlooked in patients more than 40 years of age who experience its tell-tale visual and ocular symptoms.

EPIDEMIOLOGY

GCA is well accepted as a disease of the aged, typically affecting individuals over the age of 55 years.^{2,3,6,17,20,33} While age specific prevalence rates vary by source

and exceptions to the rule have been reported, all support this assertion.^{3,6,17,19,32} A diagnosis of GCA at ages younger than 55 is considered by some to be one of exclusion. One estimation, provided by Glaser,¹ cites incidences under the age of 50 years as 17.4 to 28.6 per 100,000, between the ages 60 and 69 as 33 per 100,000 and over the age of 80 as 844 per 100,000. Most large series report a female to male preponderance of approximately three to one.^{1,2,4,7,12,18,19} Increased frequencies in certain ethnic populations and geographic areas support a potential genetic predisposition. The disease is almost exclusive to the Caucasian race but has been reported in the African-American and Asian races.^{2,12,17,21}

PATHOPHYSIOLOGY

The specific pathogenesis of temporal arteritis is poorly understood.^{1,20} It has been postulated that the basis for the disease

lies within abnormalities of the arterial elasticum, with disintegration of the inner elastic membrane of affected arteries, resulting in a giant cell reaction in proximity to this elasticum.^{2,4,6,8,12,17}

An alternative theory is that the initial lesion is a degeneration of the muscular layers of the artery's tunica media caused by ischaemia. This is thought to lead to fragmentation of the elasticum with the formation of giant cells occurring secondarily.²

Humoral and cellular autoimmunity have been implicated as a basis for the vasculitis.^{2,12,15} Elevated levels of serum immunoglobulins complement and immune complexes support this postulation.⁹ Cellular autoimmunity is suggested by the presence of giant cells, interdigitating reticulum cells, HLA-DR expressing macrophages and a predominance of T lymphocytes in the involved arteries. HLA-B8 and HLA-DR4 antigens have been identified as associated antigens, although this has not been definitively determined.^{2,4,17}

CLINICAL FEATURES

Systemic

The systemic features of giant cell arteritis can occur without the ophthalmic manifestations.¹⁸ These symptoms may be insidious at the onset, causing many patients to postpone examination. Patients often delay medical attention until catastrophic vision loss occurs. Systemic features usually precede ophthalmic manifestations by four to six weeks. Headache (ocular, temporal or occipital) is the most common presenting symptom.¹ As many as two out of three of patients present with headache before vision loss occurs.^{1,23} Cranial symptoms such as jaw claudication, temporal artery tenderness and scalp pain present in the majority of cases.¹⁻²⁰ Extracranial organs can be involved, although less frequently. About eight per cent of patients with GCA have been found to experience at least one of the following conditions: pleural effusion, coronary vasculitis, pericarditis, myocarditis, peripheral neuropathy, hearing loss, renal arteritis, lymph node hyperplasia and abnormal liver function.³³

Constitutional symptoms may include but are not limited to weight loss, fever, malaise, depression and polymyalgia rheumatica (PMR).^{1,3,12,14,34} PMR is a major symptom of GCA but can occur in isolation. It is characterised by aching and stiffness of the proximal joints, namely, the shoulders, hips and neck of at least one month duration. It is especially exacerbated in the morning. Like GCA, PMR occurs mainly in people older than 50 years of age. It is associated with an elevated ESR and is treated with systemic steroids. Approximately 20 per cent of patients with PMR develop GCA, especially in cases that are left untreated. Some suggestions have been made that PMR and GCA may be different manifestations of the same disease process.³⁵⁻³⁷ GCA may also present in an occult form, where the disease process is present but without systemic signs and symptoms.²⁹ Hayreh and co-workers²⁹ estimated that up to 21 per cent of all cases exist as the occult form. While systemic signs and symptoms are

important for making diagnostic decisions, they are not necessarily essential for identifying the syndrome.²⁹ If too much weight is placed on the presence of specific signs and symptoms, diagnostic decision-making may be postponed or overlooked in a clinical scenario that might be life threatening.²⁹

Ophthalmologic

The rate of ophthalmic involvement in GCA has been reported to be as high as 50 per cent.¹ The ocular signs and symptoms of GCA are summarised in Table 1. Loss of visual acuity presents as the first symptom in up to 36 per cent of cases.¹⁸ Anterior segment findings may include hyperaemia of the conjunctiva and episcleral vessels. A relative afferent pupillary defect (RAPD) is common. Corneal oedema, decreased intraocular pressure and iritis are prevalent. Progressive cataract and iris neovascularisation (rubeosis), due to the involvement of the ophthalmic artery, are present in severe cases.

Anterior ischaemic optic neuropathy (AION) results secondary to involvement of the ophthalmic, posterior ciliary, vertebral and temporal arteries.^{1,2,14,20} Ophthalmoscopically, the optic disc may appear

Symptoms	Signs
Generalised head pain	Pale, swollen disc/AION
Decreased visual acuity	Haemorrhage around ONH
Amaurosis fugax	CRAO
Diplopia	BRAO
Muting of colour vision	CWS
Visual field defect	Conjunctival hyperaemia
Temporal headache	Episcleral hyperaemia
Jaw claudication	RAPD
Fatigue	Corneal oedema
Weight loss/loss of appetite	Decreased IOP
Scalp tenderness	Iritis
Aching/stiffness of joints	EOM restriction
Tender/palpable temporal artery	Colour vision defect
Non-pulsatile temporal artery	Visual field defect
Fever	
Depression	

Table 1. Signs and symptoms of giant cell arteritis

oedematous with indistinct borders. Nerve fibre layer thickening secondary to constricted axoplasmic flow may produce an opalescence or corona, which can partially obstruct the view of other intraretinal structures (vessels). Central or cilioretinal artery occlusions are among the potential sequelae of the process.^{1,2,14} Other ocular ischaemic disease processes associated with GCA include posterior ischaemic optic neuropathy and ocular ischaemic syndrome (carotid artery stenosis).³⁸ All of these ischaemic vascular entities have been associated with posterior ciliary artery occlusion.³⁸

Cotton-wool patches, a known indicator of focal retinal ischaemia, have been observed in up to 33 per cent of eyes affected by GCA.³⁸ As GCA is a disease of the medium-sized arteries and typically does not affect the retinal arterioles, it cannot be directly responsible for these intraretinal infarctions.³⁸ Instead, the aetiology of these retinal microinfarctions is related to partial intraluminal platelet thrombosis causing microembolisation within the common trunk of the central retinal or posterior ciliary arteries.³⁸

Another important symptom of GCA is amaurosis fugax (momentary loss of

vision).³⁸ The literature documents that 30 per cent of patients with GCA experience this symptom, which is thought to be caused by the same transient optic nerve ischaemia that goes on to produce AION or PION.³⁸ Reports^{29,38} have documented that some 63 per cent of cases that present with amaurosis fugax go on to experience permanent visual loss.

Diplopia can occur without obvious motility disturbances reflecting extraocular muscle ischaemia.^{1,2,4,14} The resulting ocular motility dysfunctions do not take on the stereotypical pattern of common cranial nerve palsies. Restriction of up-gaze appears to be the most common manifestation. This is consistent with the complaint of vertical diplopia on gaze upward.²¹

Patients who are diagnosed with GCA without ocular involvement or symptoms have a greater incidence of headache, myalgia and fever. They tend to have higher ESR levels than those with ocular involvement, making the subtle, non-ocular features of the disease as important as the ocular.³⁸

In general, patients with biopsy proven GCA, who do not present with the classical signs and symptoms, tend to be from the younger end of the age range.³⁸

Anterior ischaemic optic neuropathy

Involvement of the ophthalmic and posterior ciliary arteries advances the development of anterior ischaemic optic neuropathy, a characteristic finding of GCA. AION is considered an infarction of the optic nerve at the level of the optic disc and is categorised as arteritic (AAION: systemic vasculitis) or non-arteritic (NAION: embolic, idiopathic).^{1,2,14,20}

Most cases (80 per cent) that are non-arteritic are noted by the patient on waking and are thought to be related to nocturnal arterial hypotension.^{2,38} Here, it is theorised that the optic nerve infarction is caused by a thrombus, which occurs due to stasis or decreased perfusion pressure.³⁸

The mechanism behind AAION, as seen in patients with GCA, is granulomatous thrombus formation.³⁸ Eighty-seven per cent of patients with GCA who underwent

fluorescein angiography demonstrated thrombus formation in the posterior ciliary arteries, especially the medial posterior ciliary artery, the principle source of blood for the optic nerve.³⁸

While both AAION and NAION are characterised by sudden loss of vision (less than 6/60), bilateral vision loss, dyschromatopsia, RAPD and disc oedema are more likely to occur in the arteritic form. Prodromal episodes with symptoms that include transient monocular blindness, difficulty focusing, colour vision disturbances, flashing or flickering lights, headaches, neck stiffness or unplanned weight loss may occur one to two weeks prior to a severe attack.²⁰ In arteritic cases, the second eye often becomes involved in a matter of days or weeks with severe vision loss occurring in the fellow eye despite prompt and immediate systemic treatment.^{1,2,14}

Associated findings

Cortical blindness from bilateral occipital lobe infarction has been reported in cases of AAION. Diplopia has been reported in up to 15 per cent of cases secondary to extraocular muscle ischaemia.⁴ Neuropsychiatric syndromes have been described as a result of brain stem ischaemia. Systemic and central nervous system difficulties have been reported in AAION and NAION, as a result of thromboses or emboli from carotid or vertebral arteries.^{1,20} It has been postulated that many strokes in the elderly that are thought to be a result of arteriosclerosis may be secondary to GCA.⁴

DIAGNOSIS

Today, the diagnosis of temporal arteritis is based more on impression rather than one specific laboratory test. Haematologic abnormalities and abnormal temporal artery biopsy results support the diagnosis. While an elevated erythrocyte sedimentation rate is associated with GCA, it has been documented in the setting of a normal ESR (Men = age/2; Women = (age + 10) / 2) in up to nine per cent of cases. Therefore, a normal complete blood count (CBC) and normal ESR results do not exclude the diagnosis.^{1,20} As it is not unusual for the

ESR to be normal early in the disease process, repetition of the ESR may be helpful.²¹

An elevated ESR is not pathognomonic for GCA. An elevated ESR indicates the presence of an inflammatory process such as vasculitis, collagen-vascular or autoimmune disease. The test does not possess the specificity to allow the determination of a definitive diagnosis. Macrocytosis (a condition in which the red blood cells are larger than normal),³⁹ hypercholesterolaemia (increased serum cholesterol), increased fibrinogen (a globulin of the blood that catalyses coagulation)⁴⁰ and the presence of gamma and beta globulins (proteins present in plasma defined by their electrophoretic movement)⁴¹ are a sampling of entities that may produce an elevated ESR, clouding the diagnostic process. Similarly, there are entities that may produce falsely low or reduced ESR measurements. These include but are not limited to polycythaemia (increased total red cell mass of the blood),⁴² sickle cell disease (a hereditary, genetically determined, haemolytic anaemia where crescent shaped cells are in circulation),⁴³ microcytosis (smaller than normal, non-nucleated RBCs in circulation),⁴⁴ hepatic necrosis (death of liver tissue usually connoting progressive damage via enzymes)⁴⁵ and a high white blood cell (WBC) count.

An alternative blood test for detecting the presence of non-specific inflammation is the C-reactive protein (CRP) test. The CRP is not easily influenced by the many factors that effect the ESR, such as haematologic disease and age. This makes the CRP comparatively more sensitive than the ESR for the early detection of GCA.²³ The CRP shows a distinct early, significant increase with the onset of inflammation. The CRP also reacts by promptly returning to normal (compared to the ESR) when remission is accomplished.⁴⁶

A recent report by Hayreh and co-workers²³ found that the CRP was more sensitive (100 per cent) than the ESR (92 per cent) for the early diagnosis of GCA. An elevated CRP (greater than 2.45 mg/dl) was found to have a statistically significant association with positive temporal artery biopsies. Further, patients with an elevated CRP were 3.2 times more likely to have a

positive biopsy than patients with normal CRP levels. In contrast, the investigation found no statistically significant association between elevated ESRs and temporal artery biopsy results. Nevertheless, the study concluded that maximum specificities (97 per cent) could be achieved only by using a combination of both tests.³⁴ Interestingly, while elevated ESR and CRP levels are characteristic of classic GCA, lower levels have been reported in occult cases.²⁹

Frequently, abnormalities of the blood including plasma fibrinogen (specifically the alpha-2 globulin fraction), serum alkaline phosphatase and haptoglobin levels are elevated in the acute phase of the disease.^{2,16,21} Many patients with GCA have been noted to have normochromic normocytic anaemia. In some instances, it is the first sign of GCA.²¹ A longitudinal study of anticardiolipin antibody (aCL) in PMR and GCA by Chakravarty and colleagues³⁶ revealed that the aCL may have a possible prognostic role in the course of both diseases. The study found that patients who presented with higher aCL levels suffered from more significant disease processes. PMR patients with high aCL levels frequently progressed to GCA; GCA patients with elevated aCL levels showed a trend toward developing vascular complications.³⁶ Finally, recent studies have reported that the platelet count as well as concentrations of CD8+ lymphocytes may have some diagnostic/prognostic implications for GCA patients.³¹

While these additional tests are potentially helpful, they are often omitted because the presenting constellation of signs provide adequate information to formulate a reasonably accurate diagnosis, allowing the initiation of the next phase of management. Unfortunately, costs also remain a factor in the decision-making process.

Temporal artery biopsy

Histopathologic identifications of cases diagnosed as GCA are important as the treatment that is selected varies with the aetiology of the disease. While the temporal artery is usually the vessel of choice for biopsy, segments of the occipital or facial arteries are acceptable alternatives.² Doppler flow studies have been used to iden-

tify areas in the artery that possess the highest suspicion for inflammation.⁵ A three- to five-centimetre specimen should be obtained from the left and right superficial temporal arteries, to avoid 'skip areas' (areas free from inflammation).^{1,2,4,15,20} Several points along the specimen's length should be scrutinised for the characteristic cellular changes by a pathologist familiar with GCA's processes and characteristics.²

A pathologic diagnosis for GCA is based on the presence of mononuclear or granulomatous inflammation, characterised by infiltration with histiocytes, lymphocytes, and multinucleated giant cells in the arterial wall.^{2,4,12} Using this definition, giant cells do not have to be present histologically to confirm the diagnosis of GCA. Fifty per cent of positive biopsies do not present with classic giant cells.⁴⁷ Thrombosis, intimal hyperplasia, fibrosis and infiltration of polymorphonuclear leukocytes are often present as well but are not considered pathognomonic. In cases that are questionable, the definitive means of confirming a diagnosis of GCA is ultimately decided by biopsy.^{1-20,34} The false negative

- Central retinal artery occlusion
- Acute glaucoma
- Uveitic glaucoma
- Retrobulbar optic neuritis
- Orbital abscess
- Ophthalmic migraine
- Tolosa Hunt syndrome
- Orbital and cavernous sinus compressive lesions
- Migraine headache
- Lyme disease
- Herpes zoster ophthalmicus
- Trigeminal neuralgia
- Diabetes
- Poorly controlled hypertension
- Stress related disorders
- Angina pectoris

Table 2. Differential diagnosis of giant cell arteritis^{1,3,7,20,33,48}

rate for temporal artery biopsy has been reported to range from five to nine per cent.^{1,4}

DIFFERENTIAL DIAGNOSIS

The list of potential differential diagnoses for giant cell arteritis (Table 2) includes many conditions that are commonly seen in clinical practice.^{1,3,7,48} Diseases with vascular, infectious, neoplastic, metabolic, infiltrative and inflammatory aetiologies may masquerade as giant cell arteritis and warrant due considerations during the diagnostic decision-making process. Carotid occlusive disease and the ocular ischaemic syndrome, diabetes and its complications, central retinal artery occlusion, acute pupillary block glaucoma, uveitis along with its complications, orbital abscess, orbital and cavernous sinus compressive lesions, non-arteritic ischaemic optic neuropathy, posterior ischaemic optic neuropathy, optic neuritis, retrobulbar optic neuritis, sinusitis, mucocoele and migraine headache are just a few of the possibilities that may produce a loss of vision in the presence of head or facial pain.^{1-20,48}

- Blood pressure (in both arms)^{1,2,20}
- Complete blood count (CBC) with haematocrit, differential and platelets^{20,33}
- C-reactive protein test^{1,16}
- Westergren erythrocyte sedimentation rate (ESR); results interpreted in less than 24 hours^{1-20,33,48}
- Carotid artery evaluation (Bruit)²⁰
- Carotid studies (Duplex Doppler ultrasonography)^{1,8,20}
- Fasting blood glucose (FBS)^{1,20}
- Sodium fluorescein angiography in cases with AION to rule out choroidal involvement^{1,11,20}
- Emergency ophthalmologic or neuro-ophthalmologic referral to rule out the need for immediate hospitalisation, temporal artery biopsy and IV steroidal therapy¹⁻⁵³

Table 3. Evaluation and management of patients suspected of having GCA

It is also very important to distinguish GCA from other types of vasculites, especially in the presence of extracranial organ involvement. Any systemic inflammatory disease (therefore any vasculitis) has the potential to produce an elevated ESR, making other tests necessary to differentiate among them. For example, the cytoplasmic-antineutrophil-cytoplasmic-antibody (c-ANCA) is used to separate GCA from Wegener's granulomatosis (WG). Similarly, the autoantibody anti-myeloperoxidase, which causes perinuclear staining by immunofluorescence (p-ANCA), is used to differentiate GCA from polyarteritis nodosa (PAN) and pauci-immune crescentic glomerulonephritis, among other vasculites. GCA has not been associated with either of the ANCA antibodies and has an excellent prognosis when treated compared to the aforementioned ANCA antibody associated vasculites.^{33,47}

As 81 per cent of GCA patients have AAION at some point in their disease, it is important for the clinician to be able to differentiate AAION from NAION. This is particularly important because both

diseases share some ocular and non-ocular signs, symptoms and population base.^{27,29,31,38}

In the initial stages, when the disc is oedematous, the AAION nerve tends to appear chalky-white. The disc in the NAION may be coloured normally or even hyperaemic with a haemorrhage adjacent to the margin. NAION patients often exhibit smaller optic nerves, a sign known as the 'disc-at-risk'.^{27,29,31,38}

Patients with AAION ultimately develop optic atrophy within six to eight weeks of the initial event. Ninety to 95 per cent of patients will have a significantly cupped pale disc. One study documented the average amount of cupping in AAION to be 0.85 as compared to 0.3 in normals and 0.2 or less in patients with NAION. The examiner must be cognisant of the differences between pale cupping (AAION) and pink cupping (glaucomatous cupping) so the two are not confused. Pale cupping can also signify space-occupying lesion.²⁷

Another feature that aids the clinician in distinguishing AAION from NAION is the degree of visual loss. In AAION, early visual loss is devastating (6/60 or worse).

Hayreh, Podhajsky and Zimmerman²⁹ reported that 54 per cent of the AAION patients had visual acuity of count figures to light perception, compared to 29 per cent in the NAION group. Laterality is also important. Thirty-one per cent of giant cell arteritis patients (AAION) present with bilateral vision loss. While there is no characteristic pattern to the field loss in cases of AAION, NAION classically presents with an altitudinal defect that respects the horizontal meridian.²⁹

EVALUATION

The acute phases of giant cell arteritis may yield visual acuities that range from 6/18 to no light perception. With the potential for fellow eye involvement within two days, despite appropriate treatment and an associated mortality rate that averages 20 per cent (secondary to complications of cerebrovascular disease),²⁰ giant cell arteritis is among the true ocular emergencies.¹⁻⁵ However, when properly treated with systemic steroids, the life expectancy for patients with GCA is virtually the same as that of the general population. Interestingly, there is no correlation between the risk factors of GCA and likelihood of mortality. This illustrates the extreme importance of the early diagnosis and treatment of GCA.⁶

History and patient profile are important elements in the diagnosis of GCA. A patient's age (over 65 years), race (Caucasian) and sex (females outnumber males three to one), along with the constellation of clinical signs and symptoms, almost always direct the examination into the correct algorithm.

Uncovering the data associated with ischaemic optic neuropathy may be tedious. Patients often do not volunteer information because they do not feel it is important or do not understand the relationship of their visual or ocular symptoms to their systemic condition. Specific questions should include whether the patient had experienced amaurosis fugax, headache, fever, malaise, jaw claudication and scalp tenderness.^{29,38}

In the office, the clinician should carefully evaluate the visual acuity at distance

and near. As patients with GCA often present with an acute loss of visual acuity in one or both eyes, pinhole visual acuity measurement and laser interferometry are often useful for ruling out interruptions in the ocular media or changes in refraction. Extraocular muscle motilities, Amsler grid, confrontational visual fields, automated perimetry, pupil testing, colour vision testing and brightness comparison can provide a cursory neurological assessment. Blood pressure should be measured in both arms and carotid auscultation should be performed.

Biomicroscopy should be completed along with applanation tonometry. A thorough undilated and dilated examination of the anterior and posterior segments is mandatory. Careful observations should be made so that subtle abnormalities within the aqueous and vitreous are not overlooked. Special attention should be given to the appearance of the optic disc (colour, cupping, contour, vessels and the presence or absence of a spontaneous venous pulsation).²² In cases where one suspects GCA, the clinician should observe the disc for chalky-white oedema, artery occlusion, cilio-retinal artery occlusions and/or cotton-wool patches.³⁸

If GCA is even remotely suspected, immediate laboratory testing is appropriate. The necessary studies are shown in Table 3. The minimum blood studies include the erythrocyte sedimentation rate (Westergren), the C-reactive protein test (CRP) and a complete blood count with differential. Instructions should be given to the laboratory to process the results within one hour. The results should be interpreted on the same day via a prompt, emergency referral to a neuro-ophthalmologist or a competent general ophthalmologist with experience in treating GCA. As diagnosis is infrequently straightforward in GCA and initiating treatment with oral corticosteroids is contraindicated in cases of optic neuritis,^{49,50} the need for clinical experience should not be underestimated.

MANAGEMENT

There are no steadfast guidelines that address the optimal dosage and duration

for corticosteroid therapy in cases of GCA.^{1,6,7,15,51} High doses of oral prednisone (60 mg to 100 mg) are documented as having a positive impact on vision, often within the first 24 hours of treatment.^{1-5,8,14,20,51} Pulsed intravenous corticosteroids (methylprednisolone, Solu-medrol, Upjohn, NY) has also been documented as useful within the first 36 hours of vision loss.^{2,11,14,20} Untreated, GCA leads to unilateral visual loss in 30 to 50 per cent of patients and bilateral visual loss in up to 33 per cent of patients.⁵¹ While some clinicians have implemented treatment with oral corticosteroids, reported treatment failures have led most to adopt high dose intravenous (IV) corticosteroid regimens as the modality of first choice.⁵¹ Doses of IV methylprednisolone (IVMP) ranging from 500 mg to 2000 mg have been recommended.⁵¹

The treatment of GCA remains controversial. Cornblath and Eggenberger⁵¹ reported four cases of GCA in which patients experienced severe vision loss despite at least 48 hours of IVMP treatment. Twenty-five to 58 per cent of patients with GCA who are treated with corticosteroids experience corticosteroid-related side effects (bone fractures secondary to corticosteroid induced osteoporosis, increased body fat).^{31,51} Further, the specific medication, dosage, route of administration and tapering schedule remain poorly defined. Cornblath and Eggenberger⁵¹ reviewed the literature and found that recommendations for the initial treatment of GCA ranged from 20 mg of oral prednisolone per day in the rheumatologic literature to 2000 mg of IVMP per day in the ophthalmologic literature, with no controlled studies comparing regimens or outcomes.⁵¹

The literature has reported that patients with GCA who are treated with oral corticosteroids can have visual loss in a previously involved eye, an uninvolved eye or can proceed with visual recovery.⁵¹ The literature also reports the same outcomes with IVMP. Given the slightly higher risk and greater cost associated with IVMP, Cornblath and Eggenberger⁵¹ suggest that a scientific answer, in the form of a clinical trial comparing IVMP to oral corticosteroids in acute visual loss, similar to those that have been done regarding cortico-

steroid use for optic neuritis, be pursued. Researchers³⁸ have demonstrated that following the administration of IV steroid therapy, if visual loss is to occur in the fellow eye, it will happen within one week of the start of treatment. As therapy is continued, visual function often levels off.³⁸ This confirms the concept that immediate and correct diagnosis leading to prompt and proper treatment can prevent blindness. To lessen the risk of failure or complications, treatment must be completed with the correct dosage of the correct regimen for the correct length of time.³⁸ Vision loss has been documented one to two months following abrupt, inappropriate interruption of optimal therapy.³⁸

Immunosuppressive therapy, using methotrexate, dapsone, azithioprine or cyclophosphamide, has also been reported as useful in steroid-resistant cases. However, this too remains controversial.^{8,18} Methotrexate (MTX) has been investigated for its steroid sparing effects in the treatment of GCA. Van der Veen and colleagues,³⁵ in a randomised, double-blind, placebo-controlled report, using relatively low 7.5 mg per week dosages of MTX, demonstrated that such assertions were unfounded. No statistically significant differences were found between MTX and a placebo with respect to time to achieve remission, the duration of remission or number of relapses.³⁵

In GCA, it is the duration and course of therapy that dictates the rate of remission and recurrence. Some patients finish their course of treatment in one year, some in two years, while others remain on maintenance doses of oral corticosteroids for several years.^{1,20}

A recent study of interleukin-6 (IL-6) in clinical relapses of PMR and GCA by Caplanne, Le Parc and Alexandre⁵² suggests that IL-6 may have a significant role in detecting and consequently managing GCA for relapse. IL-6 is a cytokine (chemical messenger released by mast cells) that stimulates C-reactive protein synthesis and the synthesis of other proteins that produce an elevation in the ESR.²³ ESR, CRP, haptoglobin and fibrinogen levels remain normal in 50 per cent of patients with

relapsed GCA who are still undergoing steroid treatment. Serum IL-6 levels have been found to increase significantly in cases of recurrence, even in the presence of corticosteroid treatment. While more testing is necessary in this area, it is conceivable that IL-6 may be used to follow GCA patients in the future.⁵²

PROGNOSIS

Generally, temporal arteritis has a finite course, which ranges from several months to years.^{1,20} Exacerbations and remissions are common, especially during the first year. Polymyalgia rheumatica is the most common symptom when relapses occur.^{1,4} Prompt diagnosis and treatment may prevent additional incapacitating losses.^{9,14} Jacobs and Foster¹ report that up to 15 per cent of patients with vision loss may recover a portion of useful vision, when prompt treatment is instituted.¹ Delays in treatment can result in permanent, devastating visual losses (6/240 to NLP).^{1,22} Unfortunately, despite timely treatment, vision loss can still occur in the fellow eye, presumably secondary to existing arteritic involvement in the ophthalmic circulation.^{1,14} For reasons that are poorly understood, approximately five per cent of patients suffer a decrease in visual acuity during the first week of steroid treatment.¹¹

In 15 per cent of GCA cases, death ensues from large vessel involvement, cardiac involvement (myocardial infarction) or other systemic failures related to side effects brought about by the disease or chronic corticosteroid therapy.^{6,8,10,53} A rare cause of death in GCA is aortic dissection. This is more likely to occur in hypertensive females and can be uncovered using several imaging techniques such as retrograde aortography, CT, MRI and transoesophageal echocardiography (TOE).⁵³

CONCLUSION

Even though more than 95 per cent of cases occur in patients older than 55 years, it is important to remember that age alone is not sufficient to rule out temporal arteritis. Even when considering the unique

collection of signs and symptoms, including age over 65, female predominance of three to one, headache, head tenderness or scalp tenderness, malaise, fatigue, fever and jaw claudication, the diagnosis continues to require skill and experience. Many of the systemic symptoms are nonspecific so the diagnosis may remain elusive until a majority of manifestations is present.

Vision loss and amaurosis fugax are the most prominent ocular symptoms. Diplopia, ptosis and periorbital pain are common. Once GCA is suspected, an emergent erythrocyte sedimentation rate and CRP should be ordered and interpreted. In patients who present with the classic history and clinical findings, even in the absence of an elevated ESR, the diagnosis should not be abandoned without a referral to a surgeon experienced in the recognition and treatment of GCA. Temporal artery biopsy is the only definitive method of confirming the disease and if there is a high suspicion for GCA in the presence of an elevated ESR and detectable CRP, steroids are initiated immediately while awaiting the results of the biopsy.^{24,32}

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