GIANT CELL ARTERITIS: THE INTERNIST SHOULD NOT BE A LONE RIDER IN THIS POTENTIALLY BLINDING CONDITION

BIDGOLI S, CORDONNIER M

ABSTRACT

We report the case of a 66-year-old woman with visual loss due to anterior ischaemic optic neuropathy. The diagnosis of giant cell arteritis was made on the basis of classic clinical characteristics and haematological abnormalities. Despite corticosteroid treatment, involvement of the other eye occured, resulting in a bilateral and permanent loss of vision. The follow-up was marked by two relapses within the 6 months after the first episode. In order to prevent blindness, ophthalmologists should be familiar with this disorder and should actively participate in the treatment, not leaving the internist deciding alone about tapering corticotherapy.

KEYWORDS

Giant cell arteritis, Recurrence of arteritic anterior ischaemic optic neuropathy, Visual loss, Failure to response to corticotherapy

INTRODUCTION

Giant cell arteritis (GCA), also known as temporal arteritis or Horton's disease, is the most common systemic vasculitis in the elderly. The first clinical description of this disease was made by Hutchinson in 1890 but it was Horton, in 1930, who described the typical histopathologic aspect of temporal arteries. It consists in a panarteritis of unknown etiology, involving aorta and its primary branches, particularly the extracranial arteries of the carotid circulation. GCA is clinically characterized by a wide range of systemic symptoms but the main danger lies in ophthalmic complications. We report a dramatic case which despite corticosteroid treatment and close follow-up by the internist, ended in a rapid bilateral and permanent loss of vision.

CASE REPORT

A 66-year-old woman presented at our department with a loss of vision in her left eye for 5 days. She had an history of 4 weeks frontal headache, claudication of the jaw and neck pain. She was previously healthy and her past medical story included bilateral phacoemulsification and YAG capsulotomy. Visual acuity (VA) was 10/10 on the right eye and hand motion on the left eye. Fundus examination revealed a no pale optic disc edema in the left eye consistent with an anterior ischaemic optic neuropathy (AION). Both temporal arteries were pulsatile and not tender. The right visual field was unremarkable, while the left was markedly constricted (*Fig. 1a)*.

ESR was 80 mm in the first hour, the platelet count was 706.000/mm^3 and the CRP 3.7 mg/dL. GCA was assumed on the basis of the aspect

.....

Submitted: Apr 21, 2012
Accepted: Aug 30, 2012

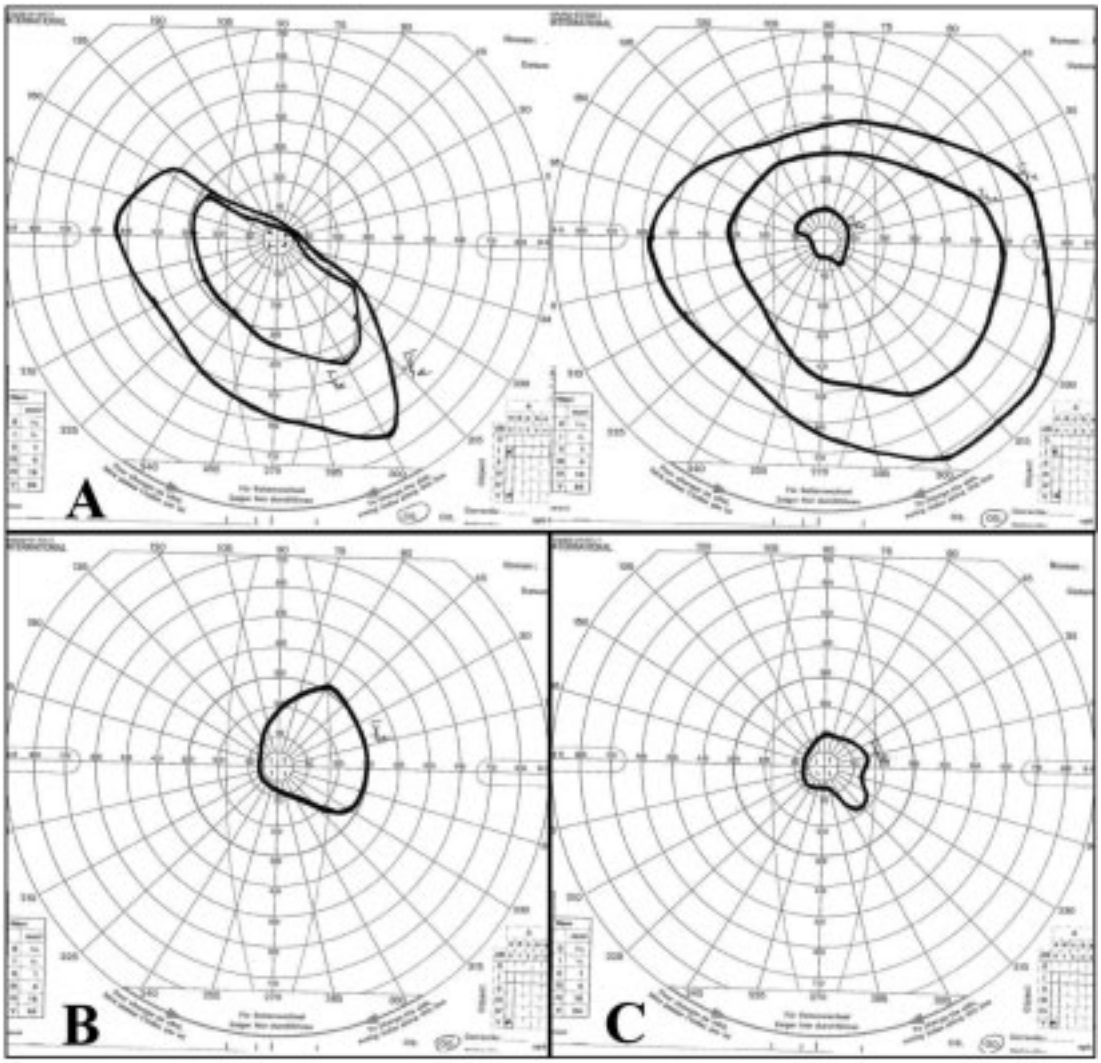

Fig. 1:
A: right and left visual fields at admission
B: right visual field at the time of discharge
C: right visual field at the second relapse

of the optic nerve and of the laboratory results. A treatment of 64 mg methylprednisolone (MP) and 100 mg acetylsalicylic acid was initiated. After 2 days, she had 10/10 acuity in the right eye and light perception in the left eye, but fundoscopy demonstrated a swelling of the nasal side of the right optic disc. She was admitted to hospital and an high dose intravenous (IV) MP therapy (750 mg/day) was administered during 3 days. After that, VA was still 10/10 in the right eye and she had no light perception on the left, but she had a bilateral disc edema and 2 flame-shaped peripapillary hemorrhages in the right eye. Steroid induced intracranial hypertension was excluded by a lumbar puncture and the treatment was increased to 900 mg/day. The following day, the VA had declined and measured 7/10 in the right eye. Two days after, the MP dose was again increased to 1500 mg/day during two days.

Given the presence of classic clinical manifestations of GCA and the biologic response to steroids, the index of suspicion was very high and a temporal artery biopsy (TAB) was not performed. After this seven-day course of high dose IV MP, she was switched to a maintenance dose of oral MP which was slowly tapered. All laboratory parameters normalised within two weeks. At the time of discharge, she had 10/10 in the right eye and hand motion in the left eye with a markedly constricted visual field of the right eye (*Fig. 1b*). During the following months, she progressively developed steroid induced diabetes. After 2 months, when the steroid dose was reduced to 40 mg/day, the patient complained again of headache and jaw pain without deterioration of visual function.

The CRP was 2,4 mg/dL and the platelet count raised to 435.000/mm^3. Methotrexate (10 mg/week) was added to her treatment in order to allow reduction of the MP dose without risking remanifestation of symptoms.

Thereafter, ESR and CRP levels decreased within one week but platelet count remained high for two months.

Six months after the first episode, the patient was admitted for a relapse while she was on 16 mg/day MP and methotrexate. She had headache, jaw pain and a sudden visual loss in her right eye but normal values of ESR, CRP and platelet count. After questioning the patient, we realised that steroids had been tapered the preceding weeks although she had episodes of transient visual loss. VA was 10/10 but a new visual field amputation was present (*Fig. 1c*). An high dose MP IV therapy (500 mg/d) was instituted for 3 days followed by oral treatment tapered gradually. Visual parameters remained stable following this episode.

DISCUSSION

Ocular manifestations of GCA are not rare with reported incidences of 14-70% (1). Ischaemia anywhere along the visual pathways (from the retina to the occipital lobe) can cause visual loss but, in the majority of cases (81,2%), visual loss is due to an arteritic AION (2). This form of AION results from an occlusive inflammation of the posterior ciliary arteries causing an infarction of the optic nerve head. Fundoscopy reveals a pallid (chalky white) disc edema. Retinal ischaemic lesions such as central retinal artery occlusion, cilioretinal artery occlusion and cotton wool spots can also be found. Choroidal ischaemia, which can be seen by fluorescein angiography (delay of choroidal filling time) may be the first ocular sign of GCA, preceding the AION (3). Permanent visual loss is preceded by transient visual loss in as much as one third of cases (4). It should be considered as an impending threat of blindness, and mandates immediate high dose corticotherapy as well as hospitalization and strict bed rest at initiation of treatment (to improve the vascularization of the head). When systemic features are missing, some fundoscopic findings like cotton-wool spots, intraretinal haemorrhages or disc swelling can help to distinguish GCA-related amaurosis from classical amaurosis. A history of amaurosis alternating between the two eyes favours GCA too (5). GCA should also be suspected in any case of diplopia or ocular pain in elderly persons. Diplopia, which is the second most common visual symptom of GCA, can result from ischaemia to extraocular muscles, cranial nerves or brainstem oculomotor pathways.

Ocular manifestations of GCA occur generally after systemic manifestations but some patients (between 5 and 38%) may have an occult presentation without any systemic symptom or sign, making the diagnosis difficult (5). The diagnosis of GCA is usually based on the criteria defined by the American College of Rheumatology (ACR) (*Table 1*). In fact, these criteria

Table 1: *The ACR criteria for the classification of GCA*

1. Age ⩾ 50 years
2. New onset of localized headache
3. Temporal artery tenderness or decreased temporal artery pulse
4. Elevated ESR (⩾ 50 mm/hr by the Westergren method)
5. Biopsy sample of a temporal artery showing necrotising arteritis with predominantly mononuclear cell infiltration or granulomatous inflammation usually with multinucleate giant cells

   The diagnosis of GCA is made when at least three of the criteria are met.

Hunder GG, Bloch DA, Michel BA et al – The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum* 1990; 33:1122-1128.

have been established for research studies to classify patients with a diagnosis of vasculitis rather than as diagnostic criteria for GCA in clinical practice (6). Indeed some criteria significant for the diagnosis like jaw claudication, neck pain and a high level of CRP are not included (*Table 2*). In our patient, classic clinical features were present and because of rapid biologic normalisation after steroid therapy, we have decided not to perform a TAB. It seems that TAB rarely influences patient management in practice. In a 10 year review of TAB, 68% of patients had sufficient information from clinical features and ESR to make a diagnosis of GCA (8). TAB could be of increasing benefit in atypical cases or in presence of only 2 criteria (9). Nevertheless, TAB is the only way to have a definite proof and should be considered whenever a diagnosis of GCA is suspected (10). Although growing, the place of imaging methods such as Doppler sonography, MRI and nuclear medicine techniques remains limited in the diagnosis.

Table 2: *Pertinent points about criteria for the diagnosis of GCA*

- The majority of patients have at least one of these symptoms at presentation: headache, jaw claudication, neck pain, myalgia, arthralgia, fever, malaise, anorexia or weight loss.
- Headache occurs in up to 90% of cases but can be due to many other diseases (5).
- Jaw claudication is the symptom most often associated with a positive TAB[1].
  It has also been linked to an increased risk of permanent visual loss (7).
- Elevated ESR, CRP and platelet count are the commonest laboratory findings.
- Thrombocytosis has the most significant positive likelihood ratio among usual clinical and laboratory findings[2].
- A positive TAB is definite proof of GCA but a negative TAB does not exclude it and an incidence of 5-13% false negative biopsies has been reported (1).

[1] Hayreh SS, Podhajsky PA, Raman R, Zimmerman B – Giant cell arteritis: validity and reliability of various diagnostic criteria. *Am J Ophthalmol* 1997; 123:285-296.

[2] Niederkohr RD, Levin LA – Management of the patient with suspected temporal arteritis a decisionanalytic approach. *Ophthalmology* 2005; 112:744-756.

The universally recognized treatment of GCA is corticosteroid therapy since Birkhead et al. have showed it in 1957, although there was no randomized controlled trial (11). The initial dose depends on clinical presentation of the disease. For patients with ocular involvement, high dose oral MP (80-100 mg/day) or high dose IV treatment (1 g MP daily for 3 days) folllowed by high dose oral therapy has been recommended (4). There is no evidence that IV administration is superior than oral way in improving vision or preventing deterioration of the affected eye but it may diminish the fellow eye involvement (12). Thus, IV therapy is suggested in presence of a history of transient amaurosis, a significant visual loss or impending signs of bilateralisation.

High dose oral MP should be maintained until the disappearance of systemic symptoms and the normalisation of laboratory markers, at least for 4-6 weeks. After that, a gradual and individual tapering of the dose is recommended to reach a maintenance dose. No generalization is possible but in most cases, the initial reduction is 5-10 mg per month to a daily dose of 10-15 mg. Then the rate of reduction should proceed only by 1mg per month (5). The duration of the treatment is variable but usually, patients are still on steroids after two years. Visual recovery is very rare and when it occurs, it is usually not accompanied by visual field or color vision improvement (13). The best predictor of recovery is early treatment, which if started within 24 hours, makes an improvement possible in 57% of cases versus only 6% if started later (7). The principal aim of steroid therapy is to prevent the involvement of the non-affected eye, which can occur within 1-10 days in 20-62% of cases without treatment (1). However, visual deterioration and bilateralisation in spite of megadose IV steroid therapy have been reported (14). The reason for this variable response to treatment is unknown. In our case, the initial therapy dose of 64 mg MP was possibly too low to control the activity of the disease. Immediate corticotherapy with an adequate dose provides the best chance to preserve vision.

More than half of patients have at least one relapse (15). Although relapse, including loss of vision can occur in patients who appear to be stable on an adequate dose of steroids, most relapses are related to the tapering (16).

Relapses can be defined clinically or by a rise of the laboratory parameters. In fact, relapses are primarly associated with recurrence of systemic symptoms and secondarily with an increase in the ESR and CRP. Because ophthalmic complications can occur without systemic manifestations (occult GCA), clinical monitoring based on symptoms alone is insufficient to guide the tapering. If ESR and CRP have both risen, the GCA is considered to have relapsed and an increase of the corticosteroid dose to the last effective dose is recommended (15). On the other hand, clinical relapses exist with normal ESR and CRP. In a GCA/polymyalgia rheumatica population, Kyle et al. reported normal ESR in 48% and normal CRP in 56% of cases during relapses (17).

During the tapering of steroids, patients must be questioned about any recurrence of symptoms particularly ocular problems. In our patient, despite the fact that she had transient amaurosis, the dose of steroid was inappropriately reduced by the internist.

We think therefore that ophthalmologists play a crucial role in the management of GCA, since visual defects may be poorly symptomatic. Questioning about visual complaints is essential, because transient visual loss and diplopia are predictive of ischemic neuro-ophthalmic complications.

Patients with GCA are not spared by adverse side effects of steroid therapy, increasing their morbidity and mortality. Bone and gastric protection should be considered as well as the monitoring of blood pressure and glucose to prevent cerebro- and cardiovascular complications. Many steroid-sparing agents have been studied but their use remains debated and there are no definite recommendations.

However, failure to respond or to wean from corticosteroids requires the consideration of adjuvant therapy like methotrexate or other immunomodulator agent.

CONCLUSION

GCA is considered as the prime medical emergency in ophthalmology because potentially leading to bilateral and irreversible blindness without treatment.

It should be suspected in any case of visual symptoms in people older than 50 years.

Altough the use of corticosteroids permits to preserve affected eyes from visual deterioration and bilateralisation, some patients fail to respond to the treatment without reason. A better knowledge of the immunologic processes involved in the pathogenesis of the disease will help to understand the variation in treatment response and to develop targeted therapies. As ophthalmologists have a primary role in the diagnosis of GCA, they must also take an active part in the treatment, not leaving the internist to be a lone rider in therapeutic options.

REFERENCES

(1) Rahman W, Rahman FZ – Giant cell (temporal) arteritis: an overview and update. *Surv Ophthalmol* 2005; 50: 415-428.

(2) Hayreh SS, Podhajsky PA, Zimmerman B – Ocular manifestations of giant cell arteritis. *Am J Ophthalmol* 1998; 125: 509-520.

(3) Slavin ML, Barondes MJ – Visual loss caused by choroidal ischemia preceding anterior ischemic optic neuropathy in giant cell arteritis. *Am J Ophthalmol* 1994; 117: 81-86.

(4) Hayreh SS, Zimmerman B – Management of giant cell arteritis. Our 27-year clinical study: new light on old controversies. *Ophthalmologica* 2003; 217: 239-259.

(5) Kawasaki A, Purvin V – Giant cell arteritis: an updated review. *Acta Ophthalmol* 2009; 87: 13-32.

(6) Hunder GG – Classification/diagnostic criteria for GCA/PMR. *Clin Exp Rheumatol* 2000; 18: S4-S5.

(7) Gonzalez-Gay MA, Blanco R, Rodriguez-Valverde V et al – Permanent visual loss and cerebrovascular accidents in giant cell arteritis: predictors and response to treatment. *Arthritis Rheum* 1998; 41: 1497-1504.

(8) Davies C, Frost B, Eshan O, McLain AD, Shandall A – Temporal artery biopsy... who needs one? *Postgrad Med J* 2006; 82: 476-478.

(9) Varma D, O'Neill D – Quantification of the role of temporal artery biopsy in diagnosing clinically suspected giant cell arteritis. *Eye (Lond)* 2004; 18: 384-388.

(10) Dasgupta B, Borg FA, Hassan N et al – BSR and BHPR guidelines for the management of giant cell arteritis. *Rheumatology (Oxford)* 2010; 49: 1594-1597.

(11) Birkhead NC, Wagener HP, Shick RM – Treatment of temporal arteritis with adrenal corticosteroids; results in fifty-five cases in which lesion was proved at biopsy. *J Am Med Assoc* 1957; 163: 821-827.

(12) Liu GT, Glaser JS, Schatz NJ, Smith JL – Visual morbidity in giant cell arteritis. Clinical characteristics and prognosis for vision. *Ophthalmology* 1994; 101: 1779-1785.
(13) Danesh-Meyer H, Savino PJ, Gamble GG – Poor prognosis of visual outcome after visual loss from giant cell arteritis. *Ophthalmology* 2005; 112: 1098-1103.
(14) Cornblath WT, Eggenberger ER – Progressive visual loss from giant cell arteritis despite high-dose intravenous methylprednisolone. *Ophthalmology* 1997; 104: 854-858.
(15) Fraser JA, Weyand CM, Newman NJ, Biousse V – The treatment of giant cell arteritis. *Rev Neurol Dis* 2008; 5: 140-152.
(16) Kyle V. Treatment of polymyalgia rheumatica/giant cell arteritis. *Baillieres Clin Rheumatol* 1991; 5: 485-491.
(17) Kyle V, Cawston TE, Hazleman BL – Erythrocyte sedimentation rate and C reactive protein in the assessment of polymyalgia rheumatica/giant cell arteritis on presentation and during follow up. *Ann Rheum Dis* 1989; 48: 667-671.

.....

Adress for correspondence:
Dr Sina BIDGOLI
Department of Ophthalmology, Erasme Hospital
808, Route de Lennik, 1070 Bruxelles
E-mail: sinabidgoli@yahoo.fr