Deterioration of Giant Cell Arteritis With Corticosteroid Therapy

Hugh Staunton, PhD, FRCPI, FRCP; Frances Stafford, FRCPI; Mary Leader, MD, FRCPath; Doon O’Riordain, FRCR

**Background:** Failure of response of giant cell arteritis (GCA) to corticosteroid therapy has invariably been attributed to the delay in diagnosing the disease or the use of inadequate corticosteroid dosage. Following our observation of progressive deterioration following the introduction of prednisolone use in a patient, we examined the possibility that worsening of the condition might be due to corticosteroid therapy rather than coincidence.

**Objective:** To determine whether corticosteroid therapy may exacerbate GCA.

**Design:** Case report and an analysis of similar cases reported in the medical literature.

**Patient:** A 64-year-old man had a 3-month history of headache, night sweats, malaise and general weakness, and anorexia and weight loss and a more recent history of jaw claudication, dysphagia, and hoarseness. Clinical findings included prominent temporal arteries with absent pulsation, abnormal saccades to the right, and eyelid retraction. Laboratory findings included an elevated erythrocyte sedimentation rate and platelet count. Results of a biopsy of the temporal artery confirmed GCA. Magnetic resonance imaging scans showed ischemic cerebellar lesions and a mature infarct in the left anterior occipital, posteroparietal region. Following corticosteroid therapy commencement, the patient’s condition deteriorated steadily for 5 days with clinical signs suggestive of an evolving vertebrobasilar stroke. Following treatment with high-dose intravenous dexamethasone sodium phosphate and heparin sodium, his symptoms improved.

**Data Sources:** The review included analysis of autopsy-based reports in which clinical details are provided and clinical reports in which major visual or cerebral complications are described. Significant complications occurred in many cases shortly following the introduction of corticosteroid therapy. In many of these cases, the symptoms indicated that GCA had been present for a significant period prior to corticosteroid therapy.

**Conclusions:** Progressively evolving occlusive strokes may occur following corticosteroid therapy in patients with GCA. In cerebrovascular complications, vascular occlusion occurs at sites of active vasculitis, usually within the vertebrobasilar system. It is not certain that the worsening of the condition following corticosteroid therapy is always coincidental, and an alternative possibility, namely a functional relationship between the initiation of corticosteroid therapy and clinical deterioration, should be borne in mind.

Arch Neurol. 2000;57:581-584

Giant Cell Arteritis (GCA) is a condition in which death rarely occurs. However, to our knowledge, there is probably not full ascertainment of GCA as a cause of death. For instance, it is unusual to have available histological information on the coronary arteries after death outside the hospital from myocardial infarction. Of 9 deaths in 1 report, 2 were due to myocardial infarction, 2 to dissecting aortic aneurysm, and 5 to cerebral stroke. Reports vary widely on neurological complications, perhaps because of ascertainment and selection. Most authors agree that visual symptoms are the most common neurological complication. Retinal ischemia usually is regarded by ophthalmologists as the cause of amaurosis, and the possibility of posterior circulation ischemia sometimes is not considered. One report suggested that the carotid artery distribution is a more common site of cerebral infarct. However, the available pathologic information suggests greater involvement of the posterior circulation territory in subjects who died of the disease, and there are numerous clinical reports of strokes in the vertebrobasilar territory. Although, in general, the intracranial vessels are claimed to escape morbidity, this is a relative state-
ment, and in complicated cases leading to death, such involvement does occur. Many such strokes appear to have occurred shortly after diagnosis of GCA. The idea that commencement (as well as sudden withdrawal) of corticosteroid therapy might have an initial deleterious effect on the patient’s condition does not appear to have been considered. In this article, we describe a patient with multiple ischemic effects, probably all within the posterior circulation territory, whose condition deteriorated steadily for 5 days following the institution of corticosteroid therapy to the point of constituting a medical emergency. This case illustrates the problems in management of GCA with central nervous system complications or the potential for such complications. Also, we advert to similar descriptions in the literature of clinical deterioration following initiation of corticosteroid therapy.

REPORT OF A CASE

A 64-year-old man with a previous history of glaucoma presented with a 3-month history of headache, night sweats, malaise and general weakness, and anorexia with weight loss of 6.3 kg. More recently he complained of jaw claudication, dysphagia, hoarseness, and a visual disturbance from the right side. His body temperature was 36.8°C to 37.8°C; pulse rate, 90 to 110 beats/min; and blood pressure, 150/90 mm Hg. Clinical findings included prominent temporal arteries with absent pulsation, abnormal saccades to the right, and eyelid retraction. The visual fields were full to confrontation, and the ophthalmoscopy of the retina was normal. The laboratory results were as follows: erythrocyte sedimentation rate, 88 mm/h; hemoglobin, 115 g/L; white blood cell count, 10.0 × 10⁹/L; hematocrit, 0.35; and platelet count, 586 × 10⁹/L. A postcontrast computed tomographic brain scan was normal. Prednisolone (60 mg/d) was commenced (day 1), and a biopsy of the temporal artery was performed on the following day. The histological results of the biopsy revealed severe vasculitis characterized by disruption of the elastic layer of the vessel wall, transmural inflammation, and poorly formed granulomas, giant cells, fibrin, and eosinophils. On day 2 he developed double vision. He was sweating profusely and complained of generalized weakness. On day 3 he became agitated. On day 4 he became drowsy and could not stand independently. Movements of the right side of the body were slower than normal. His jaw claudication and scalp tenderness had lessened. At this stage, the platelet count was 601 × 10⁹/L and hematocrit was 0.38. By day 5 he had become confused and his general condition had deteriorated. Meanwhile, magnetic resonance imaging brain scans showed a number of recent cerebellar lesions and 1 lesion in the left anterior occipital, posteroparietal region. The presence of a low signal on the T1-weighted magnetic resonance image suggested the latter lesion to be older. Results of Doppler ultrasonography showed all major neck vessels to be patent without stenosis. However, the Doppler waveform showed high-resistant blood flow in both vertebral arteries. (The results of magnetic resonance angiography that was performed 1 week later revealed no major neck vessel occlusion.) On day 5, because of continued clinical deterioration, 20 mg of dexamethasone sodium phosphate was administered intravenously immediately, and therapy with dexamethasone sodium phosphate, 4 mg 4 times a day, was subsequently commenced. Because of an episode of complete visual loss upon sitting, heparin was given intravenously within a matter hours. By the following day, his condition had generally improved (platelet count, 481 × 10⁹/L; hematocrit, 0.37), and thereafter, his condition continued to improve steadily. Heparin was replaced by warfarin sodium on day 11. By the time of discharge after 28 days of hospitalization, he was fully alert and ambulant with normal eye movements;
there was some residual unsteadiness and difficulty using the right hand, though. These deficits subsequently improved, and the erythrocyte sedimentation rate was normal. He had no memory of the period of acute illness described above and did not subsequently regain it. Results of a neuropsychological evaluation showed some continued cognitive and memory deficits. The results of the Wechsler Adult Intelligence Scale–Revised showed a verbal IQ of 124 and a performance IQ of 78. His performance was impaired in the logical memory and visual reproduction subtests of the Wechsler Memory Scale–Revised. His performance on the Rey Auditory Verbal Learning Test and Rey Complex Figure Test also showed impairment.

Other relevant and additional laboratory investigations performed during the acute illness stage that showed negative results included autoantibody screen, cardiolipin antibody assay, hepatitis B surface antigen, enzyme-linked immunosorbent assay for hepatitis C (Ortho Diagnostic Systems Inc, Raritan, NJ), neutrophil cytoplasmic antibody assay, and electrocardiography.

**COMMENT**

The patient described herein was admitted electively for investigation of symptoms slowly progressing for 3 months. Following a diagnosis of GCA and the use of prednisolone, 60 mg daily, his condition evolved into a rapidly progressive brainstem syndrome. Given the normally rapid systemic response to corticosteroid therapy in this condition, steady deterioration of the condition for 5 days following corticosteroid use raises the question of whether corticosteroid therapy might have initially compounded the problem as distinct from being an interposition on the decline. Although the concept may be novel, Conn et al referred to the use of glucocorticoid therapy in the management of systemic vasculitis as a possible “double-edged sword.” They suggested that progression of occlusion of the vessels may occur after control of inflammation. There is a diminished safety factor if such occlusion occurs in critical coronary or cerebral vessels already affected by the pathological process.

Despite the foregoing observation, the balance of probability would probably favor a coincidental relationship between the corticosteroid medication use and brainstem ischemic complications if this were a single case unsupported by other literature. However, a review of the literature reveals otherwise. In autopsy-based reports, death was usually due to a major complication at the site of vasculitis, notably vascular occlusion in the cerebral vessels (vertebral was more common than carotid vessels), coronary vessels, and aortic dissection. Where clinical details are available, a significant number of these complications occurred within a relatively short time after corticosteroid therapy induction, either in an area without apparent involvement at the time of therapy induction or as a compounding of symptoms in an area already clinically involved. Wilkinson and Russell reported results of 4 autopsies. Of these, 3 deaths occurred following the deterioration of the patients’ condition within days of the induction of corticosteroid therapy. Save-Soderbergh et al reported the results of autopsies in 9 patients in which 1 patient with typical GCA developed a coronary occlusion 4 days after therapy initiation and died a week later; 1 patient with typical polymyalgia had a stroke 12 days after initiation of corticosteroid therapy and died 2 weeks later. In all the foregoing patients, active vasculitis, usually accompanied by occlusion, in the relevant vasculature was present.

There are many similar clinically based reports. Buttner et al described 4 patients with cerebral complications. In 2, the complications followed within days of the induction of corticosteroid therapy. Of these patients, one had premonitory symptoms, including dizziness, that may have indicated a pathological condition in the cerebral vessels, while the other patient simply had headaches, mandibular pain, an erythrocyte sedimentation rate of 90 mm/h, and a biopsy specimen revealing the presence of GCA. Detailed examination of 8 cases reported by Gonzalez-Gay et al reveals a striking closeness in time between initiation of corticosteroid therapy and cerebrovascular ischemic events. Also, there are numerous reports on deterioration of GCA in previously affected eyes or in the appearance of symptoms in previously unaffected eyes following the introduction of corticosteroid therapy. In many of the cited cases, symptoms were present for weeks to months before the corticosteroid treatment initiation, and clinical deterioration occurred within a short period following corticosteroid therapy.

In the foregoing reports, the complicated outcome is invariably attributed to the delay in diagnosing the disease or the use of an inadequate dose of corticosteroid. The probable validity in many cases of such an assumption cannot be gainsaid, and we recognize that corticosteroid medication use remains the criterion standard of treatment in patients with GCA. However, in view of the proximity between initiation of corticosteroid therapy and progressive deterioration of the condition or the development of a new complication in numerous cases, we recommend that the possibility of complication following corticosteroid induction in some cases be borne in mind.

Finally, attention is drawn to the high platelet count in the case presented in this article. This phenomenon is wellknown. While a reactive thrombocytosis of this degree would not normally be expected to give rise to ischemic complications, it may be a complicating factor in a condition with already inflamed blood vessels supplying critical areas and it has been suggested that platelet-derived growth factor plays a role in arterial occlusion in GCA. Thus, active anticoagulation or thrombocyte aggregation inhibition should be considered in the presence of a potentially evolving fatal stroke.

Accepted for publication October 14, 1999.

**Doppler ultrasonography was performed by Greg Shanik, MCh.**

Reprints: Hugh Staunton, PhD, FRCPI, FRCP, Department of Neurology, Beaumont Hospital, Beaumont Road, Dublin 9, Ireland (e-mail: hugh@iol.ie).
REFERENCES


