

## Is Visual Loss Due to Giant Cell Arteritis Reversible?

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Giant cell arteritis (GCA) is a common systemic vasculitis with an unknown etiology. It mainly affects people older than 50 years of age and often presents with symptoms such as headache, jaw claudication, visual loss, polymyalgia rheumatica and increased erythrocyte sedimentation rate (ESR). Established blindness is irreversible if the steroid treatment is not administered within a few days. Here, we report a case of GCA in a patient with a normal ESR whose left eye perceived just light at the initiation of treatment. Immediately prior to the combined treatment with high dose oral steroids and cyclophosphamide, the ESR level had increased to 80 mm/h and the vision improved after the combined treatment four months later.

**Key Words:** Temporal arteritis, cyclophosphamide, steroids

### INTRODUCTION

Giant cell arteritis (GCA) is a systemic vasculitis of the elderly with a high erythrocyte sedimentation rate (ESR). Its prevalence increases with advancing age<sup>1</sup> but its cause is unclear. The disease is characterized by a granulomatous inflammation of the large and medium arteries throughout the body. Approximately 50% of all GCA patients have ocular complications. The most common complication is visual loss secondary to an ischemic optic neuropathy, central retinal artery occlusion, or rarely, cerebral ischemia.<sup>2</sup> In this report, we present a 45-year-old male patient with 20 mm/hour ESR, who lost his vision

in the right eye due to central retinal artery occlusion approximately three years ago. One year later, the vision in his left eye was also affected and it was only able to perceive light. Although it was resistant to high dose oral steroid treatment, the visual acuity of the left eye improved to 20/100 after a combination treatment with high dose oral steroids and cyclophosphamide four months later.

### CASE REPORT

A forty-five year old male patient was admitted to another hospital in February 1997 complaining of decreased vision in his right eye. The optic disc of the right eye had minimal pallor and the retinal arteries were narrowed. In the laboratory examination, ESR was within normal limits (20 mm/hour). The central retinal artery occlusion was diagnosed by fundus fluorescein angiography (FFA). The patient was not given any treatment at that time. In July 1997, he also noticed decreased vision in his left eye. In September 1997, after completely losing vision in his right eye, he was treated with oral high dose steroids. The initial steroid dose was 80 mg/day. After 10 days, the dose was tapered by 10 mg per week. However, an improvement in symptoms was not detected. He was then admitted to our Rheumatology clinic in February 1998, 1 year after the beginning of his complaints. He was not under treatment for one month and did not have any headache, jaw claudication, malaise, weight loss and any symptoms of polymyalgia rheumatica. The left temporal artery pulse was weaker than the right

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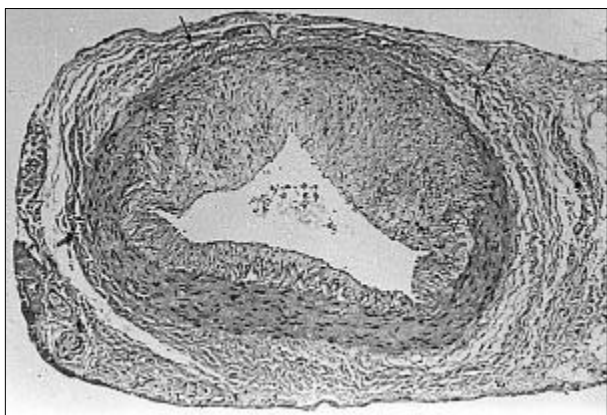
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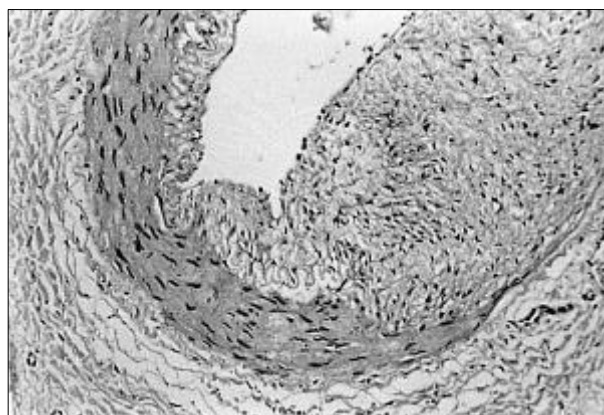
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one. The systemic blood pressure was normal. An ophthalmologic evaluation revealed that he did not have any vision in his right eye and the visual acuity of his left eye was 20/100. In the fundoscopic examination, the bilateral central retinal arteries were narrowed and bilateral cystic macula edema scarring were noticed. In the laboratory studies, a complete blood count, urine analysis, renal, liver and thyroid function tests were in the normal range. The rheumatoid factor, C reactive protein (CRP), antinuclear, anticardiolipin and antineutrophil cytoplasmic antibodies were negative. ESR (Westgren) was 7 mm/hour. A five-cm long left temporal artery biopsy was done. In the histopathological examination of the left temporal artery, subintimal fibrosis, small aggregates of lymphocytes, destruction and irregular fibrosis of the medial muscle layer were revealed (Fig. 1 and 2). There was also an interruption in the internal elastic membrane (Fig. 3). These histopathological changes suggested inactive temporal arteritis. After the biopsy, the visual acuity of the left eye was further impaired the eye was only able to perceive light. According to the clinical presentation, laboratory and histopathologic features, the patient was diagnosed as GCA.<sup>3</sup> Steroid treatment was commenced at 60-mg/day. Because there was no change in vision after 3 weeks, the steroids dose was tapered by 2.5 mg every two days. After the end of two months, at the control visit, there was no improvement in vision. However, an increase in the ESR (80 mm/hour) was found. There was no other pathology, such as infection, that

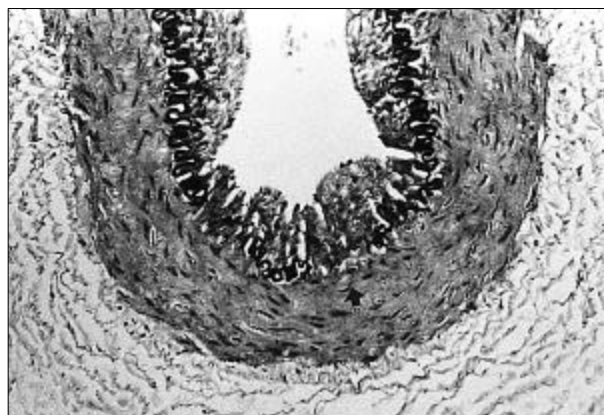
could explain the elevated ESR. The elevated ESR was found to be due to the activation of the disease. The steroids dose was increased to 60 mg/day and cyclophosphamide (150 mg/day orally) was added. After two weeks the steroids dose was tapered by 2.5 mg every four days to 40 mg/day. The daily steroid treatment was then changed to an alternate day steroid treatment. After two months, while he was under cyclophosphamide (150 mg/day) and steroids (40 mg every other day) treatment, the visual acuity in his left eye improved to 20/100 and the ESR had decreased to 20 mm/hour. Later, the steroids dose was tapered by 2.5 mg monthly. The cyclophosphamide dose was reduced to 100 mg/day. Currently, he is under (100 mg/day) and steroid (17.5 mg every other day) treatment, and the visual acuity in his left eye is still 20/100.



**Fig. 1.** Intimal fibrosis and small aggregates of lymphocytes in the vessel wall (arrow) (Hematoxylin + Eosin  $\times 40$ ).



**Fig. 2.** Destruction and irregular fibrosis of the muscle layer (Hematoxylin+Eosin  $\times 100$ ).



**Fig. 3.** Interruption of the internal elastic layer (arrow) (Verhoeff's Elastic Stain,  $\times 100$ ).

## DISCUSSION

Many types of vasculitis can affect the temporal arteries.<sup>4</sup> GCA is one of those types of vasculitis that occur in people over 50 years of age. Moreover, 90% of patients are over the age of 60 at onset, and an increased incidence with increasing age has also been reported.<sup>1</sup> Women are affected about twice as much as men.<sup>5</sup> The onset may be abrupt, but in most instances the constitutional symptoms of polymyalgia rheumatica such as fatigue, anorexia, fever, weight loss, and stiffness are present for weeks or months before a diagnosis is established.<sup>1,2</sup> Elevated ESR and CRP are the most common laboratory findings of the disease. In contrast to this clinical presentation, as in our patient, patients may have only ocular involvement without systemic symptoms and signs, or a normal ESR. In a large study, 18 (21.2%) out of 85 patients with ocular involvement caused by GCA reported to no systemic symptoms or signs of GCA including their ESR values. Even those with higher than normal levels were significantly lower than the others.<sup>6</sup> One of those patients had central retinal artery occlusion, which was noted in our patient. However, our patient was younger and had a normal ESR value at the initial visit.

Blindness is the most severe complication of GCA. Bilateral eye involvements at the first admission have been reported in 28.8-31% of patients.<sup>7-9</sup> The usual interval between the involvement of two eyes was 1 to 14 days, but in one case, it was reported to be as long as 9 months.<sup>7-9</sup> The involvement of the second eye in this patient occurred over five months, which is a long time for GCA.

In GCA, inflammation is detected most often in vessels originating from the arch of the aorta.<sup>10</sup> The inflammation tends to affect the vessels in a segmental or patchy fashion.<sup>11</sup> In early cases or in regions of the arteries with minimal involvement, collections of lymphocytes may be confined to the region of the internal or external elastic lamina or the adventitia. Intimal thickening, with prominent cellular infiltration is usually present. Necrosis of some portion of the arterial wall and granulomas containing multinucleated histiocytic and foreign body giant cells, histocytes, lymphocytes, some

plasma cells and fibroblasts are often found in specimens. The inflammatory process is usually marked in the inner portion of the media adjacent to the internal elastic lamina. However, giant cells are not seen in all sections and are therefore not required for a diagnosis if other features are compatible.<sup>12</sup> In our case, giant cells were not observed but subintimal fibrosis, small aggregates of lymphocytes, destruction and irregular fibrosis of the medial muscle layer, and an interruption in the internal elastic membrane were observed (Fig. 1 - 3).

Steroids have been found to be quite effective in treating GCA, as they suppress arterial inflammation and minimize the ischemic complications of the disease. Since their introduction, the incidence of blindness due to GCA has fallen considerably.<sup>13-15</sup> To be effective, it is important to commence steroid treatment within days. Therefore, if there is any suspicion of GCA, high dose steroid treatment should be started immediately, and a temporal artery biopsy should be done as soon as possible in order to either verify or rule out the diagnosis. In one study, it was shown that temporal artery biopsy specimens can show arteritis even after more than 14 days of steroid therapy in the presence of clinical indications of the active disease.<sup>16</sup> Moreover, Guevara reported a case in which GCA was shown after 6 months of steroid treatment.<sup>17</sup> To give a proper diagnosis and treatment, temporal artery biopsy is recommended, even in patients who received previous steroid treatment.

The second choice treatment for patients with steroid resistance or a relapsed disease while under steroid therapy is methotrexate treatment. However its use is limited.<sup>18</sup> Azathioprine has also been used as a steroid-sparing agent in GCA with limited success. Overall, methotrexate appears to have a better effect than azathioprine.<sup>19</sup>

Cyclophosphamide is one of the most potent immunosuppressive agents. It is well established in the treatment of some disease such as systemic lupus erythematosus, and vasculitis like Wegener's granulomatosis.<sup>20</sup> It has also been used in patients with GCA. It was reported to be as effective in a patient with GCA who developed subsequently renal failure while on steroid treatment.<sup>21</sup> Cyclophosphamide was also effective

in a patient with cerebral vasculitis.<sup>22</sup>

As far as the authors are aware, this case is the first case that responded to four months of combined treatment (steroid and cyclophosphamide) after a non effective two months of high oral steroid treatment. His vision on the left eye is still 20/100 and he has not shown any sign of activation for two years. It is believed that cyclophosphamide may be used in steroid resistant GCA patients, either as a second line drug or as a steroid sparing agent. Further studies for confirmation are recommended.

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