CASE REPORT

Arteritic anterior ischemic optic neuropathy treated with intravenous prostaglandin E_1 and steroids

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RD Steigerwalt Jr, MR Cesarone, G Belcaro, et al. Arteritic anterior ischemic optic neuropathy treated with intravenous prostaglandin E_1 and steroids. Int J Angiol 2010;19(3):e113-e115.

Arteritic anterior ischemic optic neuropathy (AAION) is an acute ischemia of the posterior ciliary arteries and/or ophthalmic artery due to inflammation. Therapy is immediate intervention with systemic steroids, especially to protect against vision loss in the other eye. The addition of a potent vasodilator to the steroids could help restore ocular blood flow and improve visual acuity. The objective of the current report was to present the use of prostaglandin E_1 (PGE_1) – a powerful vasodilator of the microcirculation – in the treatment of AAION. Two patients with AAION were treated with intravenous steroids and PGE_1. The visual acuity improved from 4/50 (less than 20/200) to 6/10 (20/35) in one patient and from 1/50 (20/400) to 1/10 (20/200) in the second patient. The visual fields in both patients maintained small central islands of vision. No complications due to the use of PGE_1 were seen. Intravenous PGE_1 should be considered in addition to steroids in cases of AAION to immediately restore blood flow to the optic nerve and improve visual acuity while the steroids reduce the inflammation.

Key Words: *AAION; Arteritic anterior ischemic optic neuropathy; Giant cell arteritis; PGE_1; Prostaglandin E_1*

Arteritic anterior ischemic optic neuropathy (AAION), also known as giant cell arteritis, is caused by an ischemia of the posterior ciliary arteries and/or the ophthalmic artery. The ischemia is due to a granulomatous vasculitis of the vessel walls. Therapy is immediate intervention with systemic steroids, especially to protect against vision loss in the other eye. Other retinal signs of ischemia may also be present (1). Prostaglandin E_1 (PGE_1) is a potent vasodilator of the microcirculation. Intravenous (IV) PGE_1 has been successfully used to treat seven of eight cases of non-AAION, three cases of chronic ischemia in high myopia and a branch retinal arterial occlusion (2-4). It has also been shown to improve ocular blood flow in patients with decreased flow in the presence of peripheral vascular disease and diabetes (5). Because AAION is due to ischemia caused by inflammation, the use of a potent vasodilator of the microcirculation, together with systemic steroids, may help in its treatment.

The current report presents two patients with AAION who were treated with IV steroids and IV PGE_1.

CASE PRESENTATIONS

Case 1

In December 2006, a 75-year-old white woman presented to the emergency room at the Ophthalmic Hospital (Rome, Italy) with a sudden loss of vision in her right eye (OD). She had a two-month history of general muscle pain, jaw claudication and right-sided temporal pain. She was being treated for diabetes and hypertension, and underwent a complete dilated eye examination. Her best corrected visual acuity (BCVA) in the OD, using the Snellen visual acuity chart, was 4/50 (less than 20/200), recognizing only one of two letters with a –0.75 sphere. Her BCVA in the left eye (OS) was 5/10 (20/40) with a –1.50 sphere. Her intraocular pressures were normal and she had mild cataracts. The fundus examination revealed optic disc edema (ODE) in the OD, a normal-appearing optic nerve head (ONH) in the OS and mild retinal pigmentary epithelial changes in the macula of both eyes. Her blood work revealed an erythrocyte sedimentation rate (ESR) of 125 mm/h (the normal value is less than 20 mm/h for the Westergren test), a glucose level of 250 mmol/L and a C-reactive protein (CRP) level of 14.87 mg/L (the normal value is less than 5 mg/L). She was then seen by an internist for a medical examination, who made the diagnosis of AAION. She refused a temporal artery biopsy. Once the diagnosis was made and after explaining the experimental nature of the treatment, written consent was obtained and the patient was rapidly given 20 mg of IV 6-methylprednisolone. This was followed by 80 µg of PGE_1 with 2 mEq of potassium in 250 mL of IV physiological solution (NaCl 0.9%) over 3 h. Normally, a higher dose of IV 6-methylprednisolone would have been used as a starting dose but, due to the patient's diabetes, the internist used only 20 mg. Her pulse and systemic blood pressure were monitored every 15 min. On the following morning, the same treatment was repeated first with 20 mg of IV 6-methylprednisolone immediately followed by 80 µg of PGE_1 with 2 mEq of potassium by IV infusion over 3 h. The next day, 48 h after the first IV infusion, the vision in the OD had improved to 5/10 (20/40) with a reduction in the ODE. The OS was unchanged. After one week, the visual acuity was unchanged and the optic disc in the OD was pale without edema. At six months, the BCVA, using the Snellen chart, in the OD improved to 6/10 (20/35) and was unchanged in the OS. After the first two IV infusions of 80 µg of PGE_1, no further PGE_1 treatments were given. She was followed by the internist. After the first two days of IV 6-methylprednisolone, she was started on 25 mg of prednisone once daily for three days followed by 12.5 mg once daily for 45 days. The steroids were gradually reduced to 5 mg a day and stopped. After one week of treatment, the ESR was 72 mm/h and the CRP level was 1.42 mg/L (normal was lower than

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1 mg/L). This second CRP level was measured in a different laboratory with different normal values. After two weeks of treatment, the ESR was 12 mm/h and the CRP level was 0.95 mg/L (again, the normal CRP level was lower than 1 mg/L). Her medical complaints of general muscle pain, jaw claudication and right-sided temporal pain disappeared. Octopus (Haag-Streit International, Switzerland) visual fields (VFs) were measured six and 12 months after treatment, and were essentially the same. The mean deviation (MD) was –22 dB with a dense peripheral scotoma of 360° and a small island of central vision extending nasally.

Case 2

In January 2007, an 84-year-old diabetic white woman presented to the emergency room at the Ophthalmic Hospital with a sudden loss of vision in the OS. She had a one-month history of jaw claudication and left-sided temporal pain. Her BCVA using the Snellen visual acuity chart was 3/10 (20/70) in the OD and 1/50 (20/400) in the OS. Her intraocular pressures were normal. She had mild cataracts and mild macular degeneration in both eyes. The ONH was pale in the OD and there was ODE in the OS. Her blood work revealed an ESR of 82 mm/h and a CRP level of 8.7 mg/L (normal was lower than 5 mg/L). After a medical examination by an internist, a diagnosis of AAION was made. A temporal artery biopsy was not obtained. After explaining the experimental nature of the treatment, written consent was obtained and the patient rapidly received 40 mg of IV 6-methylprednisolone followed by 80 µg of PGE_1 with 2 mEq of potassium by IV infusion as described for the first patient. The same treatment was repeated on the second day. On the third day, she was started on 25 mg of predisone two times a day by mouth. She was then seen one week after the beginning of therapy. Her visual acuity was the same in the OD but had improved to 1/10 (20/200) in the OS, recognizing both letters of the Snellen chart. The ODE was still present in the OS. After two weeks, the visual acuity was the same, the ESR was 23 mm/h and the CRP was 4.8 mg/L (normal CRP level is less than 5 mg/L). The jaw claudication and left-sided temporal pain were no longer present. The ODE had disappeared and both optic nerves were pale. An Octopus VF measurement at that time showed an MD of –23.3 dB with a dense peripheral scotoma of 360° with a small island of central VF. At two months, results of the ocular examination were the same. The patient was followed by the internist who gradually reduced the steroids. Three months after treatment, the VF was unchanged with an MD of –22.8 dB.

DISCUSSION

PGE_1 is a safe, potent vasodilator of the peripheral vascular system (microcirculation or capillary system) that is used to treat patients with peripheral vascular disease such as intermittent claudication and peripheral diabetic ulcers (5,6). A two-day IV treatment with PGE_1 causes a vasodilation of the capillary system that can last for four weeks or longer in patients with peripheral vascular disease (7). It is well tolerated with few side effects, and can be used in patients who are hypotensive. It is important to monitor the systemic blood pressure frequently (every 15 min to 20 min) during its IV administration (5-7). The main mechanism of action of PGE_1 is a vasodilation of the microcirculation (capillary system). PGE_1 has a direct action on the smooth muscle of the vascular wall, leading to vascular dilation and increased flow. PGE_1 is also known to inhibit platelet aggregation. PGE1 is rapidly metabolized by oxidation during passage through the pulmonary circulation. It is excreted in the urine as metabolites within approximately 24 h (8). This rapid elimination also contributes to its safety.

AAION is a granulomatous vasculitis of the vessel walls of the posterior ciliary arteries and/or ophthalmic artery, and therapy is immediate high-dose IV steroids, especially to protect against vision loss in the other eye (1). Two published studies (9,10) reported visual acuity improvement in patients with AAION using IV steroid therapy. In the first study (9), the visual acuity improved in 7% of 41 consecutive patients treated with IV steroid therapy. In the second study (10), the visual acuity improved in 13% of 39 consecutive patients. In the two cases treated with IV steroids and PGE_1 reported in the present article, there was visual acuity improvement in both. Normally, high-dose steroids are given immediately, but the internist elected to use low doses in these two cases because of the presence of diabetes in both patients. High-dose steroids would have made diabetic management difficult and the patients here immediately responded well to the low-dose steroids together with the PGE_1. In the current study, we used IV steroids for an additional two reasons. The first was that ODE was present due to swelling of the axons caused by axoplasmis flow stasis. Swollen axons in a restricted space in the opening of Bruch's membrane and the scleral ring in the ONH can compress the capillaries between the nerve fibre bundles. It is possible that increasing the blood flow with PGE_1 in the capillaries would cause more tissue swelling at the level of the ONH. We did not want further swelling in an already congested area with the risk of further damage to the nerve fibres, and believed that IV steroids may help reduce this swelling and risk. The second reason for the use of IV steroids was to try to reduce ischemia-reperfusion (I-R) injury. The immediate reinstitution of blood is necessary to prevent further tissue damage, but the reperfusion itself may cause further tissue damage (ie, reperfusion injury). Infiltrating leukocytes are believed to play a major role in I-R injury and was one of the reasons we used IV steroids before the use of IV PGE_1 (11,12). Steroids were continued orally after PGE_1 because of the granulomatous vasculitis and potential for I-R injury in the immediate post-treatment period.

Because the decrease in visual acuity is due to ischemia, the addition of a potent vasodilator to immediately re-establish blood flow while the systemic steroids take effect could be important. PGE_1 has been shown to improve ocular blood flow in patients with decreased ocular blood flow in the presence of peripheral vascular disease and diabetes (5). It has been used to treat acute ocular ischemia in the form of non-AAION and a branch retinal arterial occlusion (2,4). One IV infusion of PGE_1 improves blood flow for up to four weeks in patients with peripheral vascular disease (7). For these reasons, we decided to add PGE_1 to the treatment of AAION. In both patients, treatment with PGE_1 was given for only two days. The vasodilatory effect of two IV administrations of PGE_1 probably lasted long enough for the systemic steroids to take effect and reduce the ischemia. In both patients, the systemic steroids were gradually reduced by the internist as the ESR and CRP decreased. A total of 2 mEq of potassium was added to each 250 mL IV infusion to avoid cardiac arrhythmias.

These are only two cases involving the addition of PGE_1 to the normal treatment of AAION with systemic steroids. The use of a potent systemic vasodilator to immediately improve ocular blood flow could help improve visual acuity in the ischemic eye while the steroids take effect. The authors normally use higher doses of steroids to treat AAION. It was only because of the presence of diabetes in these two cases that lower doses of steroids were used. The visual acuity initially improved and remained stable on all follow-up visits in both cases. The VFs were obtained only after treatment so that the start of PGE_1 and steroid therapy would not be delayed. Despite the improved visual acuity, the VFs were markedly diminished, with only a small island of central vision remaining in the affected eyes of both patients. The use of PGE_1 appeared to be effective without causing any systemic or ocular side effects, but larger studies are necessary to evaluate its use.

DISCLOSURES: The authors have no conflicts of interest and no proprietary interest in the products mentioned in this case report. The authors alone are responsible for the content and writing of this report.

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