Two Patients with a Rapid Increase in the Ocular Pressure after Carotid Artery Stenting for Cervical Internal Carotid Artery Stenosis with Ocular Ischemic Syndrome

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Objective: We report two patients with a rapid increase in the ocular pressure after carotid artery stenting (CAS) for cervical internal carotid artery stenosis with ocular ischemic syndrome.

Case Presentations: Case 1 was a 67-year-old male. Case 2 was a 70-year-old male. In the two patients, a reduction in vision and transient hemiparesis had persisted for a few months, leading to a diagnosis of severe internal carotid artery stenosis. Furthermore, they were diagnosed with ocular ischemic syndrome and neovascular glaucoma. Panretinal photocoagulation was performed before CAS in the Department of Ophthalmology. In Case 1, ocular pain appeared 9 days after CAS. In Case 2, it appeared the day after CAS, and increased ocular pressure was noted. After conservative treatment, trabeculectomy was performed, but the visual prognosis was unfavorable.

Conclusion: In patients with severe internal carotid artery stenosis and ocular ischemic syndrome, there may be a rapid increase in the ocular pressure after revascularization. Therefore, it is necessary to establish a cross-sectional treatment strategy in cooperation with ophthalmologists.

Keywords: cervical internal carotid artery stenosis, stenting, neovascular glaucoma, ocular ischemic syndrome, diabetic retinopathy

Introduction

Ocular ischemic syndrome is an ocular complication in which chronic circulatory failure of the eyes causes various symptoms. It is frequently complicated by internal carotid artery lesions.1–3) In particular, when neovascularization in the anterior ocular region induces rubeosis iridis or neovascular glaucoma, the visual prognosis is unfavorable.1,2) Carotid endarterectomy (CEA) or carotid artery stenting (CAS) as revascularization is considered to be effective treatment for circulatory failure of the eyes, and several reports demonstrated the improved visual function following revascularization.4–7)

In this study, we report two patients with carotid artery stenosis accompanying ocular ischemic syndrome, who suffered a rapid increase in the ocular pressure requiring ophthalmological treatment.

Case Presentations

Case 1 was a 67-year-old male. He had a 6-month history of reduced vision of the left eye, transient amaurosis, and transient hemiparesis of the right half of the body. He was referred from the Department of Ophthalmology. Angiography showed a stenotic lesion at the origin of the left internal carotid artery (North American Symptomatic
Carotid Endarterectomy Trial [NASCET: 90%]). Surgery was considered due to the symptomatic, severe stenotic lesion. Preoperative systemic examination showed diabetes mellitus (HbA1c: 7.2%), hypertension, and dyslipidemia. In addition, a severe stenotic lesion of the coronary artery was detected, and percutaneous coronary intervention (PCI) was performed 1.5 months before CAS. On ophthalmological evaluation 3 months before CAS, the corrected vision of the left eye was 0.06, and the prolongation of the intra-retinal circulation time (21 seconds), which reflects ocular ischemia, for the left eye, petechial fundal hemorrhage, and rubeosis iridis were observed (Fig. 1). The angle was occluded (50%). The left ocular pressure was 15 mmHg, being within the normal range. To prevent further neovascularization, panretinal photocoagulation was performed. After 1 month, the corrected vision of the left eye was 0.03, showing slight exacerbation. However, rubeosis iridis slightly reduced.

Prior to PCI, the oral administration of aspirin at 100 mg/day and clopidogrel at 75 mg/day was started and continued until CAS. Under distal protection with a Filterwire EZ (Boston Scientific, Natick, MA, USA), CAS was performed. Using a Sterling (3.0 mm/30 mm; Boston Scientific), predilation was conducted for 30 seconds at 5 atmospheric pressures, and a Carotid Wallstent Monorail (10 × 24 mm; Boston Scientific) was deployed. Using a Sterling (4.0 mm/30 mm; Boston Scientific), postdilation was conducted for 30 seconds at 5 atmospheric pressures, leading to favorable vasodilation (Fig. 2). There was no debris in the filter collected. On left internal carotid angiogram before CAS, the left ophthalmic artery was visualized through retrograde circulation mediated by a collateral pathway from the left external carotid artery (Fig. 3A and 3B), but the origin of the left ophthalmic artery was visualized on left internal carotid angiogram immediately after CAS, showing anterograde blood flow (Fig. 3C).

Left ocular pain appeared 9 days after surgery. Detailed examination in the Department of Ophthalmology showed a marked increase in the left ocular pressure (36 mmHg) in comparison with the preoperative value, leading to a diagnosis of neovascular glaucoma. The drip infusion of Mannitol and treatment with an eye drop preparation were
Two Patients with a Rapid Increase in the Ocular Pressure after CAS

To treat right carotid artery stenosis, CAS was selected, considering a history of severe heart disease. Under distal protection with a Carotid Guardwire PS (Medtronic, Minneapolis, MN, USA), the procedure was performed. Using...
Neovascular glaucoma appears in the terminal phase of ocular ischemic syndrome, and the visual function prognosis is unfavorable. In our patients, surgery was performed, but it was difficult to maintain the visual function. Concerning the pathogenesis of neovascular glaucoma, chronic anterior ocular ischemia may induce functional or structural occlusion of the angle related to neovascularization around the iris, which is termed rubeosis iridis, and neovascular membrane, increasing the ocular pressure through aqueous humor outflow disorder.\textsuperscript{2,3,8) Ocular ischemic syndrome is a condition in which $\geq 90\%$ stenosis to complete occlusion of the carotid artery causes ischemic symptoms of the ipsilateral eye.\textsuperscript{2–7) This syndrome is characterized by ocular pain and suddenly or gradually exacerbating low vision. Posterior ocular lesions, including retinal lesions, are more frequent than anterior ocular lesions such as iridal/lens lesions.\textsuperscript{3) Furthermore, chronic retinal ischemia causes narrowing of the retinal arteries, dilation of the retinal veins, petechial/blot hemorrhage, and vitiligo.\textsuperscript{3,7) Ocular ischemic syndrome is observed in 4\%–18\% of patients with carotid artery lesions.\textsuperscript{1) Therefore, physicians often encounter ocular ischemic syndrome or neovascular glaucoma when performing the treatment of carotid artery lesions such as CAS.

For the diagnosis of ocular ischemic syndrome, it is important to differentiate it from diabetic retinopathy. In particular, many patients with advanced ocular ischemic
syndrome have diabetic retinopathy, and ocular ischemia should not be overlooked. In 80% of patients with ocular ischemic syndrome, the unilateral eye is affected, whereas diabetic retinopathy involves the bilateral eyes. If there is a ≥20% difference in retinopathy findings between the left and right eyes, ocular ischemic syndrome should be suspected, and detailed examination of a carotid artery lesion should be conducted. Furthermore, retinal hemorrhage related to ocular ischemic syndrome is less frequent than in patients with diabetic retinopathy. In those with diabetic retinopathy, lesions are localized around the posterior pole of the eyeball, whereas an extensive area involving the anterior ocular region is affected in those with ischemic ocular pathology. Cotton-wool patches of the fundus are observed in both patients, but hard spots are detected only in those with diabetic retinopathy. These characteristics are useful for differential diagnosis.

To our knowledge, 12 patients with neovascular glaucoma after CEA have been reported in the field of neurosurgery. Furthermore, neovascular glaucoma after CAS is rare, and only one case report has been published, excluding the present cases (Table 1). However, recently, CAS for cervical internal carotid artery stenosis has been increasingly indicated for patients with heart diseases, such as coronary artery stenosis, in comparison with CEA, as demonstrated in the Stent and Angioplasty with Patients at High Risk for Endarterectomy (SAPPHIRE) trial. A study suggested the association with coronary artery lesions in patients with ocular ischemic syndrome. In the future, the number of patients with neovascular glaucoma after CAS may increase.

The mechanism of neovascular glaucoma after revascularization is hypothesized as follows: in the presence of ocular ischemic syndrome, marked stenosis of the carotid artery may decrease the cerebral perfusion pressure, reducing the production of aqueous humor in the initial phase. When ocular ischemic syndrome is advanced, ruberosis iridis may appear. However, even aqueous humor outflow disorder related to ruberosis iridis may not increase the ocular pressure if a balance is maintained through a reduction in the production of aqueous humor. When revascularization improves the cerebral perfusion pressure, the balance may be destroyed through a rapid increase in the production of aqueous humor, increasing the ocular pressure. In our patients, the angle was occluded (≥50%) before the ocular pressure increased; therefore, the production of aqueous humor may have been inhibited due to internal carotid artery occlusion despite the presence of aqueous humor outflow disorder before CAS, and a CAS-related improvement in ocular blood flow may have improved the production of aqueous humor, resulting in a rapid, marked increase in the ocular pressure. Thus, even if the ocular pressure before revascularization is normal in patients with ocular ischemic syndrome, neovascular glaucoma may occur after surgery. On the other hand, when neovascular glaucoma is present before revascularization, as demonstrated in Case 2, the possibility of a rapid increase in the ocular pressure after revascularization should always be considered.

According to previous studies, the interval from revascularization until the appearance of glaucoma attacks ranges from 0 to 16 days. However, such attacks occurred within 7 days after surgery in most cases. In our patients, there was a rapid increase in the ocular pressure 9 days after surgery and the day after surgery. This was consistent with the results of previous studies (Table 1). The onset of glaucoma attacks within 2 weeks after revascularization must be considered. The timing is consistent with that of postoperative hyperperfusion syndrome appearance. In addition, hyperperfusion syndrome frequently causes severe ocular pain or unilateral headache, and these symptoms resemble those related to a rapid increase in the ocular pressure; they may be misdiagnosed. If patients are misdiagnosed with hyperperfusion syndrome, sedation may delay glaucoma treatment. If ocular pain or headache is observed after revascularization for cervical internal carotid artery stenosis with ocular ischemic syndrome, ophthalmological assessment should be promptly conducted after confirming pupil findings. Even if there is no symptom, it may be necessary to clarify the condition by evaluating the visual function after revascularization through ophthalmological assessment before discharge.

It is difficult to predict the onset of neovascular glaucoma based on the pattern of ophthalmic artery visualization on angiography before and after CAS. In Case 1, retrograde circulation of the affected-side ophthalmic artery changed to anterograde circulation after CAS (Fig. 3). However, in Case 2, anterograde circulation was noted before and after CAS (Fig. 5). To our knowledge, there was only one case report describing the pattern of ophthalmic artery visualization among case reports on neovascular glaucoma after revascularization. Katsuta et al. reported that the ophthalmic artery ipsilateral to an internal carotid artery lesion was anterogradely visualized on internal carotid angiography before CEA. Thus, neovascular glaucoma may occur regardless of the pattern of ophthalmic artery visualization, but this issue should be further examined in a larger number of patients.

For the effective treatment of ocular ischemic syndrome, it is necessary to reduce ocular ischemia.
Table 1  Reported case of neovascular glaucoma related to surgical procedure for internal carotid artery stenosis

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Author (year)</th>
<th>Age/ Sex</th>
<th>IC stenosis, side</th>
<th>Surgical procedure</th>
<th>Onset of symptom Post-surgery (days)</th>
<th>Ocular symptom Post-surgery</th>
<th>Intraocular pressure (mmHg) Pre-surgery/ Post-surgery (side)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Coppeto et al. (1985)</td>
<td>67/F</td>
<td>95%, Right</td>
<td>CEA</td>
<td>14</td>
<td>90%, Left</td>
<td>18/44–46 (Right)</td>
</tr>
<tr>
<td>2</td>
<td>Coppeto et al. (1985)</td>
<td>49/M</td>
<td>95%, Left</td>
<td>CEA</td>
<td>5</td>
<td>70%, Right</td>
<td>21–23/43 (Left)</td>
</tr>
<tr>
<td>3</td>
<td>Melamed et al. (1987)</td>
<td>60/M</td>
<td>“severe”, Right</td>
<td>CEA</td>
<td>3</td>
<td>Headache</td>
<td>24/38 (Right)</td>
</tr>
<tr>
<td>4</td>
<td>Melamed et al. (1987)</td>
<td>46/M</td>
<td>Evanescent, Right</td>
<td>CEA</td>
<td>1</td>
<td>Blurred vision</td>
<td>18/42 (Right)</td>
</tr>
<tr>
<td>5</td>
<td>Wagner et al. (1988)</td>
<td>54/F</td>
<td>&gt;90%, Left</td>
<td>CEA</td>
<td>16</td>
<td>Right orbital pain, exophthalmos</td>
<td>17/59 (Left)</td>
</tr>
<tr>
<td>6</td>
<td>Daels et al. (1992)</td>
<td>60/M</td>
<td>100%, Right</td>
<td>CEA</td>
<td>4</td>
<td>Right orbital pain, exophthalmos</td>
<td>16/50 (Right)</td>
</tr>
<tr>
<td>7</td>
<td>Nguyen et al. (1996)</td>
<td>72/F</td>
<td>70%, Left</td>
<td>CEA</td>
<td>–</td>
<td>–</td>
<td>12/38 (Left)</td>
</tr>
<tr>
<td>8</td>
<td>Masuoka et al. (1997)</td>
<td>58/M</td>
<td>95%, Right</td>
<td>CEA</td>
<td>1</td>
<td>Ocular pain, blurred vision</td>
<td>–/66 (Left)</td>
</tr>
<tr>
<td>9</td>
<td>Cuevas-Lestienne et al.</td>
<td>2000)</td>
<td>–, Left</td>
<td>CEA</td>
<td>1</td>
<td>–</td>
<td>30/45 (Right)</td>
</tr>
<tr>
<td>10</td>
<td>Takagi et al. (2005)</td>
<td>59/M</td>
<td>99%, Right</td>
<td>CEA</td>
<td>1</td>
<td>Right orbital pain</td>
<td>18/44–46 (Right)</td>
</tr>
<tr>
<td>11</td>
<td>Katsuta et al. (2013)</td>
<td>64/M</td>
<td>83%, Right</td>
<td>CEA</td>
<td>1</td>
<td>Headache, Blurred vision</td>
<td>10–18/51 (Right)</td>
</tr>
<tr>
<td>12</td>
<td>Lee et al. (2018)</td>
<td>74/M</td>
<td>&gt;70%, Right</td>
<td>PTA</td>
<td>5</td>
<td>Right ocular pain</td>
<td>–/43 (Right)</td>
</tr>
<tr>
<td>13</td>
<td>Present case 1</td>
<td>67/M</td>
<td>90%, Left</td>
<td>CAS (two-staged)</td>
<td>2</td>
<td>Right ocular pain</td>
<td>16/30 (Right)</td>
</tr>
<tr>
<td>14</td>
<td>Present case 2</td>
<td>70/M</td>
<td>99%, Right</td>
<td>CAS</td>
<td>1</td>
<td>Left ocular pain</td>
<td>15/36 (Left)</td>
</tr>
</tbody>
</table>

CAS: carotid artery stenting; CEA: carotid endarterectomy; PTA: percutaneous transluminal angioplasty
neovascularization around the iris a few days after treatment, suggesting its usefulness for reducing symptoms of neovascular glaucoma. Currently, the vitreous body injection of anti-VEGF antibody for neovascular glaucoma is sometimes performed to reduce intra-chamber hemorrhage before surgery, but this is not approved in Japan.23,24 Furthermore, it may be ineffective when angle occlusion is marked. The intra-ocular injection of anti-VEGF antibody before CAS may be considered with close discussion between neurosurgeons and ophthalmologists. However, this treatment should be considered in high-risk patients for glaucoma attacks after cerebral revascularization.

## Conclusion

We experienced two patients with neovascular glaucoma after cerebral revascularization for severe internal carotid artery stenosis with ocular ischemic syndrome. Neovascular glaucoma is rare, but it may be an important complication following CAS that may lead to the loss of the visual function. When treating severe stenotic lesions of the carotid artery with ocular ischemic syndrome, perioperative cross-sectional treatment by neurosurgeons and ophthalmologists is necessary.

## Disclosure Statement

There is no conflict of interest for the first author and coauthors.

## References