Central Retinal Vein Occlusion (CRVO) —Visual Disorder in Patients of Middle and Advanced Age —

Ikuo TOBARI

Professor, Second Department of Ophthalmology,
Toho University School of Medicine

Abstract: Patients with central retinal vein occlusion (CRVO) have retinal hemorrhages in all four retinal quadrants around the posterior pole, with a markedly dilated and tortuous venous system. CRVO frequently develops in patients at 60–69 years of age, and approximately 90% of the incidence is noted in patients at 50 years of age or older. It usually occurs in one eye, but occasionally in both eyes if patients have an increased blood-viscosity condition, including hypervolemia and hyperlipemia. CRVO is generally associated with systemic complications, including hypertension and arteriosclerosis. Younger patients with CRVO principally caused by inflammation and blood disease often have favorable prognosis because their vision is improved by treating underlying diseases and using drug therapy. In nonischemic CRVO that develops in patients at 50–69 years of age, who had a specific level of vision at the onset of the disease, the prognosis varies according to whether arteriolar sclerosis is present, and to the duration of retina circulation time. In the absence of arteriolar sclerosis and delayed retina circulation time, visual acuity can be improved in most cases. In ischemic CRVO, which occurs in patients at 60–79 years of age who have poor vision at the onset of the disease, the condition is usually associated with arteriolar sclerosis and delayed retina circulation time, and thus the visual acuity is rarely improved. Laser photocoagulation is used to prevent the development of neovascular glaucoma.

Key words: Central retinal vein occlusion; Retina circulation time; Retinal arteriolar sclerosis; Laser photocoagulation

Introduction

The incidence of central retinal vein occlusion (CRVO) is not high, but it is frequently associated with poor prognosis. Therefore, although CRVO is easy to diagnose, subsequent treatment is somewhat problematic. We describe our clinical findings, clinical types of
the disease, and therapeutic procedures.

**Clinical Characteristics**

CRVO is associated with hemorrhages over all four retinal quadrants and a markedly dilated and tortuous venous system. It commonly occurs in patients at 60–69 years of age, and those at 50 years of age or older account for 90% of all patients with CRVO, with a slightly higher proportion of males. CRVO in younger patients is induced by inflammation, including optic disk angitis and retinal angitis. The disease usually involves one eye, but occasionally both eyes in patients with hyperlipemia, and hypervolemia with increased blood viscosity. The systemic complications observed in CRVO include hypertension, diabetes mellitus, cardiovascular disease, and cerebrovascular disease.

The typical funduscopic appearance is hemorrhages in all quadrants with the optic disk in the center, involving the superficial and middle layers of the retina. A markedly dilated and tortuous venous system, and edema of the retina and optic disk are observed. The early-stage appearance of the disease principally consists of a dilated and tortuous venous system with only slight retinal hemorrhage but no edema. In advanced-stage CRVO, marked retinal hemorrhage and edema are present, which are occasionally associated with soft exudates, and vascular occlusion in the periphery of the optic disk. Findings in end-stage CRVO include vitreous hemorrhage caused by retinal and optic disk neovascularization, traction retinal detachment, angle and iris neovascularization, and occasionally, neovascular glaucoma.

**Clinical Types**

CRVO is classified into two groups according to impending or complete occlusion, venous stasis retinopathy or hemorrhagic retinopathy, and nonischemic or ischemic characteristics, respectively.

The difference between impending and complete occlusion is based on the time after onset. Impending occlusion frequently advances to complete occlusion. Patients with CRVO due to inflammatory disease and blood disease are under the condition of impending occlusion, but the treatment of the causative diseases can sometimes lead to cure within several months.

Hayreh conducted an experiment in monkeys, and discovered that occlusion of only the central retinal vein caused no hemorrhage but that transient occlusion of both the central retinal vein and artery resulted in hemorrhage in the fundus. Therefore, Hayreh considered that there are two types of CRVO, i.e., venous stasis retinopathy with central retinal vein occlusion without circulatory disorder of the central retinal artery, and hemorrhagic retinopathy with central retinal vein occlusion and circulatory disorder of the central retinal artery, which are induced by different mechanisms of pathogenesis, and whose funduscopic findings, complications, and prognosis of visual acuity differ from each other.

In clinical practice, however, we have encountered patients whose funduscopic findings are of venous stasis retinopathy but associated with the complications usually seen in hemorrhagic retinopathy, suggestive of an intermediate type. Inomata considered that if the ophthalmic artery and vein, proximal to the optic nerve, are occluded in monkeys, central retinal artery occlusion must occur, and indicated that the above classification is inconsistent with the pathogenesis of CRVO.

Although CRVO is classified as a nonischemic and ischemic disease on the basis of visual acuity, funduscopic findings, fluorescent fundus angiographic findings, and electroretinogram (ERG), there is an intermediate type, and differences in neovascularization were seen according to the severity of ischemia. Some nonischemic diseases develop into ischemic disease. The classification into two types poses clinical issues, and it appears to be inappropriate from the standpoint of treatment.

In retinal hemorrhage in CRVO, whether
Ischemic or nonischemic, not only central retinal vein with occlusion and narrowing but central retinal artery with circulatory disorder are involved. The narrowing of the lumen due to arteriolar sclerosis reduces the blood flow into the eye, and this is considered to have an effect on the prognosis of CRVO. The reduced intraretinal blood flow due to arteriolar sclerosis causes retinal ischemia, impeded blood flow, and occlusion of the capillaries, leading to fusion of the occluded areas making more extensive vascular occlusion to establish typical ischemic CRVO.

Most ischemic CRVO are associated with arteriolar sclerosis, and CRVO with marked arteriolar sclerosis is associated with delayed retina circulation time. Patients with a retina circulation time of 20 seconds or longer are considered to have poor prognosis.

Younger CRVO patients without associated arteriolar sclerosis, and patients with ischemic CRVO who have no underlying diseases such as hypertension or arteriosclerosis have no or slightly delayed retina circulation time, and most have favorable prognosis of visual acuity, which could be improved by drug therapy alone.

The prognosis for elderly patients with CRVO frequently with associated arteriosclerosis is poor. Extremely reduced intraocular blood flow induces occlusion of the cilioretinal artery, which then causes severe edema and opacity over the optic disk and the macula retinae, leading to very poor prognosis of CRVO.

**Clinical Types and Prognosis of Visual Acuity**

1. **Early-onset CRVO**

90% of CRVO develops in patients at 50 years of age or older. However, CRVO due to inflammation and blood disease frequently occurs in patients under 50 years of age. In the absence of hypertension and arteriosclerosis, visual acuity can often be improved by the treatment of the underlying disease and medication for CRVO, generally resulting in favorable prognosis. At the time of onset of CRVO, patients usually have good vision, and fundus findings show a dilated and tortuous venous system but only slight retinal hemorrhage with no or slight macular edema. Fluorescent fundus angiography showed no delay in retina circulation time, no leakage of fluorescent dye from blood vessels, and no abnormality in parafoveal capillaries. The impending occlusion type of the disease with minimal retinal hemorrhage can occasionally be cured.
without further progression.

2. Nonischemic CRVO (Fig. 1)

The visual acuity and age of patients varies widely at the onset of the disease. Visual acuity ranges from 0.2 to 1.0 at onset, varying according to the degree of macular hemorrhage and edema. The disease can occur in younger patients but commonly occurs in patients at 50–69 years of age. Funduscopic findings in nonischemic CRVO show a markedly dilated and tortuous venous system, and retinal hemorrhages in all four retinal quadrants around the posterior pole, but relatively mild macular edema and hemorrhage. The optic disk frequently has redness and swelling with hemorrhagic involvement of the periphery. Arteriolar sclerosis is rarely observed and mild if present. Fluorescent fundus angiography revealed slightly delayed venous perfusion, slight leakage of fluorescent dye from the capillaries, and no vascular occlusion.

If patients maintain their visual acuity despite relatively severe hemorrhage, they are treated with aggressive drug therapy. Basically, thrombolytic therapy, vascular-reinforcing agent, anti-inflammatory enzyme drug, and vitamin C are administered, and antiplatelet agent and anticoagulant are added where necessary. If macular edema is present, acetazolamide and steroids are used, and if the visual acuity declines to 0.2–0.3, laser photocoagulation should be performed immediately to absorb edema and hemorrhage and thereby to prevent cystoid macular edema. Laser photocoagulation is sometimes useful to prevent macular dysfunction, and progress to ischemic CRVO.

The clinical findings of CRVO which are expected to cure or restore the vision include relatively well maintained vision, only slight leakage of fluorescent dye from the blood vessels, absence or mild arteriolar sclerosis, and early bypass formation.4 If patients are of advanced age, and have marked arteriolar sclerosis, marked delayed retina circulation time, marked fluorescence-dye leakage at the macula retinae, even a combination of drug therapy and laser photocoagulation results in poor outcomes.4 Therefore, when many unfavorable prognostic factors are present, laser photocoagulation is used at an early stage in combination with drug therapy. In patients with many favorable prognostic factors, CRVO can be treated by drug therapy alone. A grid pattern of laser photocoagulation performed after the establishment of cystoid macular edema is not sufficiently effective to improve the vision, although edema may be improved.

Fig. 2 68-year-old male—right eye—ischemic CRVO

a: Marked retinal hemorrhage, soft exudates in the surroundings of the optic disk and along arterial and venous vessels

Visual acuity: 0.08

b: Visual acuity after 5-month laser photocoagulation: 0.1

Hemorrhage, exudates absorbed, and optic disk atrophy
Therapeutic approaches to treat diffuse macular edema due to CRVO include drug therapy, laser photocoagulation, compressed oxygen therapy, and vitrectomy. In drug therapy, carbonic anhydrase inhibitor is used, and in laser photocoagulation, a grid pattern of laser photocoagulation is used. However, although these approaches are useful for some forms of nonischemic CRVO, they are not efficacious for ischemic CRVO. Compressed oxygen therapy has never been useful in elderly patients, patients with poor visual acuity at the onset of the disease, or patients with ischemic CRVO. Surgical resection of the vitrectomy together with the internal limiting membrane of retina improves edema in most cases but visual acuity is only improved in a few cases.

3. Ischemic CRVO (Fig. 2)

If patients develop ischemic CRVO at 60–79 years of age, with a visual acuity of approximately 0.1 at the onset of the disease, marked retinal hemorrhage in all four retinal quadrants around the posterior pole, a markedly dilated and tortuous venous system, and occasionally soft exudates in the surroundings of the optic disk and along arterial and venous vessels, the visual acuity generally remains poor. In such cases, marked arteriolar sclerosis, macular hemorrhage immediately after the onset of the disease, and progressive edema are seen. Fluorescent fundus angiography reveals delayed retina circulation time and extravascular leakage of fluoresce dye. In patients with markedly delayed retina circulation time, the disease advances rapidly, resulting in poor outcomes.

Sclerosis of the optic artery and the central retinal artery reduces intraocular blood flow, and induces a large number of soft exudates in the periphery of the optic disk, where vascular occlusion begins, leading to neovascularization at the angle and iris. Markedly decreased intraocular blood flow induces occlusion of retinal capillaries, resulting in the occurrence of severe yellowish hard exudates over the posterior pole of eyeball. The prognosis is extremely poor.

There is no definitive therapy, which is particularly effective in the treatment of the disease. CRVO is resistant to drug therapy, laser photocoagulation, compressed oxygen therapy, and surgical resection of the vitrectomy. Therefore, we perform panretinal laser photocoagulation over hemorrhage, and use adjuvant drug therapy with vascular reinforcement agent, antiinflammatory enzyme agent, vitamin C, and antiplatelet agent to prevent commonly occurring angle and iris neovascularization, vitreous hemorrhage, and neovascular glaucoma.

Electrophysiological investigation of CRVO is frequently conducted, and diminution of b wave, decreased b/a ratio, prolonged peak latency of b wave have been reported. Decreased b/a ratio is observed in ischemic CRVO, and patients with markedly decreased b/a ratio are observed to develop neovascular glaucoma.

Retinal circulatory disorder due to CRVO induces retinal ischemia, and induces retinal nerve tissue disorder of bipolar cells and amacrines cells, leading to deterioration of vision. Damage to the vascular wall, and vascular occlusion due to insufficient oxygen supply to retinal capillaries can cause damage to parafoveal capillaries, and is the major cause of visual deterioration.

REFERENCES

5) Miyamoto, H., Ogura, Y., Wakano, Y. et al.:
