Treatment of Age-related Macular Degeneration

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Introduction

Age-related macular degeneration (ARD) is a disease of the macula in the retina, the incidence of which increases with age. Since the macula is affected, patients with ARD acknowledge visual impairment from the onset of the disease. ARD is the leading cause of blindness among adults in the U.S. and Europe, and its incidence in Japan is also gradually increasing.

Epidemiological data from a study conducted in Rotterdam reported an incidence of ARD of 1.1% of the residents aged 55 and older. In a similar study conducted in Hisayama-machi, Fukuoka Pref., Japan, the incidence of ARD in residents aged 50 and older was 0.67%.

The International Classification of Diseases defines two types of maculopathy: early age-related maculopathy (drusen and retinal pigment epithelium abnormalities) and late age-related maculopathy (hemorrhage due to choroidal and subretinal neovascularization; wet and dry forms). ARD generally refers to late age-related maculopathy, and risk factors associated with it include genetic predisposition, hypertension, smoking, and exposure to sunlight. Included in the genetic factors are ATP-binding cassette transporter retina and A2E proteins.

Diagnosis

Funduscopy reveals subretinal neovascularization in the macular area, exudation from the newly formed blood vessels, retinal edema, and hemorrhage in patients with ARD. Fluorescein fundus angiography with indocyanine green is now available to identify choroidal neovascularization, in addition to conventional angiography with sodium fluorescein. Optical coherence tomography makes possible the cross-sectional examination of the retina, and plays a critical role in investigating the presence of subretinal neovascularization, the extent of retinal detachment, and in providing improved images after treatment.

These new techniques have allowed visualization of the detailed state of spread of subretinal neovascularization, which was previously impossible with conventional funduscopy examination or fluorescein fundus angiography using sodium fluorescein.

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Treatment

This section describes the pharmacotherapy, non-invasive and invasive treatments that are currently available for ARD.

1. Pharmacotherapy

Although there is no well established pharmacotherapy for ARD, therapeutics including peripheral vasodilating drugs, vitamin B12, or α and β- interferon have been used. In animal experiments, tranilast, kinase inhibitors, and peroxisome proliferator activated receptor-γ ligands have been found effective in suppressing neovascularization. Studies have also been conducted on antagonists for vascular endothelial growth factors and their receptors.

2. Non-invasive treatment

Laser photocoagulation is performed when the distance between the neovascular membrane and the center of the macula is over 200μm, as measured by fluorescein fundus angiography with sodium fluorescein or indocyanine green. The entire neovascular membrane should be thoroughly photocoagulated, or recurrence may occur in areas not coagulated. However, photocoagulation cannot be performed on bleeding areas. In addition, caution should be exercised when performing photocoagulation, as neurons within the photocoagulated areas die. Subsequently, the area of coagulation may enlarge in the healing process and reach the central portion of the macula, resulting in an unexpected deterioration of visual acuity.

Low dose radiation therapy is used to occlude newly formed vessels by irradiation of the posterior pole of the fundus with about 20 Gy. The therapy is highly effective in some cases, particularly when the hemorrhage has already reached the macula, as photocoagulation therapy is not applicable in such cases.

Photodynamic therapy (PDT) is a treatment method that has recently attracted attention. PDT is designed to selectively destroy only neovascular membranes by intravenously injecting a photosensitive agent, followed by irradiation with a laser at a specific wavelength that does not harm normal neurons. This methodology makes possible the coagulation of newly formed blood vessels in the fovea centralis of the macula, which should not be photocoagulated. Verteporfin (Visudyne) has been used as a photosensitive agent. Results of one- and two-year clinical studies have demonstrated the effectiveness of PDT with verteporfin in the wet form of ARD. Other photosensitive agents have also been studied and PDT is likely to become an important treatment option in the future.

Transpupillary thermal therapy is designed to occlude newly formed blood vessels by heating choroidal neovascular membranes with a near-infrared diode laser. Its effectiveness, however, has not been established.

3. Invasive treatment

Evacuation of subretinal hematoma is a surgical technique designed to remove hematoma, before accumulation of blood in the inferior portion of the retinal macula results in irreversible damage to retinal neurons. In this procedure, an incision is made in the retina close to the hematoma, and tissue plasminogen activator is injected via the incision into the hematoma which is dissolved and is removed. Although this technique has yielded favorable results, it must be performed before the presence of a hematoma results in retinal neuron disorders.

Surgical removal of subretinal neovascular membranes is designed to resect submacular neovascular membranes by insertion of a forceps via a retinal incision near the macula. However, the surgery results in inevitable damage to retinal pigment cells or their extraction together with resected neovascular membranes during surgery. As a result, the retinal neurons of the macula cease to function and the prognosis is by no means favorable.

Recently, a surgical procedure has been per-
formed in which pigment cells from the patient’s iris have been cultured and then transplanted to the area where retinal pigment cells were lost after surgical removal of vascular membranes. This procedure was shown to be successful and is likely to provide a promising treatment option in the future.

**Macular translocation surgery** is performed to preserve the function of photoreceptor cells of the macula. In the procedure, the entire retina is cut around the periphery, and it is rotated around the optic nerve papilla and repositioned to an area where the retinal pigment cells are healthier. Although the rotation of the retina leads to anomalous retinal correspondence, resulting in a distorted image (the extent of distortion corresponds to the degree of rotation), the patients eventually become accustomed to this new image.

**Conclusion**

The incidence of ARD is expected to increase in Japan. Although there are no well-established treatments for ARD at present, a number of promising pharmacotherapy, non-invasive and invasive treatment options are being investigated.

**REFERENCES**