

Choroidal Neovascularization Due to Pathologic Myopia

The pathogenesis of this condition is unknown, but anti-VEGF treatment has shown promising therapeutic results.

BY YASUSHI IKUNO, MD

High myopia, normally defined as myopia with refractive error less than -6.00 D, is common in Asian countries, with an incidence of 5% to 10%. In comparison, countries with a predominantly white population have a lower incidence. Complications such as macular hole with retinal detachment, myopic foveoschisis, and chorioretinal atrophy often develop with high myopia. Choroidal neovascularization (CNV) due to pathologic myopia (mCNV) is a major condition that threatens the vision of people with myopia. Its incidence is not well investigated; however, a hospital-based study reported that the condition existed in 5% to 10% of highly myopic patients.¹

Myopia is the second most common cause of secondary CNV, accounting for 62% of CNV in patients less than 50 years of age.² mCNV often stabilizes without treatment; however, chorioretinal atrophy initiated

from the CNV margin and gradually expanding during the chronic stage is a main cause of poor visual outcome over the long term. Chorioretinal atrophy is augmented by the loss of photoreceptors and by the obstruction of the choroidal vasculature and its replacement with fibrous tissue.³ Yoshida et al reported that more than 80% of eyes with mCNV had a visual acuity better than 20/200 at the onset, but vision was preserved in less than 10% of eyes after 5 to 10 years.⁴

CLINICAL MANIFESTATIONS

mCNV is normally small and grayish at the macula or adjacent to the crescent of the optic nerve head (Figure 1). This circular lesion, called Foerster-Fuchs spot, is often pigmented. According to the Verteporfin in Photodynamic Therapy study group, more than 70% of these lesions are of the classic type, and 65% of them are subfoveally located.⁵ Occult CNV and pigment

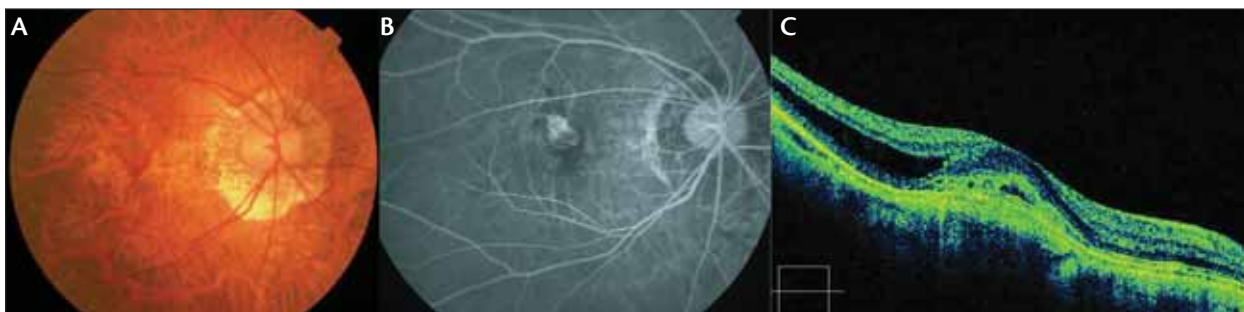


Figure 1. Typical fundus photograph (A), fluorescein angiography (B), and OCT appearance (C) of mCNV. This case presents juxtafoveal classic mCNV superotemporal to the fovea. Small subretinal hemorrhage and retinal detachment over CNV complex is observed on OCT. BCVA at this visit was 20/40.

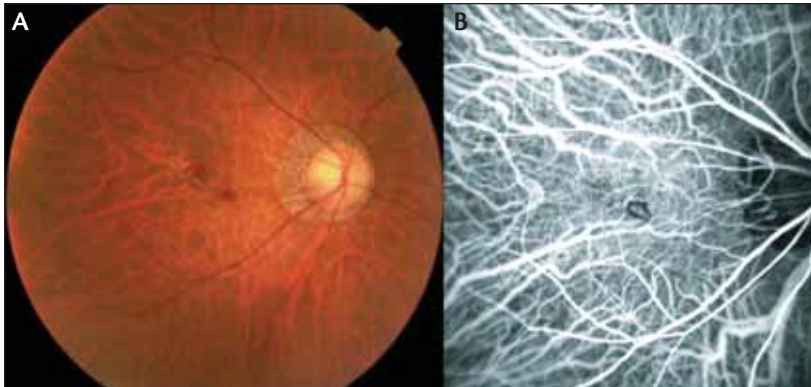


Figure 2. ICGA provides more detailed information about RPE and Bruch's membrane. Fluorescein angiography (A) and confocal ICGA (B) of a patient with obsolete mCNV. Encapsulation often occurs by migration of RPE around the CNV. This so-called dark-rim sign (B) characterized by hypofluorescence around the CNV due to the blocking effect of accumulated pigmentation.

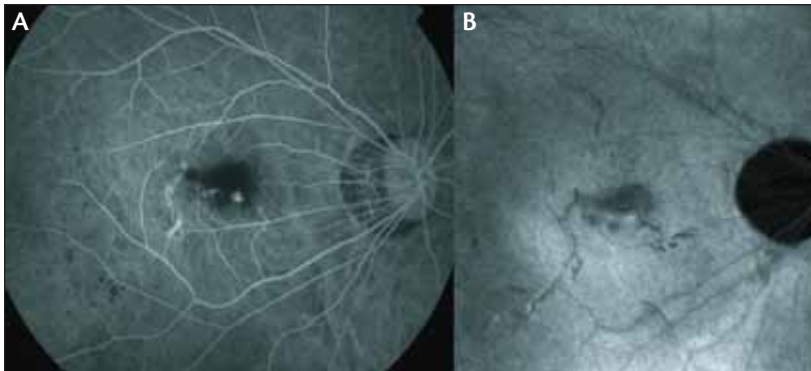


Figure 3. LCs are highly associated with mCNV. Fluorescein angiogram (A) shows a small mCNV at the macula with a horizontal LC. Late phase ICGA (B) shows LCs more clearly. Some of the cracks seen on ICGA cannot be seen on fluorescein angiography.

epithelial detachment are rarely presented. mCNV is sometimes accompanied with a small hemorrhage between the photoreceptors and the retinal pigment epithelium (RPE).

Fluorescein angiography is helpful for diagnosis. mCNV appears as a hyperfluorescence in the early phase and as a fluorescein leakage in the late stage. Indocyanine green angiography (ICGA) provides additional information about RPE and Bruch membrane. Encapsulation by the RPE (the so-called dark-rim sign) indicates that CNV is no longer active (Figure 2). The location of lacquer cracks (LCs) can be more clearly depicted in ICGA (Figure 3).

Optical coherence tomography (OCT) is also useful for diagnosis, monitoring, and determining treatment. Active mCNV presents fibrins and a low-scattering CNV complex. The presence of subretinal fluid is also a sign of active mCNV.

PATHOGENESIS

The pathogenesis of mCNV is still unknown; however, several investigators have implicated LCs. LC is a break in Bruch membrane due to an acute axial length elongation. LCs present as a white crack line in fundus photographs. They can be more prominently observed in fluorescein angiography and ICGA. LCs coexist in more than 90% of eyes with mCNV. Vascular endothelial growth factor (VEGF) is also involved, as anti-VEGF therapies such as intravitreal bevacizumab (Avastin, Genentech) or ranibizumab (Lucentis, Genentech) have been shown to shrink mCNV membranes and improve vision (Figure 4). Patients with mCNV have significantly higher rates of delay of choroidal filling of the macula in confocal ICGA,⁶ indicating that choroidal circulation abnormalities may be the cause. Spectral-domain OCT (SD-OCT) has revealed that subfoveal choroidal thickness is significantly lower in mCNV than in normal eyes.⁷

MANAGEMENT

There are several approaches to management of mCNV.

Direct photocoagulation. In the 1980s and 1990s, thermal laser photocoagulation was applied in eyes with mCNV. Later expansion of the coagulation scar is a major concern with this approach. Because the RPE and the retina are extremely stretched in highly myopic eyes, the thermal burn grows faster than in nonmyopic eyes. Moreover, the results of previous case series were not remarkable.

Surgical approach. Surgical removal of CNV offers beneficial effects in only selected patients because of RPE damage during surgery and later expansion of the atrophic area. Limited or 360° foveal translocation is an option, and this is the only method that is capable of saving the macula from chorioretinal atrophy. However, this technique is not commonly used because highly advanced techniques and skills are required.

PDT. Photodynamic therapy (PDT) is widely used as a treatment for mCNV. The Verteporfin in Photodynamic Therapy Study, a randomized, prospective clinical trial

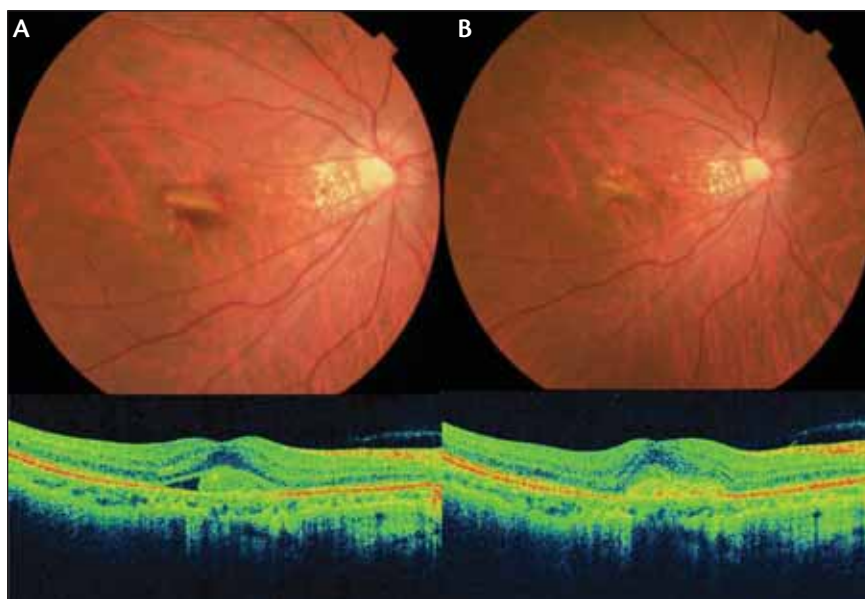


Figure 4. Fundus photo and OCT image before (A) and 3 months after intravitreal bevacizumab for mCNV (B). There was a typical small mCNV at the macula with subretinal fluid, a sign of active CNV before treatment. Three months after treatment, subretinal fluid was dramatically resolved in response to the treatment. The CNV was reduced and became a high-scattering complex, showing that mCNV was no longer active.

that tested the safety and efficacy of PDT in mCNV, found a significantly better visual outcome in patients at 12 months⁵ compared with baseline; however, this benefit was lost at 24 months,⁸ indicating that the long-term efficacy of this approach is questionable. It is agreed among the retina community that PDT effectively stabilizes mCNV, providing a 0.2 to 1 line gain in visual acuity with two to five treatment sessions during 2 years follow-up.^{8,9} PDT leads to choroidal vascular thrombosis,¹⁰ which is a major concern in an atrophic choroid in high myopia. Reduced-fluence PDT is another option to be considered; however, the safety and efficacy of this approach has not been established for this indication to date.

Anti-VEGF therapy. In my view, anti-VEGF therapy is currently the most accepted and most promising therapy for mCNV. We first injected Bevacizumab for mCNV in 8 eyes intravitreally, and vision was improved in 75%.¹¹ There are several large case series describing 60% to 70% of patients achieving significant (two lines or more) visual improvement and two to three lines of mean visual gain.^{12,13} Several prospective and retrospective investigations have shown that anti-VEGF therapies offer more beneficial effect on visual outcome compared with PDT.^{14,15} Intravitreal ranibizumab has also become a common treatment for mCNV and seems to be equally effective as bevacizumab.¹⁶

CONCLUSION

Long-term visual prognosis is poor in cases with mCNV, and intervention is needed. To date, anti-VEGF therapy has shown promising results, but prospective, randomized, multicenter clinical studies are needed to confirm its efficacy and safety. ■

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