RANIBIZUMAB IN MYOPIC CHOROIDAL NEOVASCULARIZATION:
CLINICAL EXPERIENCE ACROSS DIFFERING PATIENT PROFILES

An interview discussion with Adjunct Assistant Professor Nikolle Tan, and Honorary Clinical Associate Professor Timothy Lai

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Introduction

Pathologic myopia is a term most often used to describe a pronounced and progressive elongation of the eye, but it may also refer to specific changes in the fundus such as lacquer cracks and chorioretinal atrophy in the presence of high myopia. Pathologic myopia is a major cause of visual impairment worldwide and is reported as the underlying cause of blindness in 6% to 9% of blind Caucasian individuals and 23% of blind Chinese individuals. In the general population, pathologic myopia has a prevalence of 0.9% to 3.1%.

A frequent, vision-threatening complication of pathologic myopia is myopic choroidal neovascularization (CNV), characterized by the growth of new, fragile blood vessels beneath the retina or the retinal pigment epithelium. Myopic CNV occurs in 5.2% to 11.3% of individuals with pathologic myopia and is associated with a substantial loss in visual acuity (VA). In a 10-year follow-up of 25 patients with myopic CNV, VA deteriorated to <20/200 in 96% of patients a decade after the onset of CNV.

Several treatments are traditionally used for patients with myopic CNV, such as laser photocoagulation, verteporfin photodynamic therapy (VPDT), and surgical excision or macular translocation. These treatment options are associated with a variety of complications, limited efficacy, unpredictable outcomes, and/or a high rate of CNV recurrence. Thermal laser photocoagulation was the only treatment available for myopic CNV for many years, but is associated with considerable risks and complications, including tissue damage with laser scar expansion and high rates of disease recurrence. VPDT has also been used to treat myopic CNV, with a theoretically reduced risk of tissue damage compared to thermal laser photoagulation. However, VPDT treatment generally only stabilizes, without improving, VA, and long-term efficacy is limited. Surgical excision of CNV also has many potential complications, including chorioretinal atrophy and the development of cataracts or glaucoma.
More recently, the introduction of vascular endothelial growth factor (VEGF) inhibitors for the treatment of myopic CNV has revolutionized its management. The efficacy and safety of ranibizumab in the treatment of myopic CNV was demonstrated by the phase 2 REPAIR study and the phase 3 RADIANCE trial. The findings of the RADIANCE trial led to the approval of ranibizumab for the treatment of visual impairment due to CNV secondary to pathologic myopia (i.e., myopic CNV) in Europe in July 2013, and subsequently in over 80 countries worldwide. A recent evidence-based treatment algorithm for the clinical management of myopic CNV recommends early, urgent referral to a retinal specialist and prompt initial treatment with a single intravitreal injection of anti-VEGF therapy. Ideally, this is then followed by close monitoring to assess the need for repeat injections.

The number of patient-treatment years of experience for ranibizumab in myopic CNV will grow as more clinicians choose this treatment option over alternative therapies for their patients with myopic CNV. Here, we describe our clinical experiences of 3 very different cases of patients with myopic CNV receiving ranibizumab. These cases simultaneously highlight the real-life challenges associated with diagnosing myopic CNV, the importance of early intervention, and the possibility of long-term treatment success with few injections of ranibizumab.

Case 1: Long-term efficacy can be achieved with a single injection of ranibizumab

A Chinese female aged 61 years presented with a 2-week history of vision blurring and metamorphopsia in the left eye. The patient had previously undergone bilateral laser refractive surgery for myopia of -8 diopter (D) and had no other notable health complaints except hyperlipidemia.

On initial examination, the patient had a best-corrected VA (BCVA) of 20/20 in the right eye and 20/70 in the left eye. Fundus photography revealed a small macular hemorrhage with CNV of a grayish color that involved the fovea (Figure 1A). Optical coherence tomography (OCT) was then performed, showing subfoveal hyper-reflective material due to active CNV (B), which was confirmed by fluorescein angiography that showed actively leaking subfoveal myopic CNV (C). CNV, choroidal neovascularization.
reflective material due to active myopic CNV and exudation (Figure 1B). Fluorescein angiography (FA) confirmed the presence of subfoveal myopic CNV that was actively leaking (Figure 1C).

The patient received a single dose of intravitreal ranibizumab and was monitored for 4 years. There was an improvement in the left eye BCVA from 20/70 at presentation to 20/30 1 month after treatment, accompanied by OCT-confirmed CNV regression and minimal retinal thickening (Figure 2A).

The patient’s BCVA continued to improve, reaching 20/25 by Month 3 and 20/20 by Month 5. One year after the single ranibizumab injection, the patient’s BCVA remained at 20/20 with no evidence of CNV seen by either OCT (Figure 2B) or FA (Figure 2C). Fundus photography revealed only a small macular scar, again with no evidence of CNV (Figure 2D). BCVA of the patient was maintained at 20/20 for over 2 years before it deteriorated slightly to 20/30, owing to the development of a nuclear sclerosis cataract. At the end of the 4-year follow-up period, the final BCVA was 20/30 compared with 20/70 at presentation.

This case demonstrates a clinically significant and sustained improvement in BCVA following a single dose of intravitreal ranibizumab, indicating the potential long-term benefits of prompt ranibizumab treatment for myopic CNV.

**Figure 2:** Follow-up examinations imaging in Case 1. Optical coherence tomography showed regression of CNV and minimal thickening 1 month post ranibizumab treatment (A), with no evidence of CNV activity or recurrence 1 year post ranibizumab treatment (B). The absence of CNV at 1 year was also confirmed via fluorescein angiography (C), and fundus photography revealed a small macular scar (D). CNV, choroidal neovascularization.

**Figure 3:** Initial examination imaging in Case 2. Fluorescein angiography showed extensive staining in the macula as a result of chorioretinal scarring and old lacquer cracks. An area of masking corresponded with a submacular hemorrhage, and leakage was seen (A). Optical coherence tomography revealed macular schisis and a probable myopic CNV lesion (B). CNV, choroidal neovascularization.
Case 2: The challenge of myopic CNV diagnosis

Adjunct Assistant Professor Nikolle Tan

A 65-year-old female patient with bilateral myopia of -14 D presented with mild blurring of vision and a central scotoma in the right eye. BCVA was 20/30 in both eyes, and fundus examination showed changes consistent with severe myopia, including severe fundus tessellation, widespread chorioretinal atrophy, peripapillary atrophy, and posterior staphyloma. Old lacquer cracks and pigmented chorioretinal scars were also seen in the macula regions of both eyes but were worse in the right eye. There was a subtle submacular hemorrhage bordering an area of chorioretinal atrophy in the right macula but with no obvious macular edema.

FA was performed, revealing extensive macular staining as a result of the old lacquer cracks and chorioretinal scarring. An area of masking corresponded with the submacular hemorrhage, and leakage was seen (Figure 3A). OCT revealed macular schisis and a lesion that was likely to represent a myopic CNV within the schisis. (Figure 3B).

The patient received 1 intravitreal ranibizumab injection in her right eye and was re-examined a month later. BCVA 1 month post injection remained 20/30, but the central scotoma had resolved. FA showed cessation of active leakage (Figure 4A).

Figure 4: Follow-up examinations imaging in Case 2. One month following a single ranibizumab injection, fluorescein angiography showed cessation of active leakage (A), and optical coherence tomography confirmed regression of the myopic CNV lesion (B). Four years post treatment, fluorescein angiography revealed cystoid macular edema and extensive staining (C). Optical coherence tomography showed worsening of the macular schisis, but there was no change in the myopic CNV/scar complex (D). CNV, choroidal neovascularization.
and OCT revealed regression of the presumed myopic CNV lesion (Figure 4B). BCVA remained 20/30 for the following 3 years with no recurrence of symptoms; however, annual OCT imaging did show progression of the macular schisis.

Four years following initial presentation, a central scotoma in the right eye had returned, and BCVA had declined to 20/150. FA showed extensive areas of staining (Figure 4C), making images difficult to interpret. Cystoid macular edema was seen. OCT showed further worsening of the schisis, but there was no change in the presumed myopic CNV/scar complex (Figure 4D). Despite symptoms, the patient was reluctant to receive any treatment more invasive than intravitreal injection. She received 1 further injection of ranibizumab. OCT findings remained unchanged 1 month post injection, but BCVA improved to 20/70. The patient declined further interventions and failed to attend subsequent appointments.

This case highlights the challenges in obtaining a confident myopic CNV diagnosis in the presence of concomitant macular changes commonly seen in highly myopic eyes, such as extensive chorioretinal scarring or macular schisis. FA and OCT can be difficult to interpret in such situations. Clinical examination and close monitoring of response to treatment, in addition to a combination of ocular imaging techniques, are often required for the accurate diagnosis of myopic CNV.

Case 3: Early diagnosis of myopic CNV and rapid gains

Adjunct Assistant Professor Nikolle Tan

A 56-year-old female patient presented with several weeks of increasingly blurred vision and metamorphopsia in her left eye. Initial examination revealed high myopia in both the right and left eyes (-7.25 D and -8.5 D, respectively). BCVA was 20/20 in the right eye and 20/60 in the left eye. Fundus examination showed
changes associated with high myopia, including tessellation, peripapillary atrophy, posterior staphyloma, and diffuse chorioretinal atrophy. A large lacquer crack was observed in the left eye but no evidence of submacular hemorrhage or edema (Figure 5A). FA revealed leakage, however, around the lacquer crack in the left eye (Figure 5B). OCT confirmed macular thickening and subretinal fluid in the corresponding area (Figure 5C), leading to the diagnosis of myopic CNV.

The patient received 2 intravitreal injections of ranibizumab into the left eye 1 month apart before declining to receive further injections. BCVA in the left eye improved from 20/60 at baseline to 20/40 at Month 1. This was coupled with improved OCT findings (Figure 6A). BCVA further improved to 20/25 2 months after the initial injection. The patient was monitored monthly for 4 months following the second ranibizumab injection, during which time OCT findings remained stable (Figure 6B). After this time, the intervals between monitoring visits increased progressively from 3 to 12 months. The patient was instructed to return should symptoms recur. Both VA and OCT results remained stable during 3 years of follow-up. This case illustrates that, compared with neovascular age-related macular degeneration (nAMD), myopic CNV may not be accompanied by typical signs of active CNV such as submacular hemorrhage, macular edema, and hard exudates. Indeed, although OCT changes in this case were obvious, myopic CNV is frequently subtle and may be challenging to diagnose, particularly in the early stages of disease. It is imperative to pick these cases up early, however, for prognosis of patients with myopic CNV is generally good with early treatment and they generally require fewer anti-VEGF injections for sustained stability.9-11

**Conclusion**

Pathologic myopia is a major cause of visual impairment worldwide that is associated with numerous complications including myopic CNV. Previous therapies such as thermal laser, VPDT, and submacular surgery can be associated with a variety of complications, limited efficacy, unpredictable outcomes, and a high rate of CNV recurrence. The introduction of anti-VEGF therapy for visual impairment due to myopic CNV provides an effective treatment option for these patients.

Our clinical experience demonstrates that significant VA gains can be achieved with ranibizumab in a wide range of different patient profiles. Improvements may be seen following 1 injection or may occur after a longer-term course of treatment. Furthermore, the importance of early diagnosis to treatment success cannot be underestimated. These cases and growing real-world experience may help to support recent clinical guidelines recommending that patients with myopic CNV receive early referral to a retinal specialist and prompt treatment with intravitreal injection of anti-VEGF therapy.11

**References**


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