Jpn J Ophthalmol 2010;54:320–324
DOI 10.1007/s10384-010-0810-4


CLINICAL INVESTIGATION

# Intravitreal Bevacizumab Therapy for Idiopathic Macular Telangiectasia

Yoko Matsumoto and Mitsuko Yuzawa

Department of Ophthalmology, Nihon University Hospital, Tokyo, Japan

**Abstract**

**Purpose:** To investigate the efficacy of intravitreal bevacizumab for the treatment of idiopathic macular telangiectasia (IMT).

**Methods:** Ten eyes of eight consecutive patients with IMT were studied. Four eyes had type 1, and six had type 2 IMT according to Yannuzzi's classification. All patients were treated with intravitreal bevacizumab (1.25 mg) injections at baseline. Monthly fundus and optical coherence tomography (OCT) examinations were performed. Changes in visual acuity, macular edema on OCT, and leakage on fluorescein angiography were analyzed during 6 months of follow-up. Retreatment was considered when increased macular edema and either fluorescein leakage or visual loss were identified.

**Results:** There were no changes in the mean visual acuity in either eye in any of the patients. In one of the four eyes with type 1 IMT, the microaneurysms disappeared after bevacizumab treatment. However, there were no changes in the other three eyes. Fluorescein leakage disappeared in four, decreased in one, and was unchanged in one of the eyes with type 2 IMT. An inner lamellar cyst in each eye was unchanged in two, newly formed in one, and expanded in one eye with type 2 IMT.

**Conclusion:** Type 2 IMT improved anatomically with bevacizumab treatment despite a lack of improvement in vision. Bevacizumab effectively decreases vascular permeability and retinal edema in the short term. **Jpn J Ophthalmol** 2010;54:320–324 © Japanese Ophthalmological Society 2010

**Keywords:** aneurysmal telangiectasia, bevacizumab (Avastin), idiopathic macular telangiectasia, macular edema, perifoveal telangiectasia

## Introduction

Idiopathic juxtafoveolar retinal telangiectasis was originally reported by Gass and Oyakawa in 1982.[1] In 1993, Gass and Blodi[2] subdivided these patients into three categories: (1A) unilateral congenital parafoveal telangiectasis and (1B) unilateral idiopathic parafoveal telangiectasis; (2) bilateral acquired parafoveal telangiectasis; and (3) bilateral idiopathic perifoveal telangiectasis and capillary obliteration. In 2006, Yannuzzi et al.[3] proposed a new, simplified classification: aneurysmal telangiectasia (type 1) and perifoveal telangiectasia (type 2).

Bevacizumab (Avastin, Genentech, San Francisco, CA, USA) is a humanized monoclonal anti-vascular endothelial growth factor (VEGF) antibody approved in 2004 by the U. S. Food and Drug Administration (for intravenous use in metastatic colorectal cancer. Since May 2005, bevacizumab has been given via intravitreal injection as an off-label therapy for neovascular age-related macular degeneration (AMD).[4,5] Bevacizumab has also been explored as a treatment for idiopathic macular telangiectasia (IMT). In several reports, bevacizumab appears to have a positive effect in reducing vascular leakage on fluorescein angiography (FA), and retinal edema of type 2 IMT.[6–8] There is only one reported case of a type 1 IMT lesion for which bevacizumab was highly effective.[9] Herein, we describe four patients with unilateral type 1 IMT and six eyes of four patients with type 2 IMT, all treated with intravitreal bevacizumab injections.

Received: July 22, 2009 / Accepted: February 16, 2010
Correspondence and reprint requests to: Yoko Matsumoto, Department of Ophthalmology, Nihon University Hospital, 1-8-13 Surugadai Kanda, Chiyoda-ku, Tokyo 101-8309, Japan
e-mail: mt@med.nihon-u.ac.jp

## Subjects and Methods

Ten eyes of eight consecutive patients (three men, three eyes; five women, seven eyes) who visited Surugadai Nihon

University hospital between September 2007 and March 2008, all diagnosed as having type 1 or 2 IMT, were studied. Their mean age was 63 years (range, 56–71). Four eyes of four patients were classified as having type 1 aneurysmal telangiectasia, and six eyes of four patients as having type 2, that is, perifoveal telangiectasia, according to Yannuzzi et al.'s classification.[3] All eyes showed fluorescein dye leakage at baseline. Diabetes was ruled out in all cases. There were no signs of any other retinal disease. An initial bevacizumab (1.25 mg) injection was given to all patients, and they were then followed on a monthly schedule with complete fundus, Snellen visual acuity, and optical coherence tomography (OCT; Stratus OCT-3, Carl Zeiss Meditec, Dublin, CA, USA) imaging examinations. Cases showing visual acuity loss due to residual macular edema, or persistent fluorescein dye leakage, were treated with additional injections of bevacizumab (1.25 mg).

Persistence or absence of microaneurysms and dye leakage were analyzed with FA in eyes with type 1 IMT. The changes in inner lamellar cysts on OCT and vascular leakage on FA were followed up in eyes with type 2 IMT.

All patients were fully informed about the off-label use of bevacizumab and its potential side effects. The study was approved by the Institutional Review Board of Surugadai Hospital of Nihon University.

## Results

Of the four eyes with type 1 IMT, the microaneurysms disappeared in only one after three bevacizumab injections (case 3). The microaneurysms remained unchanged in the other three eyes despite four injections. Baseline visual acuities ranged from 0.5 to 0.9. Visual acuities at the last follow-up ranged from 0.6 to 0.9. There were no statistically significant vision changes between baseline and the final follow-up by the Wilcoxon signed-rank test (Table 1). Retinal edema at baseline was present in cases 1, 2, and 3. The edema remained unchanged during the follow-up period. Of the six eyes with type 2 IMT, three had a significant inner lamellar cyst in each eye at baseline. One of those showed cyst enlargement during follow-up, accompanied by improvement in fluorescein dye leakage. In each of the other two eyes, the inner lamellar cysts remained unchanged. In one eye, a new inner lamellar cyst formed during follow-up. Two eyes had no lamellar cysts on any examination. There was no relationship between the inner lamellar cystic changes and fluorescein dye leakage in any of the six eyes. Five of the six eyes (cases 1, 2, 4, 5, and 6) responded to the initial bevacizumab treatment with either a reduction or disappearance of vascular hyperpermeability on FA, but two (cases 1 and 2) developed recurrences. These two eyes were retreated with bevacizumab. One eye (case 4) was also retreated because of visual acuity loss from 0.8 to 0.6. One eye (case 3) showed no response to bevacizumab. The other two eyes (cases 5 and 6) were treated only once without recurrence. Bevacizumab was injected either once or twice to all six cases during the 6-month follow-up period. Baseline visual acuities ranged from 0.3 to 0.8. Visual acuities at the last follow-up ranged from 0.1 to 0.9. There were no significant vision changes between baseline and the final follow-up (Wilcoxon signed-rank test) (Table 2).

### *Case 1: Type 1 Aneurysmal Telangiectasia*

A 71-year-old woman presented with perifoveal telangiectasis, microaneurysms, and fluorescein dye leakage around the fovea on FA. OCT showed retinal edema, mainly temporal to the fovea (Fig. 1). Her visual acuity was 0.6. Bevacizumab was injected four times during the 6-month follow-up period. At 6 months, FA showed no improvement. There was no change in macular edema on OCT (Fig. 1). Visual acuity was 0.7 at the final follow-up.

**Table 1.** Type 1 aneurysmal telangiectasia changes after bevacizumab injections

| Case number | Visual acuity changes | Microaneurysms | Vascular dye leakage | Retinal edema | Number of treatments |
|---|---|---|---|---|---|
| 1 | 0.6→0.7 | No change | No change | No change | 4 |
| 2 | 0.7→0.8 | No change | No change | No change | 4 |
| 3 | 0.5→0.6 | Disappeared | Improved | No change | 3 |
| 4 | 0.9→0.9 | No change | No change | None | 4 |

**Table 2.** Type 2 perifoveal telangiectasia changes after bevacizumab injections

| Case number | Visual acuity changes | Change of inner lamellar cysts | Vascular dye leakage | Recurrence | Number of treatments |
|---|---|---|---|---|---|
| 1 | 0.3→0.1 | None | Disappeared | Yes | 2 |
| 2 | 0.7→0.9 | No change | Disappeared | Yes | 2 |
| 3 | 0.8→0.8 | No change | No change | N/A | 1 |
| 4 | 0.8→0.5 | Expanded | Decreased | No | 2 |
| 5 | 0.6→0.5 | None | Decreased | No | 1 |
| 6 | 0.7→0.5 | Newly formed | Disappeared | No | 1 |

N/A, not applicable.

Jpn J Ophthalmol
Vol 54: 320–324, 2010

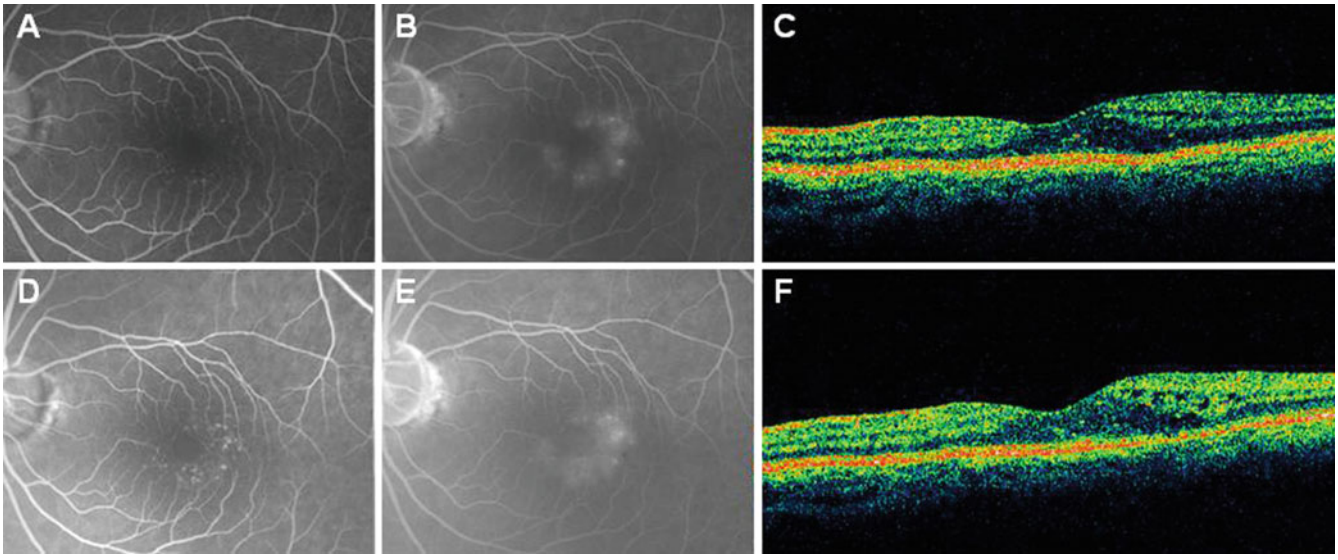


**Figure 1. A, B** Fluorescein angiography prior to bevacizumab injection shows perifoveal telangiectasia, microaneurysms, and late-phase dye leakage around the fovea. **C** Optical coherence tomography shows retinal edema. **D** After four treatments, the telangiectasia, microaneurysms, and (**E**) the late-phase dye leakage persisted, with (**F**) no change in retinal thickness.

### *Case 4: Type 2 Perifoveal Macular Telangiectasia*

A 66-year-old man presented with fluorescein leakage around the fovea without any microaneurysms. After the initial bevacizumab treatment, FA revealed persistent, reduced vascular leakage mainly temporal to the fovea. Bevacizumab was reinjected because of increased fluorescein leakage around the fovea at the 3-month follow-up examination. At 6 months, the fluorescein still leakage persisted, mainly temporal to the fovea, with enlargement of an inner lamellar cystic change at the fovea on OCT (Fig. 2). Visual acuity decreased from 0.8 at baseline to 0.5 at the final follow-up.

### *Case 6: Type 2 Perifoveal Macular Telangiectasia*

A 56-year-old woman presented with slight vascular leakage temporal to the fovea on FA. There were no abnormalities on OCT at baseline. After the initial bevacizumab injection, fluorescein dye leakage disappeared completely with no recurrence up to 6 months post-treatment (Fig. 3). Visual acuity changed from 0.7 at baseline to 0.5 at the final follow-up.

## Discussion

Although visual acuity in patients with IMT remains relatively stable for many years, most patients experience vision loss during the course of this disease.

Laser photocoagulation, intravitreal injection of triamcinolone acetonide, and posterior juxtascleral administration of anecortave acetate have been reported as treatments, but none has consistently improved vision.[10–12]

As an off-label treatment, intravitreal bevacizumab has been used worldwide since 2005 for patients with choroidal neovascularization (CNV) due to exudative AMD, myopia, angioid streaks, uveitis, and so on. Because of its anti-VEGF action, bevacizumab can be used for patients with abnormal retinal vascular hyperpermeability, such as diabetic retinopathy, and for macular edema due to retinal vein occlusion. Macular telangiectasia has also reportedly been treated with bevacizumab[6–9] because of its efficacy in controlling abnormal hyperpermeability.

In our case series, eyes with type 1 (aneurysmal telangiectasia) IMT were treated either three or four times with bevacizumab during follow-up because of persistent retinal edema and microaneurysms. However, most of the microaneurysms and macular edema in those cases showed no change. Only one eye in a previous case report of type 1 IMT treated with bevacizumab showed improved vision and reduced macular edema 1 year after treatment.[9] It would not be appropriate to judge the efficacy of bevacizumab in type 1 IMT because of the disparate results obtained and the small number of cases reported by the previous and the present study.

Six eyes with type 2 (perifoveal macular telangiectasia) IMT were treated either once or twice in 6 months. Five of the six eyes responded to the initial bevacizumab treatment with either a reduction or disappearance of vascular hyperpermeability on FA, but two eyes experienced recurrences. Inner lamellar cysts remained unchanged in two eyes, became enlarged in one, and newly appeared in one during follow-up. Because the pathology of inner lamellar cysts may involve Müller cell degeneration, anti-VEGF drugs,

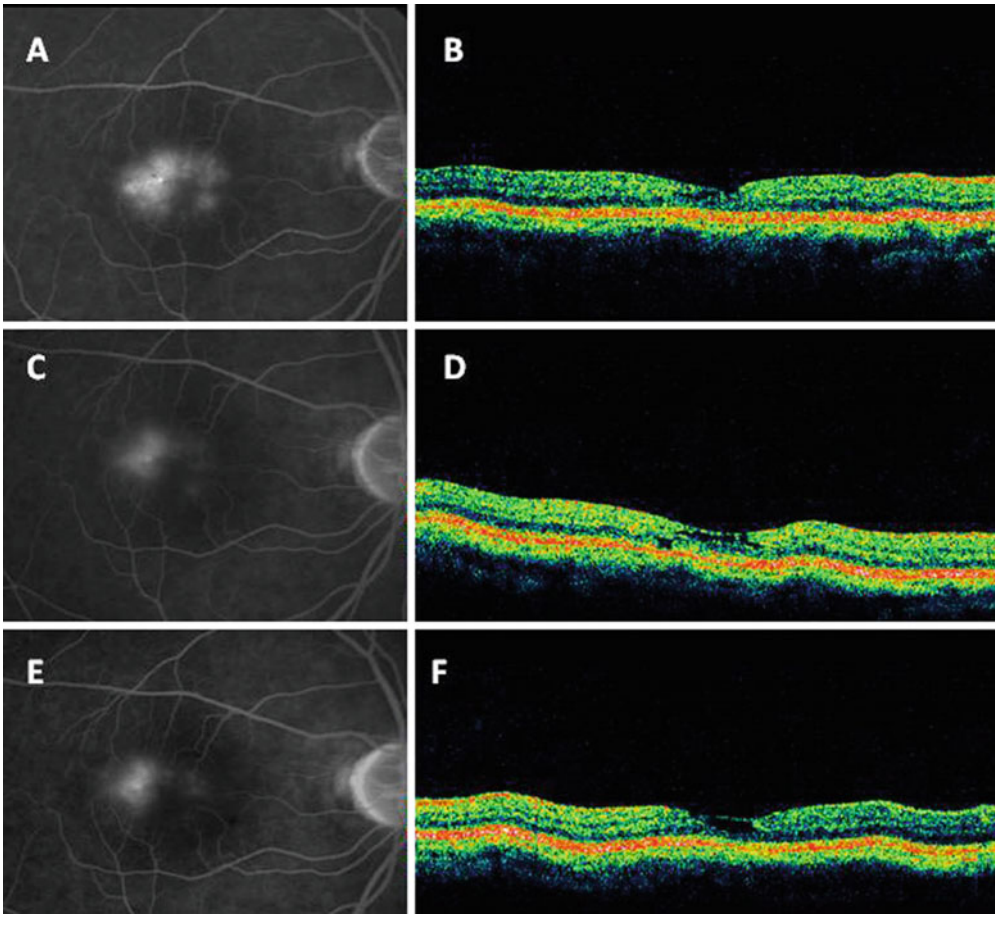


**Figure 2A–F.** Fluorescein angiography shows dye leakage around the fovea (**A**) without retinal edema on optical coherence tomography (**B**). **C** One month after the initial treatment, dye leakage was reduced but persisted, mainly temporal to the fovea without retinal edema. **D** Bevacizumab was reinjected at 3 and 6 months, but dye leakage (**E**) was the same as at 1 month. **B, D, F** An inner lamellar cyst showed gradual enlargement.

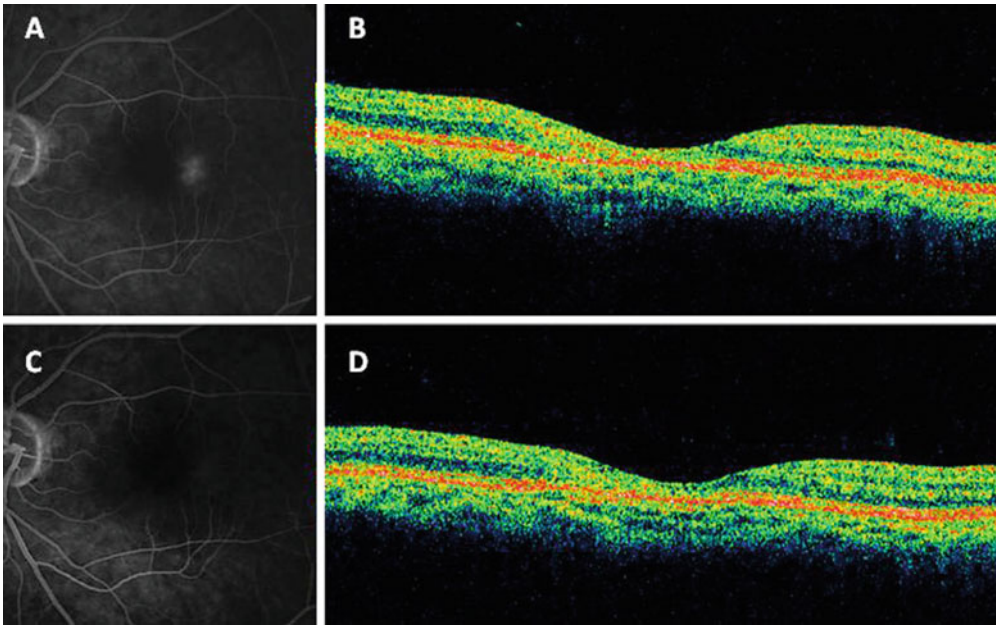


**Figure 3. A** Before the bevacizumab injection, there is slight vascular dye leakage temporal to the fovea on fluorescein angiography, without any abnormalities on optical coherence tomography (**B**). **C** After the initial bevacizumab treatment, fluorescein leakage disappeared completely, with no change on optical coherence tomography (**D**). These findings persisted until the 6-month follow-up examinations.

which act on vascular hyperpermeability and neovascularization, would be ineffective. The visual acuities changed slightly, but these changes were unrelated to both the FA and OCT findings. In three previous reports, all 11 eyes with nonproliferative type 2 IMT studied showed reduced dye leakage on FA.[6–8] Vision improved in seven of the 11 eyes. Charbel et al.[7] reported retinal thickness to be significantly decreased after bevacizumab treatment in some sections around the fovea, whereas thickening, compared with baseline, was seen in all sectors except the fovea at 3–4 months after treatment. According to our results and those of previous reports, bevacizumab reduces vascular leakage and macular edema while improving visual acuities in cases with nonproliferative type 2 (perifoveal macular telangiectasia) IMT. However, recurrence may develop soon after treatment. Longer follow-up is needed to clarify the efficacy of bevacizumab in maintaining vision over the long term in comparison with alternative treatments.

The visual prognosis of our cases differed from those reported by Charbel et al.[7] The difference between their series and our cases might reflect differing baseline retinal function. Our cases exhibited no retinal edema, whereas theirs showed some degree of edema. Half of our cases were type 2 IMT with inner lamellar cysts at baseline. Charbel et al.[7] did not mention any cysts. Baseline retinal conditions can affect visual prognosis in both treated and untreated cases.

This study has several limitations. First, bevacizumab is an off-label drug for IMT, and the short-term follow-up cannot clarify the efficacy of this treatment. The natural course of this disease is long, and most patients experience only moderate visual loss even without treatment. Also, as yet unknown side effects must be considered. None of our patients had CNV. Secondary CNV may be the best target of bevacizumab treatment for IMT.[13]

## References

1. Gass JD, Oyakawa RT. Idiopathic juxtafoveolar retinal telangiectasis. Arch Ophthalmol 1982;100:769–780.
2. Gass JDM, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis: update of classification and follow-up study. Ophthalmology 1993;100:1536–1546.
3. Yannuzzi LA, Bardal AMC, Freund KB, Chen KJ, Eandi CM, Blodi B. Idiopathic macular telangiectasia. Arch Ophthamol 2006;124: 450–460.
4. Presta LG, Chen H, O'Connor SJ, et al. Humanization of an antivascular endothelial growth factor monoclonal antibody for the therapy of solid tumors and other disorders. Cancer Res 1997; 57:4593–4599.
5. Ferrara N. VEGF as a therapeutic target in cancer. Oncology 2005; 69:11–16.
6. Kovach JL, Rosenfeld PJ. Bevacizumab (Avastin) therapy for idiopathic macular telangiectasia type II. Retina 2009;29:27–32.
7. Charbel Issa P, Finger RP, Holtz FG, Scholl HP. Eighteen-months follow up of intravitreal bevacizumab in type 2 idiopathic macular telangiectasia. Br J Ophthalmol 2007;92:941–945.
8. Moon SJ, Berger AS, Misch DM. Intravitreal bevacizumab for macular edema from idiopathic juxtafoveal retinal telangiectasis. Ophthalmol Surg Lasers Imaging 2007;38:164–166.
9. Gamulescu MA, Walter A, Sachs H, Helbig H. Bevacizumab in the treatment of idiopathic macular telangiectasia. Graefes Arch Clin Ophthalmol 2008;246:1189–1193.
10. Park DW, Schatz H, McDonald HR, Johnson RN. Grid laser photocoagulation for macular edema in bilateral juxtafoveal telangiectasis. Ophthalmology 1997;104:1838–1846.
11. Cakir M, Kapran Z, Basar D, Utine CA, Eroglu F, Perente I. Optical coherence tomography evaluation of macular edema after intravitreal triamcinolone acetonide in patients with parafoveal telangiectasis. Euro J Ophthalmol 2006;16:711–717.
12. Eandi CM, Ober MD, Freund KB, et al. Anecortave acetate for the treatment of idiopathic perifoveal telangiectasia: a pilot study. Retina 2006;26:780–785.
13. Jorge R, Costa RA, Calucci D, Scott IU. Intravitreal bevacizumab (Avastin) associated with the regression of subretinal neovascularization in idiopathic juxtafoveolar retinal telangiectasis. Graefes Arch Clin Ophthalmol 2007;245:1045–1048.