심기능 저하가 없는 뒤센근위축증 환자에서 발생한 증식성 망막병증

Proliferative Retinopathy Developed in a Duchenne Muscular Dystrophy Patient with Normal Cardiac Function

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Purpose: To report a case of severe proliferative retinopathy that developed in both eyes of a Duchenne muscular dystrophy (DMD) patient with normal cardiac function.

Case summary: A 30-year-old male patient with DMD was referred to our hospital due to decreased vision on both eyes. Best-corrected visual acuity (BCVA) was 20/1,000 in the right eye and finger counting in the left eye. Extensive retinal neovascularization with fibrovascular proliferation and dense vitreous hemorrhage was noted in both eyes. There was no cardiopulmonary insufficiency. Bevacizumab was injected as preoperative treatment 2 days prior to surgery; pars plana vitrectomy with laser photocoagulation and silicone oil injection was performed on both eyes. One month postoperatively, BCVA was 20/300 without subretinal fluid, and silicone oil was removed from both eyes. The retina remained attached without re-proliferation at the last follow-up, 18 months postoperatively.

Conclusions: Rapidly progressive bilateral proliferative retinopathy can occur in DMD patients without severe cardiopulmonary insufficiency. Considering its rapid progression, regular fundus examination and early intervention is recommended for proliferative retinopathy in DMD patients, for a better prognosis.

Keywords: Duchenne muscular dystrophy; Retinal diseases; Retinal neovascularization; Vitrectomy

Introduction

Duchenne muscular dystrophy (DMD) is a rare, severe muscular dystrophy that exhibits an X-linked recessive inheritance pattern. DMD The dystrophy results from a gene mu-

tation that leads to altered or absent dystrophin production [1]. Dystrophin plays a critical role in connecting the cytoskeleton of muscle fibers to the extracellular matrix. Voluntary muscles become gradually involved with DMD in childhood, followed by respiratory and cardiac muscles in later stages,

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potentially leading to death by respiratory or cardiac failure.

Dystrophy is known to be normally expressed in the retina, localized to photoreceptor terminals and around retinal vessels. Retinal vascular abnormalities have been reported in a few cases of DMD having compromised cardiopulmonary function [2,3] However, retinopathy developed in DMD is extremely rare, and extant clinical information is lacking in risk factors, natural history, treatment, and prognosis for this condition. In the present report, we describe a case of severe proliferative retinopathy that developed in both eyes of a DMD patient with normal cardiac function, and was managed with vitreous surgery.

Case Report

A 30-year-old Korean man with DMD was referred for decreased vision of two months duration in both eyes. He had been diagnosed with diabetes mellitus (DM) and received panretinal photocoagulation for presumed proliferative diabetic retinopathy in another hospital two months prior to the presentation. The hemoglobin A1c (HbA1c) was 6.4%, and he had no hypertension. Loss of vision had progressed and best-corrected visual acuity (BCVA) was 20/1,000 in the right eye and finger counting in the left eye. The intraocular pressure was 13 and 15 mmHg, respectively. Anterior segment examination was unremarkable except for mild cataracts in both eyes; there was no iris neovascularization. Ophthalmoscopy revealed extensive, bilateral retinal neovascularization with fibrovascular proliferation and dense vitreous hemorrhage. The posterior pole was obscured by proliferative changes in both eyes (Fig. 1).

Laboratory examination showed mild anemia with a hemoglobin of 13.5 g/dL; erythrocyte sedimentation ratio was

71 mm/h. Coagulation test and arterial blood gas analysis result were normal. The cardiac ejection fraction was 70% of the predicted level, and he used a home ventilator for 5-6 hours while sleeping.

We recommended vitreous surgery in both eyes sequentially under local anesthesia; the left eye first, then the right. Bevacizumab (1.25 mg in 0.05 mL, Roche Pharma, Reinach, Switzerland) was injected into the vitreous cavity of the left eye as preoperative treatment two days prior to surgery. Pars plana vitrectomy was performed on the left eye. The posterior vitreous was partially detached and connected to the proliferative membrane. The vitreous was removed as completely as possible with scleral indentation. The proliferative membrane was also removed completely using the vitreous forceps and vitrectomy cutter, without iatrogenic retinal break. Bleeding was controlled by elevating infusion pressure and applying intraocular electrocautery. Laser photocoagulation was performed and silicone oil was injected as tamponade after fluid-air exchange. Preoperative bevacizumab was injected into the right eye in the same day. Two days later, the same procedure was performed on the right eye.

After 1 week, BCVA was 20/1,000 in the right eye and 20/200 in the left eye. Fundoscopic examination and optical coherence tomography demonstrated subretinal fluid with cystoid macular edema in the right eye. One month postoperatively, BCVA was 20/300 without subretinal fluid in both eyes. Macular pucker was noted in the right eye. Silicone oil was removed from both eyes. For the right eye, the epiretinal membrane and internal limiting membrane were peeled and laser photocoagulation was performed additionally. Two weeks after silicone oil removal, macular edema improved with BCVA of 20/125 in the right and 20/60 in the left eye (Fig. 2). The retina maintained attached without re-proliferation for 18 months postoperatively.

Figure 1. Ocular findings on the patient's first visit. Wide fundus photos showed dense vitreous hemorrhage and fibrotic vascular proliferations in both eyes.

Discussion

The mutation in DMD is found on the gene encoding dystrophin, a 427-kD protein localized to the inner surface of the sarcolemma of muscle fibers [1]. Ocular manifestations include a diminished electroretinogram (ERG) signal and less commonly, retinal neovascularization, which may result from a variant in the dystrophin mutation [4]. The pathogenesis of severe proliferative retinopathy with neovascularization, how-

Figure 2. (A, B) Wide fundus photos and optical coherence tomography (OCT) images at postoperative 1 week. Fovea off retinal detachment and cystoid macular edema are noted in the right eye. Flat retina and 50% level of silicone oils are observed in the left eye. (C, D) Wide fundus photos and OCT images at postoperative 1 month. The retina is flat in both eyes with macular pucker in the right eye. (E, F) Wide fundus photos and OCT images 2 weeks after silicone oil removal. Macular thickness is decreased in the right eye.

ever, remains unknown and case reports are rare.

Previous reports have discussed several factors that may be involved in DMD-associated proliferative retinopathy. Louie et al. [2] reported bilateral retinal ischemia complicated with neovascularization and proposed that chronic hypoxia secondary to cardiomyopathy and ventilator failure played a predominant role in the development of retinopathy. Ober et al. [3] speculated that chronic anemia and cardiovascular

compromise would surpass the threshold beyond which retinal neovascularization is stimulated, resulting in proliferative retinopathy. However, these hypotheses cannot explain the pathogenesis of proliferative retinopathy in our patient who had neither cardiopulmonary compromise nor anemia, but diabetes mellitus.

Dystrophin is present in the retina in the internal limiting membrane and around retinal vessels. Nico et al. [5] found that abnormal neuronal vascular permeability causing cerebral edema was a part of the phenotype in an animal model of DMD. It has also been reported that certain mouse models of dystrophin deficiency were more susceptible to retinal ischemia [6]. Therefore, we suggest that lack of dystrophin may be involved in up-regulating retinal angiogenesis and endothelial permeability by increasing susceptibility to systemic conditions causing retinal ischemia, such as cardiomyopathy, anemia, and diabetes mellitus.

Although his clinical findings of the retinopathy showed those of proliferative diabetic retinopathy, we speculated that the retinopathy was caused by DMD. The duration of DM was only two months. As he had been received regular check-ups due to DMD, it was less likely to have undiagnosed diabetes mellitus for a long time enough for development proliferative diabetic retinopathy. Furthermore the level of HbA1c was not high as 6.4% at the diagnosis. He did not have hypertension.

Retinopathy in DMD appeared to share mechanisms and clinical characteristics with other ischemic retinopathies, including proliferative diabetic retinopathy. Fagan et al. [7] reported a case of bilateral proliferative retinopathy associated with DMD where, after a single injection of bevacizumab, resolution of the microvascular abnormalities and regression of the neovascularization was observed. Neovascularization in that case responded to anti-vascular endothelial growth factor treatment, and we believe that pretreatment with bevacizumab facilitated removal of fibrovascular membrane during vitrectomy in our case as well. However, proliferative retinopathy in DMD may progress rapidly and aggressively as evidenced in our case. Meticulous removal of proliferative membrane and retinal photocoagulation resulted in long-term stability in this case.

In summary, rapidly progressive bilateral proliferative retinopathy occurred in a patient with DMD but without severe cardiopulmonary insufficiency. The complicated tractional detachment and vitreous hemorrhage were managed successfully with surgical treatment, including pars plana vitrectomy.

Improvement in vision and retinal stability was maintained without aggravation of retinopathy over 18 months of follow-up. Considering its rapid progression, regular fundus examination and early intervention is recommended for proliferative retinopathy in DMD patients for a better prognosis.

Conflicts of Interest

J. E. L. (advisory board, consultant for Alcon, Allergan, Bayer, and Novartis, honorarium from Alcon, Allergan, Bayer and Novartis, research fund from Bayer and Novartis). S. W. P. (honorarium from Allergan), None of the other authors have any financial or other conflicts of interest to disclose.

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