

덱사메타손 임플란트 삽입 후 발생한 비문증에서 야그레이저를 이용한 유리체해리술의 효과

Dexamethasone Implant-associated Vitreous Floaters and Symptom Improvement by YAG Laser Vitreolysis

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Purpose: To investigate the incidence of symptomatic floaters following intravitreal dexamethasone implant therapy and to propose implant repositioning using neodymium-doped yttrium aluminum garnet (Nd:YAG) vitreolysis around the implant for treatment.

Case summary: Nd:YAG vitreolysis was performed on the superior vitreous adjacent to the dexamethasone implant in eyes with persistent symptomatic floaters following intravitreal dexamethasone implant injection using 2.0-3.0 mJ energy. Among 172 injections of the dexamethasone implant, 11 (6.4%) resulted in symptomatic floaters at the 1-month visit. Three (1.7%) eyes exhibited persistent and visually significant vitreous floaters, upon which Nd:YAG vitreolysis was performed. Immediately after the superior vitreolysis adjacent to the implant, the implants were repositioned to the inferior vitreous. Floater symptoms were resolved in all patients without any damage to the implant or other ocular complications.

Conclusions: Superior vitreolysis adjacent to dexamethasone implants may be an effective and safe treatment for persistent symptomatic floaters following intravitreal dexamethasone implant injection.

Keywords: Dexamethasone implant; Floaters; Nd:YAG; Vitreolysis

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Introduction

Vitreous floater is a visual phenomenon caused by vitreous opacities accompanied by shadows with dark spots that usually move with eye and head movement [1]. They can develop as a result of structural changes in the vitreous body or from exogenous sources, such as asteroid bodies, blood, foreign bodies, and/or parasites. In particular, intraocular injections, commonly performed in current clinical practice, sometimes produce vitreous floaters in patients undergoing treatment [1], which should be considered an unfavorable side effect of therapy.

The dexamethasone implant (Ozurdex; Allergan Inc., Irvine, CA, USA) is a biodegradable, sustained-release implant containing 700 mg of dexamethasone within a poly (D, L-lactide-co-glycolide) (PLGA) polymer matrix [2]. The United States Food and Drug Administration has approved the use of dexamethasone-PLGA matrix in the treatment of macular edema (ME) secondary to retinal vein occlusion (RVO) or diabetic retinopathy (DR) and noninfectious uveitis affecting the posterior segment [3-5]. Intravitreal injections of the implant are widely performed for the treatment of ME, and several studies have reported successful results in anatomical and functional outcomes [2,3].

Although intravitreal therapy using the dexamethasone implant is considered to be relatively safe, several drug-related side effects have been reported. In particular, due to differences in formulation between the implant (a rod-shaped solid) and other injectable drugs targeting vascular endothelial growth factor (VEGF [a liquid]), vitreous floaters are more common following treatment with a dexamethasone implant compared with other anti-VEGF injections. The reported incidence of vitreous floaters following intravitreal dexamethasone implant therapy ranges from 3.1% to 17% [4,6,7]. Because vitreous floaters following dexamethasone implant therapy can be considerably symptomatic, this adverse event cannot be neglected and should be assessed carefully following therapy.

In the present report, we describe three cases of symptomatic floaters following intravitreal dexamethasone implant therapy that were successfully resolved with neodymium-doped yttrium aluminum garnet (Nd:YAG) vitreolysis adjacent to the implant.

Case Report

Among 172 injections of the dexamethasone implant for the treatment of ME secondary to RVO, DR, and uveitis, 11 (6.4%) resulted in symptomatic floaters, which occurred following therapy and were noted at the 1-month visit. For 8 of 11 (72.7%) injections, including 5 pseudophakic and 3 phakic eyes, patients reported that the symptoms had been improving during the initial month following treatment, or the symptoms were not visually significant at the time of the follow-up visit. However, 3 of 11 (27.3%) patients complained of persistent and significant vitreous floaters for which they sought treatment. These patients were treated with Nd:YAG laser vitreolysis. Three months following intravitreal injection of the dexamethasone implant, 2 of 172 (1.2%) injections resulted in symptomatic floaters, which had been improving and were not significant since the onset of symptom(s). The institutional review board/ethics committee of the authors' institution ruled that approval was not required for this case study.

Case 1

A 79-year-old man complained of floaters 1 week after intravitreal dexamethasone implant injection in the left eye. He had undergone cataract extraction and posterior chamber

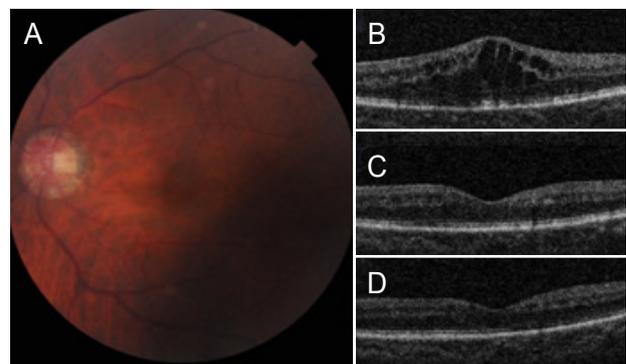


Figure 1. Fundus photograph before dexamethasone implant injection (A) and optical coherence tomography images before (B) and 1 (C) and 2 (D) months after the implant injection in case 1 with macular edema secondary to central retinal vein occlusion. One month after intravitreal dexamethasone implant therapy, the macular edema was resolved (C). One month after superior vitreolysis, neither damage to the macula nor recurrence of macular edema was noted (D).

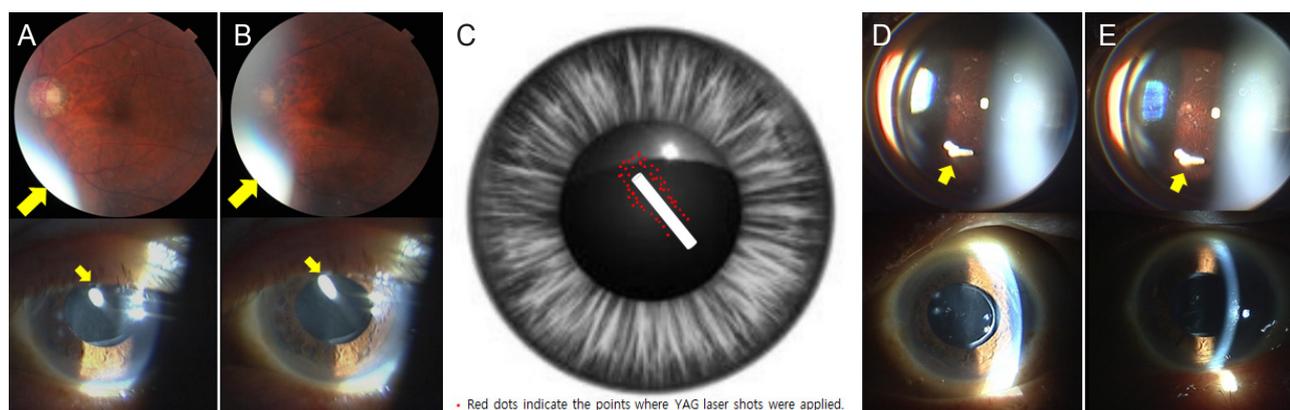


Figure 2. (A, B) Fundus and anterior segment photographs 1 week (A) and 1 month (B) after intravitreal dexamethasone implant injection in case 1. Following the implant injection, the implant was situated in the anterior vitreous and also in the visual axis, causing a symptomatic floater. There is virtually no change in the position of the implant (yellow arrows) between 1 week and 1 month after the intravitreal injection. The patient experienced a considerably symptomatic floater for 1 month following the intravitreal injection. (C-E) Illustration indicating the area treated by laser vitreolysis (C) and anterior segment and fundus photographs at the immediate post-treatment period (D) and 1 month following the laser vitreolysis (E). Following superior vitreolysis around the dexamethasone implant, the implant disappeared on the anterior segment photograph as it dropped into the inferior vitreous (yellow arrow in D). The implant could not be identified by conventional 45° fundus photography, but it was identified using fundus examination with a wide-field contact lens (SuperQuad 160; Volk Optical Inc., Mentor, OH, USA). One month following vitreolysis, the patient was symptom-free because the implant was located in the inferior vitreous (yellow arrow in E).

intraocular lens implantation in the eye 3 months previously. He had been diagnosed with ME secondary to central RVO (CRVO) and received intravitreal dexamethasone implant therapy twice (8 and 17 months before presentation), which resulted in successful resolution of ME. Optical coherence tomography (OCT) images acquired before the most recent intravitreal dexamethasone implant injection revealed the recurrence of ME (Fig. 1), and an intravitreal injection of dexamethasone implant (Ozurdex) had been performed uneventfully. On slit-lamp examination, the intraocular pressure measurement and fundus examination on the day of presentation revealed no abnormal findings other than the implant situated in the anterior vitreous, obscuring the visual axis (Fig. 2A). The patient was reassured that the symptoms would be relieved in the ensuing months.

When he returned to the clinic 1 month later, he continued to experience significant floaters that had not improved. Anterior segment photography revealed no significant positional change of the implant, as demonstrated in Fig. 2B. He reported that the impact of the floaters on his quality of life was greater than that of the visual decline associated with ME secondary to CRVO. Although the best-corrected visual acuity in the left eye had improved from 20/100 to 20/40 after the implant therapy, he requested relief of the symptom

by any means, even if it required removal of the implant. After he was informed of the available treatment options, including vitrectomy, and the potential risks of laser vitreolysis, Nd:YAG vitreolysis was performed on the superior vitreous adjacent to the implant, as presented in Fig. 2C. After dilating the pupil with 0.5% tropicamide and phenylephrine, the superior vitreous fibers attached to the implant—which support the floating implant against gravity in the vitreous cavity—were severed using 46 shots of 2.5–3.0 mJ YAG laser using a Peyman Wide Field YAG laser lens (OPY-12.5; Ocular Instruments Inc., Bellevue, WA, USA) with a 12.5 mm anterior radius for anterior vitreous. The laser was applied around the implant at virtually the same plane of the implant, with a distance of approximately one-half of the entire width of the implant. Posterior capsulotomy was also performed during the application of the YAG laser for the anterior part of the implant. The implant shook at the time of laser vitreolysis due to the mechanical force of the laser exerted on the attached vitreous and, subsequently, gradually sank into the inferior vitreous as the superior vitreous fibers attached to the implant were cut and separated, releasing the implant. The patient did not experience any pain or discomfort during the therapy, and the entire procedure was completed within 5 minutes. No topical medication was prescribed following the

laser therapy.

Immediately after the laser vitreolysis, the floaters was not observed, and slit-lamp examination revealed no visible implant obscuring the visual axis in the anterior vitreous (Fig. 2D). Fundus examination revealed an inferiorly located dexamethasone implant, which could be visualized in the inferior vitreous on downgaze only. No abnormal findings or retinal complications were observed. One month later, the patient was satisfied with the disappearance of the discomfort, and the implant was situated in the inferior vitreous (Fig. 2E). OCT imaging revealed resolved ME without any retinal damage, as demonstrated in the Fig. 1D.

Five months after the therapy, the patient experienced recurrent ME, and intravitreal dexamethasone implant therapy was performed again. Following this second therapy, however, the patient had no complaints of symptomatic floaters at the 1-week and 1-month visits.

Case 2

A 74-year-old woman with ME due to branch RVO (BRVO) complained of vitreous floaters following intravitreal dexamethasone implant therapy that persisted for 1 month in the right eye. Anterior segment photographs revealed the implant in the anterior vitreous obscuring the visual axis the day after the injection (Fig. 3A) and almost no movement of the implant at 1 month following therapy (Fig. 3B). Accordingly, Nd:YAG superior vitreolysis was performed around the implant using 28 shots of 2.5 mJ YAG laser, as described in case 1. An anterior segment photograph captured immediately after vitreolysis revealed the disappearance of the implant in the anterior vitreous (Fig. 3C). At the next visit (1 month later), the patient was satisfied with the symptomatic improvement. There were no intraocular complications.

Case 3

A 70-year-old woman presented with vitreous floaters at 6 weeks following intravitreal dexamethasone implant therapy. She had been previously diagnosed with BRVO and received intravitreal dexamethasone implant injections three times for secondary ME. After the previous injections, she experienced vitreous floaters for up to 1 month, which subsequently resolved. The implant was not observed with the slit lamp (Fig. 4A, left), but fundus examination showed that the im-

plant was located in the center of the vitreous cavity, obscuring the visual axis (Fig. 4A, right). Her vision improved from 20/50 before the intravitreal dexamethasone implant therapy to 20/40 after the therapy. Nevertheless, she experienced persistent symptomatic floaters for which she sought treatment. After explaining the potential risks, Nd:YAG vitreolysis was performed for the superior vitreous around the implant.

For the vitreolysis, 2.0-2.5 mJ energy was used to sever the superior vitreous fibers attached to the implant with a Peyman Wide Field YAG laser lens (OPY-25) with a 25 mm radius for deep vitreous. A total of 32 shots were used, which was sufficient to drop the implant into the inferior vitreous.

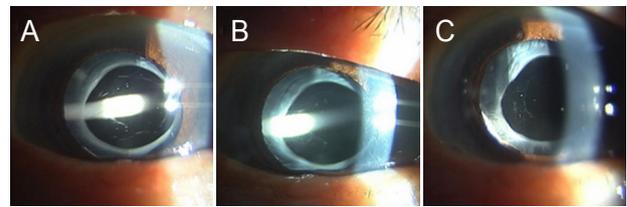


Figure 3. Anterior segment photographs in case 2 before (the day after intravitreal implant injection [A]) and 1 month after the injection [B]) and immediately after (C) neodymium-doped yttrium aluminum garnet vitreolysis. After laser vitreolysis, the implant disappeared from the anterior vitreous and out of the visual axis, and the patient was satisfied with her symptom improvement.

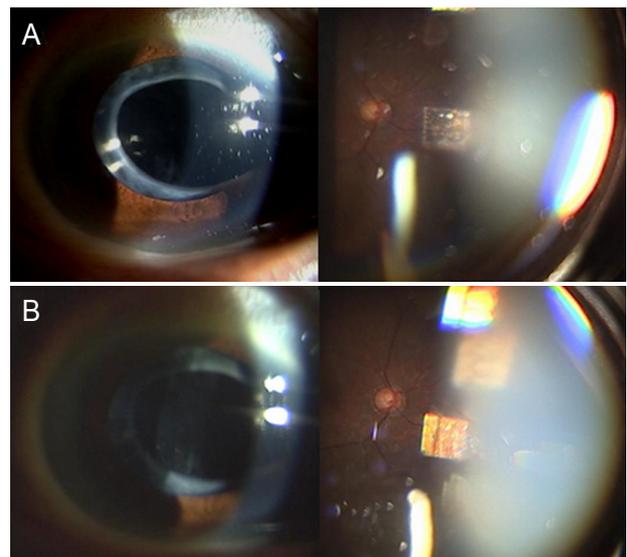


Figure 4. Anterior segment and fundus photographs in case 3 before (A) and after superior vitreolysis around the dexamethasone implant (B). After laser vitreolysis, the implant showed inferior repositioning, and the patient experienced symptomatic improvement.

The minimum number of laser shots was used with the minimal energy because the implant was fairly posterior in location. Fundus examination revealed an inferiorly-migrated dexamethasone implant (Fig. 4B), and she reported that the floater symptoms had been relieved.

One month later, the patient was satisfied with the symptomatic improvement, and fundus examination revealed that the implant was located in the inferior vitreous. Slit-lamp, fundus, and OCT examinations revealed neither retinal complications nor edema on the macular area.

Discussion

Floaters can have a significantly negative impact on the quality of life [8,9]. For persistent and significantly symptomatic floaters, interventional options, such as vitrectomy and laser vitreolysis, are increasingly being considered [10,11]. Although vitreous floaters following intravitreal dexamethasone implant therapy are not rare [4-6], appropriate management has not been extensively discussed. In the present study, 6.4% of patients experienced symptomatic floaters following intravitreal dexamethasone implant therapy, and 1.7% experienced persistent (> 1 month) and significant vitreous floaters, which required proper management. For treatment, Nd:YAG vitreolysis may be a non-invasive, effective, and safe option.

Although vitrectomy is definitive for resolution of symptomatic floaters by removal of the implant, it is associated with the potential risk for ocular complications, such as endophthalmitis, retinal detachment, intraocular pressure problems, vitreous hemorrhage, and cataract progression. In addition, the dexamethasone implant becomes friable over time, and grasping it with forceps during vitrectomy sometimes fractures it into multiple pieces, which makes removal complicated. Furthermore, if the implant is removed for symptomatic improvement, the drug is no longer effective, and other therapeutic options should be considered for treatment of ME. Alternatively, the implant may be repositioned during vitrectomy so that it is not in the visual axis. Nevertheless, vitrectomized eyes have a greater likelihood of anterior segment migration, and several authors have suggested that vitrectomy is an important risk factor for migration [12-14].

In contrast, Nd:YAG, which is most commonly used for posterior capsule opacification following cataract surgery,

is performed without sclerotomy and has markedly fewer ocular complications compared with intraocular surgery. Nd:YAG vitreolysis has been attempted for symptomatic floaters, and previous studies have reported successful results for symptom improvement. This procedure appears to be safe, given that we observed no ocular complications other than a transient rise in intraocular pressure and intraocular inflammation after treatment. Additionally, this office-based laser treatment can be performed in less than 10 minutes.

Regarding the extent of vitreolysis, one may argue that complete vitreolysis around the implant would reduce the risk for recurrence of floaters by facilitating settlement of the implant into the inferior vitreous or retinal surface by gravity. However, the possibility of anterior migration of the dexamethasone implant should be considered because there is no vitreous attached to the implant and, thus, no force holding the implant in the vitreous and preventing its anterior migration. Indeed, following superior vitreolysis, the implant slightly moved with eye movement as it contacted the inferior vitreous; however, in our cases, it did not cause floaters because of the location outside the visual axis. Biodegradation of the implant may be affected by laser vitreolysis; however, we believe there is no significant biodegradation effect given that we noted that the implant disappeared at the 4- and 5-month visits in 2 and 1 patient(s), respectively.

Our study does not necessarily support vitreolysis for all patients with symptomatic floaters following intravitreal dexamethasone implant therapy. Most patients (72.7% in our study) with symptomatic floaters following therapy exhibit gradual resolution of their symptoms without any treatment as the implant gradually moves into the inferior vitreous or dissolves. Furthermore, although laser vitreolysis results in inferior migration of the implant, symptoms may persist. Therefore, reassurance without any treatment at the time of initial complaint may be sufficient for the management of symptomatic floaters following implant therapy. However, some patients, who exhibit virtually no positional change in the implant during the follow-up period and yet still experience significant floaters, will insist on removal despite recommendations that they should wait for several months until the implant disappears. In such cases, the impact of symptomatic floaters should be seriously considered to determine optimal management, and the natural course and risks of vitreolysis should be carefully discussed with patients. Risks associated with laser vitreolysis, such as mechanical dam-

age to the retina or crystalline lens from the laser, should be carefully considered. Additionally, posterior capsule injury, damage or anterior migration of the implant, and retinal or vitreous hemorrhage may be other potential adverse effects of laser vitreolysis. Thus, we believe that eyes with an implant distant from the retina (and also crystalline lenses in phakic eyes) causing persistent symptomatic floaters are better candidates for laser therapy. Depending on the location of the implant, laser energy should be tailored to minimize mechanical damage to the retina and crystalline lens.

In conclusion, our study revealed that implant repositioning using superior vitreolysis around the dexamethasone implant may be a safe and effective treatment to resolve symptomatic and persistent floaters following intravitreal dexamethasone implant injection. This technique may be applicable to floaters caused by other types of intravitreal implants. Further studies confirming the effectiveness and safety of the technique in a larger number of patients are warranted.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this article.

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