Başarısız İntravitreal Deksametazon İmplant Uygulaması

Failure of Intravitreal Dexamethasone Implant Application

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ÖZ

İntravitreal deksametazon implantı (İVDİ) retina ven tıkanıklığı, diyabetik makülopati ve arka üveite bağlı gelişen maküla ödemi endikasyonlarında kullanıma sunulmuştur. Kliniğimizde diyabetik maküla ödemi tanısıyla intravitreal anti-vasküler endotelyal büyüme faktörü enjeksiyonu uygulanan ve her iki gözünde tedaviye yeterli yanıt alınamayan 65 yaşında erkek hastaya bilateral İVDİ uygulaması planlandı. Sağ gözüne sorunsuz olarak İVDİ uygulanan olgunun, sol göz İVDİ uygulaması sırasında implant aplikatörü ile tam kat skleral giriş yapılamadığından İVDİ uygulaması yapılamadı. Başarısız uygulama sonrası aplikatör kontrol edildiğinde implantın kısmen aplikatör iğnesinin konik kısmından hafif taşmış olduğu saptandı. İVDİ uygulaması öncesi aplikatör iğnesi ve implant pozisyonunun kontrol edilmesi uygulama başarısı açısından önemlidir.

Anahtar Kelimeler: Anti-vasküler endotelyal büyüme faktörü, deksametazon implantı, diyabetik maküla ödemi.

ABSTRACT

Intravitreal dexamethasone implantation (IVDI) has been introduced for indications of retinal venous occlusion, diabetic maculopathy and macular edema due to posterior uveitis. A 65-year-old man, who developed bilateral diabetic macular edema and had limited response to bilateral intravitreal anti-vascular endothelial growth factor injections, was planned to undergo bilateral IVDI. The IVDI was performed without any complication in the right eye but it could not be performed in the left eye due to failure of full-scleral access with the implant applicator during IVDI application in the left eye. When the applicator was checked after failed application, it was determined that the implant partially spilled slightly from the conical part of the applicator needle. Controlling applicator needle and implant position prior to IVDI application is important for application success.

Key Words: Anti-vascular endothelial growth factor, diabetic macular edema, dexamethasone implant.

INTRODUCTION

Diabetes mellitus is a considered as a disorder which has long been known dating back to BC 16th century and even described in Egyptian papyrus.[1] In developed countries, it is one of the most important causes of vision loss and diabetic macular edema (DME) is the most common pathology resulting in decreased vision.[2] In the randomized-controlled studies, intravitreal anti-vascular endothelial growth factor and corticosteroid injections are found to be beneficial in DME treatment.[3,4]

Ozurdex (Allergan Inc., Irvine, CA, USA) is a dexamethasone implant (0.7 mg) approved for retinal vein occlusion, posterior uveitis-related macular edema and diabetic retinopathy-related macular edema by US Food and Drug Administration (FDA).

In this study, we presented failure of intravitreal dexamethasone implant (IVDI) in the left eye of a patient who scheduled bilateral IVDI administration due to unresponsiveness to repeated anti-VGEF injections performed due to bilateral DME.

CASE REPORT

In a 65-years old man with known type 2 diabetes mellitus, intravitreal ranibizumab injection was performed for 13

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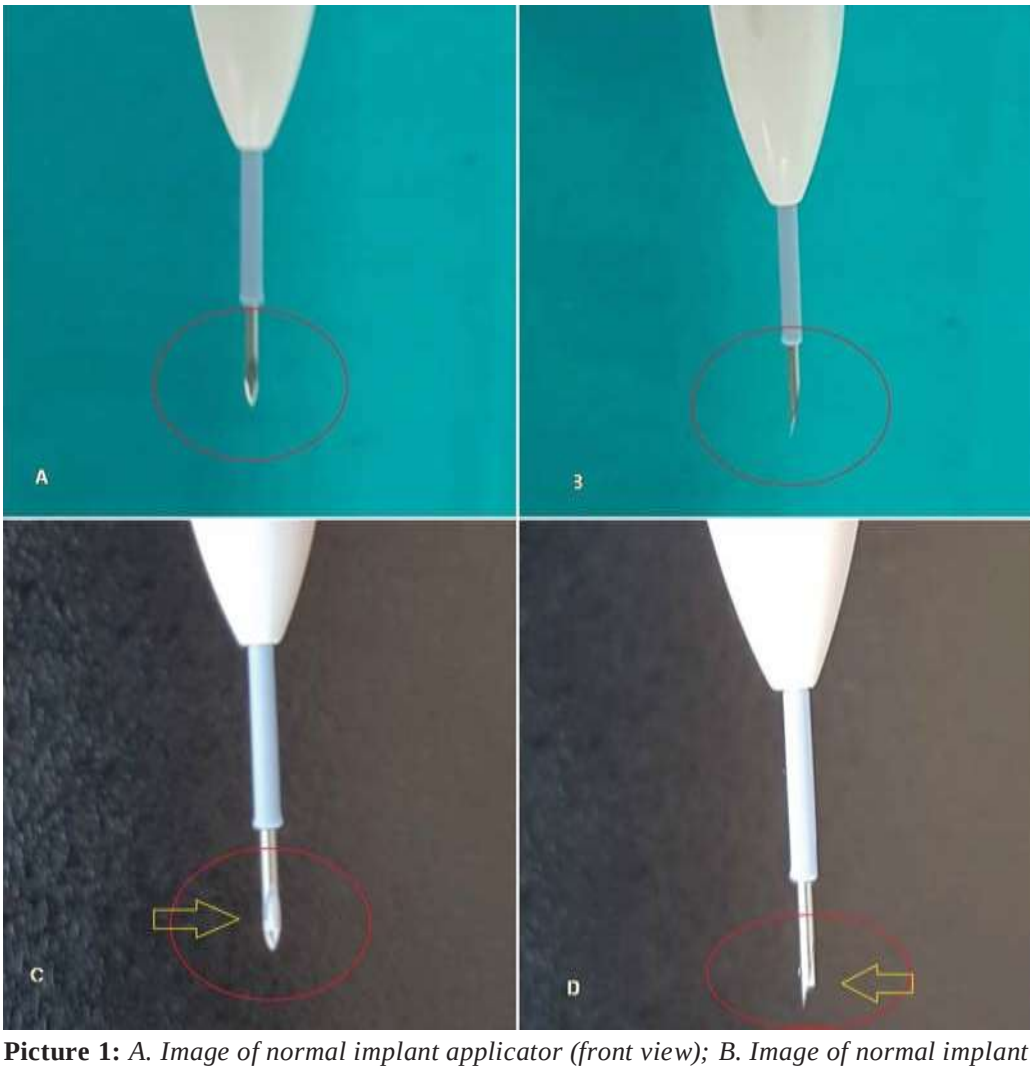
times in the right eye and 10 times in the left eye in combination with bilateral laser photocoagulation due to recurrent DME during follow-up. In the recent period, monthly anti-VGEF injections (3 injections) were administered bilaterally for DME; however, no clinical response was achieved and bilateral IVDI was scheduled to the patient.

The best corrected visual acuity was 0.1 in right eye and 0.2 in the left eye. The intraocular pressure was 15 and 11 mmHg in right and left eyes, respectively. There was nuclear sclerosis in the right while pseudophakia in the left eye. The fundus examination revealed bilateral DME, retinal photocoagulation scar, diffuse micro-hemorrhage and plaques of hard exudate. On optical coherence tomography (OCT) imaging, diffuse macular edema was found to be persistent in the patient with inadequate clinical response despite multiple anti-VGEF injections. The IVDI application was planned for treatment of bilateral DME and informed consent was obtained from the patient after providing information about risks of treatment.

It was planned to administer IVDI in the right eye first and then in the left eye after a week. The injection was performed uneventfully in the right eye. In the left eye, after preparation under topical anesthesia with 0.5% proparacaine HCl, the injection site was marked as being 3.5 mm distant from limbus by a pair of compass and injection procedure was initiated at inferior temporal quadrant. By using injector of IVDI applicator, sclera was accessed with an angle of 30° via lamellar manner. The lamellar access was maintained until disappearance of conical part of needle within sclera. After achieving lamellar access, applicator was moved to a perpendicular position (90°) and it was attempted to access into eye; however, IVDI could not be performed since it was failed to achieve full-scleral access with applicator at perpendicular position. When needle of applicator was checked to reveal cause of failure, it was seen that there was no problem in the needle but implant was displaced to conical part of needle where implant should not be appear (Picture 1). Despite intensive efforts during IVDI implication in the left eye,



Picture 1: *A. Image of normal implant applicator (front view); B. Image of normal implant applicator (side view); C. Image of displaced implant applicator (front view; D. Image of displaced implant applicator (side view)*

no complication other than mild sub-conjunctival hemorrhage was observed in the left eye.

Two weeks after failure, the new IVDI provided by manufacturer due to defective product was injected to superior temporal quadrant without problem. No complication was observed in both eyes during short-term follow-up after IVDI application and marked regression with improvement in disorganization of retinal layers were observed.

DISCUSSION

The DME pathophysiology involves multifactorial complex mechanisms triggered by hyperglycemia. In the DME, disruption of retina-blood barrier is pivotal in the pathway resulting in macular edema.[4] There are several important factors involved in the disruption of retina-blood barrier integrity, including VEGF-A, placental growth factor (PlGF), IL-8, IL-6, IL-1β, TNF-α and matrix metalloproteinases.[5]

The treatment options include carbonic anhydrase inhibitors, non-steroidal anti-inflammatory agents (cyclooxygenase inhibitors), anti-angiogenic agents, corticosteroids, laser photocoagulation and vitreoretinal surgery.[1]

The corticosteroids block arachidonic acid release from cell membrane and suppress prostaglandin synthesis. They also inhibit leukocyte migration and release of pro-inflammatory mediators such as TNF-α and VEGF. In addition, corticosteroids stabilize endothelial tight-junctions by increasing number of tight junctions. Thus, they have anti-inflammatory, anti-apoptotic, anti-edematous and anti-angiogenic effects. Corticosteroids can be used via several route including systemic, topical, periocular, intravitreal injection and intravitreal implant.

In recent years, sustained-release corticosteroid implants have been introduced as a novel treatment modality. The IVDI is most widely accepted and used modality for intravitreal steroid implantation. It is injected into vitreous by a special applicator without need for sutures. The release of active substance has a biphasic pattern with high doses in first 6 weeks and lower doses until month 6 thereafter. It is a biocompatible and biosoluble and metabolizes into CO_2 and water. In clinical trials, significant improvement in visual acuity with decreased central retinal thickness was observed in DME.[5] In a study, it was reported that intravitreal dexamethasone implant is effective in vitrectomized eyes which comprises most challenging and refractory group.[6]

The complications related to IVDI implantation can be addressed in two major categories including complications related to corticosteroid suspension and those related to injection procedure. The corticosteroid suspension-related complications include IOP elevation, cataract formation and endophthalmitis as IOP elevation being most common adverse effect. The IOP elevation peaks at day 60 and returns baseline levels on day 180.[7,8] In addition, pseudo-hypopyon can be observed , which is characterized by accumulation of injection particles in anterior segment due to vitreous degeneration and zonular weakness.[8] Implant break-up during injection, implantation to lens, supra-choroidal space or sub-retinal area, decreased visual acuity, lens damage, endophthalmitis, intravitreal hemorrhage, vitreous detachment, macular contact, hypotonia, conjunctival bleeding, macular fibrosis, ocular pain, allergic reaction and xerophthalmia can develop due to injection procedure.[1,9,10]

In the literature, there is limited data regarding IVDI failure in DME cases; however, there are anecdotal reports about IVDI applications associated to failure or empty shot due to implant falling away from applicator. In addition, it was also reported that IVDI implantation was failed due to break--up of implant within applicator.[11] In our clinic, about 100 IVDI implantations were performed over 3 years but no empty shot or applicator- and/or implant-related problem was encountered. For the first time, implantation was initiated without recognizing that implant displacement to conical part of applicator needle; lamellar access was achieved without problem but full-thickness sclera access could not be achieved after positioning applicator perpendicularly despite intensive effort; thus, IVDI was failed. In addition, two weeks later, it was found that the implant was displaced similarly when applicator was checked; thus, implantation was postponed and implant exchange was requested from manufacturer.

In conclusion, IVDI can be preferred in eligible patients with DME. However, likelihood of implantation failure due to displaced implant will be reduced by checking applicator and content.

KAYNAKLAR / REFERENCES

1. Küçümen RB, Yenerel NM. Diyabetik makula ödemi ve tedavi yaklaşımları: derleme. Turk J Ophthalmol. 2012;42:53-60.
2. Yıldırım Y, Ayata A, Ünal M, et al. Klasik tedaviye dirençli diffüz diyabetik maküla ödeminde intravitreal triamsinolon asetonid etkinliği. Ret-Vit. 2005;13:261-6.
3. Nguyen QD, Shah SM, Khwaja AA, et al. Two-year outcomes of the ranibizumab for edema of the macula in diabetes (READ-2) study. Ophthalmology. 2010;117:2146-51.
4. Haller JA, Kuppermann BD, Blumenkranz MS, et al. Dexamethasone DDS Phase II Study Group. Randomized controlled trial of an intravitreous dexamethasone drug delivery system in patients with diabetic macular edema. Arch Ophthalmol. 2010;128:289-96.
5. Klaassen I, Van Noorden CJ, Schlingemann. Molecular basis of the inner blood-retinal barrier and its breakdown in diabeticmacular edema and other pathological conditions. Prog Retin Eye Res. 2013;34:19–48.
6. Boyer DS, Faber D, Gupta S, et al. for the Ozurdex CHAMPLAIN Study Group. Dexamethasone intravitreal implant for treatment of diabetic macular edema in vitrectomized patients. Retina. 2011;31:915-23.
7. Campochiaro PA, Brown DM, Pearson A, et al. FAME Study Group. Longterm benefit of sustained-delivery fluocinolone acetonide vitreous inserts for diabetic macular edema. Ophthalmology. 2011;118:626-35.
8. Özkırış A, Evereklioğlu C, İlhan Ö, Erkılıç K. İntravitreal triamsinolon asetonid enjeksiyonu sonrası endoftalmi. T Oft Gaz. 2005; 35: 519-522.
9. Boyer DS, Yoon YH, Belfort R, et al. for the Ozurdex MEAD Study Group. Three-Year, randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with diabetic macular edema. Ophthalmology. 2014; 121:1904-14.
10. Dugel PU, Bandello F,Loewenstein A. Dexamethasone intravitreal implant in the treatment of diabetic macular edema. Clin Ophthalmol. 2015;9:1321-35.
11. Rishi P, Mathur G, Rishi E. Fractured Ozurdex™ implant in the vitreous cavity. Indian J Ophthalmol. 2012; 60: 337–338.