

Case Report

Iatrogenic Retinal Penetration from Intravitreal Injections

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Keywords

Anti-VEGF · Intravitreal injection · Macular degeneration · Retinal detachment · Retinal penetration · Retinal tear · Vitreous hemorrhage

Abstract

We present 2 cases of iatrogenic retinal penetration from intravitreal (IVT) injections in a retrospective noncomparative case series of 2 patients. The first patient, an 81-year-old Caucasian male, developed dense vitreous hemorrhage soon after receiving an IVT bevacizumab injection for macular edema from central retinal vein occlusion. A 25-g vitrectomy 1 week later showed a retinal hole surrounded by fresh hemorrhages in the same quadrant as the IVT injection. The second patient, an 87-years-old male, developed a retinal detachment after 28 injections of anti-VEGF medications for neovascular AMD. A peripheral round hole was observed during vitrectomy without any lattice degeneration in the same quadrant as prior IVT injections. Both eyes were pseudophakic, had normal axial lengths, and received injections without measuring the injection site. Retinal penetration from IVT injections can result in serious sight-threatening complications. Measuring the injection site from the limbus should be part of safe IVT injection technique.

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Introduction

Intravitreal (IVT) injections have revolutionized the management of several sight-threatening retinal conditions. Approximately, 5.9 million IVT injections were administered in the USA in 2016 with an expected 10–20% annual increase [1]. Most retinal conditions require multiple IVT injections over long periods. Although well-tolerated in the majority, serious

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complications such as endophthalmitis, cataract, and retinal detachments (RDs) have been associated with IVT injections [2]. The purpose of this communication is to report 2 cases of inadvertent retinal penetration from IVT injections.

Case Reports

This study was performed according to the tenets of the Declaration of Helsinki and Health Insurance Portability and Accountability Act of 1996. The Institutional Review Board approval was not required for this retrospective case series involving 2 eyes. Written informed consent for publication was obtained from all patients. Both patients received IVT injections elsewhere with a 30-g needle under topical anesthesia in an office setting. Details of injection technique were obtained by contacting referring providers. A lid speculum was used in both eyes. However, no marking device was employed to measure the distance of injection site from the limbus. Neither patient had prominent eyebrows, deep-set eyes, or narrow palpebral fissures. The direction of the needle was perpendicular to the sclera [3]. There was no documentation of any unusual pain, eye, or head movement during the injection.

Case 1

An 81-year-old Caucasian male was referred after he noticed sudden onset of floaters in the right eye followed by rapid loss of vision 4 h after receiving his 6th IVT bevacizumab injection for macular edema caused by central retinal vein occlusion according to records provided by the referring physician. His past ocular history was significant for cataract surgery with implantation of an in-the-bag posterior chamber IOL OU 19 years ago, and disciform scar in the left eye secondary to neovascular age-related macular degeneration. He denied history of high myopia and the emmetropic IOL power in the right eye was +20 D. His past medical history was significant for atrial fibrillation with CHA₂DS₂-VASC score of 5 (2 for age, 1 each for hypertension, congestive heart failure, and type 2 diabetes) for which he was on warfarin for stroke prophylaxis with international normalized ratio maintained between 2.5 and 3 [4]. His systemic medications included 81 mg aspirin/day for stable ischemic heart disease and other medications for hypertension, oral hypoglycemic agents, and high cholesterol. His visual acuity at presentation was hand motions in the right eye and 20/400 in the left. The intraocular pressures were normal OU. The anterior segment examination showed a well-centered PCIOL with open capsules from prior YAG capsulotomies OU. The dilated fundus examination of the right eye showed dense vitreous hemorrhage (VH) without any view of the optic nerve or retina. The left eye showed a normal nerve and a disciform scar in the macula. An ultrasonography of the right eye showed vitreous opacities but no RD.

The patient underwent a 25-g pars plana vitrectomy 8 days after the onset of symptoms and after withholding warfarin for 3 days without bridging with low-molecular-weight heparin (online suppl. Video; for all online suppl. material, see www.karger.com/doi/10.1159/000512695) [5]. The international normalized ratio was 1.6 (subtherapeutic)

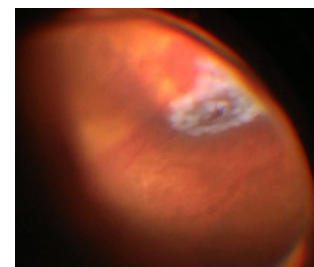


Fig. 1. Intraoperative photograph of the peripheral retina OD of Case 1 showing a peripheral round hole surrounded by endolaser adjacent to scleral depression.

on the day of surgery. After clearing the VH, a round retinal hole with surrounding retinal hemorrhages was noted at the inferotemporal periphery in the same region as the site of last IVT injection. The retinal break was treated with endolaser (Fig. 1). The patient had an uneventful recovery with return of vision to 20/30 three months after surgery. Dilated fundus examination showed a well-lasered break at the inferotemporal periphery and scattered retinal hemorrhages consistent with old central retinal vein occlusion (Fig. 2).

Case 2

An 87-years-old Caucasian male received a total of 28 IVT injections (22 bevacizumab and 6 aflibercept) in the inferotemporal quadrant OD for neovascular AMD. He developed floaters soon after his last IVT aflibercept injection followed soon after a superior visual field defect that progressed to almost complete loss of vision over a period of 2 weeks. His ocular history was significant for an uncomplicated cataract surgery OU 13 years ago. The axial length was 24.42 mm in OD. An examination revealed visual acuity of hand motions OD and 20/40 OS. The anterior segment examination showed a well-centered “in-the-bag” IOL OU. The intraocular pressures were normal. Dilated fundus examination of the right eye showed hazy view due to pigment and old hemorrhage in the vitreous cavity. A total RD was noted with a stiff retina and a break with rolled edges around the 7 o’clock position (Fig. 3). The left eye was normal except for atrophic macular degeneration, without any lattice or round holes. A 25-g vitrectomy, encircling scleral buckle, laser, and 14% C3F8 gas procedure was performed the following day. Intraoperatively, a round retinal hole without an associated lattice was noted in the inferotemporal quadrant (Fig. 4). The retina was successfully reattached intraoperatively but redetached due to proliferative vitreo-retinopathy. Repeat surgery consisting

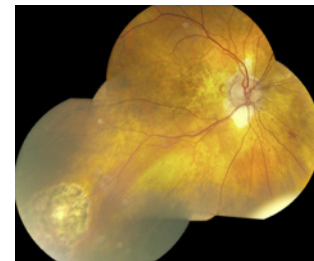


Fig. 2. Fundus photograph of Case 1 three months post op showing well-lasered retinal break at inferotemporal periphery.

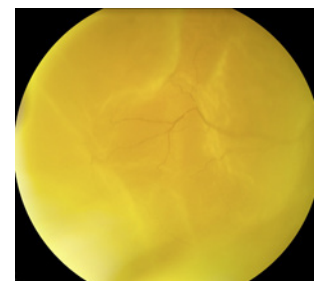


Fig. 3. Preoperative fundus photograph of OD of Case 2 showing hazy vitreous and detached retina. The causative break is not visible in this photograph.

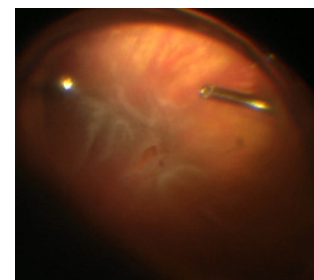


Fig. 4. Intraoperative photograph of OD of Case 2 showing a round peripheral retinal defect with rolled edges.

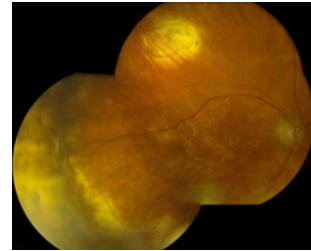


Fig. 5. Case 2. Ten months after second surgery showing attached retina.

of 25-g PPV, membrane peel, localized retinectomy, and silicone oil injection was performed 6 weeks after initial surgery resulting in retinal reattachment. Ten months after the second surgery, his pinhole vision was 20/400 with good buckle height and laser (Fig. 5). His neovascular AMD has remained quiescent without any further injections over the past 10 months.

Discussion

Retinal tears and detachment are rarely reported but well-known complications of IVT injections. Meyer et al. [6] reported 5 cases of RD 2–6 days after 35,942 IVT injection with an estimated incidence of 1 in 7,188. All injections were performed in the operating room under topical anesthesia with a 30-g needle introduced obliquely by experienced surgeons 3.5–4 mm behind the limbus using calipers for marking. Four of 5 patients were myopic. Retinal tears were identified in the same quadrant as that of injection in 2 eyes. The relationship between the location of tear (superonasal in 1, inferotemporal in 1, and unknown in 1), and the injection site was not available for the remaining 3 eyes. The retinal breaks were tears as opposed to holes in each case. The authors concluded that precise placement of a small (<30-g) needle 3.5–4 mm behind the limbus and tunneled insertion to avoid vitreous incarceration with resulting traction may minimize the risk of RD following IVT injections.

Karabag et al. [7] reported 3 cases of retinal tears or detachments after 3,907 IVT injections (1 in 1,300 injections). Injections were performed in the operating room with sterile drape and lid speculums 3.5 (pseudophakic) to 4 mm (phakic) posterior to limbus. All breaks occurred in the inferotemporal quadrant, the location of IVT injections. However, 1 eye had history of posterior capsular rupture during cataract surgery 2 months prior to developing a RD. The second patient developed a retinal tear in the untreated fellow eye 1 year after developing a RD in the first eye likely indicating pre-existing predisposition to retinal breaks.

Storey et al. [8] reported 24 cases of RD following 180,671 IVT injections (1 in 7,532 injections) [8]. A retinal break was located in the quadrant of the injection site in 62.5%. All injections were performed in office and only 3 of 36 (8%) physicians used calipers or tip of a 1-mL syringe to measure the injection site. Approximately, 20% of patients showed preoperative proliferative vitreo-retinopathy. The nature of retinal breaks (tears vs. holes) was not provided. Although no association was noted between measuring the injection site versus not measuring regarding the occurrence of retinal detachment, this retrospective study involving only 24 cases of RD was likely underpowered to detect such an outcome.

Current US guidelines for IVT injections recommend injecting 3.5 mm behind the limbus in pseudophakic and 4 mm in phakic eyes [3]. An injection site that is too anterior risks lens or ciliary body damage [9, 10] and too posterior injection risks damage to vitreous base, ora serrata, or even retina [11]. Potential for retinal injury also exists if the needle is inserted obliquely in a posterior direction. A 2011 survey of US retina specialists revealed that 424/765 (56%) respondents measured the injection site from the limbus and 96% injected straight, as

opposed to tunnel, into the vitreous cavity [12]. A recent survey, however, showed that only 86/281 (31%) US physicians measured the distance from the limbus ($p < 0.00001$ compared to 2011 survey) [13]. The reason for this decline in measuring in the USA is not clear but may involve lack of Level 1 evidence for measuring, complacency due to the perception of IVT injections as commonly performed simple office procedures, and/or need for expediency in view of an ever increasing volume of IVT injections.

Iatrogenic retinal penetration has been reported after retrobulbar or peribulbar block [14], scleral buckle surgery [15], strabismus surgery [16], botulinum toxin injection for strabismus [17], acupuncture [18], and recently by electromyography electrodes placed for neurophysiologic monitoring during intracranial surgery [19]. While some of them can result in VH, subretinal hemorrhage, retinal tear, or RD, many are asymptomatic [16]. It is, therefore, plausible that some cases of iatrogenic retinal penetration following IVT injections might remain undiagnosed.

Despite our careful search these appear to be the only cases of inadvertent retinal penetration following IVT injections. We find diminishing use of calipers or a suitable marking device in the USA particularly concerning. Castroviejo calipers may not be practical for a high-volume office-based procedure due to their cost and inconvenience associated with cleaning, sterilization, and storage. However, the backend of Alcon MIVS trocar (Alcon, Ft Worth, TX, USA) can be autoclaved in the same pouch as an eyelid speculum and used off-label as a measuring device and is readily available to most of us free of cost [20]. There is a need for further evolution of evidence-based guidelines for IVT injection technique that further enhance patient safety.

Statement of Ethics

This study was performed according to the tenets of the Declaration of Helsinki and Health Insurance Portability and Accountability Act of 1996. Both patients provided their informed written consent for this publication. The Institutional Review Board approval was not required for this retrospective case series involving 2 eyes.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

K.K. performed surgery on the subjects and contributed to the creation and editing of the manuscript. D.M. and K.H. contributed to the literature review and editing of the manuscript.

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