

Intravitreal Silicone Oil Droplets after Multiple Avastin Injections



Brenton Kinker JD¹, Asheesh Tewari MD^{1,3} and Joaquin Tosi^{1,2,3}

¹School of Medicine, Wayne State University, USA

² Health Sciences Center, University of New Mexico, USA

³Kresge Eye Institute, Wayne State University, USA

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***Corresponding author:** Brenton Kinker JD, School of Medicine, Wayne State University, 1301 Orleans Str. Apt 715E, Detroit, USA,
Email: bkinker@gmail.com

Abstract

A 77 year old man presented with worsening vision and a history of diabetic retinopathy with previous intravitreal injections. Fundus examination showed diabetic macular edema in the right eye and bilateral moderate non proliferative diabetic retinopathy. It was decided to start treatment with the anti-Vascular Endothelial Growth Factor Bevacizumab (Avastin®). After multiple Avastin injections in OD, fundus examination revealed previously unobserved silicone oil bubbles in the eye. Patient denied noticing any visual interference from the silicone bubbles, and continued receiving his scheduled Avastin injections with close monitoring. Silicone oil accumulation in this patient may be the result of the lubricant used in the syringes during his intravitreal injections. These silicone oil droplets have persisted in the patient's vitreous chamber, though their long term effects are unknown. Further studies are needed to assess the long term safety of silicone oil accumulation secondary to intravitreal injections.

Keywords: Silicone oil; Avastin; Bevacizumab; Lucentis; Eylea; Droplet; Injection; Intraocular; Intravitreal; Bubbles; Syringe

Introduction

Intravitreal injection use has increased markedly with the discovery of agents that can hinder the progression of many vascular endothelial growth factor (anti-VEGF)-mediated diseases, including choroidal neovascularization, diabetic macular edema (DME), diabetic retinopathy and retinal venous occlusive disease. There are many procedure-related complications of intravitreal injections, including damage to the lens, sterile and infectious endophthalmitis, retinal tears, retinal detachment, intraocular inflammation and vitreous hemorrhage. We report a case of intravitreal silicone oil bubbles found in the eye of a patient after receiving multiple Avastin injections.

Case Report

A 77 year old man with a history of hypertension, type 2 diabetes mellitus, deep vein thrombosis and pulmonary embolism on anticoagulation medication presented with gradually progressing loss of vision in his right eye. His ophthalmologic history is significant for right sided cataract removal, bilateral primary open angle glaucoma treated

with Dorzolamide-Timolol and Bimatoprost, moderate non-proliferative diabetic retinopathy (Figure 1 & 2) and diabetic macular edema requiring multiple Avastin injections.

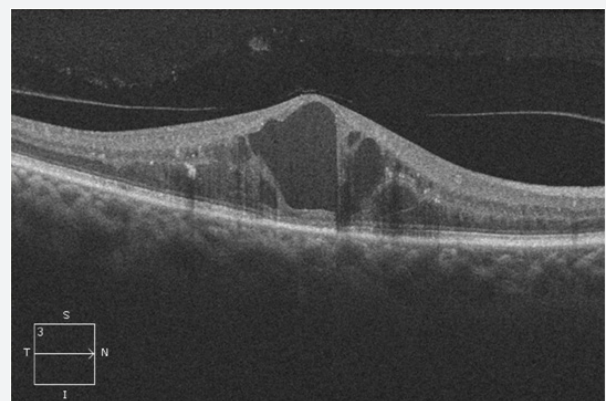


Figure 1: OCT showing central cystic changes due to diabetic macular edema, with secondary disorganization of the sensory retinal layers. Note also the vitreomacular adhesion (VMA).



Figure 2: Fluorescein Angiogram of right eye. Note the periferoveolar focal laser scars, diffuse leakage causing DME and increased foveal avascular zone (FAZ) due to macular ischemia.

Evaluation revealed visual acuity of 20/4000D and 20/200S, and intraocular pressure was 11mmHg OD and 13mmHg OS. Dilated fundus examination revealed right sided macular ischemia and diabetic macular edema, along with bilateral, moderate nonproliferative diabetic retinopathy. During the retina exam, silicone oil bubbles in the vitreous cavity were noticed as seen in Figure 3. The patient’s right diabetic macular edema was treated with an Avastin 1.25mg/0.5ml injection. Upon follow-up 4 weeks later, the patient reported vision improvement in his right eye to 20/200 so it was decided to continue with Avastin injections to attain the resolution of his diabetic macular edema. Patient denied awareness of silicone bubbles on his vision test. Given that no visual deficits or pathology were identified, no further interventions were warranted, and patient continued with his previous schedule of care.



Figure 3: Fundoscopic view of right eye. Note the silicone oil droplet on the retinal surface.

Discussion

Macular edema secondary to microaneurysms is the primary mechanism by which vision loss occurs in diabetic retinopathy [1]. Current treatment options include intravitreal injections of anti-VEGF agents, steroids, and laser management. Steroids

induced glaucoma, and the limitations of using laser treatment in parafoveal microaneurysms favor the use of anti-VEGF agents such as Bevacizumab (Avastin), Ranibizumab (Lucentis) and Aflibercept (Eylea) [2].

Avastin injection formulations do not contain silicone oil. Rather, silicone oil is a syringe lubricant, which may eventually build up in the eyes of patients undergoing numerous injections. Certain staked-on syringe designs may increase the risk of silicone oil accumulation, while other luer syringes may lessen this risk. In a study by Scott et al. [3] staked-on syringe and luer designs were compared for silicone oil residues in the eye after Triamcinolone Acetonide injections. In patients receiving only luer cone syringe injections, no silicone oil droplets were found, while the patients receiving injections only with staked-on syringes were found to have silicone oil droplets in 44% of the cases examined. These results were attributed to a 50µL residual space in the needle hub which “squeegeed” silicone oil from the needle as the plunger was pushed down. Others have estimated oil expulsion on the plunger tips of disposable staked-on syringes at around 24% of the silicone lubricant [4] with between 0.15mg and 0.25mg of silicone oil ejected after three plunger pushes to expel air droplets [5].

Handling of syringes may also be a factor, especially the repackaging, shipping, and handling of injectables. A study by Liu et al. [6] found that freeze-thawed samples of injectable Bevacizumab, along with samples that were mechanically disturbed (via dropping of package), led to large increases in intravitreal silicone oil findings. The authors posited that the plastic syringes into which Bevacizumab is often repackaged were not designed to deliver intra-ocular injections, with looser parameters for the silicone oil lubricant.

Although intraocular silicone oil has been associated with a number of ocular diseases in larger volumes, the effects of smaller volumes has not yet been sufficiently studied. Relatively small injections may induce keratopathy, movement of silicone oil into the anterior chamber, and emulsification [7]. However, larger amounts may lead to elevated post-surgical intraocular pressure, pupillary block, angle closure with pupillary block, and idiopathic closed-angle glaucoma. Long-term intraocular silicone oil exposure may be associated with optic nerve damage, including demyelination and vacuoles, along with retinal damage [8]. These changes are associated with the larger volumes of oil used in retinal surgeries, but have yet to be found in the smaller volumes used in intra-ocular injections.

Silicone oil may also have pharmacokinetic effects, slowing down bevacizumab distribution to ocular tissues in rabbit eyes [9]. Indeed, the efficacy of a number of drugs (e.g. insulin) may be compromised by silicone oil. Although it is unlikely that the relatively small volumes of silicone oil in intra-ocular injections would produce detectable effects, care should be taken when monitoring patient progress.

Conclusion

This case illustrates the rare yet predictable potential for intraocular silicone oil buildup following multiple Avastin injections. Recognition of the risk factors for intravitreal silicone oil accumulation and close monitoring following injections may foreclose the risk of potential negative side effects.

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