Case report

Chronic retinal detachment and neovascular glaucoma after intravitreal stem cell injection for Usher Syndrome

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1. Introduction

The hype in stem cell treatment for numerous medical disorders has caused a surge in “stem cell” clinics in the United States and internationally. Those clinics offer unproven and unregulated “stem cell” therapies without the oversight of regulatory agencies, such as the U.S. Food and Drug Administration (FDA). Although there are ongoing FDA-regulated clinical trials studying the use of stem cell technology for ocular diseases, no FDA-approved stem cell treatments exist for any ocular conditions. Here, we report a case of neovascular glaucoma (NVG) following intravitreal injection of autologous adipose tissue-derived “stem cell” performed in the Dominican Republic by a U.S. licensed family medicine physician for the treatment of retinitis pigmentosa.

1.1. Case report

A 42-year-old Nicaraguan female was diagnosed at the Bascom Palmer Eye Institute (BPEI) with retinitis pigmentosa. Her best-corrected visual acuity was 20/70 OD and 1/200 OS. Five months later the patient elected to undergo autologous adipose tissue-derived stem cell injection (AASCI) in her left eye in the Dominican Republic by a family medicine doctor licensed in Florida. Prior to intravitreal injection, the patient’s best-corrected visual acuity (BCVA) was 1/200. The patient experienced decreased vision gradually over a 3-month period. The patient presented with no light perception (NLP) vision with a total funnel retinal detachment, as well as hyphema, iris neovascularization, and nearly 360° posterior synechiae of the iris to the lens capsule. The patient suffered from ocular pain with an intraocular pressure (IOP) of 37 mm Hg. Transcleral cyclocryocoagulation was performed. The IOP was 6 mm Hg six weeks after treatment and the patient was pain free.
2. Discussion

Autologous adipose tissue-derived stem cell injection has been increasing in frequency and is a growing trend in the United States due to a surge in the number of for-profit “stem cell” clinics.\(^1\) In a phase one/two clinic trial, stem cell transplantation of retinal pigment epithelial cells led to improvement of vision and vision-related quality of life measures for Stargardt’s disease and age-related macular degeneration.\(^2\) However, no stem cell therapy has been approved by the FDA for any ocular conditions at this time. Despite FDA statements on the need for oversight and warnings to consumers, multiple “stem cell” clinics in the United States and around the world continue to offer unproven treatments.\(^3\)

Retinal detachment following sub-retinal injection of autologous bone marrow-derived stem cells was first reported by Leung et al., in 2016 on a patient with Stargardt’s macular dystrophy.\(^1\) Boudreault et al. reported a case of peribulbar stem cell injection in a patient with retinitis pigmentosa that resulted in central retinal artery occlusion and subsequently led to severe vision loss.\(^4\) In 2017, Kuriyan et al. reported a case series of six eyes in three patients who were treated at a “stem cell” clinic in Florida for macular degeneration. These patients developed profound vision loss ranging from 20/200 to no light perception after treatment. Five out of 6 injected eyes developed a combined tractional/rhegmatogenous retinal detachment with proliferative vitreoretinopathy in a delayed manner ranging from 3 days to 38 days. One eye resulted in retinal atrophy.\(^5\) Saraf et al. reported similar complications in a patient who underwent bilateral intravitreal injection of stem cell in Georgia for macular degeneration.\(^7\) Rong et al. reported similar complications in a patient who underwent intravitreal autologous adipose-tissue derived stem cell injection in his right eye for retinitis pigmentosa.

To our knowledge this is the first reported case of a patient developing glaucoma after intravitreal injection of autologous adipose tissue-derived stem cell injection for Usher syndrome associated retinitis pigmentosa. Diagnosis of uveitis-glaucoma-hyphema (UGH) syndrome was also considered. At initial presentation it was not clear whether the patient had inflammatory or red blood cells in the anterior chamber. On subsequent examination, the acute pathology appears to have been hemorrhage from neovascularization in the setting of a chronic retina detachment. UGH syndrome arises from repetitive mechanical iris trauma by a malpositioned or subluxed intraocular lens (IOL).\(^10\) Patient was phakic and ultrasonography did not suggest such a lens malposition.

Neovascular glaucoma is frequently observed in patients with ischemic diseases such as diabetic retinopathy, central retinal vein occlusion, central retinal artery, sickle-cell retinopathy, and retinopathy of prematurity. One can postulate in this case that the injection of “stem cells” may have caused a retinal artery or vein occlusion, which subsequently resulted in neovascularization secondary to ischemia. Cells and flare at initial presentation is likely a result of inflammatory response to the adipose stem cell injection. Chronic inflammation is also another stimulus for neovascularization.

Another postulated mechanism is that “stem cells” may settle on the retinal surface and differentiate improperly into myofibroblast-like cells which may increase oxygen demands, inducing ischemic microvascular changes which subsequently leads to neovascularization, in addition to tractional retinal detachment. As for the mechanism behind delayed tractional detachment, Kuriyan et al. proposed “stem cells” themselves form tractional scaffolds rather than the injection technique causing retinal detachment, especially since retinal detachment was often delayed and time is needed for cellular proliferation. “Stem cells” that may improperly differentiate into myofibroblast-like cells may produce contractile membranes similar to proliferative vitreoretinopathy.\(^5\)

3. Conclusions

The prevalence of “stem cell” clinics is a rising trend in the United States and around the world.\(^5\) Although there have been advances in treatment of macular degeneration and Stargardt’s macular dystrophy
using human embryonic stem cell-derived retinal pigment epithelium, the poor outcome and the “stem cell” clinic direct-to-consumer advertisement for therapies without FDA oversight is concerning. Improved patient education on evidence-based treatments as well as the danger of undergoing unproven therapy such as “stem cell” injection is important to decrease the incidence of complications from stem cell transplantation.

Patient consent

The patient consent for research is included in the Bascom Palmer Eye Institute general consent as well as surgery consent.

Declaration of competing interest

The authors declared that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2020.100647.

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