



Case report

Complication associated with intravitreal injection of tissue plasminogen activator for treatment of submacular hemorrhage due to rupture of retinal arterial macroaneurysm

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ABSTRACT

Purpose: To report the possible complications of intravitreal injection of tissue plasminogen activator (t-PA) for the treatment of submacular hemorrhage associated with retinal arterial macroaneurysm (RAM).

Observations: A 75-year-old man complained of a sudden diminution of visual acuity in his left eye. Fundus examination of this eye revealed rupture of a RAM (0.5 disc diameters (DD) in size), submacular hemorrhage and hemorrhage under the internal limiting membrane (ILM). The patient had untreated hypertension and his systolic blood pressure was over 200 mmHg. Intravitreal injection of t-PA (42,000 units/0.07 ml) was given 1 day before undergoing vitrectomy. On the following day, the fundus was no longer visible because of a dense vitreous hemorrhage. After performing vitrectomy to remove the dense vitreous hemorrhage, we confirmed a marked increase in subretinal hemorrhage, and seemed to have markedly enlarged the macroaneurysm (6 DD). In addition, macular hole was found to have occurred. One week after surgery, the macular hole closed. Four months after surgery, best-corrected visual acuity improved from 20/400 to 20/40.

Conclusions and Importance: Untreated hypertension and the use of t-PA can cause re-ruptured RAM and deterioration of subretinal hemorrhage. In this case, a macular hole was also occurred. Since there are risks of various complications, it is necessary to be careful in the use of t-PA for RAM.

1. Introduction

Although intravitreal injection of tissue plasminogen activator (t-PA) and gas in patients placed in a postoperative face-down position is a commonly used treatment for subretinal hemorrhage secondary to age-related macular degeneration or retinal arterial macroaneurysm (RAM), there are also many reports of complications when using this technique.^{1–5} Breakthrough vitreous hemorrhage is one of the common complications observed when using this procedure.^{2,3} Furthermore, enlarged submacular hemorrhages with dense vitreous hemorrhage and macular hole have also been noted after administering an intravitreal injection of t-PA.^{4,5} We report a case of macular hole and deterioration of a subretinal hemorrhage with dense vitreous hemorrhage after an intravitreal injection of t-PA.

2. Case report

A 75-year-old man developed sudden vision loss in his left eye 6 days prior to his first visit to our hospital. Best-corrected visual acuity

(BCVA) of his left eye was 20/400. Fundus examination of this eye revealed rupture of the RAM, submacular hemorrhage and hemorrhage under the internal limiting membrane (ILM). This macroaneurysm was 0.5 disc diameters (DD) in size, and located in the upper temporal part of the macula. Fig. 1 showed the fundus photograph and the optical coherence tomography (OCT) image at the first visit. Although macular traction existed, macular hole was not detected in the OCT image (Fig. 1B). After being hospitalized on the following day, blood pressure measurements showed that he had untreated hypertension, with a systolic blood pressure over 200 mmHg. On the same day, he was started on an oral antihypertensive medication (amlodipine besilate 5 mg), with an intravitreal injection of t-PA (alteplase; 42,000 units/0.07 ml) given on the day prior to the vitrectomy. On day of the operation (the day after the t-PA injection), the patient's vision had decreased to hand motion, and his fundus was no longer visible due to a dense vitreous hemorrhage. Pars plana vitrectomy was performed. After using 25G pars plana vitrectomy to remove the dense vitreous hemorrhage, we confirmed a marked increase in subretinal hemorrhage and re-ruptured RAM, and the RAM seemed to be enlarged to 6 DD (Fig. 2A).

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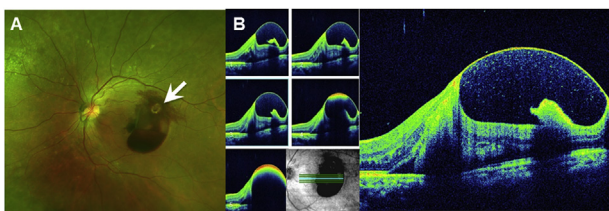


Fig. 1. Fundus photography and optical coherence tomography finding at the first visit. There were the rupture of the retinal arterial macroaneurysm (solid arrow; 0.5 disc diameters), submacular hemorrhage and hemorrhage under the internal limiting membrane formed nivoau (A). Although the macular traction was present, there was no macular hole (B).

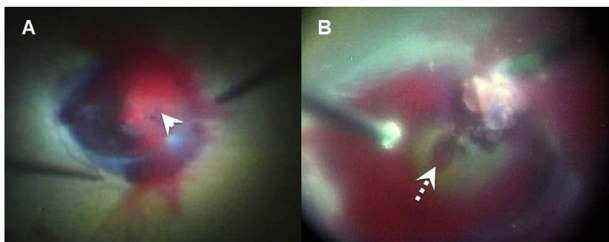


Fig. 2. Intraoperative fundus photographs. After vitrectomy to remove the dense vitreous hemorrhage, re-raptured RAM surrounded with hematoma (arrow head; 6 disc diameters) was detected along with a marked increase in the subretinal hemorrhage (A). After removal of the internal limiting membrane (ILM) and aspiration of the sub-ILM blood, macular hole (dashed arrow) was revealed (B).

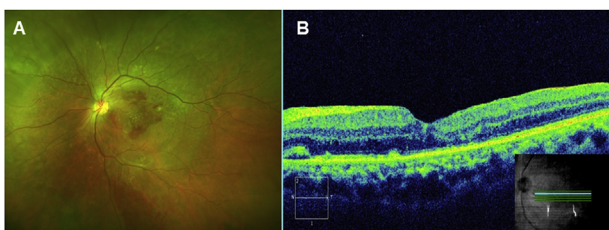


Fig. 3. Fundus photography and optical coherence tomography finding at 1 month after surgery. There was no hemorrhage under the fovea (A), the macular hole had closed (B).

These were Removal of the ILM and aspiration of the sub-ILM blood aspirated using a silicone-tipped extrusion cannula revealed a macular hole (Fig. 2B). Due to the presence of macular hole, the subretinal blood was completely removed, followed by performing air and sulfur hexafluoride (SF6) gas tamponade. The patient continued to maintain an intermittent facedown position for 7 days. One month after surgery, there was no hemorrhage under the fovea, the macular hole had closed, and his visual acuity was 20/125 (Fig. 3). Five months after the surgery, the patient's visual acuity had improved to 20/40.

3. Discussion

Heriot¹ was the first to describe the treatment of submacular hemorrhage by administering an intravitreal injection of t-PA and pneumatic displacement of the subfoveal hemorrhages. This simple procedure provides a high anatomic success rate with few complications. However, Kokame² reported two cases of severe vitreous hemorrhage that occurred at 1 day after an intravitreal injection of SF6 gas with t-PA in eyes with submacular hemorrhage associated with RAM. Mizutani et al.³ also reported that t-PA should not be recommended for ruptured RAM, due to a higher incidence of subsequent vitreous hemorrhage. Thus, the need for t-PA remains controversial. Furthermore, there have also been some studies that have reported finding macular

hole formation after the rupture of a RAM.^{4,5} Sagara et al.⁵ suggested that the presence of subretinal and sub-ILM hemorrhages after the rupture of a RAM might contribute to the formation of macular hole. In our case, it was speculated that hemorrhage at first visit expanded by re-rupture and caused macular hole.

Although the ability of intravitreal t-PA to penetrate through the ILM and into the subretinal space is controversial, our current case suggests that t-PA was able to penetrate the ILM to the level of the RAM. Previous experimental work in the rabbit, which does not have a foveal region and has a thinner ILM in the fovea as compared to humans, showed that the injection of molecules as large as t-PA (70 kD) into the vitreous cavity could not penetrate the ILM or the subretinal space.⁶ Although severe vitreous hemorrhage was not noted in our current case prior to the t-PA injection, we noted sub-ILM hemorrhage. Thus, sub-ILM hemorrhage could have potentially allowed increased intraretinal penetration of the intravitreal t-PA via the macular hole and displacement of the ILM, thereby predisposing the eye to the potential complication of increased bleeding from the retinal macroaneurysm. Moreover, our patient was also found to have had untreated hypertension. Thus, our findings suggest that various factors were all related to the complications seen in this patient, eg, the use of t-PA and untreated hypertension overlap caused re-raptured RAM, the increase of sub-ILM hemorrhages strengthened traction, and the macular hole was occurred. Furthermore, because there is a possibility to occur macular hole, we thought that it is necessary to pay close attention to use of t-PA for ruptured RAM.

Patient consent

Written informed consent for the treat was recieved from the patient. Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Conflicts of interest

All authors have no financial disclosures.

Authorship

All authors attest to satisfying the ICMJE criteria for Authorship.

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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.2019.100556>.

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