

## **TREATING SUBMACULAR HEMORRHAGE WITH INTRAVITREAL tPA INJECTION AND PNEUMATIC DISPLACEMENT**

### **ABSTRACT:**

*Background:* This report describes the clinical outcome in an adult male with spontaneous submacular hemorrhage who underwent successful intravitreal tPA injection and pneumatic displacement. *Case Presentation:* A 30 yr old male patient presented with complaints of sudden painless diminution of vision in left eye since one day. The vision on presentation was Hand Movements +. Fundus showed a submacular hemorrhage with breakthrough vitreous hemorrhage. Injection tPA (25 $\mu$ g in 0.05 mL) and pure sulfur hexafluoride (SF6, 0.3 mL) was injected into the vitreous cavity. After surgery the patient was instructed to maintain a prone position. This was followed by a vitrectomy after 2 weeks. Postoperatively, patient had significantly improved having an unaided vision of 6/9P in the left eye which improved to 6/6 on correction. *Conclusion:* Intravitreal tPA and pneumatic displacement using pure SF6 is an effective treatment for submacular hemorrhage.

Key Words: Submacular Hemorrhage, Pneumatic Displacement, tPA, SF6 Gas

### **INTRODUCTION:**

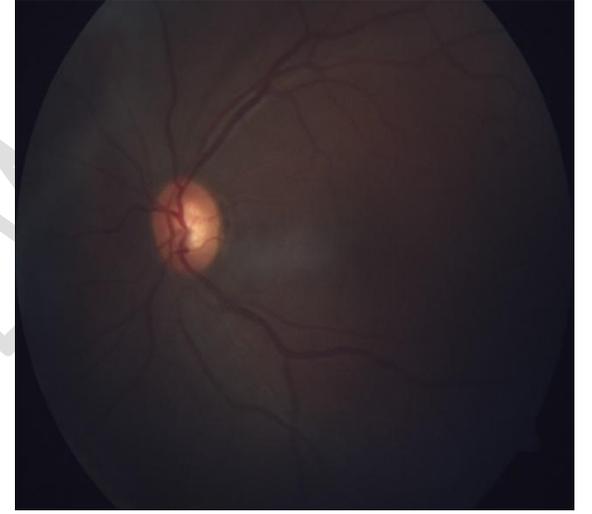
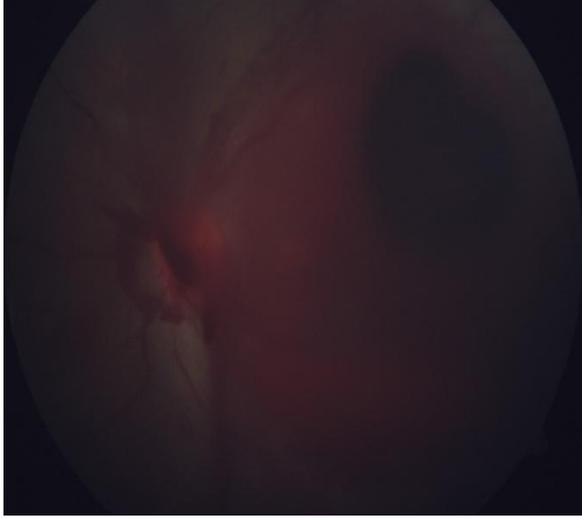
**Submacular hemorrhage** (SMH) is a term which describes a condition characterized by the presence of blood in the potential space between the retinal pigment epithelium and the neurosensory retina in the macular region. It occurs in several conditions,

but most commonly is associated with age-related macular degeneration, presumed ocular histoplasmosis, high myopia, retinal arterial macroaneurysm, angoid streaks and trauma. SMH is a sight threatening condition requiring urgent attention. [1]

In 1996, Herriot reported a technique for treating submacular hemorrhage using intravitreal tissue plasminogen activator (tPA) and gas injection. [2] We used this procedure with vitrectomy to good result in a young patient with spontaneous submacular hemorrhage.

### **CASE PRESENTATION:**

A 30 yr old male patient was referred to us from a local hospital with complaints of sudden painless diminution of vision in left eye since one day. There was no history of trauma or any systemic illness. The vision on presentation was Hand Movements + in Left Eye and 6/6 in Right Eye. The Anterior Segment examination was normal and intraocular pressure was 10mmHg OS. Fundus showed a hemorrhage in the submacular area with breakthrough vitreous hemorrhage (Figure 1). B Scan of the left eye showed a submacular hemorrhage, vitreous hemorrhage and retina was attached. Paracentesis (0.3 mL) was done under local anaesthesia to reduce the intraocular pressure. Next, tPA (25 $\mu$ g in 0.05 mL) was injected into the vitreous cavity and we waited 15 minutes for the hemorrhage to dissolve. Then a further paracentesis (0.1 mL) was done, followed by injection of pure sulfur hexafluoride (SF<sub>6</sub>, 0.3 mL) into the vitreous cavity. After surgery, the patient was instructed to maintain a prone position. This was followed by a vitrectomy after 2 weeks. Intraoperatively, a retinal break was identified at 12 o'clock position which was lasered. 3 weeks postoperatively, patient had significantly improved (Figure 2), macula was intact (Figure 3), having an unaided vision of 6/9P in the left eye which improved to 6/6 on correction.

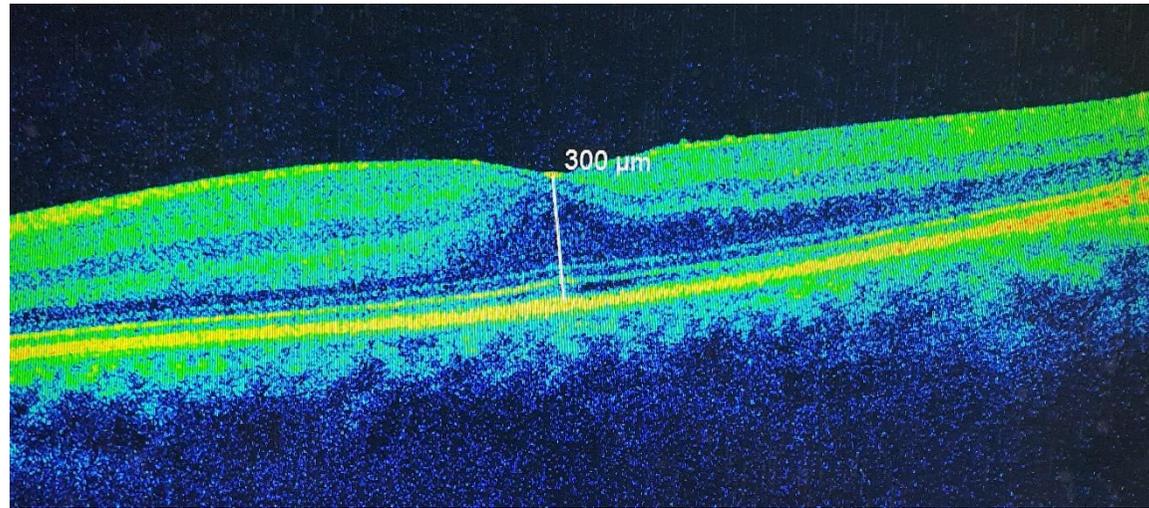


UNDER PEER REVIEW

Figure 1: Fundus image showing submacular hemorrhage and breakthrough vitreous hemorrhage

Figure 2: Postoperative Fundus image

Figure 3: Postoperative OCT image showing intact macula



## DISCUSSION

Submacular hemorrhage is an accumulation of blood between the neurosensory retina and the Retinal Pigment Epithelium (RPE) arising from the choroidal or retinal circulation. The most common etiology is Choroidal Neovascularization in patients with Age Related Macular Degeneration. VEGF present in CNV may cause opening of capillary fenestrae increasing permeability and risk of

bleeding. The other causes include High myopia, Trauma, Angoid Streaks, Ocular Histoplasmosis, Retinal Macroaneurysms, Sickle Cell Disease, Coagulopathies, Central Retinal Vein Occlusion, Diabetic Retinopathy, Inflammation of the retina/ choroid, Idiopathic.[1,2,3]

The patient presents with sudden, profound, painless loss of central vision with metamorphopsia.

The mechanism by which subretinal blood damages the overlying neurosensory retina may be explained as there is disruption of the connections between the RPE and photoreceptor cells which inhibits the normal diffusion between them leading to rapid photoreceptor atrophy. Contraction of the fibrin clots lead to shear stress on the attached retina forming scars and fibrovascular proliferations. Iron derived from hemoglobin may have a toxic effect on the outer layers of the retina.[3,4,5]

A Submacular hemorrhage is a vision threatening condition that requires treatment by clot removal on an urgent basis. Retrospective reports of the natural history of SMH demonstrated poor prognosis.[6] Without treatment, SMH usually end up with poor final vision.

Tissue plasminogen activator (tPA) is a serine protease with fibrin-specific thrombolytic activity that forms a complex with fibrin to activate plasminogen to plasmin which then cleaves fibrin and dissolves the clot. Advantages include decreased fibrin-mediated photoreceptor damage, early lysis allowing earlier removal of hemorrhage and shorter duration of toxic and barrier effect of blood on retina.[3,7]

There has been some doubt with regard to whether intravitreal tPA is able to penetrate into the subretinal space in sufficient quantities to induce clot liquefaction Coll et al. reported that intravitreal injection of tPA can penetrate the subretinal space via the intact rabbit retina and promote lysis of blood clots that have been present under the retina for 24 hours.[9,10,11] Boone et al. demonstrated that subretinal clots were partially liquefied 24 hours after administration of intravitreal tPA in a pig model.[12]

In 1996, Herriot introduced a simple technique using intravitreal tPA injection to liquefy the subretinal blood clot and long-acting intravitreal injection of expansile gas in combination with postoperative face-down positioning to displace the submacular hemorrhage pneumatically. This technique reported a high anatomic success rate with few complications. [2,4,5,8]

Goldman et al. reported that pneumatic displacement using SF<sub>6</sub> gas improved visual acuity in a 25yr patient with traumatic submacular hemorrhage.[13] Holland and Wiechens reported that pneumatic displacement using tPA (50 µg per 0.1 mL) and SF<sub>6</sub> gas was an effective treatment for traumatic submacular hemorrhage in a 37-year-old man.[14] Tsuyama et al. reported displacement of submacular hemorrhage and improvement in final visual acuity of a 10yr old boy with traumatic macular

hemorrhage using pneumatic displacement using tPA (12.5  $\mu$ g in 0.05 mL) and 0.3 mL of pure sulfur hexafluoride gas injection in the vitreous.[15]

Other treatment modalities include Intravitreal injection of Anti-Vascular Endothelial Growth Factor drugs , Pneumatic displacement without tissue plasminogen activator, Vitrectomy and removal of the clot or the subretinal neovascularization, Photodynamic therapy, Macular translocation.

The prognosis of submacular hemorrhage depends on various factors including thickness, size and extend, underlying pathology (e.g CNV, choroidal rupture, pathological myopia) , time and mode of intervention.[3,7,9,12]

### **Conclusion**

In conclusion, pneumatic displacement is an effective and simple treatment for submacular hemorrhage. However, this is a single case report, and a prospective randomized controlled trial in a larger number of patients would be needed to assess the benefit of this technique in the management of patients with submacular hemorrhage of various etiologies.[6,7,12]

### **CONSENT:**

Written informed consent for publication was obtained from the patient

### **ETHICAL CLEARANCE:**

Authors have obtained ethical approval from Institutional Ethical Committee.

### **REFERENCES:**

- [1] Abdelkader E, Yip KP, Cornish KS, "Pneumatic displacement of submacular haemorrhage," Saudi Journal of Ophthalmology, vol 30, 221–226, 2016.
- [2] W. J. Herriot, Intravitreal Gas and TPA: An Outpatient Procedure for Submacular Hemorrhage, AAO Annual Vitreoretinal Update, Chicago, Ill, USA, 1996.

- [3] Hochman MA, Seery CM, Zarbin MA, "Pathophysiology and Management of Subretinal Hemorrhage" Survey of Ophthalmology Vol 4'2. Number 3 | Nov-Dec1997
- [4] L. Hesse, "Treating subretinal hemorrhage with tissue plasminogen activator," Archives of Ophthalmology, vol. 120, no. 1, pp. 102–203, 2002.
- [5] S. Doi, S. Kimura, Y. Morizane et al., "Successful displacement of a traumatic submacular hemorrhage in a 13-year-old boy treated by vitrectomy, subretinal injection of tissue plasminogen activator and intravitreal air tamponade: a case report," BMC Ophthalmology, vol. 15, article 94, 2015.
- [6] L. Hesse, J. Schmidt, and P. Kroll, "Management of acute submacular hemorrhage using recombinant tissue plasminogen activator and gas," Graefe's Archive for Clinical and Experimental Ophthalmology, vol. 237, no. 4, pp. 273–277, 1999.
- [7] L. Hesse, B. Schroeder, G. Heller, and P. Kroll, "Quantitative effect of intravitreally injected tissue plasminogen activator and gas on subretinal hemorrhage," Retina, vol. 20, no. 5, pp. 500–505, 2000.
- [8] S.-N. Chen, T.-C. Yang, C.-L. Ho, Y.-H. Kuo, Y. Yip, and A.N. Chao, "Retinal toxicity of intravitreal tissue plasminogen activator: case report and literature review," Ophthalmology, vol.110, no. 4, pp. 704–708, 2003.
- [9] H. Lewis, S. C. Resnick, J. G. Flannery, and B. R. Straatsma, "Tissue plasminogen activator treatment of experimental subretinal hemorrhage," American Journal of Ophthalmology, vol. 111, no.2, pp. 197–204, 1991.
- [10] C. J. Hrach, M. W. Johnson, A. S. Hassan, B. Lei, P. A. Sieving, and V. M. Elner, "Retinal toxicity of commercial intravitreal tissue plasminogen activator solution in cat eyes," Archives of Ophthalmology, vol. 118, no. 5, pp. 659–663, 2000.
- [11] G. E. Coll, J. R. Sparrow, A. Marinovic, and S. Chang, "Effect of intravitreal tissue plasminogen activator on experimental subretinal hemorrhage," Retina, vol. 15, no. 4, pp. 319–326, 1995.

- [12] D. E. Boone, H. C. Boldt, R. D. Ross, J. C. Folk, and A. E. Kimura, "The use of intravitreal tissue plasminogen activator in the treatment of experimental subretinal hemorrhage in the pig model," *Retina*, vol. 16, no. 6, pp. 518–524, 1996.
- [13] D. R. Goldman, R. A. Vora, and E. Reichel, "Traumatic choroidal rupture with submacular hemorrhage treated with pneumatic displacement," *Retina*, vol. 34, no. 6, pp. 1258–1260, 2014.
- [14] D. Holland and B. Wiechens, "Intravitreal r-TPA and gas injection in traumatic submacular hemorrhage," *Ophthalmologica*, vol. 218, no. 1, pp. 64–69, 2004.
- [15] Tsuyama T, Hirose H, Hattori T, "Intravitreal tPA Injection and Pneumatic Displacement for Submacular Hemorrhage in a 10-Year-Old Child" Hindawi Publishing Corporation, *Case Reports in Ophthalmological Medicine*, Vol 2016, Article ID: 9809583