LETTER TO THE EDITOR

To the Editor

Retinal and Choroidal Haemorrhage after Tissue Plasminogen Activator Administration

Keywords: Ischemic stroke, tissue plasminogen activator, retinal haemorrhage, choroidal haemorrhage, computed tomography, thrombolysis

In Canada, stroke ranks as a leading cause of disability. Effective therapies now exist for the treatment of ischemic stroke, and therefore rapid assessment and early management are critical. Patients presenting within a 4.5-hour window of symptom onset should be considered for treatment with intravenous tissue plasminogen activator (t-PA).[1] Timely administration of t-PA results in better patient outcomes.[2]

The major risks associated with intravenous t-PA include intracranial haemorrhage, major systemic haemorrhage including urinary and gastrointestinal haemorrhage, and hemilingual angioedema.[3] Intraocular haemorrhages are not part of the routine discussion of t-PA-associated risk in ischemic strokes due to the rarity of these events. Vitreo-retinal haemorrhage has been reported in an 84-year-old male with a history of type II diabetes mellitus with diabetic retinopathy, hypertension, dyslipidemia, and bilateral cataracts[4] who was treated with t-PA for stroke. The patient was left with only light perception in the affected eye. Intraocular haemorrhages have also been described with t-PA use in the context of acute myocardial infarction (MI).[5,6] One patient within the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO)–I trial developed a choroidal haemorrhage with t-PA use.[7] Retinal and choroidal haemorrhages have also been reported after administration of reteplase for an acute MI in a 66-year-old male with hypertensive retinopathy.[8] As far as we can tell, after an extensive literature review, there are no documented cases of retinal or choroidal haemorrhage in patients without known retinal disease after t-PA administration for an acute ischemic stroke.

Thrombolysis can be a life-saving intervention, resulting in dramatic functional independence in patients with an acute ischemic event. The unfortunate side effect of retinal and choroidal haemorrhage is not routinely discussed due to its low prevalence, but it can create a large burden and have a severe functional impact on patients and their well-being.

Herein we describe what we believe to be the first case of a left-sided retinal and choroidal haemorrhage leading to impaired vision, post-intravenous t-PA administration for an acute ischemic stroke in a patient without known retinal disease.

An 81-year-old female presented to the emergency department after developing sudden-onset left facial droop, as well as left arm and left leg weakness. She did not have any documented history of vascular risk factors. She was known to have had a cataract removed from the left eye 10 years previously but had no known retinal disease.

Her vital signs were stable, apart from an elevated blood pressure (210/122 mmHg). Her physical exam was consistent with a right hemispheric stroke, and the Acute Stroke Protocol was activated. An urgent computed tomography (CT) scan of the head showed no evidence of acute infarction (Figure 1). Her blood pressure was managed with a labetolol infusion, and she was treated with intravenous t-PA as per protocol after consent was obtained.

Following the administration of the t-PA, the patient remained neurologically and hemodynamically stable. A 24-hour repeat CT showed a new left intraocular haemorrhage (Figure 2). There was no evidence of new stroke or intracranial haemorrhage. After informing the patient of the CT findings, she mentioned that she was experiencing "cloudy" vision in her left eye, which was new for her. Her visual fields were full to confrontation.

Throughout her hospital stay, her left arm and leg weakness improved significantly, but she continued to experience what she described as "a cloud" in her left eye. Ophthalmology was consulted to rule out any possible underlying pathology that could have predisposed her to bleeding. Her visual acuity at near distances was determined to be 6/30 (20/100) in her left eye and 6/21 (20/70) in her right eye. Intraocular pressures were normal at 17 mmHg bilaterally. Posterior pole examination revealed both a retinal and a choroidal haemorrhage in the infranasal quadrant of the left eye. Other investigations were negative. Her visual deficit persisted throughout her stay on the neurology stroke service. She was eventually able to ambulate independently with the aid of a two-wheel walker and was subsequently transferred to a restorative care service to undergo further physiotherapy, prior to being discharged home.

Following an extensive search of the literature, we found one previously reported case of a retinal haemorrhage due to t-PA in a patient presenting with an acute ischemic stroke. That patient had a history of bilateral retinopathy secondary to diabetes, which does represent an underlying pathological process that could predispose to haemorrhage. To our knowledge, our case

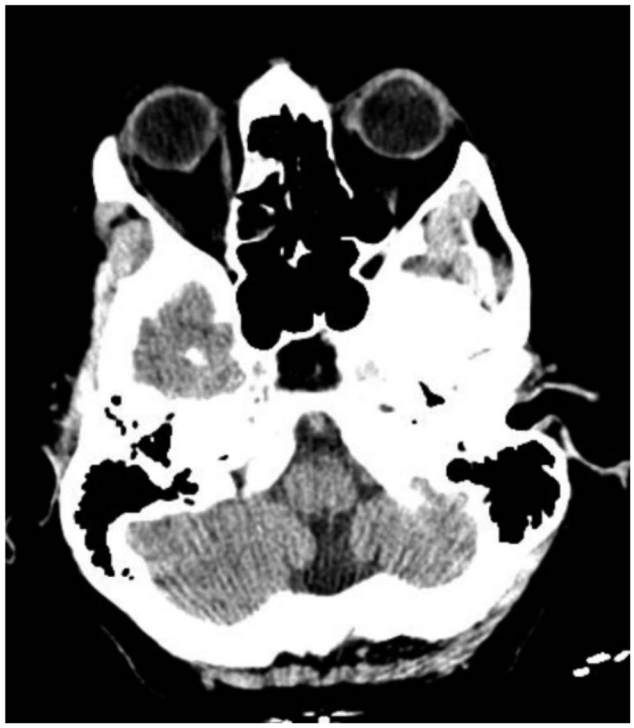

Figure 1: *Initial non-contrast head CT, prior to t-PA.*

https://doi.org/10.1017/cjn.2017.35 Published online by Cambridge University Press

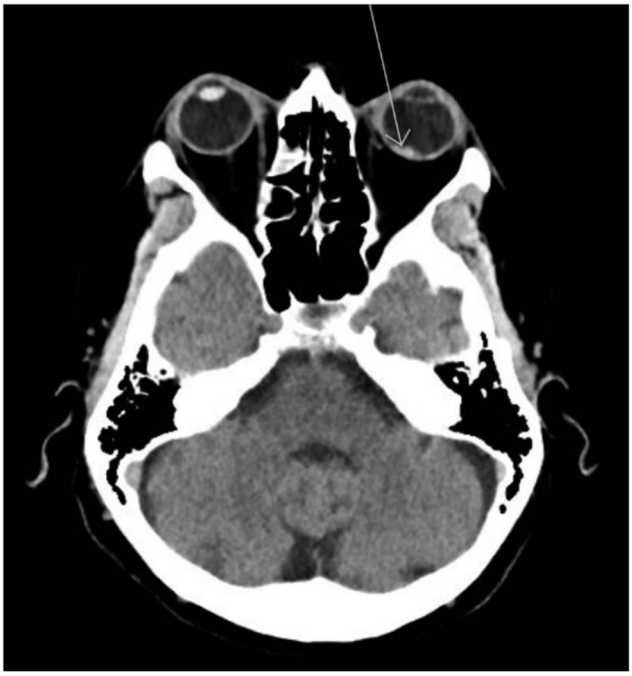

Figure 2: *Follow-up non-contrast head CT, 24 hours post t-PA, showing a new left intraocular haemorrhage.*

represents the first documented case of a patient without underlying retinal disease suffering retinal and choroidal haemorrhages following t-PA administration for treatment of an acute ischemic stroke. Our case report, in combination with the aforementioned reports, lends support for the relationship between t-PA and intraocular haemorrhage.

There are known significant bleeding risks with t-PA. These should be routinely discussed with patients or their substitute decision makers prior to t-PA administration. While an intraocular haemorrhage is not life-threatening, it can result in severe functional impairment in patients, particularly if they do not recover their vision. It may be reasonable to include intraocular haemorrhage as one of the possible adverse effects associated with t-PA in acute ischemic stroke.

Disclosures

None of the authors have any conflicts of interest to disclose.

Statement of Authorship

Dr. Scott Lee was the primary author. He obtained informed consent from the patient presented, reviewed her medical information, and conducted a literature review. He also completed the first draft of the article.

Dr. Harald Gjerde saw the patient in ophthalmology clinic. He obtained the visual diagnostic information. He also completed the ophthalmology section of the case report, conducted a literature review and provided edits to the completed article.

Dr. Gordon Gubitz was the attending physician to the patient on the neurology service. He was also the supervisor for the article, providing revisions and guiding its presentation.

Scott Lee
Department of Medicine, Dalhousie University
Halifax, Nova Scotia, Canada
Email: sdlee@dal.ca

Harald Gjerde
Department of Ophthalmology and Visual Sciences, Dalhousie University Halifax, Nova Scotia, Canada

Gordon Gubitz
Assistant Professor, Division of Neurology, Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

References

1. Casaubon LK, Boulanger JM, Blacquiere D, et al. Canadian Stroke Best Practices Recommendations: Hyperacute Stroke Care Guidelines, Update 2015. Int J Stroke. 2015;10(6):924-40. Epub ahead of print Jul 6. Available at: http://journals.sagepub.com/doi/pdf/10.1111/ijs.12551.
2. Emberson J, Lees KR, Lyden P, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014; 384(9958):1929-35. Epub ahead of print Aug 5. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4441266/.
3. Miller D, Simpson J, Silver B. Safety of thrombolysis in acute ischemic stroke: a review of complications, risk factors and newer technologies. Neurohospitalist. 2011;1(3):138-47. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3726129/.
4. Hormese M, Wichter M. Vitreo-retinal hemorrhage after thrombolysis in a patient with acute ischemic stroke: a case report. Front Neurol. 2012;3:71–3. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3347041/pdf/fneur-03-00071.pdf.
5. Barsam A, Heatley, Herbert L. Spontaneous suprachoroidal hemorrhage secondary to thrombolysis for the treatment of myocardial infarction. Clin Exp Ophthamol. 2006;34(2):177-9.
6. Berry C, Weir C, Hammer H. A case of intraocular hemorrhage secondary to thrombolytic therapy. Acta Ophthalmol Scand. 2002;80(5):561-2. Available at: http://onlinelibrary.wiley.com/doi/10.1034/j.1600-0420.2002.800522_1.x/full.
7. Mahaffey K, Granger C, Toth C, et al. Diabetic retinopathy should not be a complication to thrombolytic therapy for acute myocardial infarction: review of ocular hemorrhage incidence and location in the GUSTO–I trial. Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries. J Am Coll Cardiol. 1997;30(7):1610-6. Available at: http://www.sciencedirect.com/science/article/pii/S073510979700394X?np=y&npKey=d771fdb8812c6de43346b0cd0e6f1e557a2789cac855ef9cd2dea0c3829a3dde.
8. Kaba RA, Cox D, Lewis A, et al. Intraocular haemorrhage after thrombolysis. Lancet. 2005;365(9456):330. Available at: http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(05)17788-5.pdf.

https://doi.org/10.1017/cjn.2017.35 Published online by Cambridge University Press