

# Treatment of Post-Traumatic Trabecular Mashwork Thrombosis and Secondary Glaucoma with Intracameral Tissue Plasminogen Activator in Previously Unrecognized Sickle Cell Anemia

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## ABSTRACT

*Intracameral tissue plasminogen activator (t-PA) application in a child with previously unrecognized sickle cell anemia, post-traumatic hyphema, thrombosis in trabecular mashwork and consecutive acute glaucoma showed positive results. Thirteen year-old boy, son of African father and Caucasian mother, was admitted to hospital, with symptoms of acute glaucoma and partial hyphema after right eye trauma. Visual acuity of affected eye was 0.5 and intraocular pressure (IOP) 46 mm Hg. Despite a common therapy three days later clinical condition of patient's right eye was getting worst. Visual acuity was only hand motion (HM) and IOP 53 mmHg. At this point rose suspicion of sickle cell disease (SCD) and decision about injecting t-PA (20 µg) into anterior chamber was made. Cytological examination of aqueous humor revealed 10% sickled erythrocytes. Hemoglobin electrophoresis discovered hemoglobin S so that diagnosis of SCD was confirmed. Intraocular application of t-PA showed excellent results in post-traumatic hyphema with trabecular mashwork thrombosis in the patient with sickle cell anemia. Two-years follow up confirmed permanent normalisation of IOP and visual acuity. Successful outcome with anterior chamber paracentesis and intracameral injection of t-PA is promising novel approach, which we recommend in treatment of post-traumatic hyphema in SCD.*

**Key words:** sickle cell anemia, t-PA, thrombosis, glaucoma, treatment

## Introduction

Sickle cell disease is inherited hematological disorder characterized with sickle cell hemoglobin (Hb S), which differs from the normal only by one amino acid substitution in the  $\beta$ -chain of hemoglobin (Hb $\beta^S$ ), resulting with less flexible sickle red blood cells (SS RBCs)<sup>1</sup>. Sickle cell anemia is a recessive disease characterized with sickling of the red cells under reduced oxygen tension. The major cause of morbidity and mortality in sickle cell disease (SCD) is vascular occlusion. Episodic occurrence of vasoocclusive events precipitate with acute painful episodes leading to organ failure and death. The severity of SCD increases with higher leukocyte count because of their adherence to vascular endo-

thelium facilitating vasoocclusion. The ophthalmic manifestations of SCD are present in various segments of the eye, i. e. conjunctiva, iris, retina and optic nerve. After traumatic hyphema patients with SCD tend to have more severe ophthalmic complications, such as glaucoma and vasoocclusive retinopathy leading to retinal detachments and vitreous hemorrhages<sup>2</sup>. Sickling phenomenon and consecutive thrombosis may cause obstruction of trabecular mashwork and increased IOP.

Most reports about traumatic hyphema indicate prevalence of 70% or greater in pediatric population, and the average duration of the uncomplicated hyphema is 5 to 6 days<sup>3</sup>. Usually, traumatic hyphema is successfully

treated topically with mydriatics and antibiotics. There is no consensus regarding use of systemic antifibrinolytic agents, indications for hospitalization, or timing for surgical intervention in management of traumatic hyphema<sup>4</sup>. Clinical benefit of so far used therapy is questionable. Up to date intracameral injection of t-PA seems to be safe and effective method for the treatment of unresolved total hyphema and several studies indicates the promising features of this drug. However, to our knowledge, intracameral application of t-PA in treatment of post-traumatic hyphema in patients with SCD was not recorded yet.

### Case report

A previously healthy 13-year-old boy, born in marriage of African father and Caucasian mother, was admitted to our department 4 hours after being accidentally hit in the right eye by handball. He complained of headache, right eye pain, photophobia and epiphora. His father died of heart attack when he was 36-year-old.

Slit lamp examination of the affected eye revealed ciliary injected conjunctiva, corneal edema with 2 mm hyphema, marked aqueous cells and flare, and irregular and enlarged pupil with poor light reflex reaction. Visual acuity of the same eye was 0.5 and IOP amounted to 46 mmHg (normal < 18 mmHg). Detailed fundus examination was not possible because of corneal edema. Results of diagnostic work-up, which included a complete blood count, electrolytes, urine analysis, x-ray and computed tomography of the orbit, were unremarkable.

Traumatic hyphema, iritis and secondary glaucoma of the right eye were diagnosed. Initial treatment included topical and subconjunctival steroids, topical timolol, oral acetazolamide, and systemic 10% mannitol. Despite the treatment, three days later affected eye developed total hyphema with IOP of 53 mm Hg and visual acuity of only hand motion (Figure 1). Suspicion of sickle cell anemia rose according to clinical condition, boy's background (African) and therapy failure.



Fig. 1. Post-traumatic total hyphema of the right eye.

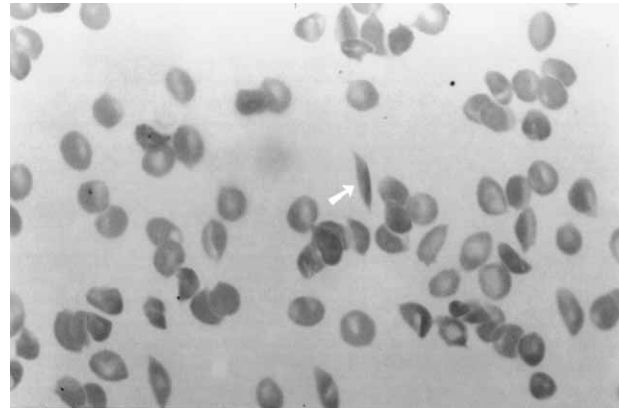


Fig. 2. Photomicrograph of aqueous humor (May-Grunwald, Giemsa, x100). Arrow indicates erythrocyte from hyphema with alteration in sickle cell shape.

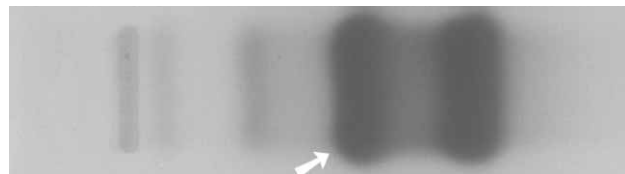


Fig. 3. Hemoglobin electrophoresis on cellulose acetate at pH 8.6 following staining with Ponceau-S. Arrow indicates prominent band for HbS trait.

At this point, anterior chamber lavage and partial evacuation of blood clot were performed in order to evacuate hyphema and 20 µg of t-PA were injected to dissolve the clot rest. After the surgery transcorneal oxygen therapy was applied, as well as 1000 ml of 0.9% NaCl with 5% glucose solution per day. Surgery temporarily decreased IOP and ameliorated symptoms, but the day after IOP rose again and persisted at high levels (≈ 30 mmHg). However, only partial hyphema remained (1 mm) with anterior chamber cells and flare present.

The surgical procedure was repeated four days later. During paracentesis aqueous humor with hyphema was aspirated and a cytological examination of the specimen was done. Fresh and stained preparations of aqueous humor have revealed that 10% of erythrocytes from hyphema were sickle cells (Figure 2). In the meantime hemoglobin electrophoresis revealed hemoglobin S (Figure 3). After second surgery IOP normalized, cornea became completely clear, corneal edema resolved, cell and flare in the anterior chamber were negative, while the pupil remained irregular. Fundus examination revealed normal optic nerve disc, two peripheral retinal blot hemorrhages, and peripheral retinal artery occlusions with ischemical lesions at 5, 6 and 11 hours. Visual acuity was 1.0.

Folic acid, acetylsalicylic acid and vasodilators (verapamil) were included in therapy in occasion of patient's discharge from hospital. On later controls the patient continued to feel well, and his IOP remained normal as well as his vision. Examination, 24 days after injury,

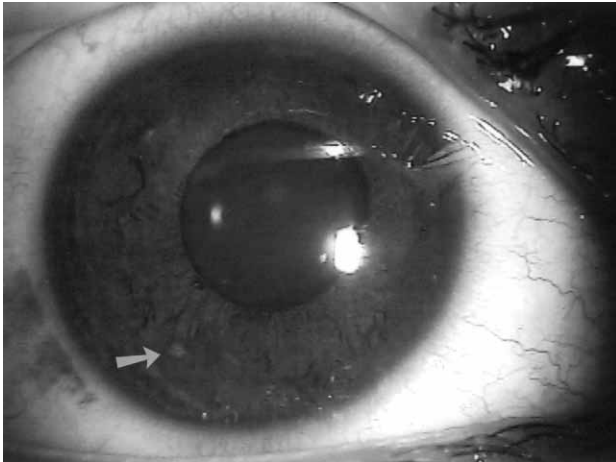


Fig. 4. Right eye after treatment, arrow indicates partial iris atrophy.

showed partial iris atrophy, for which we believed to be secondary to the vasoocclusive process in the iris (Figure 4). Sickle cell retinopathy remained unchanged for first three months, but follow-up after four months showed normal retina with no signs of retinal artery occlusions.

On the beginning pattern visual evoked potentials (VEP) of the right eye have shown normal P 100 wave amplitude and elongated latency (116.6 ms), but four months later, the latency normalized. Visual field was normal all the time. Two-years follow up confirmed permanent normalization of IOP, visual acuity, and fundus findings.

## Discussion

Sickle cell anemia has to be considered in differential diagnosis of hyphema when it is combined with increased IOP. Although peripheral blood examination of our patient did not show sickle red cells, 10% of red cells from hyphema in the anterior chamber had sickle cell shape. All that points out how important is to perform cytological examination of aqueous humor when complications of traumatic hyphema occur.

Successful outcome with anterior chamber paracentesis and intracameral injection of t-PA is our promising novel approach, which we highly recommend in treatment of post-traumatic hyphema in SCD. Tissue plas-

minogen activator is a fibrin specific fibrinolytic and potent thrombolytic agent that has been shown to be effective in accelerating the clearance of fibrin clots from anterior chamber. The results in five eyes with post-traumatic total hyphema (in patients without SCD) suggest that t-PA is a useful addition in managing of total hyphema<sup>5,6</sup>.

The management of traumatic hyphema has been controversial for many years. Several double-masked studies clearly establish the value of systemic aminocaproic acid (ACA) in prevention of recurrent hemorrhages<sup>7</sup>, but we still have unanswered questions whether the therapy of hyphema with antifibrinolytics is as effective in children as in adults, in white patients as in black, and in patients with normal hemoglobin as well as in those with sickle cell hemoglobinopathies<sup>8</sup>. Accordingly to present experience we can conclude that application of antifibrinolytics is contraindicated for blocking the cloth lysis in patients with hyphema and SCD.

Our experience did not confirm what some authors described that transcorneal oxygen therapy could reduce intraocular pressure in patients with SCD and glaucoma caused by hyphema<sup>9</sup>. Hyphemas in patients with sickle cell hemoglobinopathies, whether traumatically or surgically induced, may have devastating effects on the eye. Early anterior chamber paracentesis may be the best treatment for this type of hyphema induced secondary glaucoma<sup>10</sup>. Complications of traumatic hyphema include increased IOP, peripheral anterior synechiae, optic atrophy, corneal bloodstaining, secondary hemorrhage, and accommodative impairment<sup>11</sup>. In addition, occlusions of retinal blood vessels are the initiating event in sickle cell retinopathy, which in its advanced form may be complicated by preretinal neovascularization, vitreous hemorrhage, and retinal detachment<sup>12</sup>. In our case acetylsalicylic acid and vasodilators improved reperfusion of the peripheral retinal vessels.

The fact that acute chest syndrome is a leading cause of death among patients with SCD<sup>12</sup>, it can be presumed that our patient's father also had SCD that unfortunately was unrecognized and therefore untreated.

Knowing that SCD may cause blinding or sight-threatening damage to the retina or optic nerve, we can conclude that an appropriate screening and management of those patients are very important public health issues, which can guarantee them satisfactory quality of life.

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## **LIJEČENJE TRABEKULARNE TROMBOZE I SEKUNDARNOG GLAUKOMA TKIVNIM AKTIVATOROM PLAZMINOGENA KOD RANIJE NEPREPOZNATE ANEMIJE SRPASTIH STANICA**

### **S A Ž E T A K**

Intrakamerularna primjena tkivnog aktivatora plazminogena (t-PA) djelovala je povoljno na posttraumatsku hifemu, trombozu trabekuluma i sekundarni glaukom kod dječaka sa ranije neprepoznom anemijom srpastih stanica (ASS). Trinaestogodišnji dječak, mulat, je hospitaliziran zbog akutnog glaukoma i djelomične hifeme nakon traume desnog oka. Vidna oštrina iznosila je 0.5 a intraokularni tlak (IOT) 46 mmHg. Nakon tri dana, usprkos uobičajnoj terapiji, klinička slika se pogoršala. Vidna oštrina bila je mahanje ruke a IOT 53 mmHg. Tada je postavljena sumnja na ASS i 20 µg t-PA je injicirano u prednju sobicu. Citološka analiza sobne vodice dokazala je prisutnost srpastih eritrocita (10%). Elektroforezom hemoglobina (Hb) potvrđena je prisutnost HbS i tako je potvrđena dijagnoza ASS. Intraokularna primjena t-PA dala je zadovoljavajuće rezultate kod posttraumatske hifeme sa trabekularnom trombozom u pacijenata sa ASS. Pacijent je bio praćen naredne dvije godine te je stalno imao normalan IOT i vidnu oštrinu. Stoga uspješno liječenje paracentezom i intrakamerularnom aplikacijom t-PA je novost koju preporučamo u liječenju posttraumatske hifeme u pacijenata oboljelih od ASS.