# A Case with Acute Angle Closure Glaucoma Misdiagnosed as Herpetic Keratouveitis

*Tulay SIMSEK[1], Onur OZALP[2]*

**ABSTRACT**

Findings of acute glaucoma crisis was detected in a patient who previously diagnosed as a glaucoma secondary to herpetic keratouveitis and given medical treatment in an another facility. The patient was receiving treatment for herpes virus infection in addition to maximum anti-glaucomatous treatment. The biomicroscopic examination, gonioscopy, and anterior segment optical coherence tomography imaging were considered as acute glaucoma crisis due to primary angle closure and the treatment was re-arranged accordingly. Intraocular pressure was decreased while corneal edema was resolved by treatment; thus, YAG laser iridotomy was performed on day 4. Here, acute angle closure glaucoma diagnosis, differential diagnosis and treatment were discussed in the context of a case with acute angle closure glaucoma misdiagnosed as herpetic keratouveitis.

**Key Words:** Angle closure glaucoma, Herpetic keratouveitis, Laser iridotomy, Pilocarpine.

## INTRODUCTION

Glaucoma is a leading cause of blindness worldwide and it is estimated that glaucoma affects approximately 60 million people. Patients with primary angle closure glaucoma (PACG) accounts for one-third of all glaucoma cases and one-half of patients developed blindness secondary to glaucoma. Primary angle-closure is defined as the closure of the anterior chamber angle appositionally or synechially with the periphery of the iris. The angle closure can be prevented in patients who were identified before synechial angle closure.[1]

Uveitis is another cause of glaucoma. Approximately 5% of adult uveitis cases are secondary to Herpes virus infection. In cases with Herpes simplex-related disciform keratouveitis or stromal ulcer, inflammation occurring trabecular region can increase intraocular pressure (IOP) due to edema and occlusion of trabecular network.[2-5] In particular, the IOP is extremely high in disciform endotheliitis. In addition, there may be findings similar to angle closure such as corneal edema, keratic precipitates in endothelium, iris atrophy and dysmorphic pupils; thus, it may be confused with acute angle closure in rare occasions.[6]

Here, we discussed diagnosis, differential diagnosis and management of acute PACG in the context of a patient who was referred to our clinic with the diagnosis of treatment-resistant herpetic keratouveitis from another hospital but diagnosed as acute primary angle closure glaucoma and treated successfully in our clinic.

## CASE REPORT

A 63-years old woman without known systemic disease and medication presented to an ophthalmology outpatient clinic of another hospital with complaints of watery eye and pain in left eye. The patient was considered as ocular infection and a topical agent was prescribed. However, the patient presented to same center with persistent complaints 2 weeks after first visit. In the second visit, the patient was considered as herpetic keratouveitis based on ocular examination and valacyclovir (oral tablet, 1x500 mg) and ganciclovir (topical gel, 1x1) and dexamethasone (eye drop, 3x1). However, 3 days after second visit, the

1- MD., Prof., Eskisehir Osmangazi University Faculty of Medicine Department of Ophthalmology, Eskisehir, Turkey

2- MD., Eskisehir Osmangazi University Faculty of Medicine Department of Ophthalmology, Eskisehir, Turkey

**Received:** 20.08.2018
**Accepted:** 14.02.2020
*Glo-Kat 2020; 15: 189- 193*
DOİ: 10.37844/glauc.cat.2020.15.33

**Correspondence Adress:**
Tulay SIMSEK
Eskisehir Osmangazi University Faculty of Medicine Department of Ophthalmology, Eskisehir, Turkey
**Phone:**
**E-mail:** tulaysimsek@hotmail.com

patient presented to a second medical center due to lack of regression in her complaints and she was referred to our clinic with initial diagnosis of herpetic keratouveitis and trabeculitis based on ocular findings including corneal edema and fix, dilated pupil in left eye and IOP reaching up to 47 mmHg.

At presentation to our clinic, corrected visual acuity was found to be full (with +1.00) in right eye while finger counting at 20 cm in left eye. Refractive the value could not be recorded in left eye. The in biomicroscopic examination, there was mild nuclear sclerosis with narrow anterior chamber at periphery in right eye while hyperemic conjunctiva, edematous cornea, the mid-dilated and irregular pupil, occasional atrophy and pupillary margin of iris and narrow anterior chamber in left eye. In the fundus examination, cup: disc (CD) ratio the was found as 0.3 in the right eye and 0.7 in the left eye. The IOP was measured as 11 mmHg in the right eye and 40 mmHg in the left eye. Corneal sensitivity was detected in both eyes.

Anterior segment OCT, retinal nerve fiber layer thickness and ganglion cell complex analysis were performed, corneal thickness was measured. Gonioscopic examination could not be performed in the left eye due to corneal edema while appositional angle closure was detected in the right eye. On OCT, both eyes were considered as having narrowed angle (Figure 1). Thus, patient was considered as acute angle closure and treatment with brimonidine tartrate plus timolol maleate combination (eye drop, 2x1), pilocarpine HCl %2 (eye drop, 2x1), fluorometholone 5% (eye drop, 3x1) and acetazolamide (oral tablet, 2x1) was initiated. A single dose intravenous mannitol (20%, 300 cc) was given. Ganciclovir and valacyclovir were withdrawn.

The IOP was reduced to 26 mmHg in the left eye and corneal edema was regressed. YAG laser iridotomy (YAG Li) was performed in both eyes on the 4th day (right eye for prophylactic purposes). The anterior chamber angle was found to be open in the anterior segment OCT which performed after medical treatment and YAG Li. (Figure 2).

The IOP was measured as 18 mmHg after laser iridotomy. The patient was discharged by dexamethasone (eye drop, 1x1), pilocarpine HCl %2 (eye drop, 2x1), brimonidine tartrate plus timolol maleate combination (eye drop, 2x1) and acetazolamide (oral tablet, 2x1). Follow-up visits were also scheduled.

In the control visit on week 2, oral acetazolamide was withdrawn. After then trabeculectomy was performed due to IOP measurement of 36 mmHg in the second follow-up visit.

## DISCUSSION

Although multiple mechanisms are involved in the acute angle closure glaucoma, it most commonly occurs due to disruption of humor aqueous circulation as are result of pupillary blockade in eyes with narrow angle which are predisposed to angle closure.[1, 7, 8]

The most widely accepted clinical classification for angle closure includes pre-clinical stage, attack stage, intermittent stage, chronic stage and absolute stage.[9] The attack stage includes two types as mild and acute severe attacks. In mild attack, there may be complaints such as blurred vision, mild redness and pain at nasal region resulting from slight elevation in IOP due to incomplete angle closure. The mild attacks are generally resolved following miosis with pilocarpine. In acute, severe attacks, IOP can be reach over 70 mmHg as a result of complete angle closure. Symptoms such as severe pain, marked decrease in vision, headache at attack site, nausea and vomiting can occur in the patients.

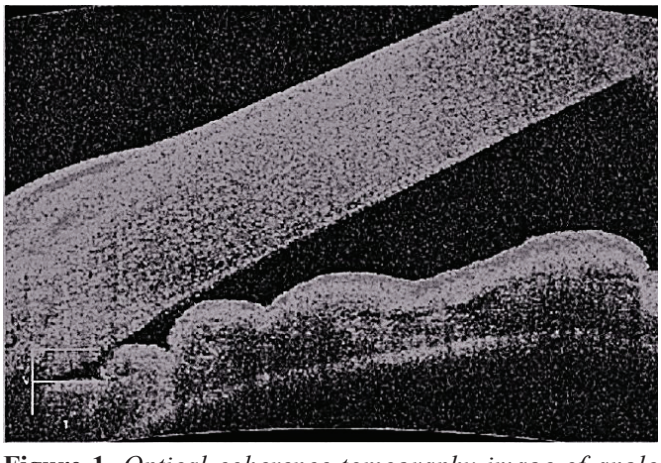

**Figure 1.** *Optical coherence tomography image of angle before pilocarpine therapy.*

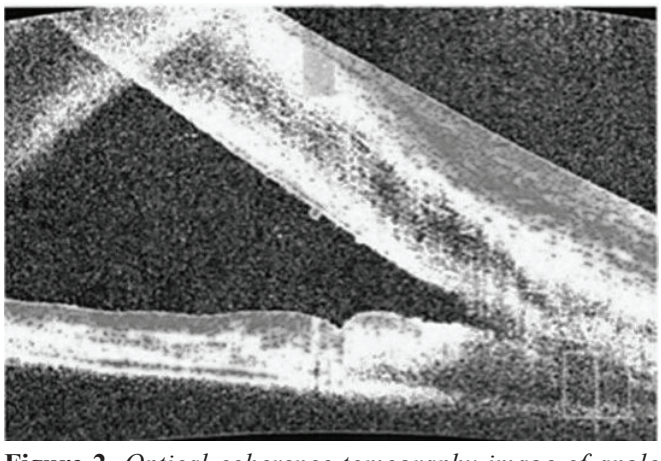

**Figure 2.** *Optical coherence tomography image of angle after pilocarpine therapy and laser iridotomy.*

Clinical findings include marked conjunctival hyperemia, corneal edema, fix, mid-dilated pupil, iris pigments of anterior chamber, cellular exudation and narrow anterior chamber.[9] In addition, pigmented precipitates at cornea, irregular iris atrophy and subcapsular opacities at anterior margin of lens termed as glaukomaflecken can also be seen.[7, 8]

Herpetic keratouveitis can be confused with attack stage of acute angle closure given the presence of corneal edema, mid-sized keratik precipitates in the corneal endothelium, atrophic areas in the iris and elevated IOP as it was the case in our patient. There may be reaction in anterior chamber in case of primary angle closure, mimicking acute uveitis; however, pupil is generally miotic in uveitis.[10]

In adults, Herpes viruses account for 5% of uveitis.[11] In herpetic uveitis, most common complication is uveitic glaucoma, which is typically unilateral and associated with open angle.[12] On contrary, acute angle closure glaucoma is generally bilateral with findings of angle closure at contralateral eye.[9] Thus, it is important to examine ocular angle in differential diagnosis. The frequency of secondary glaucoma is 10% in the herpetic keratouveitis.[12] In a study by Hoeksema et al., it was reported that secondary glaucoma developed within median 3.9 years after herpetic keratouveitis.[13] In our case, keratouveitis was excluded given the presence of glaucomatous optic disc appearance at index presentation and lack of previous history of keratouveitis-like attacks.

Uveitic glaucoma pathogenesis involves blockage of humor aqueous efflux due to trabeculitis and occlusion of trabecular network by inflammatory cells, which is supported by normalization of IOP by corticosteroids. IOP returns normal levels within 3-8 weeks by regression of inflammation.[6, 12] In our case, no regression was observed despite treatment directing herpetic keratouveitis over 2-3 weeks and IOP remained high. In uveitic glaucoma related to Herpes virus infection, open angle is seen in anterior chamber angle assessment if there is no anterior or posterior synechia or pupillary block. Iris atrophy at pupillary margin suggests Herpes simplex uveitis while wedge-like iris atrophy suggests Herpes zoster uveitis.[6] In acute angle closure glaucoma, there are irregular atrophic areas at iris due to ischemia, which are generally localized at margin of pupil and causes impaired pupillary morphology.[7]

To best of our knowledge, there is no herpetic keratouveitis case mimicking PACG although there are cases of simultaneous PACG and systemic Herpes virus infection and angle closure secondary to panscleritis in a case with suspected PACG. In a study by Halel et al., Herpes zoster infection involving T2 dermatome was detected and ciliary congestion, corneal edema, narrow anterior chamber and mid-dilated pupils were observed on day 5 of treatment. Treatment with systemic mannitol, oral acetazolamide, pilocarpine eye drop and dexamethasone was initiated in the patient and LI was performed on day 2 after initiation of treatment, which lowered IOP. Authors suggested that sympathetic discharge due to pain concurrent with Herpes infection, resulting in angle closure caused by mydriasis.[14] In the case report by Bashir et al., the patient was initially considered as primary angle closure; however, it was found that there was scleral tenderness, clear cornea, reactive pupil, limited ocular movements and deep anterior chamber in the contralateral eye despite presence of conjunctival chemosis, narrow anterior chamber and IOP elevation. Thus, the patient was diagnosed as angle closure secondary to panscleritis.[15]

One must keep angle closure glaucoma in addition to Herpes uveitis in case of corneal edema, elevated IOP level and presence of precipitates in cornea; biomicroscopic examination and anterior chamber the gonioscopy should have to be performed cautiously. In addition, gonioscopy in the contralateral eye provides important clues for differential diagnosis. In cases in which gonioscopy cannot be performed due to corneal edema, optical coherence tomography and sonographic biomicroscopy are helpful in the diagnosis. In biomicroscopic examination, conjunctival hyperemia, corneal edema and shallow anterior chamber as well as presence of pigmented precipitates, glaukomaflecken and irregular iris atrophy should suggest angle closure glaucoma and treatment should be started as soon as possible. IOP elevation, less pigmented precipitates in the area of corneal edema, open anterior chamber angle and presence of previous history of similar complaints should suggest herpetic keratouveitis and secondary glaucoma.

Treatment differs in acute angle closure glaucoma and herpetic uveitis-related secondary glaucoma. In acute angle closure glaucoma, first-line treatment modality is LI after resolution of inflammation and regression of corneal edema. Topical corticosteroids used to reduce inflammation until laser iridotomy prevent development of peripheral anterior synechia and preserve normal structure and functions of angle.[16] Topical pilocarpine preparations provide opening of angle by mechanically removing peripheral iris via miosis and a dramatic IOP reduction in acute angle closure glaucoma while they are contraindicated in herpetic keratouveitis as they aggravate inflammation.[17] In our patient, IOP was decreased after pilocarpine but it was re-increased thereafter. We attributed the increase in IOP to synechial closure resulting from prolonged attack stage. In addition to pilocarpine, timolol maleate- dorzolamide or timolol maleate-brimonidine

fixed combination, oral carbonic anhydrase inhibitors and hyper-osmotic agents are also used to reduce humor aqueous production. In the literature, it was reported that brimonidine contributes to pupillary miosis; thus, fixed combination including brimonidine ensure more effective IOP reduction in angle closure glaucoma.[18] Therefore, we preferred timolol maleate-brimonidine fixed combination in our patient. If medical treatment and LI fail to decrease IOP, argon laser peripheral iridoplasty, clear lens extraction alone or in combination with goniosynechialysis or trabeculectomy are alternative treatment modalities.[19] Although there are studies from Fareast that reported that clear lens extraction is effective in acute angle closure glaucoma, the effectiveness of the method is still unclear in Caucasians due to anatomical variations. It was reported that lens extraction alone is effective in controlling IOP in primary angle closure glaucoma but long-term outcomes haven't been established yet.[20] In a study comparing trabeculectomy and lens extraction, it was found that extent of synechial angle closure was significantly decreased following lens extraction.[21] Razeghinejad et al. reported that low IOP values are achieved by lens extraction in PACG regardless of peripheral anterior synechia; however, combination with trabeculectomy is preferred in advanced cases in clinical practice.[22] In a previous study, it was found that anterior chamber is more crowded with thicker lens in eyes with angle closure glaucoma, particularly in Japanese people.[23] There is no consensus on timing of clear lens extraction in acute angle closure glaucoma. Some surgeons recommend that it can be performed a few days after achieving relief in the attack in order to prevent peripheral anterior synechia it is widely accepted not to perform until complete resolution. However, of inflammation and corneal edema.[20] In addition, lens extraction can cause complications as a result of factors such as choroid expansion which is involved in attacks at early period.[24] Thus, we preferred trabeculectomy since IOP remained high despite LI and maximum medical therapy, which controlled IOP. In a previous study comparing trabeculectomy and phacoemulsification in angle closure glaucoma, it was found that the extent of IOP reduction was higher while need for anti-glaucomatous agents was lesser in trabeculectomy group compared to phacoemulsification group.[25]

In conclusion, acute angle closure can rarely be confused by disorders accompanied by corneal edema and IOP elevation such as herpetic keratouveitis. Detailed history, bilateral gonioscopy and clinical assessment are of important in the diagnosis. Although pilocarpine has a historical value, it should be kept in mind in the medical treatment of angle closure glaucoma.

## REFERENCES


1. Prum BE, Jr Herndon LW, Jr Moroi SE et al. Primary Angle Closure Preferred Practice Pattern((R)) Guidelines. Ophthalmology 2016;123:P1-P40.
2. Falcon MG, Williams HP. Herpes simplex kerato-uveitis and glaucoma. Trans Ophthalmol Soc U K 1978;98:101-4.
3. Johns KJ, O'Day DM, Webb RA, et al. Anterior segment ischemia in chronic herpes simplex keratouveitis. Curr Eye Res 1991;10 Suppl:117-24.
4. Teitelbaum CS, Streeten BW, Dawson CR. Histopathology of herpes simplex virus keratouveitis. Curr Eye Res 1987;6:189-94.
5. Townsend WM, Kaufman HE. Pathogenesis of glaucoma and endothelial changes in herpetic kerato-uveitis in rabbits. Am J Ophthalmol 1971;71:904-10.
6. Munoz-Negrete FJ, Moreno-Montanes J, Hernandez-Martinez P, et al. Current Approach in the Diagnosis and Management of Uveitic Glaucoma. Biomed Res Int 2015;2015:742792.
7. Sun X, Dai Y, Chen Y, et al. Primary angle closure glaucoma: What we know and what we don't know. Prog Retin Eye Res 2017;57:26-45.
8. Wright C, Tawfik MA, Waisbourd M, et al. Primary angle-closure glaucoma: an update. Acta Ophthalmol 2016;94:217-25.
9. Simsek T. Current Diagnosis and Management of Primary Angle Closure Glaucoma. Osmangazi Journal of Medicine 2018;40:90-100.
10. Sampaolesi R, Jogi R, Boyd S. In: Boyd S, Sampaolesi J, eds. Diagnostic Pearls in Glaucoma2014; v. 1.
11. Panek WC, Holland GN, Lee DA et al. Glaucoma in patients with uveitis. Br J Ophthalmol 1990;74(4):223-7.
12. Gedik Ş, Akova YA, Şanal Doğan A. Üveitik Glokomlar. Turkiye Klinikleri J Ophthalmol 2005;14:130-6.
13. Hoeksema L, Jansonius NM, Los LI. Risk Factors for Secondary Glaucoma in Herpetic Anterior Uveitis. Am J Ophthalmol 2017;181:55-60.
14. al Halel A, Hirsh A, Melamed S, et al. Bilateral simultaneous spontaneous acute angle closure glaucoma in a herpes zoster patient. Br J Ophthalmol 1991;75:510.
15. Bashir H, Sridhar U, Mazumdar S, et al. Panscleritis masquerading as an attack of primary acute angle closure glaucoma. GMS Ophthalmol Cases 2019;9:Doc31.
16. Emanuel ME, Parrish RK 2nd, Gedde SJ. Evidence-based management of primary angle closure glaucoma. Curr Opin Ophthalmol 2014;25:89-92.
17. Hung L, Yang CH, Chen MS. Effect of pilocarpine on anterior chamber angles. J Ocul Pharmacol Ther 1995;11:221-6.
18. Kim JM, Park KH, Kim CY, et al. Effects of brimonidine timolol fixed combination therapy on anterior ocular segment configuration. Jpn J Ophthalmol 2011;55:356-61.

19. Amoozgar B, Moghimi S, Han Y, et al. An update on therapeutic modalities for the prevention of angle closure glaucoma. Curr Opin Ophthalmol 2017;28:175-80.
20. Trikha S, Perera SA, Husain R, et al. The role of lens extraction in the current management of primary angle-closure glaucoma. Curr Opin Ophthalmol 2015;26:128-34.
21. Man X, Chan NC, Baig N, et al. Anatomical effects of clear lens extraction by phacoemulsification versus trabeculectomy on anterior chamber drainage angle in primary angle-closure glaucoma (PACG) patients. Graefes Arch Clin Exp Ophthalmol 2015;253:773-8.
22. Razeghinejad MR, Myers JS. Contemporary approach to the diagnosis and management of primary angle-closure disease. Surv Ophthalmol 2018;63:754-68.
23. Ho H, Ozaki M, Mizoguchi T, et al. Angle-closure glaucoma in Asians: comparison of biometric and anterior segment parameters between Japanese and Chinese subjects. Graefes Arch Clin Exp Ophthalmol 2015;253:601-8.
24. Yang M, Aung T, Husain R, et al. Choroidal expansion as a mechanism for acute primary angle closure: an investigation into the change of biometric parameters in the first 2 weeks. Br J Ophthalmol 2005;89:288-90.
25. Tham CC, Kwong YY, Baig N, et al. Phacoemulsification versus trabeculectomy in medically uncontrolled chronic angle-closure glaucoma without cataract. Ophthalmology 2013;120:62-7.