Case Report

Taiwan J Ophthalmol 2017;7:104-107

Access this article online

Quick Response Code:

Website:
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DOI:
10.4103/tjo.tjo_41_17

# Acute angle closure following periorbital botulinum toxin injection in a patient with retinitis pigmentosa

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**Abstract:**

A 50-year-old female presented with bilateral retinitis pigmentosa (RP) and acute angle closure (AAC) with fixed mid-dilated pupil and high intraocular pressure (IOP) in the left eye following left side periorbital botulinum toxin A injection for blepharospasm. Glaucomatous optic neuropathy and retinal nerve fiber layer defect were observed in the affected eye using optical coherence tomography although the IOP was maintained at <21 mmHg after the treatment. Botulinum toxin acts at the cholinergic synapse and inhibits acetylcholine release; hence, it can cause transient mydriasis and may lead to AAC in high-risk populations such as patients with RP. Patients should be explained about the possible development of mydriasis associated with botulinum toxin injection, and clinicians must evaluate the level of risk for AAC before administration of botulinum toxin around the eyelid. In cases showing side effects associated with botulinum toxin injection, early diagnosis and treatment is required to prevent blindness.

**Keywords:**

Acute angle closure, botulinum toxin, glaucoma, retinitis pigmentosa

## Introduction

The prevalence of glaucoma among patients with retinitis pigmentosa (RP) is high, and previous reports have indicated a strong association between RP and primary angle closure glaucoma (PACG).[1,2] It has also been reported that compared to controls, patients with RP have a higher risk of developing acute angle closure (AAC).[3]

Botulinum toxin A is used to treat hemifacial spasm and blepharospasm. Its effect starts 3–4 days after its administration and lasts for 4–6 months.[4] It acts primarily at the peripheral cholinergic synapse and inhibits acetylcholine release and can cause transient mydriasis, which may be present for over 3 weeks.[5,6] Furthermore, AAC may develop in high-risk groups after administration of botulinum toxin around the eyelid during cosmetic procedures or for blepharospasm.[7-9]

The present study reports a case of RP with AAC following periorbital botulinum toxin injection for blepharospasm.

## Case Report

A 50-year-old female presented with left-sided headache and eye pain and had blurred vision in her left eye (OS) for several days. She had a history of bilateral RP with poor vision and night blindness for over 10 years. Before the episode, the patient received a botulinum toxin type A injection (30U) around the left eyelid for blepharospasm by a neurologist. Unfortunately, the left-sided headache and pain in the left eye occurred intermittently about 1–2 weeks following the botulinum injection. However, the symptoms did not improve after analgesic treatment. Then, the patient visited the ophthalmologist

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Submission: 12-12-2016
Accepted: 20-03-2017



**How to cite this article:** Tsai JC. Acute angle closure following periorbital botulinum toxin injection in a patient with retinitis pigmentosa. Taiwan J Ophthalmol 2017;7:104-7.

for examination. Ocular examination of the anterior segments of the right eye (OD) showed no abnormalities except mild nuclear sclerosis, gonioscopic findings were narrow angle with anterior trabecular meshwork visible, and intraocular pressure (IOP) was 11 mmHg. The retina showed signs of typical RP including bony spicule-like pigmentation, changes in the retinal pigment epithelium, and attenuation of the retinal vessel. The optic disc appeared normal, and the cup-to-disc (C/D) ratio was 0.2. Ocular examination of the left eye (OS) revealed corneal edema, shallow anterior chamber, and fixed mid-dilated pupil [Figure 1]. The gonioscopic findings were closed angle with totally synechial closure. The IOP was 52 mmHg, the retinal examination showed signs of typical RP, and hyperemia was observed in the optic disc (OS). The visual acuity was 20/800 (OD) and light perception (OS). Therefore, a diagnosis of AAC (OS) and RP (OU) was made.[10]

Following treatment with oral acetazolamide, topical 2% carteolol, 0.15% brimonidine, and 2% pilocarpine solution, the IOP was maintained at 41 mmHg (OS). As a patent iridotomy was not able to be obtained, the patient received trabeculectomy (OS). Follow-up examinations were performed over a period of 6 months postoperation. The IOP was maintained at <20 mmHg (OS) after glaucoma medications, the left eye showed the clear appearance of the cornea, and glaucomatous optic neuropathy (GON) with a C/D ratio of 0.8 was observed. The patient received prophylactic laser iridotomy in the unaffected eye (OD). Automated perimetry using a Humphrey 30-2 threshold revealed severe peripheral visual field (VF) restriction (OU). The average peripapillary retinal nerve fiber layer (RNFL) thickness, measured using Spectralis optical coherence tomography, was 39 μm (OS) in the affected eye [Figure 2] and 92 μm (OD) in the unaffected eye [Figure 3]. The best-corrected visual acuity was 20/400 (OD) and 20/800 (OS).

## Discussion

Botulinum toxins act primarily at the cholinergic synapses, including the skeletal muscle neuromuscular junction, causing transient muscle paresis by inhibiting the release of acetylcholine.[4,9] Botulinum toxins could cause ptosis and pupillary dilation when administered periorbitally. These toxins diffuse toward the ciliary ganglion and block its activity or act at the pupillary sphincter muscle of the iris; transient mydriasis may be present for 3 weeks, after which it disappears gradually.[5,6] However, AAC with pupillary block may develop during periods of the transient mydriasis following administration of botulinum toxin around the eyelid during cosmetic procedures or for blepharospasm in high-risk populations for AAC.[7,8]

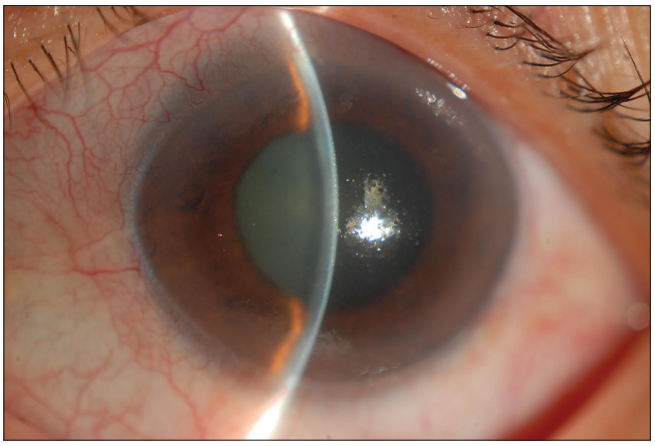

**Figure 1:** Acute angle closure revealed corneal edema, shallow anterior chamber, and fixed mid-dilated pupil following periorbital injection of botulinum toxin

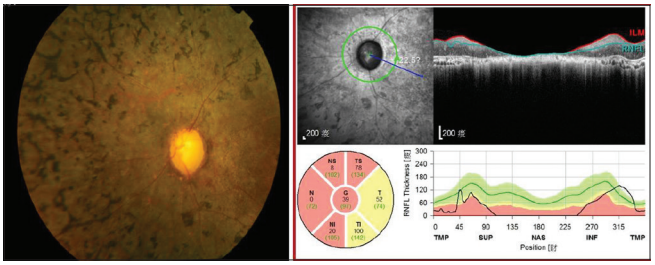

**Figure 2:** Glaucomatous optic neuropathy with large cup/disc ratio in optic disc; retinal photographs after acute angle closure remission in the affected eye of the patient with retinitis pigmentosa (left). The average retinal nerve fiber layer thickness (G), measured using Spectralis optical coherence tomography, was 39 μm in the affected eye after an episode of acute angle closure remission in the patient with retinitis pigmentosa (right)

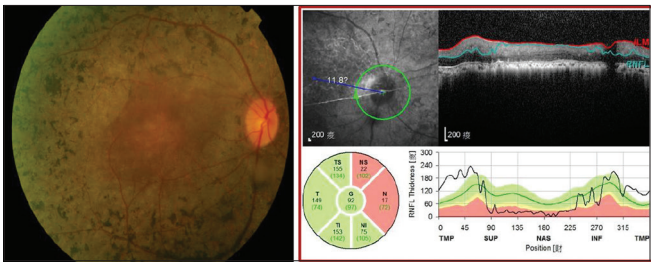

**Figure 3:** Optic disc and retinal photographs in the unaffected eye after acute angle closure in the patient with retinitis pigmentosa (left). The average retinal nerve fiber layer thickness (G), measured using Spectralis optical coherence tomography, was 92 μm in the unaffected eye after acute angle closure in the patient with retinitis pigmentosa (right)

The risk of AAC is higher in people of Asian ethnicity, elderly people, females, and people with hypermetropia. Certain anatomical features can also increase the risk for AAC; these include thick crystalline lens, narrow iridocorneal angles, and plateau iris configuration.[11]

Previous studies have shown that majority of AAC presentations caused by pupillary block occur in participants who were not aware that they were at risk for AAC because of the narrow iridocorneal angles.[7-9]

RP is a hereditary retinal degenerative disease that primarily affects the photoreceptor rods; typically, patients lose night vision and peripheral vision during adolescence and young adulthood, develop progressive peripheral vision restriction, develop tunnel vision at a later stage of the disease, and show decreased central visual acuity at a later stage because of progressive loss of the rod and cone photoreceptor cells. Evaluation of retinal function using electroretinography (ERG) shows that photoreceptor function is usually diminished.[10]

The diagnosis of RP is made when a patient shows bilateral retinal degeneration with typical pigmentations on fundus examination or rod dysfunction on standard ERG examination and has a degenerative retina. The typical retinal findings include changes in the retinal pigment epithelium (88.8%), bony spicule pigmentation (79.7%), attenuation of the retinal vessel (76.2%), waxy disc pallor (12.6%), and cystoid macular edema (0.5%).[10,12]

It has been reported that glaucoma and RP were the first and fourth leading causes of legal blindness and low vision in Taipei during 1995–2004.[13] In a multiple center study, glaucoma was the cause of blindness in 15% of cases with RP-related blindness; this was second only to RP itself.[1] The prevalence of primary open-angle glaucoma in patients with RP ranges from 2% to 12%. Badeeb *et al*. reported a strong association between RP and PACG; the prevalence of PACG among RP patients over 40 years of age was 1.03% in Canada,[2] whereas the prevalence of PACG was 0.1%–02% in populations-based studies among Caucasians over the age of 40 years.[14] The prevalence of PACG reported in Asian population-based studies was 0.96%, ranged from 0.12% in Singapore to 2.5% in Myanmar.[15]

Ko *et al*. found that compared to controls, RP patients in Taiwan had an increased risk of AAC. The mean age of patients with AAC was 53 years in RP patients and 64 years in controls. RP patients had 3.6-fold greater risk of developing AAC.[3] The association of AAC and RP in patients was not clearly understood. However, the associated ocular findings in RP, such as nanophthalmos and zonular insufficiency, may explain the increased prevalence of angle closure glaucoma in patients with RP.[16]

In the present case, as the patient already had poor vision due to RP, the patient paid attention to the headache symptom but neglected the eye-related symptoms until the ocular pain and blurred vision exacerbated. Then, the patient visited the ophthalmologist for examination. Prolonged AAC with high IOP caused irreversible GON although the IOP reduced after the treatment. Delayed recognition of the symptoms and delayed treatment might result in the development of complete blindness.

As observed in the present case, it is difficult to detect glaucomatous standard VF defect in the affected eye of AAC based on signs such as bilateral severe VF restriction and decreased central vision in the later stage of RP.[17]

However, the average RNFL thickness (39 μm) was less in the affected eye showing GON appearance and larger C/D ratio than in the unaffected eye showing normal appearance of optic disc (92 μm). This was the most useful sign associated with glaucomatous optic nerve head damage after AAC.[18]

Oishi *et al*. reported that RNFL thickness in RP patients was not correlated with visual function, but with aging, as observed in the normal participants. The average RNFL thickness was 104.1 ± 21.7 μm in patients with RP. RNFL thickness was not correlated with visual acuity or the extent of VF defect. The results are consistent with the fact that the inner retinal structures such as RNFL are relatively retained despite the profound loss of photoreceptors.[18] Another study involving RP patients found that the RNFL thickness was lesser in RP patients showing pallor of the optic disc than in those showing normal appearance of the optic disc.[19]

In conclusion, AAC may occur during periods of transient mydriasis caused by the administration of botulinum toxin around the eyelid during cosmetic procedures or for blepharospasm in the high-risk population such as patients with RP. Grading the level of risk for AAC and performing gonioscopic examination for iridocorneal angle in the high-risk populations before periorbital injection of botulinum toxin is necessary. Patients receiving treatment with botulinum toxin should be explained about the possible development of mydriasis, which may be present for several weeks. If these side effects are observed, close follow-up evaluation of IOP and patient awareness about the typical AAC symptoms such as acute onset of headache, nausea, ocular pain, and blurred vision, followed by early diagnosis and treatment of AAC can prevent blindness.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.


## Financial support and sponsorship

Nil.

## Conflicts of interest

The author has no any conflicts of interest to declare.

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