Acute angle closure glaucoma

ABSTRACT

Acute angle closure is an emergent ophthalmic condition that develops as a result of an obstructed outflow of aqueous humour between the anterior and posterior chambers of the eye, leading to a sudden rise in intraocular pressure and secondary optic neuropathy if left untreated. The most common primary cause is a pupillary block in patients with pre-existing narrow angles, such as those who are long-sighted. However, awareness should be raised to identify secondary causes of angle closure, including the use of commonly prescribed medications. A detailed interrogation is essential to exclude other possible confounding disorders that present similarly, especially those originating in the CNS. Angle closure should be excluded in all patients presenting with sudden onset of red eye associated with pupillary dilation, dull pain and headache. Basic examination of the eye should include assessment of the anterior segment with a bright light, measurement of intraocular pressure and a full neurological exam. Immediate treatment must be initiated whenever there is high clinical suspicion of acute angle closure, with the administration of systemic ocular hypotensive therapy to prevent damage to the optic nerve and limit visual loss. An urgent referral to the ophthalmologist is mandatory to dictate definitive management.

Acute angle closure is a potentially blinding ophthalmic emergency that occurs as a result of obstruction of the eye's drainage angle – the structure in which aqueous humour outflow takes place. Reduced drainage leads to raised intraocular pressure, which potentially causes damage to the optic nerve. Traditionally, acute angle closure was synonymous with glaucoma; however, the term glaucoma should be reserved for patients with confirmed optic neuropathy.

Optic nerve damage secondary to angle closure can be prevented with prompt management. Acute angle closure is one of the few conditions in ophthalmology that requires immediate treatment as irreversible blindness can occur within hours or days of onset. It is therefore important to be alert to the possibility of acute angle closure in all patients presenting with a painful red eye (especially those with associated headache, nausea and vomiting), particularly as these patients tend to initially seek consultation with non-ophthalmologists. This article provides an overview of the diagnosis and management of this condition.

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Anatomy and pathophysiology of angle closure

Intraocular pressure depends on the balance between aqueous humour production (in the ciliary body) and drainage (primarily through the trabecular meshwork: a fine sieve-like structure in the eye's iridocorneal angle, located between the anterior surface of the iris and the inner surface of the peripheral cornea). In the normal eye, aqueous humour passes from the ciliary body through the pupil to reach the anterior chamber and trabecular meshwork. The iris and lens may come into contact in eyes with an anatomical predisposition, preventing aqueous moving through the pupil into the anterior chamber. This condition, known as pupillary block, leads to a build-up of aqueous behind the iris that causes it to bow forward (iris bombe) and to make contact with the trabecular meshwork, hence obstructing outflow (Quigley, 2009) (*Figure 1*).

Pupillary block is the primary cause of the majority of cases of angle closure, but this condition can also develop as a result of secondary mechanisms:

1. Conditions that exert posterior pressure on the iris causing it to move forward and come into contact with the trabecular meshwork (e.g. mature cataracts, lens dislocation, intraocular tumours, and swelling of the uvea as a result of inflammation)
2. Neovascularization (e.g. diabetic retinopathy, retinal vascular occlusions and ocular ischaemia)
3. Medications.

Natural history

The spectrum of primary angle closure disease ranges from asymptomatic patients with anatomically narrow angles but

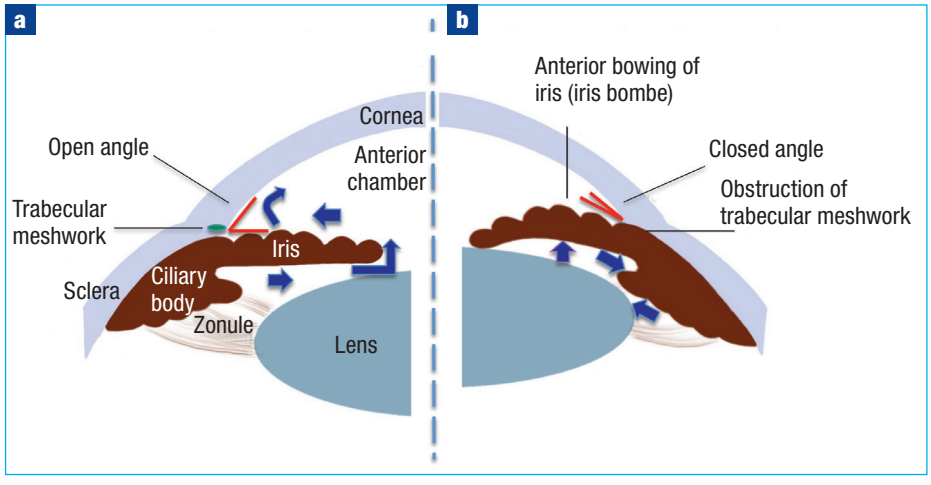

Figure 1. Aqueous humour outflow. **a.** Normal passage. **b.** Blocked outflow.

normal intraocular pressure to patients with narrow angles along with raised intraocular pressure and optic nerve damage (primary angle closure glaucoma) (Foster et al, 2002). Patients with narrow angles could potentially be treated to restore proper aqueous outflow before the development of glaucoma.

An estimated 15.7 million people worldwide are affected by primary angle closure glaucoma, with Asian populations particularly at risk. Primary angle closure glaucoma is less common than primary open angle glaucoma but it is more aggressive; the proportion of patients with primary angle closure glaucoma and significant visual impairment is almost three times higher (Annoh et al, 2019). However, most cases of primary angle closure glaucoma do not present acutely as loss of vision develops slowly over time, similar to that seen in patients with open angle glaucoma. A large amount of visual field can be lost before the patient becomes aware that there is a problem and therefore detection relies primarily on opportunistic case finding by community optometrists. Acute angle closure is typically associated with much higher levels of intraocular pressure and, because of the acute onset, presents with symptoms such as red eye, headache and blurred vision. If appropriate measures to lower intraocular pressure are not quickly instigated, damage to the optic nerve can occur within minutes or hours.

Risk factors

The main risk factors for angle closure include:

- Older age
- Female gender
- Asian ethnicity
- Having an anatomically predisposed eye, meaning an eye of short length, with a pre-existing narrow angle.

Anatomical predisposition commonly occurs in hypermetropia or long-sightedness (Xu et al, 2008). Normal age-related enlargement of the crystalline lens (e.g. cataract) causes crowding of intraocular structures and increased propensity for pupillary block (Rojanapongpun and Suwanpimolkul, 2014; Wright et al, 2016; Zhang et al, 2017; Walland, 2018). Although most cases are sporadic, there is an increased prevalence of angle closure in patients with affected first-degree relatives (Wright et al, 2016).

Table 1. Medications that can trigger acute angle closure

Drug class	Examples	Triggering mechanism
Sulfonamide-containing medications	Topiramate Diuretics (hydrochlorathiazide, furosemide) Sulfonylureas Antibiotics (trimethoprim-sulfamethoxazole, dapsone, sulfadiazine) Triptans Probenecid	Ciliochoroidal effusion with subsequent anterior rotation of ciliary body and displacement of iris–lens diaphragm
Dopamine D2 receptor agonist	Cabergoline	
Adrenergic agonists	Phenylephrine Ephedrine	Pupillary dilation and block
Anticholinergic medications or with anticholinergic side effects	Cycloplegics (tropicamide, atropine, cyclopentolate) Ipratropium bromide Disopyramide Botulinum toxin Antihistamines (promethazine, ranitidine and cimetidine) Tricyclic antidepressants (imipramine, clomipramine, amitriptyline) Serotonin reuptake inhibitor (fluoxetine, venlafaxine, citalopram) Benzodiazepines Antipsychotics (trifluoperazine, perphenazine, fluphenazine)	
Cholinergic medications	Pilocarpine Acetylcholine Carbachol	Anterior displacement of iris–lens diaphragm
Anticoagulants	Heparin Warfarin	Massive choroidal haemorrhage with subsequent anterior displacement of lens–iris diaphragm

From Razenghinejad et al (2011); Khurana et al (2012); Ah-kee et al (2015)

The use of medications as a risk factor warrants special attention since many commonly prescribed topical and systemic drugs can trigger an episode of angle closure. Most of these cases occur in patients with pre-existing narrow angles (Razeghinejad et al, 2011). One of the most common causes is the use of dilating drops such as tropicamide, as they are routinely used to perform fundus examinations and have direct effects on the iris and ciliary body. Dilating drops precipitate 1 in 5 cases of acute angle closure (Chua et al, 2017).

It is important to ask patients with symptoms of acute angle closure whether they have recently seen an optometrist and whether they may have had drops instilled to dilate their pupils. However, the overall risk of a patient developing acute angle closure after pupillary dilation is still very low, reported to occur in only 0.006–0.03% of dilated patients (Liew et al, 2006). The Northern Ireland Diabetic Retinopathy Screening Programme calculated an annual incidence of acute angle closure of 0.75 cases per year, and a risk of 1 in 31 755 cases among patients who underwent pupillary dilation with tropicamide followed by fundus clinical photography (Lagan et al, 2016).

Other medications may also precipitate acute angle closure, including drugs that have sympathomimetic or parasympathetic properties (*Table 1*).

Table 2. Acute angle closure clinical presentation

Common signs and symptoms	■ Unilateral presentation (90% of cases) ■ Sudden blurring of vision and halos around lights ■ Dull pain (intermittent or continuous) and localized to the eye, but possibly referred to the retrobulbar space and other periocular areas (eyebrows, head, paranasal sinuses, maxillary and auricular areas) ■ Red and swollen eye, associated with tearing ■ Systemic findings: nausea and vomiting, sweating, and anxiety in severe cases
Ocular examination	■ Reduced visual acuity (<6/60 in 50% of cases) ■ Elevated intraocular pressure (>30 mmHg) ■ Shallow anterior chamber ■ Corneal oedema (cloudy cornea) ■ Fixed (or poorly reactive) and mid-dilated pupil
Features that suggest an alternative diagnosis	■ Bilateral presentation ■ Painless red eye ■ Normally reactive pupil on affected eye or with a smaller size (miosis) ■ Clear cornea ■ Normal intraocular pressure ■ Purulent discharge ■ History of immediate ocular trauma ■ Optic nerve swelling ■ Headache localized away from the affected eye or associated with neurological signs

From Rojanapongpun and Suwanpimolkul (2014); Chua et al (2017)

Clinical presentation

Acute angle closure usually develops abruptly, but there may be a history of intermittent symptoms of headache or blurred vision leading up to the acute attack. Classically, patients present with a unilateral red eye associated with blurry vision, a fixed semi-dilated pupil, and ocular or periocular pain that could induce nausea and vomiting. *Table 2* describes the most common clinical findings.

Examination

Visual acuity should always be assessed. If the patient is unable to read any letters on a Snellen chart, it should be determined whether he/she can count fingers, or perceive hand movements or light.

Although a slit lamp is required for definitive diagnosis, examination can be performed without specialist equipment. A bright light source (e.g. ophthalmoscope, pen torch) can be used to examine for clouding of the cornea (corneal oedema), which occurs as a result of the inability of corneal endothelial cells to maintain corneal clarity against the high-pressure gradient caused by raised intraocular pressure. The light source can also be used to examine the pupil; in acute angle closure, it is typically round but mid-dilated and reacts poorly to light. Additionally, the light source can be used to estimate anterior chamber depth by shining it from the temporal side of the eye at the level of the iris. In eyes with a deep anterior chamber, the iris is flat and its entire surface will be illuminated. In eyes with a shallow anterior chamber, the iris blocks passage of light (*Figure 2*).

It is also useful to examine the patient's glasses to determine if the patient is at risk of acute angle closure. Most patients with acute angle closure are hypermetropic, meaning that they have a positive prescription for their spectacles (near-sighted, e.g. +3 dioptres). Patients with high degrees of refractive errors tend to have very thick lenses in their glasses. Angle closure in a patient who does not wear glasses or who is myopic (short-sighted, e.g. -3 dioptres) is rare. A simple way to identify the type of prescription in a lens is to look at an object through it. Objects appear bigger when viewed through a high power positive lens (hypermetropic patients) and they appear smaller when viewed through a high power negative lens (myopic patients).

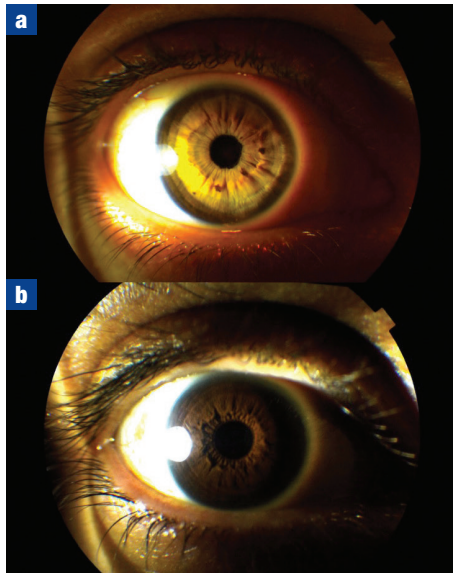

Figure 2. Estimation of anterior chamber depth with a pen torch. a. The whole surface of the iris is illuminated all the way across the nasal side in an emmetropic patient with a deep anterior chamber. b. Partial obscuration of the nasal surface of the iris in a hypermetropic patient with a shallow anterior chamber.

Gonioscopy and tonometry

Gonioscopy is the gold-standard test to assess the iridocorneal angle, but this test is difficult to perform and not practical for use without ophthalmic training. Gonioscopy involves placing a contact lens containing a mirror on the surface of the eye, which allows visualization of the angle.

Tonometry refers to the measurement of intraocular pressure and a range of devices is available for this purpose. Goldmann applanation tonometry, which is the gold standard, requires instillation of a topical anaesthetic and fluorescein. Intraocular pressure is recorded using a probe that makes gentle contact with the surface of the cornea. Normally, intraocular pressure ranges between 10 and 21 mmHg; in acute angle closure it is not uncommon to observe intraocular pressure of over 50 mmHg (Rojanapongpun and Suwanpimolkul, 2014).

Goldmann applanation tonometry also requires considerable training, but newer tonometers may be more widely available and are easier to use. For instance, the iCare tonometer is a hand-held rebound device that does not require instillation of any eye drops before testing. Intraocular pressure can also be roughly estimated using digital palpation (comparing the tension of one eye

to another through a closed lid using both index fingers). Baum et al (1995) showed that digital assessment could be useful to warn about the possibility of intraocular pressure elevations above 30 mmHg, whenever the eye offers resistance against digital indentation and its wall feels hard. However, this method is inaccurate and not recommended as standard practice.

Differential diagnosis

The main differential diagnoses of acute angle closure include alternative causes of red eye and headache (*Table 3*).

Painful red eye

The first step is to determine whether this is a unilateral or bilateral presentation. Most cases of severe dryness and conjunctivitis will lead to symptoms in both eyes, including itchy and gritty sensations associated with tearing or discharge. Uncommonly, bilateral acute angle closure attacks can occur secondary to systemic medications. There is a well-known association between topiramate and bilateral acute angle closure as a result of drug-induced swelling of the choroid, causing forward movement of the iris and lens.

Causes of unilateral red eye include eyelid, corneal or uveal tract pathology. Of these, the most important cause to exclude is uveitis. This presents with painful red eye and potentially raised intraocular pressure; however, pressures tend to be lower compared to acute angle closure, onset is slower, and the pupil may be irregular as a result of adhesions between the iris and lens surface (posterior synechiae).

Headache with nausea and vomiting

This is a common presenting complaint to the emergency department. It is crucial to always evaluate bilateral pupillary reflexes and rule out the presence of focal signs, meningismus or reduced level of consciousness that would indicate the need for urgent neurological investigations, making the diagnosis of acute angle closure very unlikely.

Acutely raised intracranial pressure (e.g. in the context of an intracranial haemorrhage) can present with a dilated pupil if the third cranial nerve is compromised (Tabatabai and Swadron, 2016). However, other focal neurological deficits will be found as well, and ocular examination may reveal bilateral optic nerve swelling or retinal haemorrhages that will be visible through a clear cornea.

In rare instances, migraine might cause episodes of unilateral dilated pupil as a result of autonomic dysfunction (Skeik and Jabr, 2011). More commonly, ocular symptoms in migraine present as part of visual aura: characteristic enlarging zigzag or flickering positive scotomas (starting centrally and expanding peripherally) and different patterns of visual loss. These symptoms could be accompanied or followed by headache and photophobia. This clinical presentation is completely reversible and usually of short duration, which differs from that of an acute angle closure attack.

Treatment

The initial treatment of acute angle closure focuses on prompt reduction of intraocular pressure to avoid optic nerve damage and development of glaucoma. The standard first-line treatment includes intravenous acetazolamide, coupled with analgesia and

Table 3. Differential diagnosis of acute angle closure

Painful red eye	Conjunctivitis	■ Allergic ■ Viral ■ Bacterial
	Severe dry eye syndrome	
	Eyelid malpositions with secondary ocular surface pathology	■ Ectropion or entropion ■ Trichiasis
	Keratitis	■ Infectious (contact lens wear, trauma with organic material, established ocular surface disease, immunocompromised, topical steroids) ■ Non-infectious (corneal abrasion, foreign body, chemical injury)
	Uveitis (possible association with autoimmune systemic diseases)	■ Scleritis ■ Iritis ■ Panuveitis
	Ocular trauma	
Headache with ocular involvement +/- nausea and vomiting	Cluster headache	■ Severe facial and ocular pain ■ Autonomic features (conjunctival injection, profuse tearing, eyelid oedema)
	Giant cell arteritis	■ Transient obscurations (amaurosis fugax) or permanent visual loss ■ Ipsilateral optic nerve swelling
	Migraine with visual aura	■ Foggy vision, tunnel vision or complete visual loss ■ Scintillating scotomas ■ Frontotemporal or periocular pain with photophobia
	Meningitis	■ Photophobia ■ Subconjunctival haemorrhages ■ Possible optic nerve involvement and visual loss
	Raised intracranial pressure	■ Visual loss ■ Ocular motility disturbance ■ Bilateral optic nerve swelling (papilloedema) ■ Retinal haemorrhages surrounding the optic nerve

From Tabatabal and Swadron (2016); Denniston and Murray (2018)

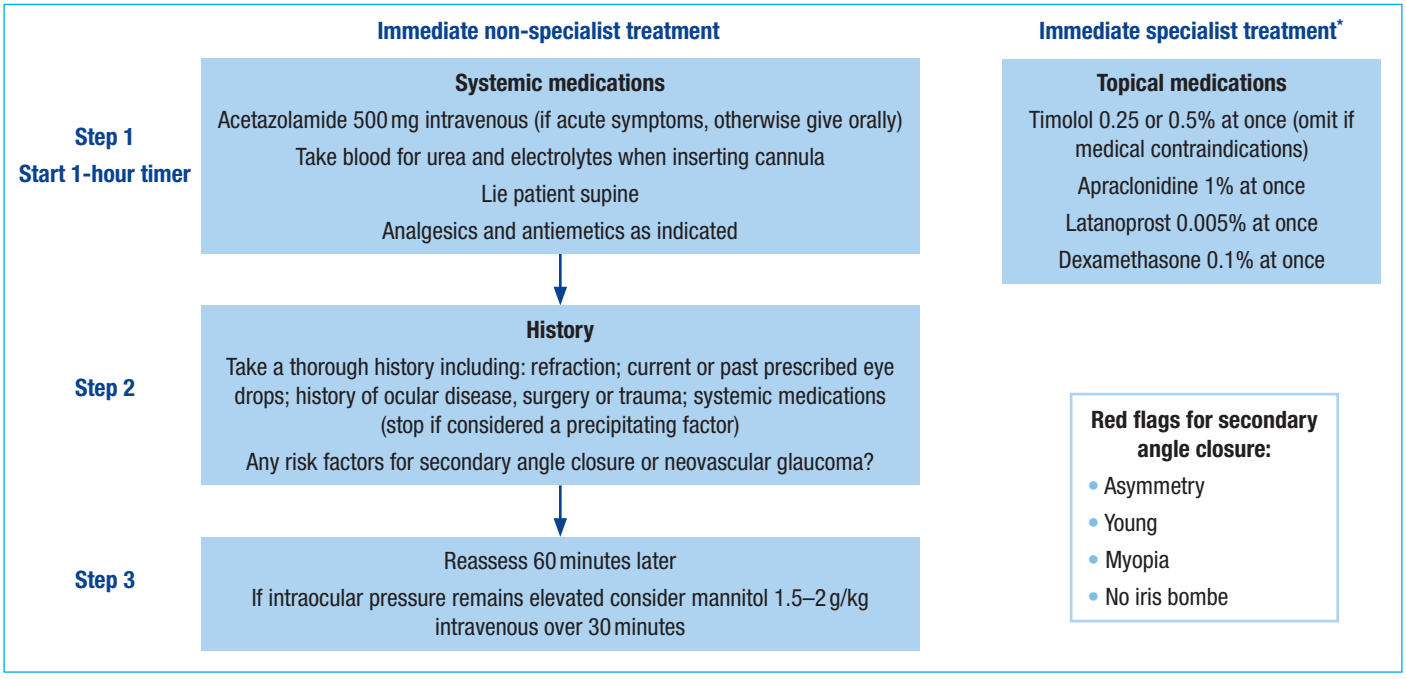

Figure 3. Flow chart for initial treatment of acute angle closure. *This treatment should be administered to the affected eye along with systemic medications whenever available in the primary care setting.

antiemetics. Topical medication is unlikely to be sufficient because ocular ischaemia impairs its efficacy. *Figure 3* summarizes the initial medical treatment.

Depending on how soon the patient is likely to be seen by an ophthalmologist, it may be prudent for the primary care or emergency department team to initiate immediate treatment with acetazolamide. The emphasis should be on urgent intraocular pressure reduction so that later on an ophthalmologist can complete a detailed examination to determine the cause and subsequent steps in management. Patients with acute angle closure should not be discharged until the acute attack has been adequately controlled and they have received or have plans in place for definitive treatment.

Most patients with pupillary block undergo laser treatment to punch a small hole through the iris to restore flow of aqueous into the anterior chamber (laser peripheral iridotomy). Laser is typically performed within a few hours of the acute attack, as soon as the cornea is sufficiently clear (Razeghinejad and Myers, 2018). Laser treatment should be performed in both eyes as the anatomical predisposition to angle closure is bilateral. *Figure 4* shows optical coherence tomography imaging of a patient with acute angle closure before and after laser peripheral iridotomy. Lens extraction is an alternative surgical option, indicated even if there is no cataract in selected cases. A multicentre randomized controlled clinical trial demonstrated that in patients with primary angle closure and intraocular pressure ≥30 mmHg or those with primary angle closure glaucoma, lens extraction was better at controlling intraocular pressure at

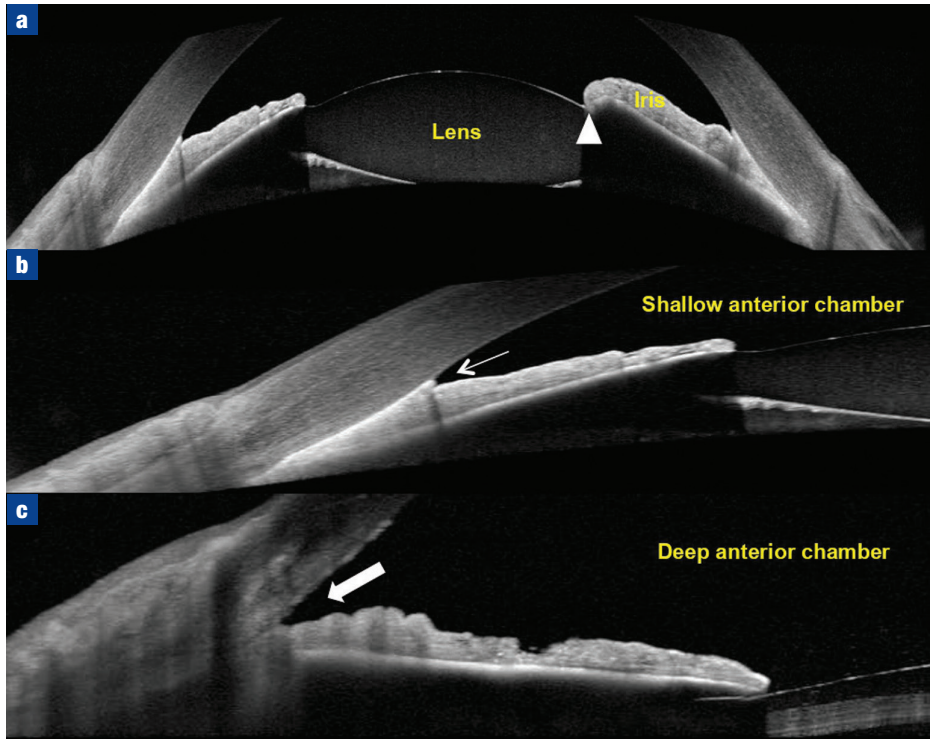

Figure 4. Horizontal anterior segment optical coherence tomography images showing a pupillary block. **a.** Contact between anterior surface of the lens and posterior surface of the iris (arrow head) before treatment. **b.** Close-up image showing closed angle (arrow) caused by forward bowing of peripheral iris and obstruction of trabecular meshwork. **c.** Open angle (block arrow) after treatment.

CURRICULUM CHECKLIST

This article addresses the following requirements from the general internal medicine training curriculum

- Managing an acute specialty-related take
- Managing medical problems in patients in other specialties and special cases

3 years and fewer patients required further treatment when compared to laser iridotomy (Azuara-Blanco et al, 2016).

Prognosis

Despite adequate treatment, 3–12% of patients with acute angle closure develop long-term severe visual impairment, mainly as a result of glaucomatous optic neuropathy (Andreatta et al, 2015). The most important risk factor that predisposes to development of primary angle closure glaucoma and visual loss is a delayed presentation of >3 days (Chua et al, 2017).

Conclusions

Acute angle closure is an ophthalmic emergency that potentially leads to rapid irreversible loss of vision. Doctors working in primary and acute care settings should be particularly aware of the clinical features of this condition and refer the patient immediately to an ophthalmologist if there is high clinical suspicion. Early recognition of acute angle closure and appropriate management can prevent the development of glaucoma and preserve sight. **BJHM**

Conflict of interest: none.

Ah-kee EY, Egong E, Shafi A, Lim LT, Yim JL. A review of drug-induced acute angle closure glaucoma for non-ophthalmologists. Qatar Med J. 2015 Apr;2015(1):6. https://doi.org/10.5339/qmj.2015.6

Andreatta W, Elaroud I, Nightingale P, Nessim M. Long-term outcomes after acute primary angle closure in a White Caucasian population. BMC Ophthalmol 2015 Aug 19;15:108. https://doi.org/ 10.1186/s12886-015-0100-5

Annoh R, Loo CY, Hogan B, Tan HL, Tang LS, Tatham AJ. Accuracy of detection of patients with narrow angles by community optometrists in Scotland. Ophthalmic Physiol Opt. 2019 Mar;39(2):104–112. https://doi.org/10.1111/opo.12601

Azuara-Blanco A, Burr J, Ramsay C et al; EAGLE study group. Effectiveness of early lens extraction for the treatment of primary angle-closure glaucoma (EAGLE): a randomised controlled trial. Lancet. 2016 Oct 1;388(10052):1389–1397. https://doi.org/10.1016/S0140-6736(16)30956-4

Baum J, Chaturvedi N, Netland PA, Dreyer EB. Assessment of intraocular pressure by palpation. Am J Ophthalmol. 1995 May;119(5):650–651. https://doi.org/10.1016/s0002-9394(14)70227-2

Chua PY, Day AC, Lai KL et al. The incidence of acute angle closure in Scotland: a prospective surveillance study. Br J Ophthalmol. 2017 Aug 09;102:bjophthalmol-2017-310725. https://doi.org/10.1136/bjophthalmol-2017-310725

Denniston AKO, Murray PI. 2018. Oxford Handbook of Ophthalmology. 4th edn. Oxford: Oxford University Press.

Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002 Feb 1;86(2):238–242. https://doi.org/10.1136/bjo.86.2.238

Khurana B, Khurana AK, Khurana AK. Drug-induced angle-closure glaucoma. J Curr Glaucoma Pract. 2012 Apr;6(1):6–8. https://doi.org/10.5005/jp-journals-10008-1100

Lagan MA, O'Gallagher MK, Johnston SE, Hart PM. Angle closure glaucoma in the Northern Ireland Diabetic Retinopathy Screening Programme. Eye (Lond). 2016 Aug;30(8):1091–1093. https://doi.org/10.1038/eye.2016.98

Liew G, Mitchell P, Wang JJ, Wong TY. Fundoscopy: to dilate or not to dilate? BMJ. 2006 Jan 7;332(7532):3. https://doi.org/10.1136/bmj.332.7532.3

Quigley HA. Angle-closure glaucoma-simpler answers to complex mechanisms: LXVI Edward Jackson Memorial Lecture. Am J Ophthalmol. 2009 Nov;148(5):657–669.e1. https://doi.org/10.1016/j.ajo.2009.08.009

Razeghinejad MR, Myers JS. Contemporary approach to the diagnosis and management of primary angle-closure disease. Surv Ophthalmol. 2018 Nov;63(6):754–768. https://doi.org/10.1016/j.survophthal.2018.05.001

Razeghinejad MR, Pro MJ, Katz LJ. Non-steroidal drug-induced glaucoma. Eye (Lond). 2011 Aug;25(8):971–980. https://doi.org/10.1038/eye.2011.128

Rojanapongpun P, Suwanpimolkul O. 2014. Acute intraocular pressure rise. In: Shaarawy T, Sherwood M, Hitchings R, Crowston J, eds. Glaucoma. 2nd edn, Vol. 1. Philadelphia: Elsevier Saunders Ltd: 598–606

Skeik N, Jabr F. Migraine with benign episodic unilateral mydriasis. Int J Gen Med. 2011 Jun;4:501–503. https://doi.org/10.2147/IJGM.S18613

Tabatabai RR, Swadron SP. Headache in the emergency department: avoiding misdiagnosis of dangerous secondary causes. Emerg Med Clin North Am. 2016 Nov;34(4):695–716. https://doi.org/10.1016/j.emc.2016.06.003

Walland MJ. Acute angle closure glaucoma? Clin Exp Ophthalmol. 2018 Apr;46(3):211–212. https://doi.org/10.1111/ceo.13189

Wright C, Tawfik MA, Waisbourd M, Katz LJ. Primary angle-closure glaucoma: an update. Acta Ophthalmologica. 2016 May;94(3):217–225. https://doi.org/10.1111/aos.12784

Xu L, Cao WF, Wang YX, Chen CX, Jonas JB. Anterior Chamber Depth and Chamber Angle and Their Associations with Ocular and General Parameters: The Beijing Eye Study. Am J Ophthalmol. 2008 May;145(5):929–936. https://doi.org/10.1016/j.ajo.2008.01.004

Zhang X, Liu Y, Wang W et al. Why does acute primary angle closure happen? Potential risk factors for acute primary angle closure. Surv Ophthalmol. 2017 Sep - Oct;62(5):635–647. https://doi.org/10.1016/j.survophthal.2017.04.002

KEY POINTS

- Acute angle closure is an ophthalmic emergency that can rapidly lead to blindness if left untreated.
- The most common cause is pupil block, which prevents aqueous humour passing into the anterior chamber, leading to forward bowing of the iris.
- Angle closure tends to occur in patients with small eyes.
- Suggestive clinical features include a painful red eye with a mild-dilated pupil associated with headache, nausea and vomiting. Angle closure should be considered in all patients presenting with abrupt severe headache.
- Immediate treatment involves use of oral or intravenous acetazolamide, analgesics and antiemetics, as well as urgent referral to an ophthalmologist for definitive surgical treatment.