An Evidence-Based Approach to Phacomorphic Glaucoma

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Abstract

Phacomorphic angle-closure is a secondary angle-closure caused by a mature cataract. The definitive treatment is cataract extraction. The objective of this review is to highlight the epidemiology, risk factors, and diagnostic and treatment strategies to optimize final visual acuity.

Background

Cataract maturation is associated with anteroposterior lens diameter increase which, in some patients, particularly those with anatomically narrow anterior chambers, can lead to pupillary block and peripheral iridotrabecular apposition [1,2]. In other patients with previously deep anterior chambers and wide open angles, the cataract may become so swollen that it physically pushes the iris anteriorly, leading to iridotrabecular apposition [3]. The role of pupillary block in the pathophysiology of phacomorphic angle-closure is still uncertain. Limited evidence suggests that early in the course of the disease, the lens swelling is only large enough to cause pupillary block [4]. Progressive enlargement of the lens may then lead directly to peripheral iridotrabecular apposition. When the iridotrabecular apposition raises the intraocular pressure (IOP) enough to cause the signs and symptoms of an acute attack of secondary angle-closure glaucoma, it is called acute phacomorphic angle-closure. Historically this entity has been labeled phacomorphic glaucoma. As pointed out by Tham, however, using the word glaucoma implies an optic neuropathy [5]. Since many patients (as will be analyzed below) do not show glaucomatous optic neuropathy following the resolution of the acute angle-closure, it may be more accurate to call this disease acute phacomorphic angle-closure. The dense white cataract labeled as a mature cataract is an advanced form of cortical cataract, with widely hydrated cortex [6]. If the lens continues to mature and the lens protein begins to denature, the resulting hyperosmolarity leads to continued hydration and the lens continues to mature and the lens protein begins to denature which, in some patients, particularly those with anatomically narrow anterior chambers, can lead to pupillary block and peripheral iridotrabecular apposition [3,10]. To narrow the chamber and so a measurement during an attack would not be representative of the depth of the anterior chamber prior to the attack. Studies to further evaluate this would need to prospectively measure these values in healthy patients and follow them to identify risk factors, but the ethics involved with observing the development of phacomorphic angle-closure without treatment precludes a fully prospective trial. Furthermore, sex may be a risk factor, with a female predominance [10,11] reported to be as high as 3:1 [12] but this has not been a consistent finding.

It should be noted that some phacomorphic angle-closure patients will not have any identifiable risk factors. Although not consistent with the historical definition involving a mature cataract, phacomorphic angle-closure of the same mechanism has been reported in myopic eyes. In at least one case, the patient had increased lens thickness (5.33 mm) which required a clear lens extraction [13]. A 40 year-old highly myopic male (~15 diopters in the right and ~18 in the left)

Table 1: Risk Factors for Phacomorphic Angle-Closure.

<table>
<thead>
<tr>
<th>Confirmed Risk Factors</th>
<th>Possible Risk Factors</th>
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<tr>
<td>Age over 60 [3,10]</td>
<td>Narrow anterior chamber [4]</td>
</tr>
<tr>
<td>Axial length &lt;= 23.7 mm²</td>
<td>Female gender [10,12]</td>
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Reported risk factors are listed below in Table 1. Among reported risk factors for the development of phacomorphic angle-closure, the most commonly cited is age [3]. One small study (49 patients) found that patients over 60 years old had an increased risk (odds ratio 2.7) of developing phacomorphic angle-closure [10]. More mature cataracts develop over time, and age is also a risk factor for primary angle-closure glaucoma, placing these patients at increased risk from having crowded angles. A retrospective case-control study compared 100 patients with phacomorphic angle-closure (the average age was 73 years old) to age-and gender-matched control eyes with mature cataracts [3]. The study showed that shortened axial length is a risk factor: the average axial length in their control group was 23.7 mm versus 23.1 mm in the phacomorphic angle-closure group. Having an axial length ≤ 23.7 mm increased the risk of phacomorphic angle-closure by a factor of 4.3. Although narrow anterior chamber depth has been previously cited as a risk factor for this secondary form of angle-closure glaucoma [4], this particular study did not find any statistically significant correlation. However, this study used anterior chamber depth measurements from the fellow eye because the attack of angle closure would be expected to narrow the chamber and so a measurement during an attack would not be representative of the depth of the anterior chamber prior to the attack. Studies to further evaluate this would need to prospectively measure these values in healthy patients and follow them to identify risk factors, but the ethics involved with observing the development of phacomorphic angle-closure without treatment precludes a fully prospective trial. Furthermore, sex may be a risk factor, with a female predominance [10,11] reported to be as high as 3:1 [12] but this has not been a consistent finding.

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had bilateral phacomorphic angle-closure secondary to isolated spherophakia confirmed with ultrasound-biomicroscopy (UBM) [14]. A 16-year-old female with poorly controlled type 1 diabetes was also reported to have bilateral phacomorphic angle-closure, likely from the acute hyperosmolar myopic shift that occurs with hyperglycemia [15]. Zonular laxity can lead to both anterior lens shift and increased anteroposterior lens diameter. Phacomorphic angle-closure from zonular laxity was reported in cases of Weill-Marchesani syndrome (despite a patent peripheral iridotomy) [16], as well as in patients with a familial Marfanoid appearance [17].

**Diagnosis and Work-up**

Multiple publications [1,3,10,18] report using the same criteria for diagnosis of phacomorphic angle-closure. The common cutoff of IOP above 21 mmHg was used, though the average presenting IOP is often over 40 mmHg [1,3,19]. As this is a secondary form of angle-closure, findings include injection, corneal edema, mid-dilated pupil, shallow anterior chamber, and a mature cataract. Of 100 patients, 71% complained of eye pain while 16% described it as a headache [1]. Nausea was reported by 8%. A B-scan should be done given an inadequate view of the fundus. Phacomorphic angle-closure caused by a choroidal melanoma causing anterior lens shift has been reported [20]. Between the acute attack and the dense cataract, the presenting vision is often extremely poor, averaging light perception only [1,3]. One study included biometry as diagnostic criteria, requiring a lens thickness of at least 5 mm (the average lens thickness is 4.63 mm) [21], and an anterior chamber depth less than 2 mm [19].

A vital part of the exam is gonioscopy to confirm a closed angle. If the corneal edema is severe, this may not be possible in the involved eye. Indentation gonioscopy may relieve the pupillary block component of the attack. Since the main differential for phacomorphic angle-closure is acute angle-closure glaucoma, gonioscopy of the fellow eye should be done to ensure that it is not occludable. The angle in the fellow eye may also be narrow, as 60% of 49 patients with phacomorphic angle-closure had a moderately narrow angle with a maximum angle width of 20 degrees in the fellow eye [10]. The fellow eye should have less of a dense cataract with a normal IOP, although this can vary depending on how much time passes between the attack and when the patient is seen. In one study of 49 patients, 80% had an immature cataract in the fellow eye [10].

In examining the cataract, it is important to evaluate for zonular laxity since it is associated with both main causes of the intumescent cataract, trauma and aging. There is also a possible association with pseudoexfoliation syndrome, in which the zonular laxity can predispose the patient to anterior lens movement. Pseudoexfoliation syndrome was present in 50% of cases in a small case series [4]. Since the mature cataract may limit any assessment of visual acuity, ancillary testing may help evaluate postoperative potential [6]. Testing can range from Purkinje vascular enoptotic testing to visual-evoked potentials.

**Treatment**

The goal in treating phacomorphic angle-closure is to reduce the IOP before the onset of acute glaucomatous optic neuropathy. Longer duration of an attack has been correlated with a progressive increase in IOP [8]. The only definitive treatment is cataract extraction [18]. However, to avoid operating on an inflamed eye with high pressure (increasing the risk of suprachoroidal hemorrhage from rapid IOP fluctuations) [18,22], with a limited view from corneal edema and an extremely shallow chamber, the initial goal is to stabilize the eye by breaking the acute attack and lowering the IOP using either medical or laser treatment.

**Medical treatment**

The most common initial treatment is topical anti-glaucoma medications, including beta-blockers, alpha-agonists, and carbonic anhydrase inhibitors [23]. Several studies relied on a standard treatment algorithm; timolol, acetazolamide and intravenous mannitol were among the most common medications used [11,18]. Pilocarpine should be avoided because it causes a forward shift of the iris-lens diaphragm which would worsen the angle-closure, and can increase the amount of inflammation [5,24]. The use of prostaglandin analogues have not been widely reported, possibly to avoid their proinflammatory effects during an acute attack [25]. Topical treatment alone may be insufficient to break the attack. In one study, patients received a topical beta-blocker, oral acetazolamide and glycerol and only 60% of patients achieved an IOP under 30 mmHg [10]. The presence of at least 180 degrees of peripheral anterior synchiae (PAS) at presentation may be an indication that topical treatment will be insufficient to break the attack [12]. If topical treatment fails to bring the IOP into a tolerable range until cataract extraction can be performed, there are 3 options. The first is oral or intravenous medicine such as acetazolamide or mannitol. Argon laser peripheral iridoplasty (ALPI) has successfully been used to break the attack and can often be used even if corneal edema precludes a view clear enough for the third option, laser peripheral iridotomy [26]. All of these treatments are temporizing because none remove the actual etiology: the swollen lens pushing the angle closed. A relatively small number of cases report combining phacoemulsification with glaucoma procedures (trabeculectomy [27] or aqueous shunts [28,29]) for pressure control, like in 4 patients who had an uncontrollable IOP (value unspecified) despite IV mannitol at presentation. Adding operative procedures to these eyes increases the risk of complications such as prolonged uveitis in 3 of 9 patients treated with combined cataract extraction and aqueous shunts [8]. In that study the final visual acuity was worse in the combined cases than in the eyes treated only with cataract extraction and combining glaucoma surgery with cataract extraction is not currently recommended.

**Laser treatment**

Argon Laser Peripheral Iridoplasty has been suggested as a way to avoid the systemic side effects that come with oral or intravenous medicine, such as metabolic acidosis with acetazolamide or congestive heart failure with hyperosmotics [5]. The settings used vary but Thom et al. averaged 46 shots around 360 degrees of peripheral iris, with a laser spot size of 500 microns, power set at 264 mW for 0.5 second duration [5]. Despite the fact that only two of ten eyes showed any open angle on gonioscopy following iridoplasty, the average IOP was reduced from 56 at baseline, to 45 at 15 minutes following the procedure, to 34 at 50 minutes, and finally to 14 mmHg at 24 hours. UBM, which may have revealed a change in angle configuration, was not done [30]. The authors postulated that the inflammatory effects caused by the laser on the uveoscleral outflow or ciliary body may be responsible for lowering the IOP in those cases. One of the ten patients failed to achieve adequate IOP control (the IOP was 40 after two hours) and so received intravenous acetazolamide. There are no available reports on the timing of IOP reduction with systemic medications specifically for phacomorphic angle closure. To give some comparison, a randomized control trial comparing medication (intravenous acetazolamide and in some cases mannitol) to ALPI for primary acute angle-closure found that the IOP decreased much more rapidly with ALPI [31]. The eyes...
treated with ALPI reached an IOP of 31 after only 15 minutes, whereas it took 60 minutes following medication administration to reach the same IOP, suggesting ALPI may achieve lower IOP’s faster than systemic medicine. However, even though this decreases the chance of PAS formation and glaucomatous optic neuropathy by shortening the duration of an angle-closure attack, there are no longitudinal studies confirming this. Another series using iridoplasty to break the acute attack had less successful results according to a stricter protocol [24]. Two hours following the procedure, 19% of 21 patients had an IOP greater than 30 and so were taken for emergent cataract extraction.

The role of pupillary block in the pathophysiology of phacomorphic angle-closure is not completely understood. It is important to note that iridoplasty alone does not relieve pupillary block, which still would require an iridotomy, best done within 2-3 days [26]. One possible reason to do a laser iridotomy even though cataract extraction is already planned is the report of a patient who had an acute attack successfully aborted with topical medication only to sustain a second angle-closure attack precipitated by the preoperative dilating drops [4]. The intraoperative IOP climbed to 46 mmHg. A laser iridotomy will not relieve angle-closure in advanced cases where the lens is large enough to directly push the peripheral iris into the trabecular meshwork [4]. Finally, neither laser is an option if the cornea is too edematous to visualize the iris despite glycerol, or if the anterior chamber appears so narrow that the laser will damage the corneal endothelium [5].

**Surgical technique**

Cataract extraction of the intumescent lens necessitates preparation due to the increased risk of complications. Specific risks include higher positive pressure, risk of expulsive hemorrhage, and vacuum of 140 mmHg [7]. During chopping, using a longer tip may be utilized instead. Intraoperative miosis may be improved through a paracentesis to deepen the chamber. Although this deepened the chamber and facilitated successful phacoemulsification, the sclerotomy carries its own risks of retinal dialysis, tear or detachment, necessitating a comprehensive retinal exam at post-op visits.

To achieve a continuous curvilinear capsulorhexis, it will likely be necessary to improve visualization on the capsule by using a dye such as trypan blue which will also be of use throughout the case by keeping the edge of the capsulorhexis in constant view. Another aid that has been used is oblique illumination held at the limbus [36]. Focal calcifications of the capsule may necessitate redirecting the capsulorhexis around the plaque or using scissors to cut through it [37]. Since hydrated cortex may escape from the mature lens into the anterior chamber when the capsulorhexis is started, one method to clear the view is to pierce the capsule with a bent 26 gauge needle to allow initial egress and decompensation. The free cortex can be removed with a small syringe before capsulorhexis is continued under high magnification. To reduce the intralenticular pressure to keep the tractional forces on the capsulorhexis flat, a 30 gauge needle can be used to directly withdraw cortex from the lens [36]. Excess viscoelastic will raise the intraocular pressure even further, and if liquefied cortex escapes and mixes with viscoelastic it will stay near the capsulotomy site, obscuring the view [38]. Since the cortex is already hydrated in an intumescent cataract, hydrodissection may not be useful and may make the lens excessively mobile.

Sufficient dispersive viscoelastic should be used to protect the corneal endothelium. This can be used in combination with a cohesive viscoelastic which helps negate the positive posterior pressure, helping to neutralize radialization forces in a soft-shell technique [39]. In this technique, a low-viscosity dispersive agent is injected over the lens, followed by a high-viscosity cohesive agent injected posteriorly, forcing the dispersive agent anteriorly to form a protective coating on the corneal endothelium. One definitive option to deal with increased positive posterior pressure is to do a partial vitrectomy prior to the cataract extraction, aspirating 0.2 cc of vitreous [35]. Dada et al. report on a blind, single-site 23 gauge partial-core pars plana vitrectomy prior to phacoemulsification [22]. At the same time, they injected viscoelastic into the anterior chamber through a paracentesis to deepen the chamber. Although this deepened the chamber and facilitated successful phacoemulsification, the sclerotomy carries its own risks of retinal dialysis, tear or detachment, necessitating a comprehensive retinal exam at post-op visits.

A divide and conquer method would be suboptimal because cracking would be difficult with such a large lens in a weakened capsule with possible zonular laxity. Employing a stop and chop method will thin the nucleus and offer an improved chance of successful chopping. During sculpting, high power will likely be needed, with one suggested setting detailing power of 80%, aspiration flow rate of 25 cc per minute and vacuum of 140 mmHg [7]. During chopping, using a longer tip (1.75 mm) improves the chance of a successful chop. Another technique called cratering involves deep sculpting of the entire central core of the nucleus (leaving behind only a small posterior cushion), after which the remaining nuclear rim can be split apart with cracking or chopping [41]. Vanathi et al. applied cratering then chopping to 26 eyes with mature cataracts and there were no posterior capsule tears [41]. Only 3 patients had corneal edema on postoperative day one. Other helpful techniques include using a second instrument to physically break the dense strands connecting nuclear fragments during aspiration [6].
There is an increased risk of posterior capsule tear with mature lenses because the large, dense cataract physically stretches the capsule, which can lead to a thinning and slacking. Excess slack predisposes the capsule to come anteriorly toward the phacoemulsification tip. Finally, there is often no remaining epinucleus which normally acts as a cushion between the tip and the posterior bag. This can be prevented by injecting some viscoelastic underneath the lens as soon as some red reflex is visible after removal of the first part of the cataract, offering a cushion between the posterior capsules whilst raising the nucleus closer to the phacoemulsification tip [6].

On the day following surgery, common exam findings include severe iritis in up to 84% of patients [10], inflammatory fibrin precipitates (48%) and severe corneal edema (24%) [18]. These are expected to resolve following topical treatment. Descemet’s folds lasted an average of 6 days in one study, and their presence did not correlate with final visual acuity [19]. Hyphema has been reported in 3% [18], - 8% [10] which resolved by postoperative week one.

**Prognosis**

The visual prognosis in most cases will be defined by the final visual acuity following removal of the dense, large cataract. The other main risk factor for poor visual outcome is chronically elevated IOP. Studies have found that presenting IOP and duration of the attack may help predict final visual outcomes.

Two studies show that there is no statistically significant association between the preoperative IOP measurement and the final visual acuity [1,18]. It would seem that this one-time measurement of IOP prior to surgery does not correlate with visual outcome. Only one study found that presenting IOP over 40 mmHg [11] was a risk factor for poor visual outcome, but this study suffered from poor follow-up as only 30% of patients came for a second visit after surgery. Presenting visual acuity is also a poor indicator of final acuity: out of 18 patients who presented with light perception without projection, 83% improved to vision with light perception [18]. These are precipitates (48%) and severe corneal edema (24%) [18]. These are expected to resolve following topical treatment. Descemet’s folds lasted an average of 6 days in one study, and their presence did not correlate with final visual acuity [19]. Hyphema has been reported in 3% [18], - 8% [10] which resolved by postoperative week one.

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**Long-Term Prognosis**

The two most important factors to examine in patients with phacomorphic angle-closure are final visual acuity and how many of these patients will go on to develop chronic glaucoma from peripheral anterior synchiae. The final visual acuity varies widely in the literature. Reports detailed visual acuity in various subsets, but in order to give an overview, reports with similar groupings are averaged in Table 2. There are case reports of patients who presented with hand motion vision achieving a final visual acuity of 20/20 [4]. In a study of 74 patients, visual acuity of 20/40 or better was achieved in 68% [18]. A retrospective study followed 82 cases of phacomorphic angle-closure for up to 9 years [1]. Only 82% of the patients had any improvement in visual acuity at final follow-up. On average, 19 months after cataract extraction, the visual acuity had improved from light perception to 20/250. Yet in the largest series of cases, only 40% of 298 cases achieved vision better than 20/200 [11]. Reasons for decreased vision include decreased corneal endothelial cell count, spherical aberration from a fixed pupil, glaucomatous optic neuropathy, and other ocular comorbidities such as macular degeneration, in this elderly population who frequently sought care only after a significant delay [19]. Corneal endothelial cell loss following an attack was reported to be 15% [12].

Since the attack of angle-closure is due to the swollen lens, if there was minimal formation of peripheral anterior synchiae, the patient may not develop chronic glaucoma. One study reported that 3 years after cataract extraction, there was an average of 100 degrees of PAS [1]. Surprisingly, the degree of PAS formation did not correlate to the time delay between symptom onset and surgery, the presenting IOP, or the final IOP. Unfortunately the mean duration of symptoms was not specified, and there were no details of the gonioscopic findings at presentation (which may not be possible with corneal edema) in the affected or fellow eye. In another study, with a mean follow-up of 2 years after cataract extraction, 0 of 21 patients showed any progression of PAS [24]. As expected, cataract extraction following phacomorphic angle-closure deepens the angle: 3 years following cataract extraction, the mean Shaffer grade of 100 eyes was 3 [1].

A review of the literature reveals only a few reports investigating the occurrence of chronic glaucoma. There are only two reports investigating longitudinal changes with conventional glaucoma testing other than IOP. Looking at IOP alone in the study with the longest average follow-up (4 years) [19], the final average IOP was only 13, and only a single patient (4%) was reported as having an a late IOP elevation following cataract extraction, which was treated with two topical medicines. In the retrospective study of 100 patients, the mean final IOP was 16 mmHg [1]. Five years following cataract extraction, 94% of patients had IOP ≤ 21, though some of these patients required IOP-lowering treatment. While 81% of these patients required no glaucoma treatment following cataract extraction, 15% needed pressure-lowering drops (an average of 1.6 medications), and a total of 3 patients (4%) needed a glaucoma procedure (one laser peripheral iridotomy and 2 trabeculectomies). Although in this study the average vertical cup-to-disc ratio was 0.2 higher in the affected eye compared to the fellow eye, vertical cup-to-disc ratios were identical between the two eyes in another study [42]. The same study analyzed general indices from visual fields in the affected eye, where the mean deviation was 5.2

<table>
<thead>
<tr>
<th>Best Corrected Final Visual Acuity</th>
<th>Mean Percent of Patients</th>
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<tr>
<td>20/20-20/50</td>
<td>50</td>
</tr>
<tr>
<td>20/60-20/200</td>
<td>24</td>
</tr>
<tr>
<td>20/200-20/400</td>
<td>11</td>
</tr>
<tr>
<td>Worse than 20/400</td>
<td>15</td>
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</table>

**Table 2:** Average of reported final visual acuities following cataract extraction [10,11,18,19].
dB after 3 years. Since no comparison was given to the fellow eye, it is not known if this can be attributed solely to the phacomorphic angle-closure. In another report using visual fields, there was no statistically significant difference between the pattern standard deviation in the affected and unaffected eye [42].

The single study on Optical Coherence Tomography (OCT) analysis of the optic nerve head measured the Retinal Nerve Fiber Layer (RNFL) thickness in ten patients following an attack (no baseline measurements were available) [42]. Three months after the attack, the average RNFL thickness was statistically similar in the involved and fellow eyes. At 9 months significant thinning had occurred in the eye with phacomorphic angle-closure. The involved eye had an average RNFL thickness of 85 microns (a 9 micron decrease over the previous 6 months) versus 100 microns in the fellow eye, which was stable. The thinning was worse in the superior and inferior quadrants.

In planning long-term follow-up, because the first visit where any elevation in IOP was noted occurred at 18 months, Lee et al. recommend following patients with phacomorphic angle-closure for the development of glaucomatous changes for at least 2 years [1]. Although phacomorphic angle-closure itself should not recur after removing the cataract, aphakic pupillary block has been reported 17 months after cataract extraction (despite already having an iridectomy), providing another reason for long-term follow-up [4]. The fellow eye must receive periodic gonioscopy since up to 14% of cases were reported to have bilateral disease [8]. The duration between fellow eye involvements, however, averaged 10 years, suggesting that a prophylactic peripheral iridotomy in the fellow eye would not be needed. The fellow cataract should be aggressively monitored so that it can be removed before it can become intumescent.

Conclusion

Phacomorphic angle-closure usually occurs in elderly patients with short axial length, as a mature lens swells and forces the peripheral iris into the trabecular meshwork. Increased IOP leads to the typical signs and symptoms of acute angle-closure. The definitive treatment is cataract extraction. In order to avoid operating on an inflamed eye with increased IOP, the attack is treated first with topical IOP-lowering medicines. If further acute treatment is needed, the next step is systemic medication, a laser iridotomy, or a laser iridoplasty if the view allows and the chamber is not flat. Surgical technique for removing the cataract must be adjusted to account for the large, dense lens and positive posterior pressure. Final visual outcome varies in the literature but 80-90% of patients are expected to have an improved visual outcome. At least 80% of patients have been found not to need long-term glaucoma treatment once the lens is removed but still require regular follow-up.

References