Treatment of Periorbital Vascularity, Erythema, and Hyperpigmentation

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KEYWORDS

• Periorbital hyperpigmentation • Classification • Lightening topical • Chemical peel • Laser • Blepharoplasty

KEY POINTS

Periorbital hyperpigmentation (POH) is often multifactorial and impacts patient's emotional well-being and overall quality of life.

- POH can be classified into pigmented, vascular, structural, and mixed subtypes.
- Etiology of POH should be taken into consideration when forming a management plan.
- Treatment varies from topical therapy, chemical peels, dermal fillers, platelet-rich plasma, lasers, to blepharoplasty.

INTRODUCTION

Periorbital discoloration or periorbital hyperpigmentation (POH) is a very frequent presenting complaint of patients. It can affect the individual in many ways because of its perception as a sign of aging, appearing fatigued, and overall negative impact on quality of life (QOL). POH presents as a light to dark brown pigmentation or violaceous discoloration involving the upper and/or lower eyelids. Clinical presentation depends on the etiology and skin color of the patient. Diagnosis is made based on history and clinical examination.

Despite being a common chief complaint, POH is an ill-defined concept. Incidence and prevalence are difficult to estimate due to underreporting of the presentation. Studies are predominantly focused on Asian populations. Based on these studies, POH occurs more frequently in patients with skin of color (SOC) and women.[1]

CLASSIFICATION

The cause of POH is often multifactorial and having a better understanding of the etiology can enhance treatment success. Classification of POH can be divided into vascular, structural, pigmented, and mixed subtypes (**Fig. 1**).[2]

- *Vascular*. The vascular subtype of POH is due to the superficial location of vasculature or thin skin overlying the orbicularis oculi muscle (**Table 1**). **Fig. 2** shows an example of prominent periorbital veins contributing to a mixed vascular and structural POH. The vascular subtype can also be associated with periorbital edema.
- *Structural*. Abnormalities in the periorbital surface contours lead to structural shadows and the appearance of POH (**Fig. 3**). Orbital fat pseudoherniation, skin laxity, tear trough depression, or periorbital edema is the causes of the structural subtype (see **Table 1**).

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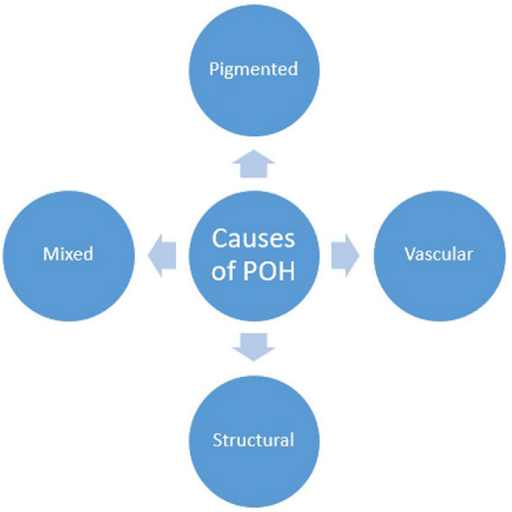

Fig. 1. Classification of POH.

- *Pigmented*. The pigmented subtype is due to increased melanin in the dermis or epidermis. Causative factors of pigmented subtype vary from genetics (**Fig. 4**), extension of pigmentary demarcation lines, nevus of Ota or Hori, dermatitis, postinflammatory hyperpigmentation (PIH), or drug induced (see **Table 1**).[2]

EVALUATION

Differentiating between the different subtypes of POH can be challenging as multiple contributing factors can be present. Manual stretching of the lower eyelid during the physical examination can help elucidate the subtype by differentiating between true pigment depositions, superficial vasculature, or shadowing effect (**Table 2**).[3]

Clinical pearls for physical examination:

1. First, evaluate discoloration with direct lighting:
   a. In the structural subtype, discoloration improves or disappears with direct lighting
2. Second, manually stretch the lower eyelid:
   a. An increase in the violaceous color indicates vasculature subtype (see **Fig. 3**)
   b. True pigment deposit would not result in any change in color (see **Fig. 4**)
   c. Structural subtype improves with manual stretching as the shadowing effect is eliminated (see **Fig. 3**)

Dermoscopy can be helpful in making the important distinction between vascular and pigmented subtypes. **Fig. 5** shows an exaggerated reticular pigment network, characteristic of melanin deposition in basal keratinocytes or at the dermoepidermal junction along rete ridges. This is a common pattern in pigmented POH. There are fine facial blood vessels near the lash line but this patient's POH is predominantly pigmented.

Table 1
Etiologies of POH. PIH: Postinflammatory hyperpigmentation

POH Type	Causes
Pigmented	Genetics PIH Extension of demarcation lines Nevus of Ota Nevus of Hori Drug induced Atopic or allergic contact dermatitis
Vascular	Superficial location of vasculature Thin overlying skin
Structural	Pseudoherniation of orbital fat pads Skin laxity Photodamage Periorbital edema

TREATMENT

Topical therapy

Topical treatments are commonly used as they are readily accessible (**Table 3**). Regimens for POH are often extrapolated from studies based on the treatment of melasma and other disorders of hyperpigmentation. An understanding of key ingredients in products targeting POH can help physicians determine optimum therapy based on the etiology.

Hydroquinone is the most widely used skin lightening agent for pigmented subtype POH, though it has not been studied as either monotherapy or in combination with a topical retinoid for this indication. Hydroquinone targets hyperpigmentation by inhibiting the tyrosinase enzyme and thus inhibiting the conversion of dopamine to melanin. Retinoids play a role in promoting keratinocyte proliferation and epidermal turnover and are hypothesized to reduce tyrosinase expression.[4] Irritation is a common side effect as hydroquinone can be difficult to tolerate on eyelids, especially in combination with a topical retinoid.

Other topical treatments include kojic acid, arbutin, azelaic acid, resveratrol, vitamin K, and caffeine pads. Azelaic acid can be considered in the setting of postinflammatory hyperpigmentation (PIH). Arbutin should be used with caution as the topical treatment can paradoxically cause

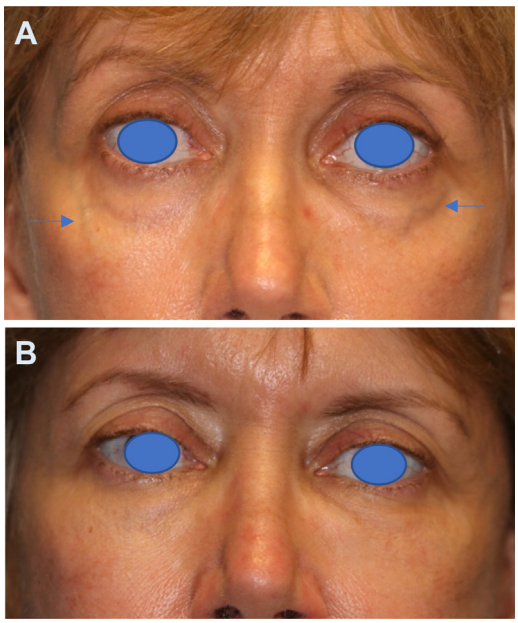

Fig. 2. (*A*) Mixed vascular and structural POH; (*B*) status post–long-pulsed Nd:YAG laser for periorbital veins and dermal filler into tear troughs and palpebromalar grooves. Her prominent preprocedural reticular veins are indicated by blue arrows which resolved after 2 laser treatments.

hyperpigmentation at high doses.[5] One study showed improvement in POH, skin elasticity, and appearance of hydration when vitamin K and caffeine were applied simultaneously compared with placebo in a split-face, single-blinded trial.[6] Resveratrol exhibited 19% improvement in dermal thickness in one study of periorbital skin.[7]

Vitamin C is hypothesized to improve POH, especially vascular subtype, by promoting collagen production to increase dermal thickness.[8] Placebo-controlled trials of topical Vitamin C for this specific indication are lacking. Although it is hypothesized that topical ascorbic acid also inhibits melanogenesis, one placebo-controlled trial did not show significant improvement in melanin content.[8]

Chemical peels

Chemical peels are commonly used to treat various causes of hyperpigmentation. Special considerations should be taken when treating patients with Fitzpatrick skin type IV–VI due to increased risk of PIH. Pretreating with topical retinoid and hydroquinone reduces the risk of PIH and may improve the appearance of POH given their mechanism of action. Pretreating with topical retinoid may also accelerate healing and thus improve downtime and patient satisfaction.[9] Topical retinoid and hydroquinone are generally discontinued 48 hours before the peel although a longer period is required if they are inducing any irritation.

One study included patients with Fitzpatrick skin types II–IV who underwent a chemical peel for the treatment of POH weekly for a total of 4 sessions with 15% lactic acid (LA) and 3.75% trichloroacetic acid (TCA).[10] The regimen resulted in significant aesthetic improvement in almost all the patients. The authors note that the aesthetic outcome remained for at least 4 to 6 months on follow-up when appropriate sun protection was used.[10]

A study by Dayal and colleagues[11] showed that 20% glycolic acid (GA) and 15% LA peel are more effective than topical vitamin C in treating mixed subtype POH. Adverse effects were reported at higher rate in the GA group and included erythema, burning sensation, irritation, dryness, and telangiectasia. Given the current findings in the literature, ascorbic acid is not recommended as monotherapy for pigmented or mixed subtype POH.

Patient's skin type and subtype of POH should be taken into consideration when selecting the depth of peel. Superficial chemical peels, such as 15% LA, 3.75% TCA, and 20% GA, are appropriate and safe for use in patients with SOC to treat the pigmented subtype of POH. The structural subtype requires a medium depth chemical peel.[12] In Fitzpatrick I–III skin, a medium depth chemical peel, such as 35% TCA or a Jessner's and TCA combination, can be applied for the treatment of periorbital rhytids and photodamage.

Lasers

Lasers are becoming increasingly integrated into treatment plans for POH. A systematic review of 10 studies (n = 143) found that 81.2% of participants had a good to excellent response to laser therapy for POH.[13] However, one of the difficulties in fully assessing the efficacy of treatment with laser therapy is that most of the studies are not based on the classification of POH or skin type. In addition to the lack of randomized controlled trials, studies vary in assessing response to treatment and time points at which the data are obtained. Despite the paucity of data, currently published studies have shown that lasers can be effective, safe, and provide satisfactory results with long-term positive outcomes when used appropriately.[13]

- *Vascular*. Facial telangiectasias are most commonly treated with pulse dye laser (PDL), potassium titanyl phosphate (KTP) laser, and intense pulse light (IPL).[14] Unlike facial telangiectasias, reticular veins are larger

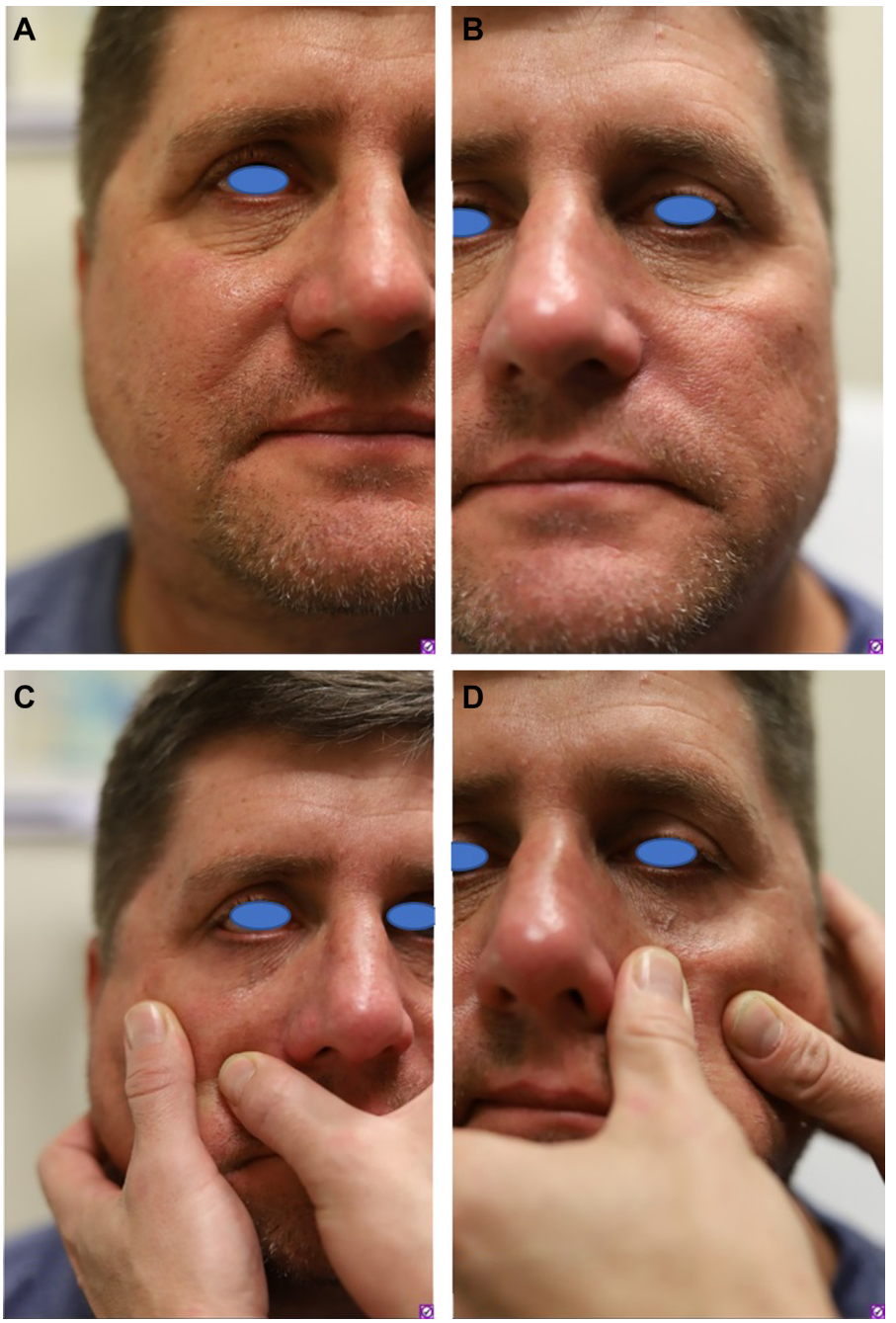

Fig. 3. (*A*, *B*) Mixed vascular and structural subtype POH; (*C*) improved shadowing effect with manual stretching of lower eyelid; (*D*) mild improvement of shadowing effect but increased prominence of periorbital reticular veins.

(1–3 mm), located deeper, and are commonly seen on the lower eyelids, infraorbital cheeks, and temples. Reticular veins can significantly contribute to vascular POH, creating a bluish hue across the lower lid. Due to their depth, deeper penetrating long-pulsed Nd:YAG is a more effective treatment of reticular veins than the aforementioned vascular lasers.[15] A study by Lai and Goldman[16] reported nearly a 100% improvement of periocular reticular veins after treatment with dynamically cooled, variable spot size 1064 nm Nd:YAG. Similar

Fig. 4. (*A*, *B*) Pigmented subtype POH; (*C*, *D*) appearance of pigmentation unchanged to slightly improved on manual stretching of lower eyelid. Patient's POH mostly pigmented subtype with mild shadowing due to periorbital edema.

Table 2
Clinical presentation and physician exam findings of POH

POH Type	Clinical Presentation	Examination
Pigmented	Patches of brown to gray discoloration	No change in pigment intensity on manual stretching
Vascular	Blue to violaceous discoloration mainly involving the lower eyelid with possible visible veins	Discoloration worsens, seems more violaceous in color when skin stretched
Structural	Eye bags, gray shadow, or hollow appearance especially in the medial inferior periorbital region	Improvement of shadows/ appearance of discoloration when eyelid stretched. No discoloration present with direct lighting.

results at the time of treatment and at 12-months follow-up were seen in a study by Ma and colleagues[17] in 26 Chinese women with Fitzpatrick skin type III and IV. Most patients require 1 to 2 sessions and treatment parameters are dependent on the size of the veins as higher energy may be needed for full-thickness penetration into the vessel.[15–17] Generally, a longer pulse duration varying from 20 to 50 ms, nonoverlapping pulses, and epidermal cooling are critical to avoid thermal injury to the epidermis.[15–17] Long-pulsed Nd:YAG is associated with a lower risk of pigmentary side effects and is safer in darker skin types as there is decreased melanin absorption at the 1064 nm wavelength.[18]

- *Pigmented*. For targeting the pigmented subtype, a few studies have looked at Q-switched lasers (QSL), either as monotherapy or in combination with other interventions. QSL, such as QS Ruby (694 nm), QS Alexandrite (755 nm), and QS Nd:YAG (1064 nm), treat pigmentary lesions through selective photothermolysis of targeted melanosomes.[19] In a study by Watanabe and colleagues,[20] 8 Japanese patients with biopsy-proven dermal melanocytosis on the lower eyelids were treated with QS 694 nm wavelength with a fluence of 6.0 to 7.0 J/cm^2 over 1 to 5 sessions. Patients treated with more than one session reported good to excellent response and side effects localized to the treated area resolved within a week.[20] A study by Lowe and colleagues[21] reported greater than 50% improvement of POH in 90% of the subjects that were treated with QS 694 nm and noted a decrease of dermal melanin deposition on posttreatment histologic evaluation.[21]

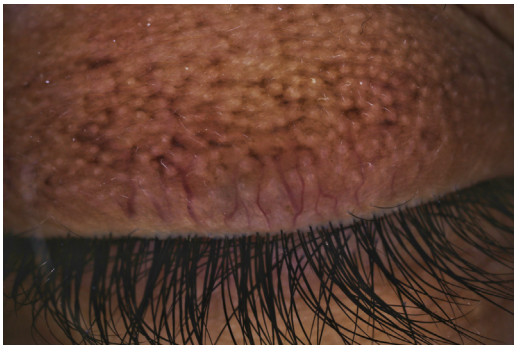

Fig. 5. Dermoscopy of upper eyelid shows exaggerated pigment network with a reticular pattern (the predominant cause of the POH in this patient). Visible veins are also located inferiorly but not in the areas of POH.

Fewer studies exist to evaluate the efficacy of QS 755 nm laser in the treatment of POH, but one would predict similar efficacy. A prospective, split-face study by Rosenbach and colleagues[22] reported similar efficacy between QS 755 nm and QS 1064 nm laser in improving hyperpigmentation. The melanin reflectance spectrometry score improved after the first session and significant clinical improvement was noted after 3 sessions. Both the QS 755 nm and QS 1064 nm lasers resulted in a significant reduction of epidermal pigmentation and melanocytes on histologic evaluation.[22]

Multiple studies have demonstrated the efficacy and safety of QS Nd:YAG laser in treating POH using low fluence and pulse duration.[22,23] In addition to clinical improvement and patient satisfaction, reflectance spectrophotometer showed a significant decrease of melanin in the upper dermis but

Table 3
Treatment modalities for consideration based on POH subtype

POH Type	Causes	Treatment Options
Pigmented	Genetics	Hydroquinone
	Extension of demarcation lines	Retinoid
		Kojic acid
	Nevus of Ota	Azelaic acid
	Nevus of Hori	Vitamin K + caffeine
		Arbutin
		Chemical peel
		Q switched or picosecond lasers
	Drug induced	+ Stop offending medication
	PIH	Treat underlying condition
	Dermatitis	
Vascular	Superficial vasculature	PDL
		Long pulsed Nd:YAG
		Vitamin C
		Carboxytherapy
	Thin skin overlying orbicularis oculi muscle	Injectable filler
		PRP
Structural	Skin laxity	Chemical peel (superficial or medium depth)
		Fractional laser resurfacing (ablative or nonablative)
	Orbital fat pad pseudoherniation	Blepharoplasty
	Tear trough deformity	Filler (HA, fat, calcium hydroxylapatite)
		Blepharoplasty
	Periorbital edema	Treat underlying cause

Abbreviations: PIH, Postinflammatory hyperpigmentation; PDL, Pulsed dye laser; PRP, Platelet-rich plasma

no significant difference in epidermal melanin in posttreatment evaluation.[23] The low fluence used in the study by Xu and colleagues[23] is extrapolated from successful treatment of other pigmented disorders with QS Nd:YAG. The pulse width of the QS Nd:YAG is not sufficient to engender vasospasm in vessels; however, some improvement of the erythema index can be noted if present along with pigmentation.[23]

A new emerging therapy for the treatment of pigmentary disorders is the picosecond laser.[24–26] A retrospective study by Levin and colleagues[27] showed comparable improvement of pigmented lesions, side effects, and patient satisfaction between the QSL group and 755 nm alexandrite picosecond laser in patients with Fitzpatrick skin types III–VI. The picosecond 755 nm laser has been shown to be effective and safe in patients with Fitzpatrick skin type IV to VI with transient side effects resolving within weeks of treatment.[24–27] One small study showed promise using picosecond lasers specifically for POH.[28] More research is needed but this newer therapy may be an effective and safe option for all skin types with lower risk of PIH due to lower photothermal damage.[25]

- *Structural*. Ablative and nonablative laser resurfacing are frequently used to improve skin texture and are often used in the treatment of POH, especially structural subtype. Fully ablative CO_2 laser resurfacing resulted in 50% clinical improvement after 9 weeks in a study by West and Alster.[29] However, there was no significant improvement in melanin measurements obtained using a handheld reflectance spectrometer pre and posttreatment.[29] Postoperative PIH was reported in 33% of patients and lasted for 12 weeks.[29] Similar results were seen in a study of 67 patients with upper eyelid dermatochalasis and periorbital rhytids with significant improvement after treatment with traditional CO_2 laser.[30]

Ablative fractional resurfacing with a CO_2 laser also improves deep wrinkles and textural irregularities but with considerably less downtime and fewer risks than traditional ablative laser.[31] Nonablative fractional laser spares the overlying epidermis, leading to more rapid healing and less downtime than traditional and fractional ablative laser resurfacing.[32] The fractionated 1550 nm

erbium-doped fiber laser has been reported in the literature to improve the pigmented POH subtype at 4-week intervals over 4 months.[32] A recent study by Horovitz and colleagues[33] reported a significant improvement of wrinkles based on physician assessment after treatment with 1565 nm Er:glass fiber laser. Although patients reported a mild-moderate improvement 8 weeks after treatment, minimal side effects and downtime were noted.[33] Physicians should discuss with patients that improvement from nonablative fractional lasers can progress over 6 months.[33] Furthermore, studies have generally supported the safety of nonablative fractional lasers in SOC.[34] However, these studies contained very few subjects with Fitzpatrick V or VI skin type so caution and conservative treatment parameters are advised.[34]

When lasers are being considered to treat POH, the possibility of PIH should be discussed with the patient. Patient counseling when using lasers in the periocular region includes appropriate protective eyewear. When feasible, targeted skin should be stretched outside the orbital rim and laser beams should be angled away from the orbit. The authors usually use metal corneal eye shields when performing laser inside the bony orbital rim.[14]

Filler

Fillers can be an effective treatment for the the structural subtype by eliminating shadows formed from tear trough depression, by subcutaneous fat loss or fat pad descent, or from overlying skin thinning. Fillers are not a substitute for surgical correction in the presence of significant orbital fat prolapse. Treatment with fillers includes hyaluronic acid (HA), calcium hydroxylapatite, and autologous fat grafts.

Small volumes of low G′, relatively thin HA fillers are most commonly used for tear trough correction and are injected into the tear trough deformity with a needle or cannula at the supraperiosteal plane, ideally deep to the orbicularis oculi muscle. More recently, a subdermal, microdroplet placement of low molecular weight HA filler has been proposed.[35] This injection method is not recommended for patients with global volume loss and significant eyelid skin laxity as it may produce eyelid or malar edema.[35]

Fat grafts are another treatment modality for structural subtype POH or translucent lower eyelid skin resulting in increased vascularity and visible orbicularis oculi muscle. Another advantage of autologous fat transplant is decreased risk of blue cast or Tyndall effect caused by the superficial placement of HA filler. However, visible fat lumps can occur resulting in poor cosmetic outcomes. Collagenase-digested fat cell grafts placed in the dermal layer can improve lower eyelid contouring while decreasing the risk of visible collections of fat.[36]

Patients with significant tear trough deformity, including postseptal fat pad pseudoherniation and redundant lower eyelid skin, may not benefit from soft tissue filler. The risk of adverse events when using volume augmentation with filler, such as Tyndall effect and blindness, should be discussed with the patient. Although the risk of intravascular occlusion events is very low with either needles or cannulas, injection with microcannula is associated with a lower risk.[37] Overall, the risk of occlusion with needle injection decreases with experience and whether a needle or cannula is appropriate ultimately depends on the patient, anatomic site, and pathology being treated.[37]

Other injectable

Platelet-rich plasma (PRP) injections decrease the visibility of underlying muscles and vasculature by increasing the thickness of the epidermis and dermis. Mehryan and colleagues[38] treated 10 patients in a single session with intradermal injections of 1.5 mL PRP into the nasojugal groove and crow's feet region. Injection of PRP resulted in significant improvement of infraorbital color homogeneity with 80% of patients achieving fair to good improvement after 3 months.[38] Although PRP has been shown to increase the thickness of the epidermis and dermis, it is not associated with significant improvement in melanin content, stratum corneum hydration, or wrinkle volume.[38] Most common side effects associated with PRP include mild/transient pain and ecchymosis that can last 1 to 2 weeks. These side effects can be minimized by using a cannula.

Although the mechanism of action of carboxytherapy is unclear, one study has shown that subcutaneous CO2 injection once a week for several weeks resulted in improvement in fine wrinkles and overall POH.[39] Carboxytherapy was slightly more effective and associated with less adverse events when injected in the periorbital region in patients with pigmented, vascular, and mixed-type POH.[39]

Surgery

Blepharoplasty should be considered in patients with advanced structural subtype POH, who possess significant lower eyelid skin laxity combined with orbital fat pad pseudoherniation. Blepharoplasty can improve POH by decreasing the shadowing effect by restoring the normal anatomy

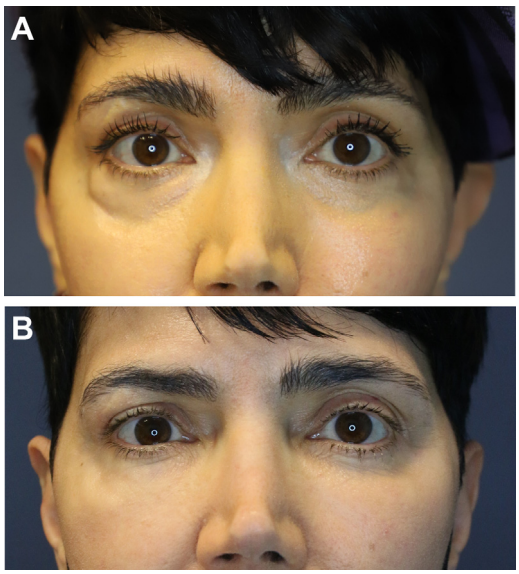

Fig. 6. (*A*) Patient with a history of prior direct transcutaneous lower eyelid fat pad resection greater than 10 years ago and inappropriately placed hyaluronic acid filler combined with prominent infraorbital reticular veins and telangiectasias. She underwent hyaluronidase injections to reverse her filler followed by 3 sessions of laser (KTP and Nd:YAG) to lower eyelids for the prominent vasculature. She then underwent revision transconjunctival bilateral lower eyelid blepharoplasty with abdominal fat transfer. (*B*). Patient 2.5 months postop. (Photos courtesy of Jessyka G. Lighthall, MD.)

and contouring of the periorbital region and removing excess skin. For complex cases, a multifaceted approach may be used to optimize patient outcomes (**Fig. 6**).

DISCUSSION

Various treatment modalities have been studied to improve the appearance of POH in patients (see **Table 3**). As discussed above, identifying the underlying etiology is crucial for effective treatment. In addition, taking into consideration the patient's skin type is important as it can impact the efficacy and safety of certain interventions.

- *Pigmented*. Pigmented subtype POH is due to melanin deposition in the epidermal or dermal layer. Treatment is aimed at reducing the melanin content.
  - For any skin type, bleaching agents such as hydroquinone and kojic acid as monotherapy or in combination with a topical retinoid are commonly prescribed as first-line therapy. Although hydroquinone is widely used, there are limited studies evaluating its efficacy and safety in the periocular region.
  - Superficial chemical peels can be added if a patient is not responding within 2 to 3 months of topical therapy and should be repeated for 3 to 4 sessions. In patients with SOC, superficial peels can be safely used and the area treated with chemical peel should be extended to include the entire face.[10,11] All patients can be pretreated with topical hydroquinone and retinoid if they are not already on this treatment.[9]
  - Lasers can be used in patients with significant periorbital melanosis or in patients who are not responding to topical therapies alone. Q-switched lasers are effective in eliminating pigment. Picosecond lasers offer a new therapeutic option with potentially increased efficacy and more safety for patients with SOC, but more studies are needed for use in POH.[27,28]
- *Vascular.* Vascular subtype POH can be due to the superficial location of vasculature or thin skin overlying the orbicularis oculi muscle.
  - Laser therapy is the most effective intervention in vascular subtype POH.
  - Lasers emitting shorter wavelengths, such as PDL and KTP are used to target facial telangiectasia.[14] For patients with prominent reticular veins as a component of their POH, long-pulsed Nd:YAG has been proven effective in 3 studies and is a reliable intervention in the authors' hands (see **Fig. 2**). In patients with darker skin color, Nd:YAG is recommended due to minimal interaction with epidermal melanin.[17,18]
  - Vitamin C can be added to the treatment plan or used as monotherapy for patients not amenable to laser intervention. Although not commonly considered first-line therapy, carboxytherapy can be used as adjunct therapy if the vascular component of POH is nonresponsive to topical and laser therapy.
  - Injectable filler and PRP are recommended for POH due to thin skin overlying muscle and vasculature. Subcutaneous PRP injection can be effective but its use is limited by the lack of tolerance to prolonged ecchymosis by patients. The authors usually can avoid this by using a cannula for injection.
- *Structural.* Mid-facial descent, tear trough deformity, and skin laxity cause a shadowing effect in the periorbital region.
  - Medium depth chemical peels can be trialed initially if photoaging is mild in patients

with lighter skin color. Fractional ablative laser resurfacing is the authors' treatment of choice for improving more advanced dermatochalasis and textural irregularities of the periorbital skin. Ablative lasers have increased risk of PIH and prolonged recovery periods in SOC. Nonablative fractional laser resurfacing is preferred in patients with SOC although more treatments are required.[30,34]

- Filler is first-line therapy for tear trough deformity (see **Fig. 2**).
- Blepharoplasty should be considered for the treatment of pronounced orbital fat pad pseudoherniation.

SUMMARY

POH is a common concern for patients due to its effect on a patient's well-being and negative impact on QOL. A number of treatment modalities exist for POH varying from over-the-counter topical treatments to surgery. Unfortunately, data from randomized controlled trials on the efficacy and safety of these interventions in POH are limited. However, successful strategies for improving POH do exist. As each treatment modality has different targets, care should be taken to identify causative factors and classification of POH. As the etiology of POH is often multifactorial, a combination of treatment options may be necessary.

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