Periorbital hyperpigmentation etiology, pathophysiology, and clinical features update A review article.

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Abstract: Periorbital hyperpigmentation (POH) is a commonly known aesthetic condition causing marked psychological stress and disfigurement. There is no sufficient information about the etiology, pathogenesis, and clinical features. POH is caused by numerous factors that may be internal and external including genetic, excessive pigmentation, periorbital puffiness, visible underlying blood vessels (veins and capillaries), shadowing effect, and tear trough. As regards the clinical aspect, it appears as round homogenous brownish or dark brown discolored patches in the periocular region always on both sides. Many factors have been established to explain the etiology and pathogenesis of POH, yet the exact mechanism is still unclear. Also, many treatment modalities have been applied to reach maximum efficacy with the least side effects. This review article aims to summarize the most recent and accepted concepts on etiology, pathogenesis and clinical features of POH which may help in finding the best lines of management with the most satisfactory outcomes.

Keywords: periorbital hyperpigmentation, etiology, pathogenesis, and clinical features.

Introduction: Periorbital hyperpigmentation (POH) represents a common aesthetic condition with an unknown definite etiopathogenesis that can have a major psychological effect on the quality of life in affected patients. POH is known by various synonyms including periorbital melanosis(1). Periorbital hyperpigmentation has many etiological factors that include constitutional pigmentation, translucent skin of eyelid leading to showing underlying blood vessels, with aging eyelid skin becomes laxer with redundancy, infraorbital puffiness, presence of melanocytes within the dermis, postinflammatory hyperpigmentation, the extension of physiological pigmentary demarcation lines, ocular hypotensive drugs, diseases like infraorbital melasma, lichen planus pigmentation, acanthosis nigricans, and environmental causes such as ultraviolet (UV) radiation, atopy, lack of sleep, stress, alcohol, and smoking(2). As regards the prevalence of POH is not clear yet due to its variable nature and absence of reasonable explanation. It is more apparent in females than males and the majority of the affected women were housewives (3).
Clinical presentation of POH is characterized by variable discoloration of eyelids skin according to underlying etiology. It is important to know that clinical examination is the cornerstone for diagnosis. POH was classified into a pigmented form that mainly appears as brown color, the vascular form that mainly appears as blue/pink/purple color, structural form, and mixed type. The eyelid stretching test is a simple tool that can help to differentiate between true pigmentation and the shadowing effect of the vasculature. In the case of pigmentation no change in color with stretching while in the case of vascularity, color improves or resolves entirely\(^{(4)}\).

**Grading of POH** was done in comparison to surrounding skin as follows: 0 – skin color comparable to surrounding skin areas of the face Grade 1 – faint discoloration of the infraorbital fold, grade 2 – pigmentation more obvious, grade 3 – deep dark color, involving all four eyelids, grade 4 – grade 3+ with involvement of skin beyond infraorbital skin \(^{(3)}\).

**Classification**

Pigmented type appears as brown color. The vascular type appears as blue, pink, or purple hue may or may not associate with infraorbital puffiness. The structural type where facial contours produce anatomical shadows. Common associations are periorbital bags, ptosis, bony prominence due to loss of subcutaneous fat. Mixed type coexistence of two or three of the previously mentioned types. It is important to specify the type of POH this will help to choose the suitable therapeutic intervention \(^{(5)}\). In another proposed classification, POH has been classified as vascular, constitutional, postinflammatory hyperpigmentation, and shadow effects\(^{(6)}\).

**Dermoscopy:** Dermoscopic finding has been classified as patterns of pigmentation, patterns of the vasculature, and pattern of skin changes: \(^{(7)}\)

- Patterns of pigmentation include blotches, coarse or fine speckled, globular, and exaggerated patterns. The pigment observed may be either epidermal or dermal origin depending on the color of the pigment.
- The pattern of vasculature includes telangiectasia and superficial veins.
- Skin changes include dermoscopy are atrophy and exaggerated skin markings.

**Wood's lamp examination:**

It can be done to detect the origin of pigmentation that may be epidermal or dermal. Epidermal pigmentation becomes more obvious, while in the case of dermal origin the contrast is less pronounced \(^{(8)}\).

**Etiology of POH:**

Many different risk factors have been claimed to be the cause of POH development. Different external and internal factors are possibly implicated in its pathogenesis\(^{(4)}\).

1) **Genetics:**

POH has been in several members of the same family with variable severity. Pigmentation may appear early young and pigmentation increased when getting older. Stress might make pigmentary changes more severe and change lifestyle seems to produce lessening of color\(^{(9)}\).

2) **Dermal melanocytosis:**

Dermal melanocytosis is characterized by excess deposition of melanocytes in the dermis. Grey or blue-grey coloration is the presenting feature. It is either congenital or acquired. It was included within the pigmentary type of Huang et al classification \(^{(10)}\).
2-1-Congenital:

2-1-1 Nevus of Ota represents a congenital form of dermal melanocytosis that it appears as spotty brown-grey to blue-black patches that may involve the skin, conjunctiva, sclera, tympanic membrane, or oral and nasal mucosa of the affected dermatomes innervated by the first and second divisions of the trigeminal nerve. Infraorbital presentation is considered an accused cause of POH (10).

2-1-2 Nevus of Hori was first described in 1984 by Hori et al and is defined as, Ota-like macules that are located on both sides and it is seen later in life. Clinically, it presents with blue-brown to slate-grey mottled pigmentation at the malar region, which may spread to the infraorbital area causing dark circles. The main differentiating sign from other forms of dermal melanocytosis is the absence of ocular or mucosal affection. Nevi of Hori may be caused by excess exposure to UV, hormonal disturbances in pregnancy, and adulthood atopy (11).

2-2-Acquired Postinflammatory hyperpigmentation:
Several conditions like atopy and allergic contact dermatitis, lichen planus pigments, and fixed drug eruptions leave beyond them post-inflammatory pigmentation. Rubbing and scratching of skin around the eyes or deposition of inflammatory fluid due to atopy and allergic contact dermatitis may explain the incidence of POH (12).

3) Superficial location of vasculature:
Another common cause of POH is the superficial position of blood vessels that have been aggravated by thin skin covering the orbicularis oculi muscle(6). POH involves more commonly the entire lower eyelids with a bluish discoloration because of visible veins and capillaries covered by light skin, more in the medial side of the eyelid, and menstruation increases that violaceous pigmentation. On stretching, pigmentation spreads out without blanching or significant lightening with deepening of pigment (14).

4) Tear through depression:
Tear troughs are defined by an anatomical location that becomes depressed with getting older, deeper over the inferior-medial orbital rim. Many factors participate in its development including, thinning of overlying skin of the orbital rim ligaments together with loss of underlying fat, also cheek descent, resulting in deepening of the orbital rim area. All these factors augment the shadowing in the tear trough causing POH (14).

5) Periorbital edema:
The spongy nature of eyelids skin precipitates in periorbital darkening by allowing fluids to accumulate. These fluids may result from systemic and local causes. Specific criteria that support the diagnosis of edema include acceleration of puffiness at early hours of the day or after intake of foods with excess salt. The difference in nature during day times and extension helps to define the effect of that puffiness on POH. It can be assessed by comparing with normal orbital fat, puffiness is retained with downward gaze with not much change during upward gaze (15).

6) Extension of pigmentary demarcation lines of the face:
Pigmentary demarcation lines (PDL) represent boundaries between more pigmented skin and lighter areas. According to the site, they have been classified from A to H lines. In the case of POH F and G lines are of specific concern.

- PDL Group F: It represents an inverted cone-shaped area of pigmentation located
over the lateral field of the face extending from the lateral orbital rim inferiorly or inferolateral

- PDL Group G: It occurs at a site similar to Group F, but with two inverted cones with a normal patch of skin in between two inverted cones forming the letter “W” (16).

7) Other causes:

7-1- Ocular hypotensive drugs:
Prostaglandin analogs are the most common causative drugs of POH, this category includes latanoprost and bimatoprost, which are used by ophthalmologists in the treatment of ocular hypertension. It is expected to develop such pigmentation among those patients between 3 to 6 months after the start of bimatoprost therapy. Fortunately, POH is completely reversible with the stoppage of the eye drops. The mechanism by which prostaglandins induce POH is the accentuation of melanogenesis in the dermal layer and increase in melanin transfer to the basal cell layer of the epidermis (17).

7-2- Environmental Causes:
Ultraviolet radiation (UV) is an important contributing factor in POH. Other lifestyle factors may contribute to developing POH, including sleep disturbances, stressful conditions, alcohol overuse, and smoking despite little sure proof (18).

Treatment of POH:
The therapeutic modalities of POH should be individualized according to the cause. The classical therapies in POH include topical whitening agents and chemical peeling. Several new options are emerging as fillers, autologous fat transplantation, and lasers as Q switched ruby laser (694 nm), Q switched alexandrite laser, and Nd: Yag laser (1064nm) with varying rates of success. Despite all these modalities, the outcomes of most of them are unsatisfactory (2).

Conclusion:
Periorbital hyperpigmentation (POH) is a common condition in dermatology practice with complicated pathogenesis, which makes its treatment is challenging. Further researches and clinical trials might be needed to understand the exact etiopathogenesis and pathophysiology which would help in reaching the optimum lines of treatment with the maximum efficacy and the least side effects.

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