Original Article

A Study of Clinicopathological Correlation of Periorbital Hyperpigmentation

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Abstract

Context: "Dark circles" are esthetic concerns that can affect individuals of any age, gender, or race. They can be familial, physiological, or associated with various medical illnesses. **Aim:** To study the clinicopathological correlation of periorbital hyperpigmentation. **Patients and Methods:** Fifty patients affected with periorbital melanosis (POM) were enrolled for the study after obtaining informed consent. Details regarding history, demographic data, and physical examination of POM were recorded, and a 2-mm punch skin biopsy was taken from the affected skin under local anesthesia and stained with hematoxylin and eosin (H and E), Fontana Masson (Melanin), Perls Prussian blue (Hemosiderin). **Results:** Twenty-three (46%) patients with POM had history of chronic illness before developing POM; 18% patients were atopic, 16% had jaundice, 18% had associated pigmentary demarcation lines (PDL) of type F and G, 8% had acanthosis nigricans, 22% patients had anemia, 16% patients gave positive family history of POM, and menstrual irregularity was seen in 16%. Histopathology revealed dermal melanin deposition with melanophages along with predominantly increased epidermal melanin and melanin in vellus follicular epithelium. Prussian blue for hemosiderin was negative in all cases. **Conclusions:** The study has elicited the multifactorial origin of POM; females are affected more than males. Dermal melanin deposition is a constant feature. Hemosiderin is not found in POM. Increased pigmentation of the vellus follicular epithelium is a feature of POM.

Keywords: *Hemosiderin, melanin, melanophages, periorbital melanosis*

Introduction

Synonyms: Raccoon eyes; Idiopathic cutaneous hyperchromia of orbital region (ICHOR).[1]

Orbital hyperchromia can be primary, also called idiopathic cutaneous hyperchromia of orbital region (ICHOR), or secondary.[1] Secondary periorbital hyperpigmentation has been attributed to dermal melanosis, postinflammatory hyperpigmentation (PIH) from atopic or allergic contact dermatitis, superficial location, and increase in vasculature,[2] hemosiderin, skin laxity, and extension of pigmentary demarcation lines (PDL) of type F and G to the infraorbital region. It can affect both males and females of any race or age.

Patients and Methods

This study was conducted at a tertiary care hospital following Institutional Ethics Committee approval from April 2011 to September 2012. Fifty patients with periorbital pigmentation, satisfying the inclusion criteria, underwent recording of medical history and physical examination and Wood's lamp examination.

Duration and age of onset, atopy/asthma/allergy to any substance or drug, daily sun exposure, daily sleep (in hours), chemical application history (cream, lotion, makeup), kohl (kajal) application history, drug intake, family history, history of jaundice, precipitating factors such as puberty, pregnancy, acute illnesses such as chickenpox, hepatitis, menstrual history, major chronic illness (tuberculosis, hepatitis, renal disease, thyroid disease), other significant illness prior to the development of periorbital hyperpigmentation and physical examination findings were recorded. A 2 mm punch biopsy taken from the affected skin under local anesthesia was processed using hematoxylin and eosin (H and E) stain, Masson-Fontana silver stain to detect melanin (dermal melanin deposition), and Perl's Prussian blue stain to detect hemosiderin deposition.

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Results

Fifty patients were enrolled for the study: 33 females and 17 males. Mean age of onset of periorbital melanosis (POM) was 30.44 years, suggesting that POM is more common in third and fourth decades (70%) [Figure 1]. Five females had onset of POM around puberty and two females attributed triggering of POM to pregnancy. Prior to the commencement of dark circles, 14% subjects had suffered acute illnesses such as viral hepatitis, chickenpox, and typhoid. Jaundice was associated with development of POM in 16% subjects, equal in each sex [Table 1].

Forty-six percent patients reported some chronic illnesses along with POM, decreased sleep <6 h/day was seen in 18% of the subjects, 8% had acanthosis nigricans, 6% patients developed POM after various surgeries (cholecystectomy, hysterectomy, renal stone removal), 4% patients had pulmonary tuberculosis prior to POM, 4% patients were diagnosed to have Lichen planus pigmentosus (LPP) [Figure 2]. POM after drug reaction was seen in one patient. "Pigmentary demarcation lines (PDL type F and G)" on face were noted in 18% [Table 2].

Histopathological assessment

Basal cell layer and lower Malpighian layer showed increase in melanin granules in 90% of biopsies along with dermal melanin and melanophages, while 10% showed only dermal melanin and melanophages. Mild perivascular lymphocytic infiltrate was seen in all.

Basal layer of vellus hair follicles showed increased melanization in 14% of the skin biopsies. Fontana Masson stain for melanin was positive in the dermis in all biopsies. Perl's Prussian blue stain for hemosiderin was negative in all biopsies.

Discussion

Very few studies correlating clinical and histopathological features of POM have been published. We correlated the clinical features and histopathology in 50 patients (M = 17, F = 33). Studies show POM affects both sexes equally[3] or show female preponderance.[4] Preponderance of females in our study probably reflects greater concern about appearance among females. Onset of POM was in the second and third decades in females and in patients with familial history of POM, while in males it was in the third decade. Two females in our study reported onset at the age of 60 years. Thirty-six percent subjects in the study are housewives with not much sun exposure.

History of atopy was found in 18% subjects of whom four patients were atopics, two had allergic contact dermatitis, and three had persistent itching around the periorbital region without any known allergy. This correlates with other studies, which attribute atopy as a cause of POM.

Table 1: Triggering factors associated with development of POM in patients

Triggering factors	Males	Females	Total (out of 50)	Percentage (%)
Puberty	1	5	6	12
Pregnancy	-	2	2	4
Acute illness, e.g., viral hepatitis, typhoid, chickenpox	2	5	7	14
Jaundice	4	4	8	16

Table 2: Prevalence of facial PDL in patients with POM

PDL	Males	Females	Total (out of 50)	Percentage (%)
F-V shaped	2	3	5	10
G-W shaped	1	3	4	8

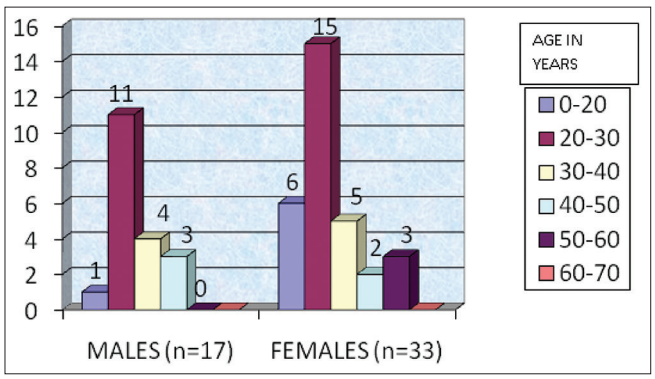

Figure 1: Age and sex among patients with POM

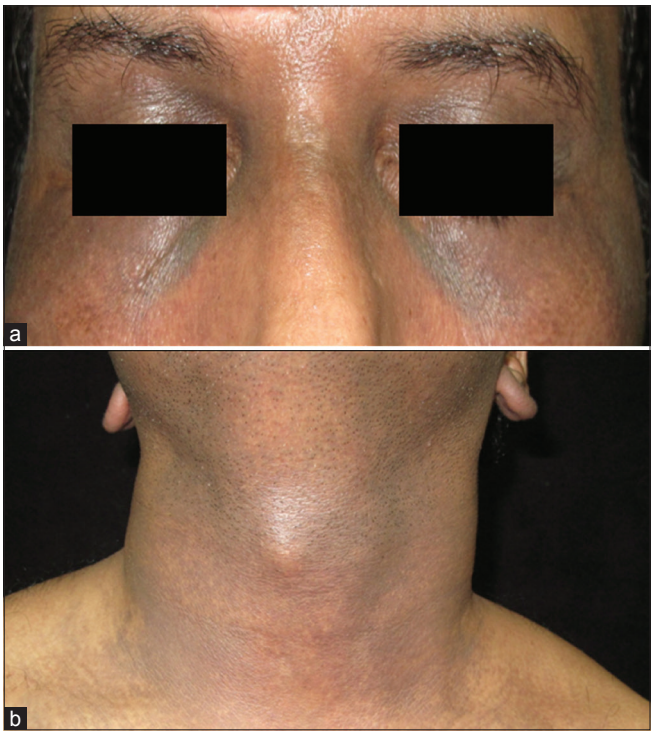

Figure 2: A patient with LPP involving the periorbital region and neck

Family history was found in 16% (male = 1; females = 7) in our study. Features of familial POM do not differ from other causes of POM. Not much data on familial POM in India are available in the literature.

Forty-six percent patients reported some chronic illnesses along with POM, decreased sleep (<6 h/day) was seen in 18% of the subjects, 8% had acanthosis nigricans, 6% patients developed POM after various surgeries (cholecystectomy, hysterectomy, renal stone removal), 4% patients had pulmonary tuberculosis prior to POM, and 4% patients were diagnosed to have LPP. POM after drug reaction was seen in one patient. Many conditions such as fatigue, anxiety, dehydration, excessive sun exposure, drugs, hormonal causes, pregnancy, chronic illnesses such as gynecological disorders, hepatobiliary disorders, thyroid disorders, chronic drug, and alcohol abuse are associated with POM.[5,6] PIH, shadow effects due to overhanging tarsal muscle, eye-bags, or a deep tear trough have also been referred to as possible causes of POM.[5]

Malakar *et al*.[7] reported various triggering factors for POM such as acute infections (viral hepatitis, typhoid fever, chickenpox) prior to development of POM. Two of our patients attributed the onset of POM to viral hepatitis as a triggering factor. One student developed POM after an attack of chickenpox. 14% patients attributed development of POM to various acute illnesses.

PDL (F and G) on face were noted in 18% patients. Malakar *et al*.[8] found that PDL-F extends to the infraorbital region as POM. Sixty-seven percent patients reported POM and PDL-F appearing at the same time.[8] They concluded that POM and facial PDL-F might represent the same entity in many patients.[8]

History of jaundice was given by 16% patients prior to development of POM. Hepatobiliary disorders giving rise to POM have been reported in the literature, though the exact cause is not known.[9] However, these factors are to be tested by case–control studies. History of kohl application was given by 10% of the patients. An Egyptian study by Omar *et al*.[10] has attributed POM to lead (Pb) in the kohl in Egyptian women who apply it around the eyes.

Sixteen percent females had history of menstrual irregularities and reported exacerbation of dark circles with each menstrual cycle. Literature reports menstrual irregularities as one of the aggravating factors in the pathogenesis of POM.[6] Pallor (anemia) was noted in 22% subjects (all females).

Pigmentation involved the entire periorbital area in 90% of the study subjects at the time of presentation though they reported that it began infraorbitally. This suggests that patients became more concerned when POM developed fully. None of the patients showed accentuation of pigmentation under Woods light.

Histopathology of POM

Analysis of biopsies showed increased basal cell and lower Malpighian layer melanization along with increased melanin granules in 90% biopsies. However, 10% patients only showed dermal melanophages and melanin deposition. Dermis showed melanin incontinence and melanophages with a mild perivascular lymphocytic infiltrate in upper dermis. This feature was consistently seen in all patients [Figure 3].

Histological characteristics of periorbital hyperpigmentation suggest that it can be both epidermal and dermal in nature.[11] Malakar *et al*.[7] reported 17 patients with POM and facial PDL (F) over lateral cheeks, both showing in the same patient. They showed melanin incontinence in the upper dermis along with melanophages in the dermis.[7] This finding led them to conclude that PDL-F lines extend as POM [Figure 4]. But the study does not mention about PDL-G (W shaped) on the face and lymphocytic infiltrate seen in POM. PDL-G extending to the infraorbital area has been reported by Al-Samary *et al*.[12] who found facial PDL and POM in two-thirds Saudi women in their study. The study concludes that both POM and PDL-F might represent the same entity. We found 1 male and 3 females with PDL-G and POM. Immunohistochemistry with S-100 and Masson Fontana stain have shown dermal melanocytosis in skin biopsies of POM.[4] We found dermal melanin incontinence, dermal melanophages, and perivascular lymphocytic infiltrate in every patient of POM. There was no evidence of hemosiderin deposition on Perl's Prussian blue staining for iron in the dermis. Goodman *et al*.[9] did not find hemosiderin on Gomori's stain for iron in skin biopsies of patients with familial POM.

An Asian study by Kurita *et al*.[13] found dermal melanocytosis along with melanophages in the patients with POM; however, this was confirmed by

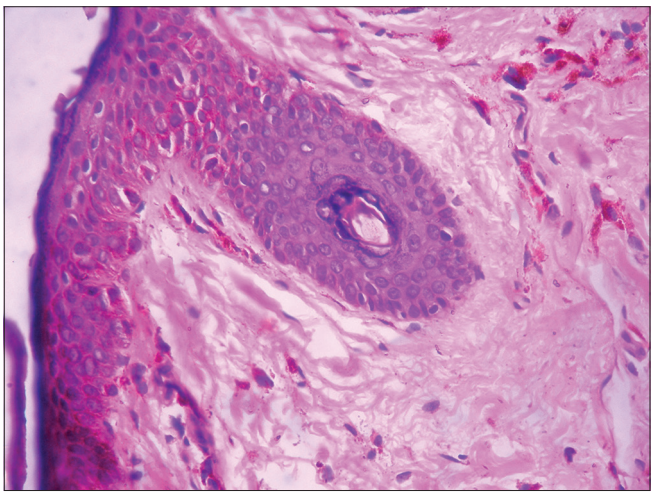

Figure 3: Hematoxylin and eosin (400×) stain showing melanophages along with lymphocytic infiltrate in the mid dermis in a perivascular distribution

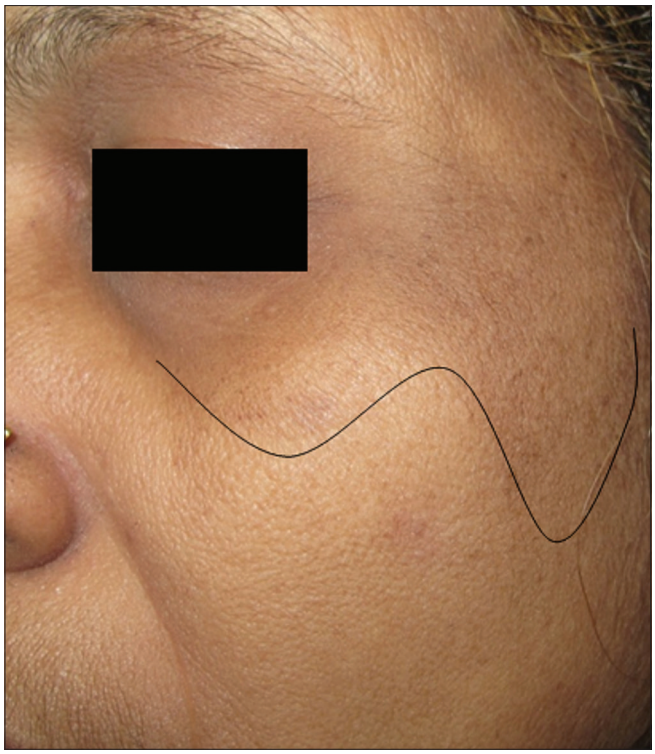

Figure 4: PDL-F lines extending as POM

immune-histochemical staining with S-100 antigen for the dermal melanocytes which was not done in our study. The dermal melanocytosis they reported has a very superficial location in the upper dermis. Interestingly, we found that the basal layer of the vellus hair follicles present in the infraorbital region also showed increased melanization and contributed to the POM [Figure 5]. This is not reported in any of the literature. POM shows dermal melanocytosis and melanophages which are difficult to get rid of. The pigmentation in POM increases and darkens the entire periorbital region over time, and this leads to relapse after some therapies such as chemical peels.

Further research should emphasize using immune-histochemical stains for TRP 1 and 2, PMEL-17, tyrosinase, S-100, CD 4+, and CD 8+ cells to know the pathogenesis of POM. In spite of these issues, our study strengthens evidence that POM is a multifactorial disorder and histopathology is similar irrespective of the cause of POM. It is probably a PIH secondary to various causes except in familial cases.

Conclusion

More females than males are affected by POM (F = 33 > M = 17). Age of onset of POM is in third decade in both the sexes. No specific population or occupation is susceptible to POM. POM can be familial, physiological, and associated with some medical disorders. Acute illnesses and physiological conditions such as puberty and pregnancy may trigger development of POM. PDL over

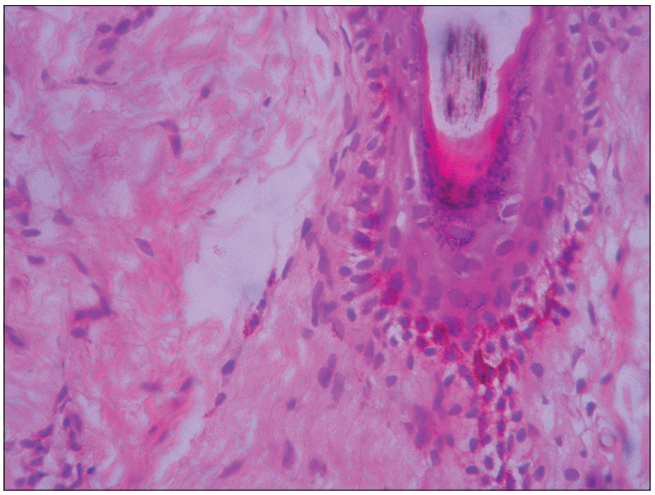

Figure 5: Hematoxylin and eosin (×400) shows increased basal cell layer melanization of one of the vellus hair follicle

face are contributory to POM. Atopic dermatitis, allergic contact dermatitis, acanthosis nigricans, and PIH can be causative of POM. Histopathology of POM reveals dermal melanocytosis and melanophages with a mild perivascular lymphocytic infiltrate, suggesting it is an inflammatory disorder and the pigmentation of a PIH. Increased vellus hair epithelial pigment is a noteworthy feature in some cases. Hemosiderin does not contribute to POM.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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