Periorbital Acquired Dermal Macular Hyperpigmentation: A Distinctive Clinical Entity in Young Adults—Observational Case-Control Study

Abstract

Introduction: Acquired dermal hyperpigmentation (ADMH) presenting on periorbital region has been described as individual case reports. We tried to characterize the features of periorbital ADMH. **Materials and Methods:** This was a retrospective case-control study among our patients who attended the pigmentary clinic during January 2016–December 2017. Clinical, dermoscopic, and histopathological features of subjects who were recruited during the study period were prospectively evaluated. **Results:** Total 19 subjects (11%) were identified among 177 ADMH patients. Periorbital ADMH patients had a relatively younger age of onset (23.26 ± 11.06 vs. 36.16 ± 13.41, $P < 0.001$). Dermoscopy of early periorbital ADMH showed only imperceptible speckled blue-gray dots that accentuated at outer-corner creases of eyes (the "outer-corner crease sign"). Clinicopathological features and prognosis of periorbital ADMH were similar to that of ADMH *per se*. **Conclusion:** Periorbital ADMH should be considered as a differential diagnosis of periorbital hyperpigmentation in children and young adults. Outer-corner crease sign on dermoscopy may help to rule out other differentials in its early presentation.

Keywords: *Acquired dermal macular hyperpigmentation, dermoscopy, lichen planus pigmentosus, outer corner crease sign, periorbital hyperpigmentation*

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Introduction

Periorbital hyperpigmentation is a common clinical entity, especially among young adults in pigmented races.[1] Diagnosis and management of these patients are often challenging. Constitutional periorbital melanosis, postinflammatory hyperpigmentation secondary to allergic or atopic dermatitis, acanthosis nigricans, and anatomical or vascular causes are a few common etiologies for periorbital hyperpigmentation. Here, we describe a series of nineteen acquired dermal macular hypermelanosis (ADMH) cases, presenting with periorbital hyperpigmentation.

Materials and Methods

This was a retrospective case-control study performed at a tertiary care center. ADMH patients with predominant periorbital involvement, registered at the pigmentary clinic of our institute from January 2016 to December 2017 were identified. Some of the patients who were seen while formulating the study were prospectively recruited. Salient features of the subjects were compared to a control arm of ADMH patients without periorbital involvement to assess for any clinico-epidemiological difference. Dermoscopic evaluation of bilateral periocular area (upper and lower eyelids, outer corners of eyes) was performed in all prospectively recruited patients (MRT) using a handheld Dermlite DL200 dermoscope at 10X magnification in polarized mode. Histopathological features were reviewed by two experienced dermatopathologists (DA and BDR).

Results

The retrospective data yielded eleven patients of periorbital ADMH. Eight more cases were seen during the study period and were prospectively recruited making a pooled total of 19 subjects. The total number of controls (ADMH without periorbital involvement) was 158. Hence, the incidence of periorbital ADMH was 11% (19/177). Compared to the control patients, the mean age of periorbital ADMH patients was significantly less, (25.05 ± 11.37 vs. 39.25 ± 13.12, $P < 0.001$). The other

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clinical and demographic characteristics of subjects and controls were similar as detailed in Table 1.

Periorbital region was the site of onset in 6/8 of the subjects in the prospective study arm. No specific precipitating factor could be elicited from any of them. Six of them had been mistreated as acanthosis nigricans or fixed drug eruption (FDE). None of the subjects had lichen planus lesions at other body sites. Topical tacrolimus and oral antioxidants were offered to all patients. However, half of them (4/8) needed oral steroids during the disease course due to the development of new lesions at other parts of the body.

Dermoscopic features showed some interesting findings in the prospective subjects. Those who presented early in their disease stage [Figure 1a and b] showed only subtle hyperpigmentation. Hence, dots and globules of early ADMH were imperceptible in the initial stages. However, there was an accentuation of dots and globules at outer corner creases of eyes ("outer corner crease sign") that helped us in early diagnosis of cases (n = 4). Histopathology showed vacuolar interface dermatitis with perivascular inflammatory infiltrates and pigment incontinence [Figure 1c]. The subjects in their later stages of disease [Figure 2a and b] demonstrated a diffuse pattern (grade 4) on dermoscopy (n = 4). Histopathology showed mainly dermal pigment incontinence with little basal cell changes [Figure 2c]. Those with milder involvement initially had also progressed to this diffuse pattern, (n = 3) as evidenced on later follow-up after 6 months.

Discussion

ADMH is an umbrella term used to describe diseases which clinically present as small to large hyperpigmented macules with histopathological evidence of current or resolved interface dermatitis and pigment incontinence without any clinically evident prior inflammatory skin lesions.[2,3] It includes diseases described earlier as Riehl's melanosis/pigmented contact dermatitis, lichen planus pigmentosus (LPPig), and ashy dermatosis

Table 1: Clinico-epidemiological features of periorbital ADMH compared to ADMH *per se*

Parameter	Periorbital ADMH (n=19)	ADMH (n=158)	P
Age (mean±SD), in years	25.05±11.37	39.25±13.12	**<0.001**
Age of onset (mean±SD), in years	23.26±11.06	36.16±13.41	**<0.001**
Female: Male	2.16	3.79	0.377
Duration of illness in months, median (IQR)	12 (8-15)	24 (9.5-48)	0.107
Symptomatic skin involvement (itching)	10/19 (53%)	53/158 (33%)	0.100
Confined to head and neck region	11/19 (58%)	63/158 (40%)	0.132
Lichen planus at other sites	0	11/158 (7%)	0.375
Precipitating factors (Mustard oil, henna, hair dye, cosmetics)	8/19 (42%)	83/158 (52%)	0.389
Associated conditions	6/19 (32%)	50/158 (32%)	0.920
Atopic dermatitis	4/19	18/158	0.263
Hypothyroidism	1/19	25/158	0.315
Treatment response - satisfactory	5/19 (26%)	55/158 (35%)	0.458

ADMH: Acquired dermal macular hyperpigmentation; SD: Standard deviation; IQR: Interquartile range; Bold letters denote significant P value at P<0.05

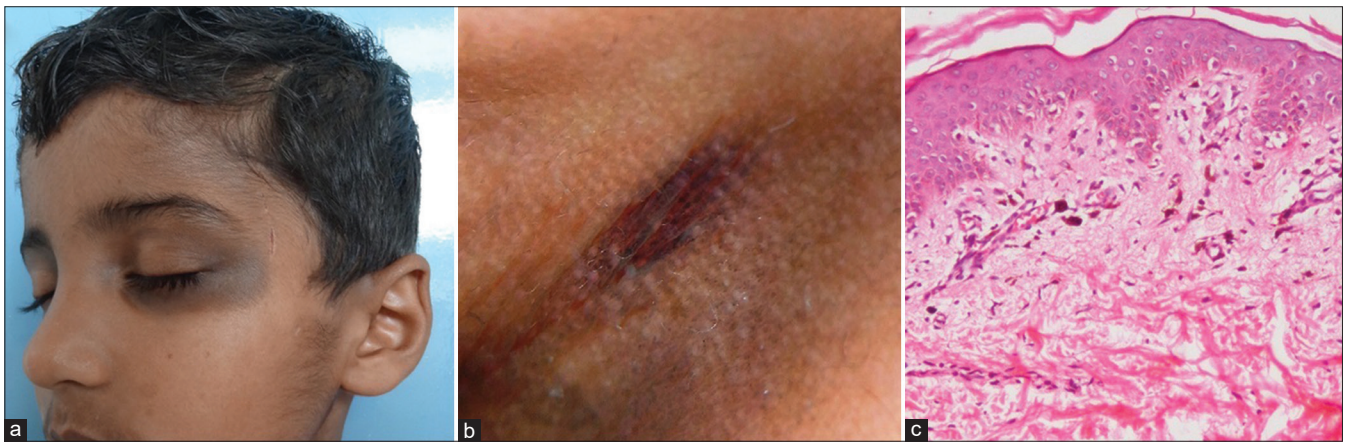

Figure 1: Early periorbital ADMH in a 9-year-old boy. (a) Barely perceptible hyperpigmented patches were noted in the infra-orbital region. (b) Discrete dots and globules that accentuated around the outer-corner creases of the eyes, the "outer-corner crease sign" on dermoscopy. (c) Early basal cell changes with minimal upper dermal perivascular inflammation. Pigment incontinence can also be appreciated. (H and E, 100×)

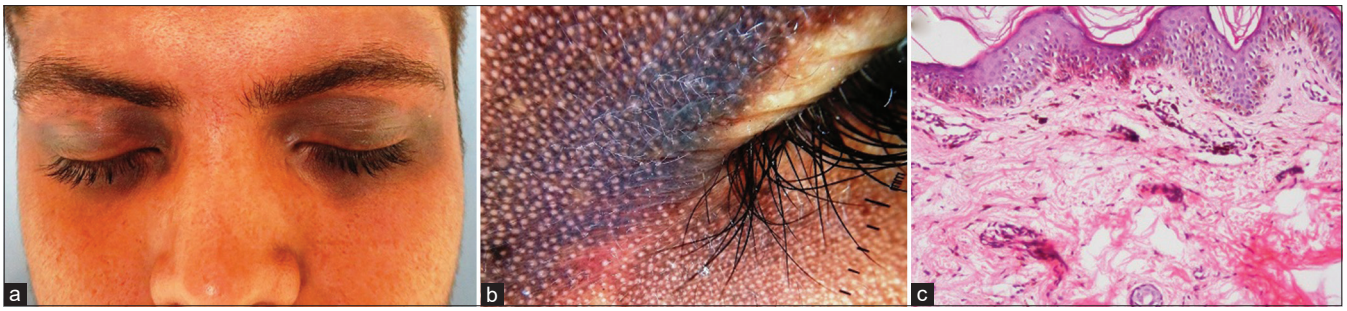

Figure 2: Late periorbital ADMH in a 16-year-old boy. (a) Easily noticeable dark slate gray pigmentation around both periorbital region. (b) Diffuse pattern of dermal pigment structures sparing eccrine openings on dermoscopy. (c) Marked dermal pigment incontinence and dermal inflammation with minimal basal cell changes. (H and E, 100×)

(erythema dyschromicum perstens, EDP). There is a scarcity of literature regarding periorbital ADMH.

In our study, periorbital ADMH was found to be associated with a younger age of onset with the median at 23 years. Accentuation of pigmented structures on dermoscopy was found to be a useful clinical tool to suspect ADMH in children presenting early in its disease course as periorbital hyperpigmentation. Treatment response of periorbital ADMH was less than satisfactory.

We could find only 6 reports of LPPig or EDP with periorbital localization in English literature. The earliest report of periorbital ADMH dates back to 1968 when Knox *et al*.[4] reported EDP involving periorbital region in a middle-aged woman. Subsequently, few more cases of EDP/LPP presenting as periorbital hypermelanosis has been reported.[5-8] Similar to our patient cohort, FDE was considered a close differential in one of those cases.[6]

An interesting and clinically useful finding in the dermoscopy of periorbital ADMH is "outer-corner crease sign." In early ADMH, there is sparse melanin incontinence that corresponds to dots and globules in dermoscopy. It is discretely distributed in early ADMH owing to the focal basal cell vacuolizations, while late ADMH shows a diffuse pattern of pigmented structures sparing only eccrine openings due to widespread basal cell damage.[3] Crowding of these discrete dots and globules in early ADMH at ridges of skin creases may be the reason for "outer-corner crease sign." Of note, inverse LPPig, the LPPig affecting flexures, show pigmentation of skin creases. Dermoscopic findings of dots and globules in early phases and diffuse pattern in late cases are consistent with the ADMH severity in early and late phases.[3] Recently, hyperpigmentation of upper eyelid with characteristic dermoscopic features of LPP has been described.[9]

Frequent misdiagnosis of periorbital ADMH as FDE or acanthosis nigricans signifies the knowledge gap among dermatologists to differentiate between these entities. The possible diagnostic confusion between ADMH and FDE has been highlighted in a report of FDE, which was initially misdiagnosed as EDP.[10] FDE has an initial erythematous phase involving entire patch compared to erythema at the periphery of the patch in EDP or no erythema in most of LPPig. The onset of the lesions at fixed sites correlating with drug intake and a histopathology showing intense hydropic degeneration of basal layer and apoptotic keratinocytes along with tissue eosinophilia characterize FDE.[6] Focal epidermal hyperpigmented spots distributed along linear crista cutis is a dermoscopic feature of acanthosis nigricans. In contrast, our periorbital ADMH cohort had dots and globules which are characteristic of dermal pigmentation distributed along the ridges of the outer corner crease area of eyes in their initial stages.

In summary, we have documented the clinico -epidemiologic, dermoscopic, histopathologic, and prognostic features of periorbital ADMH. Periorbital hyperpigmentation is not an uncommon clinical entity among young adults in pigmented races. Acquired dermal macular pigmentation may also present with periorbital hyperpigmentation, especially in younger age groups as evident from this study. Clinical course and prognosis of this entity are similar to that of ADMH *per se*. Documentation of accentuated dots and globules at the outer corner creases of the eyes on dermoscopy helps in early diagnosis of this rare entity. Careful dermoscopic evaluation of outer-corner creases of eyes should be carried out in children and young adults who present with periorbital hyperpigmentation for proper diagnosis and better prognostication of this rare entity.

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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Conflicts of interest

There are no conflicts of interest.

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