

Atopic Dirty Neck or Acquired Atopic Hyperpigmentation? An Epidemiological and Clinical Study from the National Skin Centre in Singapore

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Key Words

Acquired atopic hyperpigmentation · Atopic dirty neck ·
Rippled pigmentation · Reticulate pigmentation ·
Poikiloderma-like lesions · Atopic dermatitis

Abstract

Background: ‘Atopic dirty neck’ is a poorly understood acquired hyperpigmentation in patients with atopic dermatitis (AD). **Objective:** To report a single-centre experience with synthesis of this entity’s features. **Methods:** All patients with AD with dirty neck seen over a 5-month period at the National Skin Centre were invited to participate. **Results:** Out of 544 AD patients examined, 78 (14.3%) had acquired pigmentation of the neck. The majority had moderate-to-severe underlying eczema. Histopathology showed increased epidermal melanin and dermal melanophages, a thickened basement membrane and a dense superficial perivascular infiltrate. **Conclusion:** Acquired atopic hyperpigmentation has a high prevalence, particularly in adolescent Asian males. Clinico-pathological correlation suggests it results from both frictional melanosis and post-inflammatory hyperpigmentation. The rippled appearance and the onset in adolescence are probably due to accentuation of the juxta-clavicular beaded lines.

Optimal control of eczema may improve and potentially prevent the development, which is of importance considering the psychosocial impact of the condition.

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Introduction

First described in 1987 by Colver et al. [1], ‘atopic dirty neck’ is a peculiar acquired hyperpigmentation that predominantly affects the anterolateral aspects of the neck in patients with atopic dermatitis (AD). Other terms used to describe this condition include reticulate or rippled pigmentation of the neck and poikiloderma-like lesions on the neck in AD [2–5]. While it is a well-recognized physical sign of AD, data are limited on the epidemiology and pathogenesis of this condition [6, 7]. Hence, the aim of our study was to further elucidate this entity’s features from data generated from a single-centre experience and a review of the literature.

The study was presented at the National Skin Centre Dermatology Updates 2013 Conference on September 28, 2013.

Table 1. Demographic details of AD patients with and without acquired atopic hyperpigmentation

	AAH		p
	yes (n = 78)	no (n = 466)	
Ethnicity			
Chinese	65	377	0.91 ¹
Malay	10	53	
Indian	2	20	
Others	1	10	
Unknown	0	6	
Gender			
Male	68	304	<0.001
Female	10	162	
Median age, years	22	13	<0.001
Range	10–55	0.4–83	

AAH = Acquired atopic hyperpigmentation.
¹ p value calculation excludes unknown ethnicity.

Patients and Methods

Study Design

This was a cross-sectional study over a period of 5 months where all patients with a diagnosis of AD seen at the Paediatric Dermatology and Adult Eczema Clinic in the National Skin Centre in Singapore were examined by the attending dermatologist for acquired hyperpigmentation of the neck. The affected patients were then invited to participate in the study. Exclusion criteria included reticulate pigmentation of the neck secondary to other causes such as acanthosis nigricans, contact dermatitis and confluent and reticulate papillomatosis. After informed consent was obtained, the study subjects completed a study questionnaire, a clinical examination and photography of the neck. In addition, adult subjects aged 21 years and over were invited to undergo skin biopsies of both lesional and non-lesional skin for clinico-pathological correlation. This study was approved by the institution's Domain-Specific Review Board.

Evaluation of AD

All subjects fulfilled the UK Working Group diagnostic criteria for AD [8]. The objective Scoring Atopic Dermatitis (SCORAD) index was used for grading AD into mild (<15, range 0–83), moderate (15–40, range 0–83) and severe (>40, range 0–83) AD [9]. Quality of life (QoL) was assessed using the Patient-Orientated Eczema Measure (POEM) and the Dermatology Life Quality Index (DLQI). Other data collected included the age at onset of AD, atopic comorbidities, number of previous hospital admissions, amount of time missed from school/work because of the eczema and number of episodes of infected eczema over the neck in the previous 6 months. An infection episode was defined as follows: a skin infection with (1) clinical signs such as crusting, oozing and/or purulent discharge that necessitated systemic or topical antibiotic therapy and (2) improvement of clinical symptoms after therapy.

Evaluation of Atopic Dirty Neck

Clinical examination of the affected area was performed to determine the pattern, location and severity of the condition. Other body sites such as the face, axillae and flexures were also examined for involvement. Standardized photography was performed to document the severity and extent of pigmentation. The photographs were also used as an objective means to standardize the severity scoring of the pigmentation into mild, moderate and severe and this was performed in a blinded manner by dermatologists involved in the study. Data were collected regarding the age of onset of the pigmentation, family history, possible aggravating factors, and previous and current medications used to treat both the neck eczema and/or pigmentation. In addition, subjects completed a questionnaire that assessed specifically the impact of the neck pigmentation on their QoL (NP-QoL). The NP-QoL was modified and based on the validated Melasma Quality of Life questionnaire [10, 11].

Histological Analysis

Two 4-mm punch biopsy specimens were obtained from both lesional and non-lesional skin from the neck. All specimens were stained with haematoxylin and eosin, Fontana-Masson, periodic acid-Schiff, Congo red, HMB-45, Melan-A and tyrosinase for histological analysis.

Statistical Analysis

To associate this acquired hyperpigmentation with the various parameters measured, the χ^2 test and Fisher's exact test were used where appropriate for categorical variables and the Kruskal-Wallis test was used for continuous variables. A p value of less than 0.05 was considered to be statistically significant. Statistical analysis was performed using SPSS version 21 (Chicago, Ill., USA). Multivariate analysis was not performed as we did not have the resources to collect clinical data on the patients without atopic dirty neck.

Results

Study Selection

A total of 544 patients with AD were examined for atopic acquired hyperpigmentation of the neck. Of these, 78 patients were found to be positive for this clinical feature and were invited to participate in the study; 7 patients declined and the other 71 patients were enrolled in the study. Additionally, 4 patients aged 21 or over agreed to have biopsies done from lesional and adjacent non-lesional skin for histological analysis.

Demographics and Clinical Characteristics of AD Patients with Acquired Atopic Hyperpigmentation

Out of a total of 544 AD patients examined, 78 (14.3%) had acquired atopic hyperpigmentation of the neck. The key demographic findings are presented in table 1. Overall, the prevalence was 2.2% in subjects aged 12 years or younger compared to 23.3% for those over 12 years of age.

Table 2. Clinical characteristics of 71 AD patients with acquired atopic hyperpigmentation

Objective SCORAD	38.5 ± 12.7 [35.5]
Total SCORAD	46.9 ± 14.3 [46]
POEM	12.9 ± 7.3 [11]
Total DLQI	9.8 ± 6.6 [9]
Total AD NP-QoL	26.0 ± 15.5 [22]
Age of onset of AD	
<2 years	19 (26.8)
2–4 years	9 (12.7)
>4 years	42 (59.2)
Unknown	1 (1.4)
Allergic rhinitis	
Yes	43 (60.6)
No	26 (36.6)
Unknown	2 (2.8)
Asthma	
Yes	28 (39.2)
No	42 (59.2)
Unknown	1 (1.4)
Family history of AD	
Yes	37 (52.1)
No	27 (38)
Unknown	7 (9.9)
Family history of atopic dirty neck	
Yes	6 (8.5)
No	50 (70.4)
Unknown	15 (21.1)
Hospitalization in the past 12 months	
1–3 times	15 (21.1)
None	56 (78.9)
Number of work/school days missed due to eczema	
>10 days	12 (16.9)
1–10 days	19 (26.8)
None	40 (56.3)
Episode of infected eczema over the neck in the last 6 months	
Yes	15 (21.1)
No	53 (74.6)
Unknown	3 (4.2)
Aggravating factors	
Scratching	33 (46.5)
Food	9 (12.7)
Heat	38 (53.5)
Sweating	36 (50.7)
Regular use of the following on the neck	
Perfume	3 (4.2)
Topical traditional Chinese medication	5 (7)
Jewellery	1 (1.4)
Tight-collared shirt	9 (12.7)

Values are presented as means ± SD with medians in square brackets or numbers with percentages in parentheses.

The highest prevalence was in males between 20 and 30 years old (35.6%). Males were more likely to be affected compared to females (p value <0.001). There was no racial predilection found among the different ethnic groups represented, namely Chinese, Malay and Indian races.

The clinical profile of the patients with this acquired atopic hyperpigmentation of the neck is presented in table 2. The mean and standard deviation of the objective SCORAD index in the affected patients was 38.5 ± 12.7 (range 0–83), with 1.4, 57.7 and 40.8% having mild, moderate and severe AD, respectively; 15 patients (21.1%) had at least 1 hospital admission in the previous 12 months due to eczema and 15 patients (21.1%) also had at least 1 episode of infected eczema over the neck in the previous 6 months. The mean and standard deviation of the DLQI score was 9.8 ± 6.6 (range 0–30), with 43.7% of patients being very or extremely severely affected by their AD. The mean and standard deviation of the POEM score was 12.9 ± 7.3 (range 0–28).

The majority of subjects reported that the neck pigmentation first occurred during or after puberty (fig. 1). The anterolateral neck was most commonly affected in 36.6%, followed by whole neck involvement in 32.4%. In 29.6% of subjects, there was also axilla and/or flexural involvement. The pigmentation affecting the neck was classified as mild in 40.6%, moderate in 39.1% and severe in 20.3% (fig. 2). The pattern of pigmentation was collected in 65 subjects (91.5%). In none of the patients could the pigmentation be described as reticulate in pattern. All subjects were noted to have a rippled pattern of pigmentation and in some of those (12.7%) the pigmentation had a mixed patchy/rippled appearance.

Overall, the neck pigmentation had a significant impact on the QoL of the subjects, with a mean and standard deviation of NP-QoL score of 26.0 ± 15.5 (range 7–70). Higher NP-QoL scores were associated with increased severity of the hyperpigmentation, although this association was not statistically significant ($p = 0.262$). Patients were most disturbed by the appearance (81.9%) and felt frustrated (70.8%), embarrassed (68.1%) and unattractive (59.7%) because of it.

Associated Risk and Aggravating Factors

Self-reported aggravating factors were heat (53.5%), sweating (50.7%), scratching (46.5%) and food (12.7%). The majority of patients did not have contact with perfume, fragrances, cosmetics, deodorants, jewellery or chains, tight-collared shirts or ties.

Prior to the onset of neck pigmentation, 71.8% had a history of topical corticosteroid use on the neck, with

Fig. 1. Acquired atopic hyperpigmentation of the neck: age of onset according to the patients.

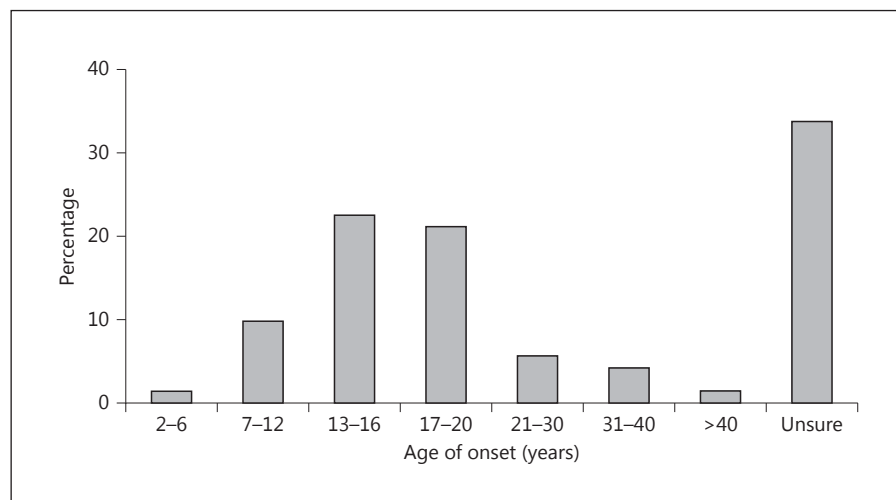


Fig. 2. Acquired atopic hyperpigmentation of the neck. **a** Mild severity. **b** Moderate severity. **c** Severe atopic dirty neck. **d** Same patient as seen in **c** showing marked improvement of the pigmentation over the neck after 2 years.

54.9% using topical corticosteroids at least 3–5 times a week; 85.9% had a history of frequent use of moisturizers on the neck. At the time of the study, 38% were using topical corticosteroids and 63.4% was using moisturizers on the neck. Previous use of topical calcineurin inhibitors was reported in 16.9%. None of the patients reported regular use of bleaching agents such as hydroquinone cream.

A history of at least 1 recent hospital admission and a higher objective SCORAD were both associated with an increased severity of the hyperpigmentation ($p = 0.006$ and $p = 0.014$, respectively).

Histopathological Features

A total of 4 subjects underwent skin biopsies for histopathological analysis (table 3). The following histological features were seen in the lesional (pigmented) skin of all cases: increased dermal melanophages, a thickened basement membrane and a denser superficial perivascular dermal infiltrate compared to non-lesional (control) skin (fig. 3a–f). Epidermal melanin pigmentation was more pronounced in 3 out of 4 lesional compared to non-lesional skin specimens.

Table 3. Histological features of patients with acquired atopic pigmentation of the neck with clinical correlation

	Clinical features		Histological features									
	active neck eczema	type of pigmentation	chronic dermatitis		epidermal melanin pigmentation		dermal melanophages		basement membrane prominence/thickening		sebaceous glands	
			pigmented skin	control skin	pigmented skin	control skin	pigmented skin	control skin	pigmented skin	control skin	pigmented skin	control skin
Case 1	+	patchy	+	–	+	+	↑↑	↑	↑	↑	–	–
Case 2	+	patchy	+	+	↑	↑	↑↑↑	↑↑	↑	↑	–	–
Case 3	–	rippled	–	–	↑	+	↑↑↑	↑	↑	–	+ and high-lying	–
Case 4	–	rippled	–	–	↑	+	↑↑↑	↑	↑	–	+ and high-lying	+

– = Absent; + = present; ↑ = mildly increased; ↑↑ = moderately increased; ↑↑↑ = markedly increased.

During the time of biopsy, 2 patients (cases 1 and 2) had active eczema around the neck area and, clinically, pigmentation around the neck was both patchy and rippled. In the biopsies taken from the lesional skin of these 2 patients, there was compact orthokeratosis and acanthosis, which was evidence of rubbing and chronic dermatitis, respectively; 1 case also showed focal spongiosis. The basement membrane was prominent in both lesional and non-lesional skin in both patients. Sebaceous glands were not visualized in the sections examined.

The other 2 patients (cases 3 and 4) did not have clinical features of active neck eczema at the time of biopsy and showed only rippled pigmentation. Sebaceous glands were seen in the biopsies taken from lesional pigmented skin and appeared high-lying compared to control skin (fig. 3g, h). The basement membrane appeared prominent in lesional skin but appeared normal in non-lesional (control) skin specimens.

Amyloid deposition was not detected with Congo red staining in all cases. Apoptotic keratinocytes were not increased in any of the biopsy specimens. Epidermal basal melanocyte numbers were within normal limits and were not increased in either the lesional or non-lesional skin on the HMB-45, Melan-A and tyrosinase stains.

Discussion

This study found that the overall prevalence of acquired hyperpigmentation of the neck in patients with AD was 14.3% in a cohort of Asian paediatric and adult patients with AD. A previous study from Japan reported a much higher prevalence of 35.5% in an adult AD cohort [5]. In contrast, a study by Trautmann et al. [12] found a lower prevalence of 5.9% in a Caucasian cohort. Our

study lends support to the hypothesis that acquired atopic pigmentation of the neck may be more common in Asian patients.

An important finding in this study was the characteristic onset of the pigmentation in puberty and early adulthood, which was similar to other studies [1, 2, 12]. While Manabe et al. [2] reported that ‘rippled pigmentation of the neck’ was not found in any patient younger than 16 years of age, we found that it can occur in children, albeit rarely. In addition, the prevalence decreased after the age of 30.

We found that it occurred more commonly in patients with severe AD, as evidenced by higher SCORAD scores and a history of recent hospitalization. In addition, affected patients also had active eczema affecting the neck, evidenced by the recent and concurrent use of topical corticosteroids over the neck and a history of infected eczema affecting the neck.

Colver et al. [1] reviewed the biopsies of 9 patients with ‘dirty neck’. Their main histological findings included epidermal acanthosis, abundant basal melanin pigmentation with lesser amounts throughout the entire thickness of the epidermis and increased numbers of upper dermal melanophages. These histological features were consistent with our findings and compatible with post-inflammatory hyperpigmentation and/or frictional melanosis [13]. Manabe et al. [2] also reported blurring and slight thickening of the basement membrane in their biopsies of patients with ‘dirty neck’. These concurred with our findings of a thickened basement membrane in lesional skin. However, they found focal basal vacuolar alteration and the presence of Civatte bodies, consistent with interface dermatitis, which were not found in this study. Interestingly, we found that biopsies from non-lesional but eczematous skin also showed the presence of a thickened

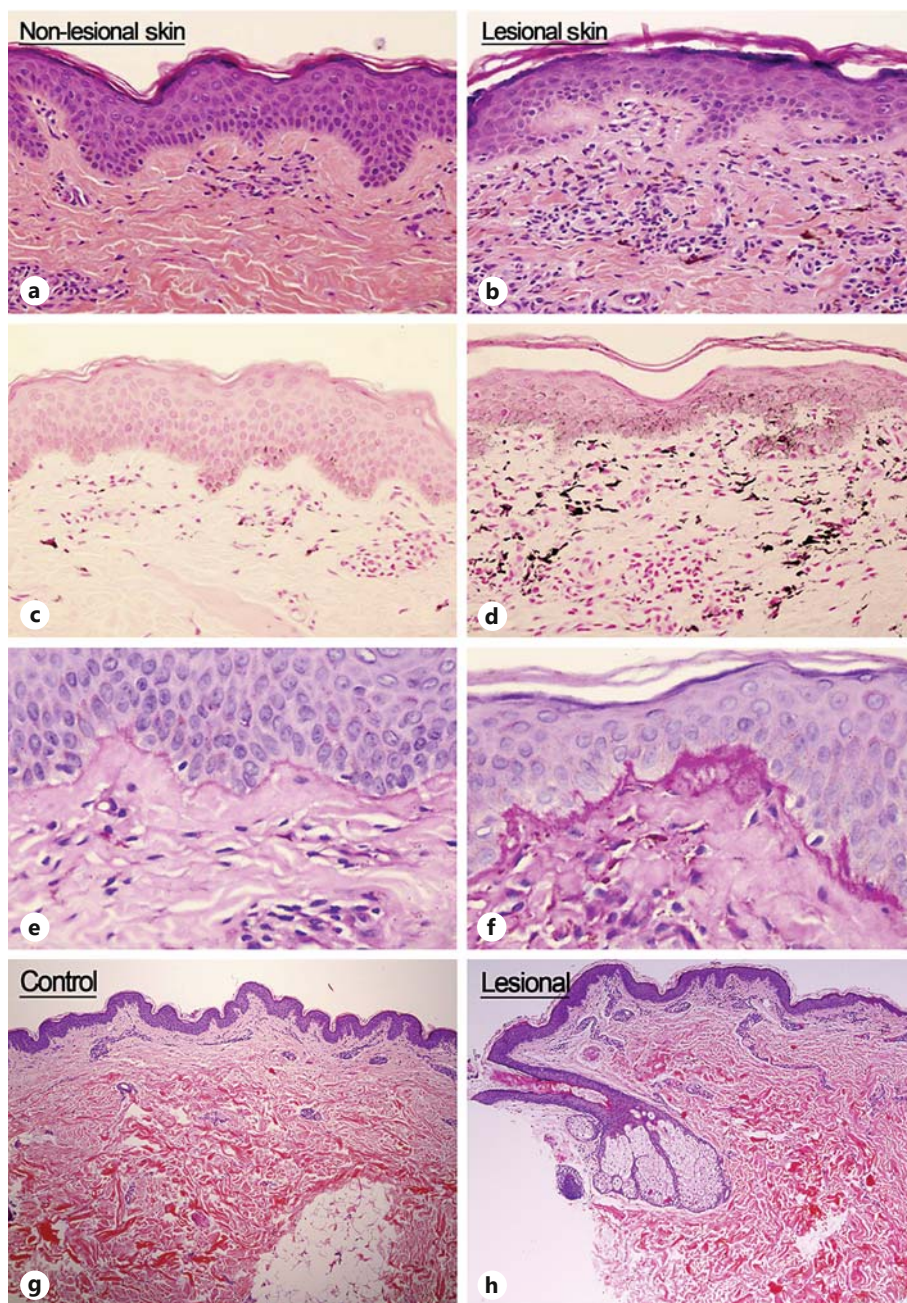


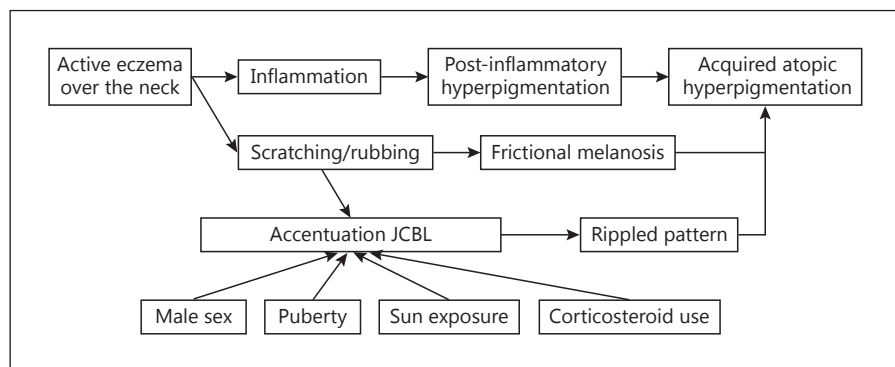
Fig. 3. Acquired atopic hyperpigmentation: histological features. Lesional vs. non-lesional skin (histological photographs taken from patient 4 of table 3; clinical photograph seen in figure 2b). **a, b** More dense superficial perivascular dermal infiltrate in lesional skin compared to non-lesional skin. HE. $\times 200$. **c, d** Increased epidermal melanin and increased melanophages in lesional skin compared to non-lesional skin. Fontana-Masson stain. $\times 200$. **e, f** Basement membrane thickening in lesional skin compared to non-lesional skin. Periodic acid-Schiff stain. $\times 400$. **g, h** Biopsy from patient 3 showing high-lying sebaceous glands in lesional skin compared to none in non-lesional skin. HE. $\times 100$.

epidermal basement membrane, while biopsies from non-lesional, non-eczematous skin showed normal thickness of the epidermal basement membrane. We postulate that the thickened basement membrane seen in acquired hyperpigmentation of the neck in patients with AD may in part be attributed to the eczematous process or chronic rubbing, which may have stimulatory effects on fibroblasts and keratinocytes, leading to increased synthesis of certain basement membrane components [14–16]. We

did not find amyloid deposits on the Congo red stain in any of our patients' biopsies, which is similar to the findings of Manabe et al. [2]. However, amyloid-like material has been observed on electron microscopy [4].

Although the entity has often been referred to as 'reticulate pigmentation of the neck', none of our patients was found to have a distinctive reticulate pattern. All patients were found to have a rippled pattern of the hyperpigmentation. We postulate that this rippled pattern seen

Fig. 4. Acquired atopic hyperpigmentation: pathogenesis. JCBL = Juxtaclavicular beaded lines.



in AD is probably due to the accentuation of the juxtaclavicular beaded lines (JCBL) (fig. 4) [17–21]. JCBL, which has also been termed *cutis punctata linearis colli*, is the normal anatomical pattern of sebaceous follicles seen in the neck, along the horizontal lines of Langer [21]. Our findings of high-lying sebaceous glands within the biopsy specimens taken from the areas of rippled pigmentation in 2 patients corroborate with this theory. The clinical manifestation and prominence of JCBL depends on several factors which influence the size of the sebaceous follicle units such as age, gender, sun exposure and friction (fig. 4). The use of topical and systemic corticosteroids has also been associated with JCBL and there is a reported case of an abrupt onset of JCBL in a transplant patient started on immunosuppressants [17, 18]. They become more evident during puberty and adulthood and are more pronounced in males compared to females [21], which may explain the male predominance and the characteristic age of onset of the pigmentation in adolescence that was found in this study. Interestingly, Mukai et al. [5] reported histological evidence of sebaceous hyperplasia in 13 of the 23 AD patients with ‘poikiloderma-like lesions on the neck’, which supports this association, although this finding was not evident in any of our biopsy specimens. Moreover, ‘juxta-clavicular’ or neck pigmentation is misleading, as similar pigmentary changes can also affect other sites such as the axillae and cubital fossae, a finding which has been reported by others [4, 12, 17, 18].

Taken together, the clinical and histological features we found in this study suggest that acquired atopic hyperpigmentation develops over time due to underlying chronicity and severity of the AD, especially over the neck, which is one of the typical pathognomonic sites of early disease involvement (fig. 4). The hyperpigmentation may initially result from chronic dermatitis and frictional melanosis with melanin incontinence, associated with sec-

ondary changes, giving rise to a prominent or thickened basement membrane. In the later stages, with the resolution of the dermatitis, the epidermis and basement membrane gradually return to their normal thickness. There is a gradual decrease in the number of dermal melanophages with time. However, within the areas in the vicinity of the high-lying sebaceous glands which correspond to JCBL, the dermal melanophages remain rather persistent, as evidenced by the increased numbers of dermal melanophages in the lesional skin of patients with purely rippled pigmentation with no eczema compared to their non-lesional skin. The reason for this delay in the clearance of dermal melanophages in areas corresponding to JCBL remains unknown. We are unable to conclude further due to the small sample size that was biopsied.

Our study also found that neck pigmentation can have negative psychological effects such as feeling frustrated, embarrassed and unattractive due to the skin appearance, comparable with the impact of melasma on the QoL [22–24]. The term ‘dirty’ neck, which is well established in the literature, is not ideal as it connotes an ‘unwashed’ appearance that results from dirt or poor hygiene. This may further increase the stigmatization of patients with this condition. We propose ‘acquired atopic hyperpigmentation’ as a less stigmatizing name for this condition, which also encompasses the fact that the acquired pigmentation is not only limited to the neck area but also involves other flexural areas such as axillae and cubital flexures in about 30% of cases.

There are very limited reports on the treatment of acquired atopic hyperpigmentation. Hira et al. [25] reported a small case series of 6 patients with acquired atopic hyperpigmentation treated successfully with tacrolimus ointment, while Hayashi et al. [26] reported that 71% of the patients improved after treatment with 10% hydroquinone ointment and 0.3% prednisolone butyl acetate

cream. In our cohort, we documented a good improvement of acquired atopic hyperpigmentation over a 2-year period in 1 patient treated with 0.1% tacrolimus ointment and long-term maintenance with azathioprine therapy.

These reports suggest that acquired atopic hyperpigmentation may be improved or even preventable with good, long-term control of the underlying eczema.

There are several limitations to this study. Apart from basic demographics, we did not have the resources to collect more clinical data on the patients without acquired atopic hyperpigmentation, which would have been useful to determine and verify prognostic or causative factors. Patients were also recruited from specialized Paediatric Dermatology and Adult Eczema Clinics in a major dermatological referral centre, which is likely to see more severe AD. While we tried to standardize the severity grading based on photography, the usage of advanced skin imaging devices may have been better for objective measurement of skin tone and pigmentation. Finally, patient responses in the questionnaires could have been affected by recall bias.

In conclusion, acquired hyperpigmentation of the neck is an important clinical finding in Asian patients with AD, with an onset after puberty and late adolescence. It is found more commonly in young male adult patients and is associated with increased disease severity. The underlying pathogenesis is probably due to frictional melanosis and post-inflammatory hyperpigmentation, which accentuate the linear arrangement of the pilosebaceous complexes in the neck, also known as JCBL, giving the pigmentation a characteristic rippled appearance.

These findings suggest that acquired atopic hyperpigmentation is potentially preventable and underscores the importance of the early recognition and treatment of the condition by optimal management of AD, especially in childhood. This study also reveals that physicians must consider the psychosocial impact of acquired atopic hyperpigmentation. We propose 'acquired atopic hyperpigmentation' as a unifying and less stigmatizing name for a condition that has been described under terms such as 'atopic dirty neck', 'rippled pigmentation of the neck', 'reticulate pigmentation of the neck' or 'poikiloderma-like changes of the neck'.

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Disclosure Statement

The authors declare no conflicts of interest.

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