Clinical Cases in Dermatology
Series Editor: Robert A. Norman

Porcia B. Love
Roopal V. Kundu *Editors*

Clinical Cases in Skin of Color

Adnexal, Inflammation, Infections, and Pigmentary Disorders

Springer

Clinical Cases in Dermatology

Series Editor
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This series of concise practical guides is designed to facilitate the clinical decision-making process by reviewing a number of cases and defining the various diagnostic and management decisions open to clinicians. Each title will be illustrated and diverse in scope, enabling the reader to obtain relevant clinical information regarding both standard and unusual cases in a rapid, easy to digest format. Each book will focus on the one disease or patient group, and will include fairly common cases to get people to know they are doing things right if they follow the case guidelines. Each will be about 15-20 cases and 100-125 pages total with key pictures for each case. The deadlines/timelines for each title will be short and facilitate rapid publication models.

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Prelude

Clinical cases are a key component of modern medical education, assisting the trainee or recertifying clinician to work through unusual cases using best practice techniques. Dermatology is an important discipline in this regard since it is a highly visual specialty requiring the reader to describe subtle differences in the presentation of patients and accurately define the diagnostic and management criteria to base their clinical decision-making on.

Census projections predict that by the year 2042, people with skin of color (including Africans, African Americans, Asians, Native Americans and Hispanic/Latinos) will represent more than half of the US population. There is now an increasing demand for dermatologic treatments in patients with skin of color, as well as an accompanying need for education and training in this quickly expanding market. Skin of color is a key topic within dermatology as specific conditions can be harder to diagnose effectively in darker skin, and their treatment can be compromised by this. Conditions such as psoriasis, eczema, and atopic dermatitis may be more difficult to diagnose in darker skin. There are various other conditions that can provide a challenge in management, including postinflammatory hyperpigmentation, melasma, scarring, alopecias, and pseudofolliculitis barbae. If these skin disorders are not diagnosed and treated properly, the initial lesions can become darker as they heal, and the darker spots can last for years in some cases. Scarring may also occur.

This book will identify the top dermatological conditions for patients with skin of color and provide essential features which contrast these conditions in darker skin types. The

reader will be able to formulate informed treatment regimens for patients with skin of color. The book will also provide clinical pearls to guide decision making, as well as important cultural beliefs that must be considered in order to provide optimal care to patients with skin of color.

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Part I
Adnexal Disorders

Chapter 1
Acne Vulgaris

Porcia B. Love

Case Presentation

A 30-year old African American female presented with a 2-year history of intermittent bumps on her face. She had previously tried numerous over the counter treatments, including topical benzoyl peroxide foams and salicylic acid cleansers. She also used shea butter on her face to help even out her skin tone. Her menstrual cycles were normal.

Physical Examination

On examination, multiple erythematous papules and pustules and enlarged pores were noted on the cheeks, nose, jawline, and chin. Hyperpigmented macules were also noted on the cheeks and the jawline. A 1 cm erythematous cyst was noted on the right nasal sidewall (Fig. 1.1). Hyperpigmented macules and papules were noted on the chest and upper back.

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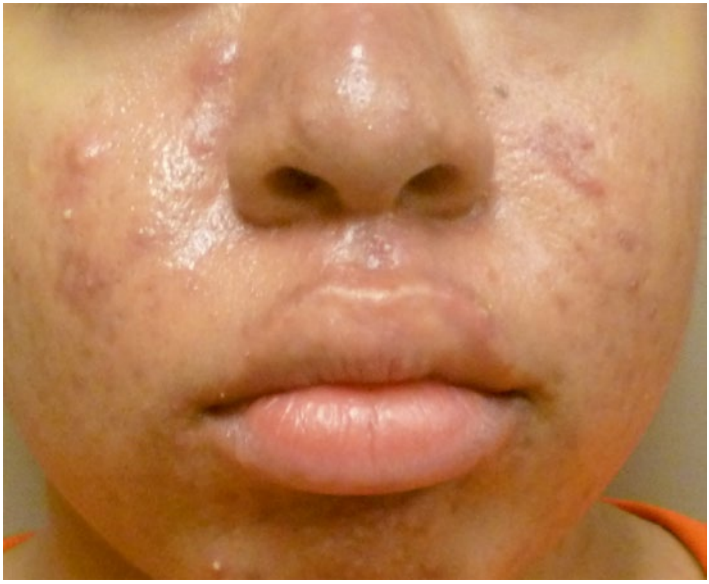

FIGURE 1.1 Inflammatory acne vulgaris. Multiple erythematous papules and pustules and enlarged pores are noted on the cheeks, nose, jawline, and chin. Hyperpigmented macules are also noted on the cheeks and the jawline. An erythematous cyst is noted on the right nasal sidewall

Differential Diagnosis

Comedonal acne should be distinguished from acneiform eruptions from follicular occlusion, like pomade and occupational acne. Sebaceous hyperplasia, characterized by yellowish, indurated papules on the forehead and cheeks, is common in adults. Inflammatory acne can be confused with folliculitis (staphylococcal, gram negative, or eosinophilic). Lesions from folliculitis are typically monomorphic papules, and comedones are not present. Papulopustular rosacea favors the forehead, malar region, and the chin. Patients also have telangiectasias and report a history of flushing. Although rosacea

typically occurs at a later age, both acne and rosacea can occur in a single individual. Perioral dermatitis is characterized by monomorphic papules and pustules, usually resulting from prolonged use of corticosteroids. Neurotic excoriations on the face, chest, and back can also be confused with acne (Zaenglein and Thiboutot 2008).

Histopathology

Acne is a clinical diagnosis, and biopsy is typically not indicated. However, biopsy of an acneiform lesion shows a microcomedo with infundibular dilatation and narrowing of the follicular opening. As the follicular epithelium distends, cystic contents rupture into the dermis. The acute inflammatory reaction is characterized by neutrophils creating pustules, foreign body granulation tissue, and subsequent end stage scarring (Zaenglein and Thiboutot 2008).

Diagnosis

Acne vulgaris

Case Treatment

A gentle cleanser was recommended for both morning and evening. A combination benzoyl peroxide/clindamycin gel was recommended for the morning, and a tretinoin 0.1 % cream was recommended for the evening. The patient was also started on doxycycline 100 mg twice daily. A moisturizer with a broad spectrum sunscreen (SPF 30) was recommended for the morning. This same moisturizer was recommended for the evening to prevent irritation from tretinoin. She was advised to discontinue her use of shea butter, as it is typically comedogenic. She was seen back in clinic in 3 months to attempt to taper the doxycycline.

Discussion

Acne is one of the most common skin disorders in people with skin of color. Practice surveys at the Skin of Color Center in New York City (Alexis et al. 2007), Howard University in Washington, D.C. (Halder et al. 1983), and in south-east London (Child et al. 1999) reported that acne vulgaris was the most common diagnosis in patients with skin of color, accounting for 28 % of dermatoses.

The pathogenesis of acne is due to four well known factors: excessive sebum production; abnormal follicular keratinization and plugging; proliferation of *Propionobacter acnes*; Hormone changes also contribute to acne pathogenesis. (Callender 2004; Leyden 1995). Although this classic pathophysiology is shared amongst all skin types, subsequent evolution of the acne lesion and the degree of inflammation at clinical presentation may vary among individuals according to their skin types. In particular, nodulocystic acne appears to be more common in Caucasians and Hispanics than in African Americans (Callender 2004; Taylor et al. 2002). Pore size may also explain differences in acne presentation, as enlarged pore size is highly correlated with sebum output and may contribute to acne pathogenesis. Epidemiologic studies demonstrate that gland pores are larger in patients with skin of color (Yin and McMichael 2014).

Clinically, acne vulgaris is characterized by open and closed comedones, papules, pustules, nodules, and cysts (Fig. 1.1). Lesions are usually present on the forehead, cheeks, jawline, chin, chest, and upper back. In patients with skin of color, postinflammatory hyperpigmentation (PIH), characterized by hyperpigmented macules, may be present after the lesions heal (Fig. 1.2).

Although acne treatment for patients with skin of color are similar to those for patients with lighter skin, specific considerations exist, especially due to the risk of PIH. Clinically, PIH presents as hyperpigmented macules or patches which correspond to the area of injury. Postinflammatory hyperpigmentation can develop in response to the acne itself or to any overly

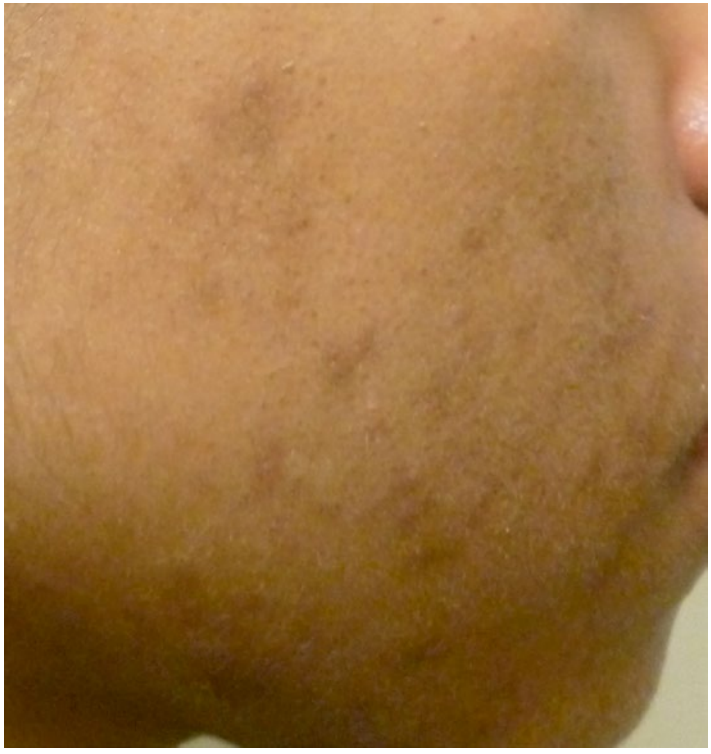

FIGURE 1.2 Postinflammatory hyperpigmentation secondary to acne. Hyperpigmented macules are noted on the forehead, cheeks, and jawline

aggressive acne treatment that disturbs the skin. Postinflammatory hyperpigmentation is thought to be a default pathophysiologic response of darker skin to cutaneous injury in which the inflammation triggers an increase in epidermal or dermal melanogenesis from labile melanocytes (Callender 2004; Taylor et al. 2002). For many patients, the lingering PIH is more psychologically disturbing than the acne itself.

Permanent and disfiguring keloid formation is also more common following acne in skin of color. The biologic basis for

a tendency for scarring in patients with skin of color may involve differences in fibroblast size and activity, immune related cellular actions, and growth factors—all of which seem to combine to promote production of excess collagen and inhibit degradation of the extracellular matrix (Callender 2004; Taylor et al. 2002).

Hair care practices among patients with skin of color may also cause a unique form of acne known as pomade acne. The daily use of pomades on the hair and scalp to overcome an inherent tendency for hair dryness and fragility often leads to a characteristic distribution of comedonal acne on the forehead and anterior hair line (Callender 2004). Additionally, corticosteroid containing skin bleaching agents that are used by some individuals with darker skin to improve hyperpigmentation may induce steroid acne, which may further worsen PIH (Shah and Alexis 2010).

Treatment

The treatment of acne in patients with skin of color can present unique challenges, both pathophysiologically (i.e., risk of PIH and keloid scarring) and culturally (i.e., use of skin and hair care products). The overall goal of acne management is to select treatment that addresses as many of its pathogenic factors as possible while minimizing potential PIH (Alexis et al. 2007). Because acne treatment can cause cutaneous irritation that initiates or exacerbates PIH in darker-skinned patients, the patient's skin should be carefully assessed to determine the risk of irritant contact dermatitis.

Topical retinoids are the top choice for first line therapy, as not only do they target hyperkeratinization and comedogenesis, but they also possess direct anti-inflammatory and antifibroblastic actions, and may block the key pathophysiologic pathways leading to PIH and keloids (Callender 2004; Alexis 2011). Special care should be taken in selecting the most appropriate retinoid vehicle. For skin of color, cream based formulations of

retinoids are often initiated because there is a decreased likelihood of irritation and resultant PIH. Retinoid formulations may also be started on an alternate-day dosing regimen to decrease irritation. Another useful strategy is to start with the lowest concentration and titrate up as tolerated to minimize retinoid dermatitis and the risk of PIH (Alexis 2011).

Topical antibiotics like clindamycin and erythromycin are effective in reducing *P. acnes* and help reduce inflammation. Adding an antimicrobial agent to a topical retinoid regimen can result in a more rapid and complete resolution of acne lesions and PIH. In addition, the use of a fixed combination agent (topical antibiotic plus benzoyl peroxide) is recommended to assist in preventing new acne lesions and reduces the risk of antibiotic resistance (Alexis 2014). Reducing potential irritation and dryness, which may adversely affect darker skin, can be achieved by using benzoyl peroxide in low concentrations and in a cream or water-based gel.

Azelaic acid has been used to treat both inflammatory and noninflammatory lesions. Because azelaic acid is considered to have a low potential for irritation, it may be suitable for patients with dark sensitive skin or with a history of PIH. Furthermore, because it inhibits melanin synthesis, it is also somewhat effective in treating PIH (Webster 2000).

Hydroquinone is the gold standard for treating PIH associated with acne. Hydroquinone inhibits conversion of tyrosine to melanin and alters several normal activities of the melanosomes. It is important to monitor extended hydroquinone use to avoid risk of exogenous ochronosis, which is characterized by asymptomatic blue-black or slate-gray speckled macules typically affecting the malar eminences, temples, and inferior cheeks. Although uncommon in the United States (Lawrence et al. 1988), hydroquinone induced exogenous ochronosis of the face can be difficult to treat. The more common adverse effects of hydroquinone include irritant and allergic contact dermatitis and temporary hypopigmentation of surrounding normal skin. Therefore, it is important to use only on dark areas, not for full facial treatment (Callender 2004).

Broad spectrum antibiotics like doxycycline, minocycline, trimethoprim-sulfamethoxazole, and cephalosporins are often added to topical medications for moderate to severe inflammatory acne. There is a preference for doxycycline over minocycline given the risk of bluish pigmentation deposition in acne scars with minocycline. Isotretinoin, a systemic retinoid, is the treatment for nodulocystic acne. Isotretinoin must be used with caution in child bearing women given its risk of teratogenicity. Androgens also play a central role in over stimulation of sebaceous glands in patients with acne. To counteract the androgenic hormones, a variety of hormonal therapies have been used, including oral contraceptives and androgen receptor blockers (i.e., spironolactone) (Callender 2004). In skin of color, a lower threshold for systemic agents may be advisable to reduce inflammation at an earlier stage, thus reducing the risk of PIH and scarring.

Adjunct therapies reserved for cases of advanced acne, include intralesional corticosteroids (especially for keloids), manual comedonal extraction, and chemical peels. Salicylic acid peels are generally safe and effective in skin of color. They are comedolytic, accelerate the clearance of epidermal melanin, and increase the penetration of topical agents (Grimes 1999). Although chemical peels can be used safely in skin of color, they should be applied conservatively, with careful consideration of any irritation that may result in PIH.

In addition to combination therapy, certain practical measures should be taken to identify and reduce exacerbating factors. First, a careful patient history should be obtained to review what patients have used to treat acne on their own. Many patients with PIH use products such as cocoa butter to attempt to even their skin tone; however, these products can be comedogenic and exacerbate acne. A careful history of hair care product use is also important, since certain hair emollients can exacerbate acne (Callender et al. 2014). In addition, patients should be counseled to avoid harsh exfoliants, which may contribute to PIH by causing irritation. A careful history may reveal that some patients have tried online "fade creams" that paradoxically contain corticosteroids, which in turn

increase acne and subsequent PIH. Finally, many skin of color patients believe that their skin is resistant to effects of ultraviolet radiation. Therefore, the daily use of a broad-spectrum sunscreen with an SPF of 30 should be recommended to help prevent exacerbation of PIH. A noncomedogenic vehicle should be selected (Callender et al. 2014).

Key Points

- Management of acne in patients with skin of color can be particularly challenging, given their potential for cosmetically disturbing complications, including postinflammatory hyperpigmentation and keloids.
- The overall goal of acne management is to select a treatment that addresses as many pathogenic factors as possible while minimizing potential postinflammatory hyperpigmentation.
- Acne treatments designed to dry the skin, such as benzoyl peroxide, should be carefully chosen. These medications may irritate the skin and prolong postinflammatory hyperpigmentation.
- Hair care practices using oil based products may cause pomade acne.
- Comedogenic moisturizers or steroid based fade creams can worsen acne in skin of color.

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Chapter 2
Rosacea

Jennifer M. Pugh and Porcia B. Love

Case Presentation

A 45-year-old African American woman presents with a 3 year history of intermittent facial flushing. She also notes persistent bumps on her cheeks and burning and stinging on her face. These symptoms worsen after exposure to heat and consumption of chocolate, alcohol, and spicy foods. She has tried over the counter benzoyl peroxide and salicylic acid cleansers without much success. Her eyes are often irritated and occasionally itch.

Physical Examination

Red papules and pustules are noted on the medial aspects of the bilateral cheeks with underlying erythema of the fore-

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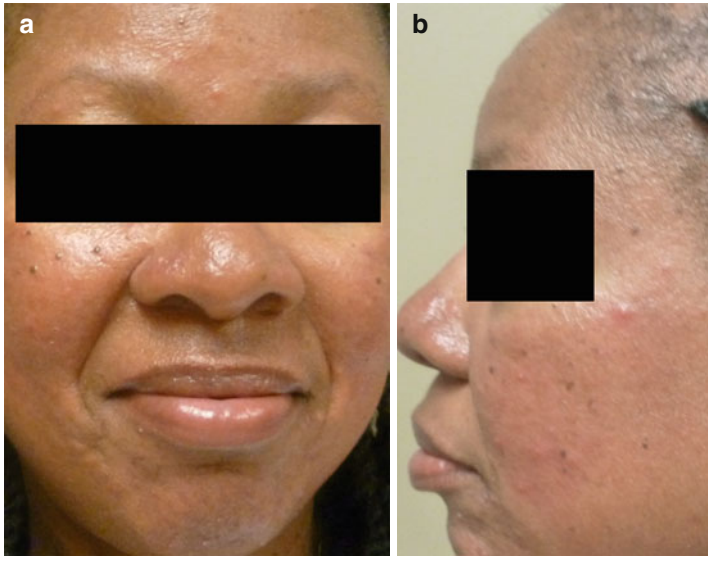

FIGURE 2.1 (**a**, **b**) Papulopustular rosacea. The patient has red papules on the forehead and cheeks, with underlying erythema of the forehead, cheeks, nose, and chin

head and malar area. Telangiectasias are noted on the nasal bridge (Fig. 2.1a, b).

Differential Diagnosis

The patient's clinical presentation was thought to be most consistent with rosacea. Acne vulgaris typically occurs in younger individuals and is characterized by open and closed comedones and inflammatory papules and pustules; however, it is possible to have acne and rosacea simultaneously. Seborrheic dermatitis often coexists with rosacea and is characterized by greasy scale in the nasolabial folds, external ear canals, glabella, and medial eyebrows. The butterfly rash or malar erythema of lupus erythematosus is often misdiagnosed as rosacea and is characterized by fine scaling, with occasional pigment change, follicular plugging, and scarring (Webster

2008). Papules and pustules are typically absent in lupus erythematosus. Sarcoidosis may also be confused with rosacea and is characterized by red and violaceous, indurated papules, plaques, and nodules that usually affect the nose, lips, cheeks, and ears. Underlying erythema of the face is typically absent.

Histopathology

Biopsy is uncommonly performed but may be considered if there is concern for lupus erythematosus or sarcoidosis. Pathology typically demonstrates vascular dilatation of upper and mid dermal vessels, perivascular and perifollicular lymphohistiocytic and granulomatous inflammation, and multinucleated giant cells and plasma cells. The most severe forms of rosacea can have non-caseating epithelioid granulomas and sinus tract formation (Webster 2008).

Diagnosis

Rosacea, papulopustular subtype

Case Treatment

The patient was started on a sodium sulfacetamide 10 %/sulfur 5 % facial wash twice a day. Ivermectin 1 % cream was recommended each morning, as well as low dose doxycycline 40 mg per day. A noncomedogenic moisturizer with sunscreen (SPF 30) was also recommended. She was advised to avoid her triggering factors, including alcohol and spicy foods.

Discussion

Rosacea is a common chronic inflammatory facial dermatosis characterized by erythema, telangiectasias, and an acneiform papulopustular eruption. It is most commonly seen in

Caucasian individuals, particularly those from Celtic and Northern European backgrounds, ranging in age from 30 to 70 years old; however, it can affect all ethnic groups. There is a spectrum of clinical features. Progression may be stepwise and range from minor cosmetic changes to severe disabling facial features. Although rosacea is less common in skin of color, it is not rare (Alexis 2010). A recent study by Al Dabagh et al analyzed the National Ambulatory Medical Care Survey of 1993–2010 for racial and ethnic distribution of patients with rosacea. Rosacea was the primary diagnosis for 8.3 % of whites and 2.2 % of blacks (Al-Dabagh et al. 2014).

There are four main types of rosacea. Erythematotelangiectatic rosacea is characterized by erythema, central facial flushing, and telangiectasias. This may be accompanied by burning or stinging, which is often exacerbated when topical agents are applied. Papulopustular rosacea is also characterized by erythema of the central portion of the face, as well as small erythematous papules surrounded by pinpoint pustules (Fig. 2.1a, b). Phymatous rosacea is characterized by marked glandular thickenings and irregular surface nodularities of the nose, chin, forehead, ears, and the eyelids. Ocular rosacea can also occur and is characterized by blepharitis, conjunctivitis, inflammation of the lids, and conjunctival telangiectasias. Patients may describe eye stinging or burning, dryness, or irritation with light. Ocular manifestations may precede the cutaneous signs by years (Crawford et al. 2004).

The symptoms that lead to the diagnosis of rosacea are commonly documented as facial flushing, erythema, telangiectasias, skin sensitivity, and an acneiform papulopustular eruption. However, these symptoms do not always appear as such on skin of color. Because erythema and telangiectasias may be more difficult to appreciate in darker skin and less cosmetic deformity may occur in early cases, many cases of rosacea amongst people with skin of color may go undiagnosed and possibly contribute to fewer physician visits (Al-Dabagh et al. 2014). Therefore, physicians should consider the diagnosis of rosacea when patients with skin of color present with facial flushing, warmth, ocular symptoms, and a papulopustular eruption of the central face.

The exact cause of rosacea is unknown. However, several factors likely play a role in its development, including changes in vasculature, climactic exposures, chemicals and ingested agents, and microbial organisms. Erythema and flushing are likely secondary to vasodilatation and increased blood flow to facial blood vessels. Harsh climatic exposures, for example extremely hot or cold temperatures or wind exposure, may also damage cutaneous blood vessels (Laquer et al. 2009). Spicy foods, alcohol, hot beverages, exercise, topicals that irritate the skin, and medications that cause flushing are traditionally thought to trigger flushing in patients with rosacea (Crawford et al. 2004). *Demodex* species (mites that normally inhabit human hair follicles) may also play a role in the pathogenesis of rosacea. Some studies suggest that *Demodex* prefers the skin regions that are affected in rosacea, such as the nose and cheeks (Bonnar et al. 1993). Studies have also shown that an immune response of helper T-cell infiltrates occurs, surrounding the *Demodex* antigens in patients with rosacea (Forton 2012). Other causes of rosacea that are being investigated include dermal matrix degeneration, pilosebaceous unit abnormalities, ferritin expression, reactive oxygen species, and dysfunction of antimicrobial peptides (Crawford et al. 2004).

Treatment

Rosacea is a chronic inflammatory skin condition that remains difficult to treat. Treatment recommendations vary based on the subtype of rosacea or on the signs and symptoms present. The first recommendation for all patients with rosacea is to avoid triggering factors, such as extreme temperatures, hot drinks, spicy foods, and alcohol. Adjunct measures include cosmetic camouflage of erythema and broad spectrum sunscreens, particularly because the use of photoprotection may help avert photodamage such as erythema and telangiectasias that contribute to the vascular changes of rosacea (Pelle et al. 2004).

In patients with persistent erythema, topical treatments with topical metronidazole, azelaic acid or sulfacetamide-sulfur should be considered (Ceilley 2004). Azelaic acid is thought to exert an anti-inflammatory effect and reduction in erythema by reducing the release of proinflammatory reactive oxygen species by neutrophils (Thiboutot et al. 2003). Brominidine tartrate 0.33 % gel has recently been approved by the FDA for treatment of persistent facial erythema. This new medication stimulates alpha-adrenergic receptors resulting in vasoconstriction (Fowler et al. 2012). When topical treatments fail, oral antibiotics, including tetracyclines (doxycycline and minocycline) and macrolides (erythromycin) can be added.

Physical treatments can also be added, especially for telangiectasias. Electrosurgery can be used to treat small vessels. The pulsed dye laser and intense pulsed light therapy can be used to treat erythema and telangiectasias. The neodymium-doped yttrium aluminum garnet (Nd:YAG) laser can target larger telangiectasias. The potassium titanyl phosphate laser (KTP) may also be used for erythema and telangiectasias; however, it is not recommended in skin of color as the higher melanin absorption can lead to epidermal damage with postinflammatory hyperpigmentation (Butterwick et al. 2006). When using lasers, it is important to appropriately select patients and set patient expectations. While improvement may be seen in 50–75 % of telangiectasias over one to two sessions, improvement is of a much lesser extent in persistent erythema, and complete resolution should not be anticipated (Butterwick et al. 2006).

Patients with papules and pustules should be treated with a combination of topical and oral therapy. Topical treatments, including metronidazole, clindamycin, sodium sulfacetamide-sulfur, and azelaic acid, are recommended. Ivermectin 1 % cream has recently been approved by the FDA to treat papulopustular rosacea. Ivermectin exhibits broad-spectrum antiparasitic activity and kills the Demodex mites that reside in the pilosebaceous units of patients with papulopustular rosacea. Ivermectin also has anti-inflammatory effects; it decreases the cellular and humoral immune responses that appear to play a dominant role in the development of rosacea

inflammatory lesions (Abokwidir and Fleischer 2015). Low dose doxycycline (40 mg/day) is recommended for less severe disease, and for severe disease, high dose tetracyclines or low dose oral isotretinoin (10 mg/day) should be considered. The anti-inflammatory properties of the tetracyclines, rather than their antibacterial properties are a primary rationale for their use in rosacea. In patients with nodules and plaques, systemic treatment with high dose tetracyclines and macrolides or isotretinoin (0.5–1 mg/kg/day) is recommended. The use of isotretinoin is considered off label for rosacea. Unlike in the treatment of acne, the use of isotretinoin may not be likely to result in remission of rosacea (Moustafa et al. 2014).

As noted, rosacea is often under recognized or misdiagnosed in patients with skin of color. Therefore, clinical trials of therapeutic agents for rosacea generally include few patients with skin of color. A recent prospective analysis was conducted to evaluate the effectiveness and safety of treatment for rosacea in patients with skin of color. Significant improvement in disease severity and erythema was obtained in patients with Fitzpatrick skin types IV-VI at week 12 who received doxycycline 40 mg capsules. Approximately 12 % of patients experienced adverse events, with no difference between the patients with Fitzpatrick skin types IV-VI compared to those with Fitzpatrick skin types I-III (Alexis et al. 2012).

Key Points

- Although rosacea is less common in skin of color, it is not rare.
- The symptoms that commonly lead to the diagnosis of rosacea do not always appear as such on skin of color because erythema and telangiectasias may be more difficult to appreciate in darker skin, and less cosmetic deformity may occur in early cases.
- Physicians should consider the diagnosis of rosacea when patients with skin of color present with facial

flushing, warmth, ocular symptoms, and a papulopustular eruption of the central face.
- The first recommendation for all patients with rosacea is to avoid triggering factors, such as extreme temperatures, hot drinks, spicy foods, and alcohol.
- Although vascular lasers are commonly used to treat telangiectasias and erythema in rosacea, they should be used in caution in patients with skin of color as the higher melanin absorption can lead to epidermal damage with postinflammatory hyperpigmentation.

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Chapter 3
Pseudofolliculitis Barbae

Brittany L. Vieira and Roopal V. Kundu

History

A 32-year old African American male presents with a 5-year history of recurrent tender, pruritic papules and pustules in the beard region. Past medical history is noncontributory. Previous treatment include topical clindamycin and oral tetracycline with temporary improvement.

Physical Examination

Physical examination revealed numerous 2–4 mm skin-colored and hyperpigmented perifollicular papules, confined to the mandible and neck (Figs. 3.1 and 3.2).

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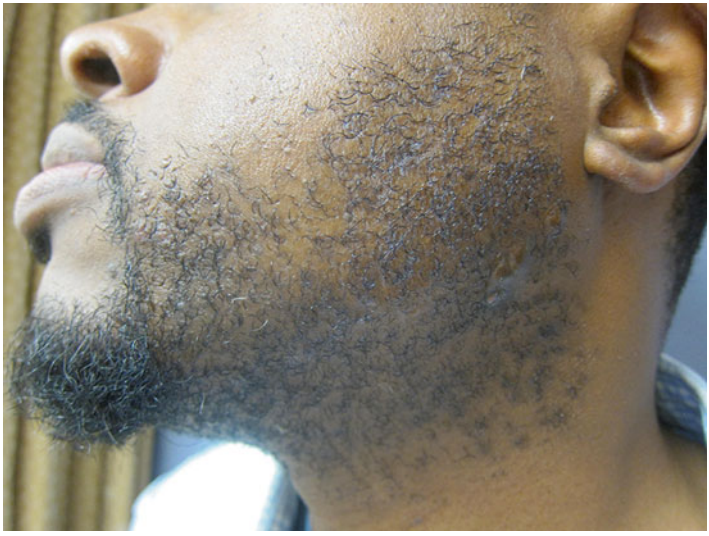

FIGURE 3.1 Pseudofolliculitis barbae. 2–4 mm skin-colored and hyperpigmented perifollicular papules, confined to the mandible and neck

Clinical Differential Diagnosis

The lesions were thought to be most consistent with pseudofolliculitis barbae. The differential included other conditions that can cause erythematous papules and pustules in the regions of terminal hair growth, such as acne vulgaris, folliculitis, tinea barbae, and acne keloidalis nuchae.

Acne vulgaris will include comedones and not is restricted to areas of terminal hair density. Primary features of bacterial folliculitis include pruritic erythematous papules and pustules, commonly observed in the beard region of men who shave. Bacterial folliculitis presents acutely, in contrast to the chronic nature of PFB. Cultures also help distinguish, as PFB is an inflammatory, sterile disorder. Tinea barbae may present as follicular pustules, inflammatory papules or scaly erythematous annular plaques. The lesions are confluent, while PFB

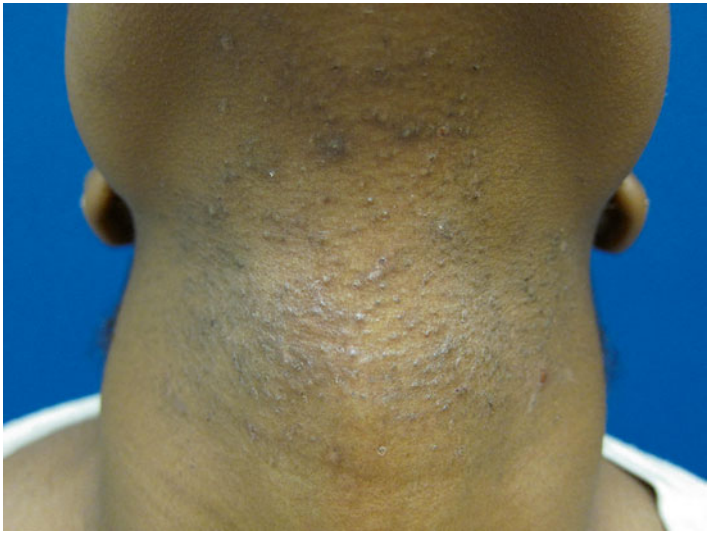

FIGURE 3.2 Pseudofolliculitis barbae in a woman. Scattered skin-colored and hyperpigmented perifollicular papules along the neck

lesions are isolated. Fungal forms can be detected with potassium hydroxide preparation. Acne keloidalis nuchae presents as perifollicular papules, pustules or keloidal plaques on the posterior scalp and, similar to PFB, disproportionally affects young men of African descent. The location on the scalp differentiates it from PFB.

Histopathology

Diagnosis can be made for this condition on clinical examination alone, and does not typically require skin biopsy. When biopsy is performed, histopathology reveals an invagination of the epidermis with intraepidermal neutrophils, granulomatous inflammation and foreign-body giant-cells surrounding an embedded hair tip. Other features include microabscess formation and fibrosis (Ramos-e-Silva and Pirmez 2014).

Diagnosis

Pseudofolliculitis barbae (PFB)

Case Treatment

The pathogenesis and chronic nature of PFB was reviewed with the patient, including the potential sequelae of post-inflammatory hyperpigmentation. Patient education is an important cornerstone of PFB management due to the multifactorial nature of treatment, which can require a combination of behavioral, procedural and pharmacologic interventions. The treatment options and reasonable expectations for each method were discussed, including cessation of shaving, alteration of shaving technique, concomitant medical treatments and permanent laser hair reduction. The patient denies personal, cultural, or occupational factors that limit his grooming practices, and therefore opted for the suggested first-line treatment of complete shaving cessation. He was advised to maintain a trimmed beard at a minimum length of 5–10 mm to prevent reactivation of the disease. He was counseled to expect his condition to persist for some time due to previously embedded hairs, and told that trapped hairs typically release from the skin naturally after 3–6 weeks of growth. The patient was instructed to contact the clinic for consideration of additional treatment options such as concomitant medical therapy if he did not experience improvement of his condition within 8 weeks.

Discussion

Pseudofolliculitis barbae is a common and chronic inflammatory condition that develops in areas of terminal hair growth as a result of hair epilation. Other names for PFB include folliculitis barbae tramatica, pili incarnate, ingrown hairs, or razor bumps. Though pseudofolliculitis can occur in all

ethnicities, it is relatively unique to skin of color (Kundu and Patterson 2013). Men of African descent are disproportionally affected, with a reported prevalence between 45 and 83 %, compared to just 3 % of white men. Hispanic and Middle Eastern men, as well as women who tweeze or pluck facial hair are also frequently susceptible to PFB. The reported incidence of PFB in women of African or Hispanic descent with hirsutism or hypertrichosis closely approximates the incidence in men (Perry et al. 2002). In addition to the potential impact on self-esteem, PFB can cause significant problems for individuals, especially those with strict occupational grooming policies, such as servicemen in the US military who are required to maintain a clean-shaven face.

The predominance of PFB in individuals of African descent is considered attributable to unique biology of African hair, particularly the prevalence of tightly coiled hair and the natural tendency of the hair shaft to curl during growth and reenter the skin. This reentry occurs through extrafollicular and transfollicular penetration. Extrafollicular penetration describes reentry of a hair shaft that has already exited the follicle; as the hair grows along its curvature it pierces the surface of the skin 1–2 mm from the follicle. Transfollicular penetration occurs when the sharpened tip of the shaved hair retracts beneath the surface of the skin and pierces the follicular wall as it grows. This type of penetration is typically caused by close-shaving practices such as shaving against the grain and pulling the skin taut while shaving. When hair cut at an acute angle (from shaving or other means of epilation) penetrates the interfollicular dermis or epidermis, it creates an invagination of the skin and forms a "pseudofollicle." This pseudofollicle can rupture, provoking an inflammatory response that manifests as firm, inflamed perifollicular papules or pustules. The ensuing inflammation can result in post-inflammatory hyperpigmentation (PIH) due to the stimulation of melanogenesis in the epidermis and an increased release of melanin in the dermis. Hypertrophic scarring or keloid formation can also develop in predisposed individuals. Often, the enduring sequelae are more cosmetically disturbing than the PFB itself.

In addition to hair removal practices, a genetic risk factor has been identified that may contribute to the pathophysiology and phenotypic expression of PFB. One study demonstrated that a single nucleotide polymorphism, which causes a disruptive Ala12 Thr substitution in the 1A α-helical segment of the hair-follicle-specific keratin 75 (previously K6hf), occurred in 36 % of individuals with PFB compared to only 9 % of unaffected individuals ($P < 0.000006$) (Winter et al. 2004). It is believed that this mutation structurally weakens the companion layer of the hair follicle and may increase the risk of PFB for some men and women, especially when combined with tightly coiled hair and shaving practices.

Pseudofolliculitis barbae presents as chronic perifollicular inflammatory papules and pustules located in regions of repetitive epilation. Lesions are most frequently observed on the anterior neck of men and on the chin of women; the moustache region is notably spared. Other commonly shaved areas, such as the axillae, pubic region, and legs are also susceptible to pseudofolliculitis. The lesions are firm, 2–4 mm in size, and may be skin-colored, erythematous, or hyperpigmented. Pain and pruritus are common symptoms. Pustules or abscesses may also develop due to a sterile inflammatory process or secondary to bacterial infection. The embedded hair may be seen within a papule, but may also manifest as a linear depression if it grows parallel to the surface of the skin.

Treatment

Pseudofolliculitis barbae is therapeutically challenging, often requiring a combination of behavioral, procedural and pharmacologic interventions. Patient education is an essential first step in the prevention and management of PFB (Madu and Kundu 2014). Preliminary consultation should begin with a detailed discussion of the condition and a stepwise approach to the variety of treatment options based on patient preferences.

PFB management relies heavily on preventative measures that reduce extrafollicular and transfollicular penetration.

The three fundamental methods include cessation of hair removal, long-term hair reduction, and modification of hair removal techniques. The importance of setting realistic patient expectations for potential treatment outcomes cannot be overstated. Although, laser therapy and discontinuation of hair removal can resolve PFB, alternative hair removal techniques are only expected to decrease the chronic activity of the condition; treatment goals should be set accordingly.

Permanent discontinuation of hair removal in the affected area is recommended as first-line treatment, as it has been shown to successfully resolve PFB in most cases (Alexis et al. 2014). Patients should be advised that after cessation of shaving, their condition is likely to persist for a few weeks due to previously embedded hairs. The trapped hairs will naturally release from the epidermis by a spring-like action at 10 mm in length, typically after three to six weeks of growth. Patients should be advised to maintain a trimmed beard at a minimum length of 5–10 mm to prevent reactivation of the disease.

Maintenance of a beard may be acceptable for some men, however for women, and due to cultural values or individual preferences, this may not always be an option. In these cases, improved hair removal methods are recommended as second-line treatment options; such options include adjustments to the shaving routine and alternatives to razors, such as electric clippers or chemical depilatories. This tier of treatment will not resolve the condition, but may decrease the severity by minimizing hair shaft reentry and reducing inflammation. To maximize the therapeutic benefit of shaving routine adjustments, patients should first allow a preliminary period of hair growth, as described above, and begin therapy once improvement is achieved. Patients who decline this transient break in hair removal should incorporate the adjustments immediately. Before shaving, the patient should use a mildly abrasive cloth to wash the affected area in circular motions to help free embedded hair shafts. Additionally, the application of warm compresses for 5–10 minutes prior to shaving softens the hair and helps minimize the sharpness of cut tips. To reduce the risk of transfollicular penetration every shave should be performed

with a sharp razor blade, and patients should avoid pulling the skin taut while shaving. Results from a recent study of 90 African American men suggest that an increased number of blades may help decrease the severity of PFB (Daniel et al. 2013). However, the literature is contradictory and additional data are needed to further evaluate the optimal number of blades, as well as directionality and frequency of shaving.

To avoid problematic close shaves with a razor, patients can use electric clippers and cut hair to the optimum length of 1–3 mm. As an alternative to shaving altogether, patients can use chemical depilatory creams, which contain either barium sulfide or calcium thioglycolate formulations that remove hair by lysing the disulfide bonds. However, irritant contact dermatitis is a relatively common complication and may limit the use of this modality. To minimize irritation, use should be limited to no more than once every other day.

Data are limited regarding the efficacy of medical therapy for pseudofolliculitis barbae. Nonetheless, the suggested pharmacologic treatments are generally well tolerated and used as adjunctive therapy. Topical therapies include mild- to medium-potency corticosteroids, antimicrobials, and retinoids. Low-potency topical corticosteroids are used to reduce the inflammatory component, most commonly applied immediately after epilation and limited to intermittent use. Topical antimicrobials (benzoyl peroxide 5 % alone or in combination with clindamycin 1 %) are also utilized for maintenance, while retinoids (e.g., tretinoin 0.025 or 0.05 %) are recommended nightly. Retinoids serve the dual purpose of improving both clinical lesions and postinflammatory hyperpigmentation commonly associated with PFB. For patients with skin of color, cream-based retinoid formulations are preferred to solutions or gels, as they reduce the risk of irritation and PIH secondary to treatment. Additional topical treatments for postinflammatory hyperpigmentation include hydroquinone, azelaic acid, kojic acid, and chemical peels. Glycolic acid and salicylic acid peels have been suggested as additional adjunctive therapies for PFB. It should be noted that pharmacologic therapy alone will not provide a cure for PFB.

Of all treatment modalities, permanent hair reduction most closely resembles a cure, as it destroys the hair follicle and thus the pathogenesis of the disease. Given the greater risk of epidermal injury with higher Fitzpatrick skin phototypes (SPT IV-VI), special care should be taken when selecting the most appropriate laser for patients with skin of color. Long-pulsed diode and neodymium:yttrium aluminum garnet (Nd:YAG) lasers provide an increased safety profile for hair removal in higher SPT. The 1064 nm long-pulsed Nd:YAG laser is preferred for patients of African ancestry. One study has shown that concomitant use of topical eflornithine hydrochloride 13.9 % (an inhibitor of hair growth) may be more effective than laser hair reduction alone (Xia et al. 2012). The potential risks of laser therapy are greatest in individuals with dark skin, and include dyspigmentation, blistering, and scarring. Electrolysis may be another option for those with limited focal involvement, such as the chin in women.

Key Points

- Pseudofolliculitis barbae is a common and chronic inflammatory condition that develops in areas of terminal hair growth as a result of hair epilation. The distal ends of cut hairs subsequently penetrate the skin, eliciting an inflammatory response.
- Though pseudofolliculitis can occur in all ethnicities, it is relatively unique to skin of color due to the higher prevalence of tightly coiled hair.
- PFB classically presents as multiple erythematous, skin-colored or hyperpigmented 2–4 mm inflammatory papules or pustules, most commonly affecting the neck in men and the chin in hirsute women.
- First line treatment for suitable patients includes discontinuation of shaving or other hair-removal practices; this approach often resolves PFB in a few months.
- Severe cases of PFB may require laser hair reduction.

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Chapter 4
Acne Keloidalis

Shirin Bajaj and Roopal V. Kundu

History

A 36-year old African American male presents complaining of painful and pruritic bumps at the nape of his neck of 2 years duration. He notes that initially he developed small pink bumps which enlarged and developed a fleshy scar-like appearance. They are itchy and bothersome.

Physical Examination

Multiple hyperpigmented follicular papules and pustules, along with hyperpigmented firm keloidal nodules, are present on the occipital scalp and posterior nape of the neck in a band-like distribution with associated areas of patchy hair-loss (Figs. 4.1 and 4.2).

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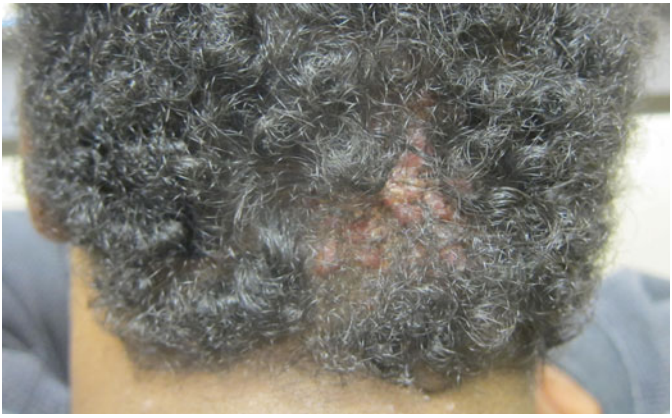

Figure 4.1 Acne keloidalis. Hyperpigmented follicular papules and pustules, along with hyperpigmented firm keloidal nodules, are present on the occipital scalp with associated areas of patchy alopecia

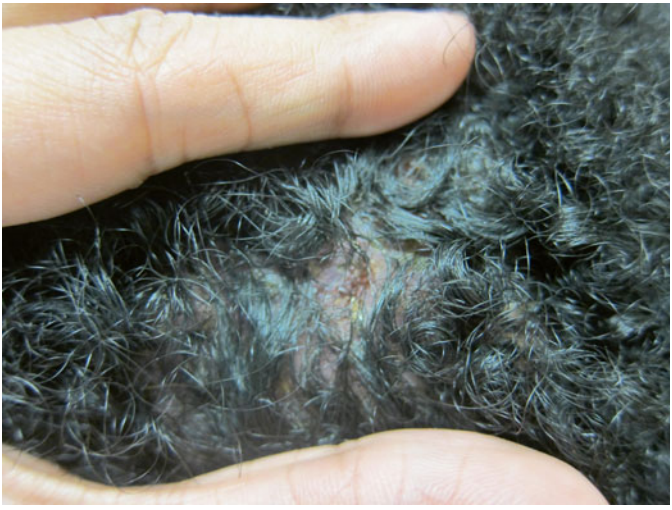

Figure 4.2 Acne keloidalis. Close up. Upon separate of the hair, erythematous follicular clustered papules with pustular drainage on the occipital scalp with patchy alopecia

Clinical Differential Diagnosis

This patient's presentation was most consistent with acne keloidalis (AK). The differential diagnosis for AK includes acne vulgaris, folliculitis decalvans, dissecting cellulitis, and hidradenitis suppurativa. However the chronic and progressive nature of symptoms in an African American male, the exclusivity of his rash to the posterior neck, and the presence of keloidal plaques without evidence of comedones or signs of infection, made each of these diagnoses unlikely (Huggins 2014).

Histopathology

This disease entity is diagnosed clinically and biopsy is not necessary for pathologic confirmation. However if performed, histopathologic examination would reveal perifollicular inflammation with a neutrophilic and/or lymphocytic infiltrate surrounding the hair follicle in early disease. During later stages, fibroplasia, absence of sebaceous glands, and naked hair shafts in the dermis are seen with associated granulomatous inflammation (Herzberg et al. 1990).

Diagnosis

Acne keloidalis (AK)

Case Treatment

The patient was informed of the diagnosis and counseled on the inflammatory nature of the disease. He was advised to avoid mechanical irritation including scratching or wearing tight fitting clothing, high-collared shirts and hats, as well as avoidance of close hair clipping and/or shaving of the neck. His large, keloidal plaques were injected with 10 mg/mL triamcinolone acetonide both for symptomatic relief and to help flatten the lesions. For treatment of the remaining

smaller lesions, he was prescribed topical clobetasol propionate 0.05 % foam, which he was instructed to use twice daily for a 2-week off-and-on regimen. In adjunct, he was prescribed topical tretinoin 0.025 % cream on an every other nightly regimen, and he was told to advance to once nightly as tolerated. The patient expressed significant concern about the cosmetic appearance of his keloidal plaques. After discussion, he agreed to return to clinic in 4–6 weeks to assess response to the intra-lesional and topical therapies and to consider the option of continued treatment with serial intralesional injections vs. surgical excision.

Discussion

Acne keloidalis (AK), also known as folliculitis keloidalis nuchae, is almost exclusively a disease of skin of color, as it predominantly affects post-pubertal men of African and Hispanic descent. Within this population, the prevalence has been estimated to range between 1.3 and 16.3 % (Huggins 2014). There are few case reports in the literature on affected black women or caucasian males.

A misnomer, acne keloidalis, is neither associated with acne vulgaris nor with true keloids. It is a progressive and chronic inflammatory folliculitis that presents with persistent pink, erythematous, or red-brown 2–4 mm papules on the occipital scalp and posterior neck that may progress overtime to form coalescing fibrotic "keloid-like" nodules. There is a risk of secondary infection, with development of pustules or purulent drainage. If infection is severe, draining sinuses and abscesses may result. Because destruction of the follicular unit is central to the pathophysiology of the disease, patients may also suffer from an associated scarring alopecia. They may also have "tufted" hairs in which multiple hair shafts emerge from one follicular orifice.

Histologic exam correlates with the evolving clinical features of the disease. During the initial inflammatory stage, there is perifollicular inflammation and subsequent weaken-

ing of the perifollicular wall. This follicular inflammation correlates with the appearance of papules on examination (Herzberg et al. 1990). In this early stage of disease, patients may be asymptomatic or may experience varying degrees of pruritus (Huggins 2014). Eventually, as the wall critically weakens, the naked hair shaft is released into the dermis. Overtime, this foreign body reaction induces surrounding granulomatous inflammation with extensive hypertrophic scarring, which manifests as fibrotic keloidal-appearing lesions (Herzberg et al. 1990). It is notable, that keloids are a distinct clinical entity, and by histology, they are characterized by an overabundant proliferation of thick collagen fibers. In later stages of AK, patients may have more severe pruritus and pain although some patients may have subclinical disease that presents only with hair loss (Huggins 2014).

While histologic examination reveals that inflammation plays a central role in the pathophysiology of the disease, the inciting trigger(s) for the inflammation is not well understood. It is likely that predisposing host biological factors, an initial trigger, and further inciting insults, act synergistically in a multifactorial manner to cause this disease.

Irritation and/or trauma may have a significant role in the pathogenesis of this condition, as the disease has high prevalence in those who have their hair cut closely with a clipper and in athletes who incur repetitive mechanical irritation from helmets (Huggins 2014). Affected patients have also reported temporal relation to the eruption of papules after close haircuts. Further evidence linking irritating trauma with onset of disease is supported by a few case reports of women who developed the disease after shaving their posterior scalp with a razor (Ramos and Pirmez 2014).

The predominance of the disease to the African American demographic suggests that specific host factors play a role in the pathogenesis. Findings by Basler and colleagues support this theory. Amongst 453 male football players, Caucasian and African American players had similar prevalence of acne mechanica (an acneiform eruption common in athletes subject to constant friction and heat), however AK preferentially

affected African American players (Alexis et al. 2014). Another relevant host factor may be African American hair morphology and texture, which differs from Caucasian hair. In cross-section African American hair is more elliptical, with the hair follicle being more spiral in shape as compared to Asians' and Caucasians' hair and hair follicles (Basler 1992). Cutting coiled and textured African American hair may require excess force that could imaginably induce inciting trauma (Ramos and Pirmez 2014).

Once the disease process has begun, secondary mechanical irritation due to pruritus may prolong the chronicity of the trauma and exacerbate disease. Genetic and anatomic host factors may also play a role. To elaborate, studies have suggested that mast cells are twice as prevalent on the nape of neck and posterior scalp as compared to the anterior scalp. Furthermore, it has been shown that the density of mast cells may depend on genetic predisposition (Ramos and Pirmez 2014). Thus, anatomic host factors including genetic factors influencing density of mast cells in affected areas may contribute to the implicated inflammatory cascade.

Other proposed contributing factors include infection, seborrhea, possible drug-induced disease (after using cyclosporine, carbamazepine), and elevated testosterone levels (Herzberg et al. 1990; Ramos and Pirmez 2014). The fact that the disease develops in males predominantly after puberty supports the possibility of androgenic interplay (Huggins 2014).

Treatment

While AK lesions are entirely benign, they can be painful and disfiguring, and therefore symptomatic relief and cosmesis are the main drivers for treatment. Furthermore, the disease is chronic and is unlikely to resolve without treatment (Ramos and Pirmez 2014).

Initial treatment should address preventative measures to minimize mechanical irritation. Patients should avoid close

hair clipping and shaving of the posterior neck, avoid wearing tightly fitting collars and hats, and avoid any self-manipulation such as rubbing or scratching of the area. Utilizing an antibacterial cleanser such as chlorhexidine or povidone iodine to minimize chance for infection can also be recommended (Ramos and Pirmez 2014).

Further treatment should be individualized based on stage of disease. In early stage disease when papules are <3 mm and if no nodules are present, treatment can be limited to topical therapy (Ramos and Pirmez 2014). A combination of topical steroids, retinoids, and/or topical antibiotics can help to reduce inflammation, improve symptoms, and treat concomitant infection if present (Huggins 2014). Authors have suggested clinical success in implementing a cyclical 2-week on and off regimen of steroid foam in treating lesions while avoiding steroid-induced atrophy (Ramos and Pirmez 2014).

If severe infection ensues, systemic antibiotic therapy can be selected appropriately based on bacterial culture results (Kundu and Patterson 2013). However, oral tetracyclines such as doxycycline and minocycline can also be instituted at low doses in the absence of infection, as their anti-inflammatory effects can be beneficial (Huggins 2014).

For larger papules and plaques, intralesional corticosteroid therapy should help to flatten lesions (recommended regimen: escalating doses of 10–40 mg/mL every 4 weeks) (Ramos and Pirmez 2014). In cases of advanced disease with large fibrotic plaques/nodules, particularly when lesions are greater than >3 cm, clinicians may discuss surgical excision. The advised technique is elliptical excision extending to subcutaneous fat. Equal success has been demonstrated using both primary closure and secondary intention healing. Despite a gap in the literature of long-term studies assessing outcomes after surgical excision, it is considered to be very successful with low rates of recurrence reported (Ramos and Pirmez 2014). This may distinguish AK from “true” keloids; for keloids surgery is rarely curative, recurrence rates are high, and patients are therefore typically counseled against surgery as a treatment option.

For patients who are amenable, long-pulsed Nd:YAG and diode lasers are therapeutic options that can be used as an adjunct to therapy in any stage of disease. If disease is minimal, laser may even serve as a sole alternative to treatment (Ramos and Pirmez 2014). Long-pulsed Nd:YAG lasers are safe lasers for use in the dark-skinned population, as they are associated with lower risk for inducing post-inflammatory hyperpigmentation (Huggins 2014). Serial treatments with the Nd:YAG laser have been proven to be effective in reducing clinically apparent disease (Ramos and Pirmez 2014).

Key Points

- AK is a disease that primarily affects post-pubertal African American males.
- AK is a misnomer, as the disease is not necessarily associated with acne vulgaris nor true keloids.
- Classic presentation is with pruritic pustules or papules on the posterior nape of the neck that can coalesce to form fibrotic keloidal plaques that may also be associated with alopecia.
- Recommend avoidance of mechanical irritation including close shaving/hair-clipping, tight-fitting clothes, and scratching of the area.
- Treatment options include topical steroids and retinoids and/or laser treatments, antibiotics for secondary infection, and intra-lesional corticosteroids and surgical excision for more extensive disease.

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Chapter 5
Dissecting Cellulitis of the Scalp

Angad Chadha and Roopal V. Kundu

History

A 25-year-old African-American male presents with an 8-month history of "a lot of bumps on my head." He first had one painful red bump on his crown, which he believed was an ingrown hair. He then developed additional bumps over the top of his head. There was associated "cheesy" drainage and alopecia. He attempted to apply his topical acne medications to the area with mild improvement. He has not had any fevers or chills.

Physical Examination

On examination, numerous erythematous papules and pustules are noted on the vertex & occiput (Fig. 5.1). There are also fluctuant cysts and nodules with connecting sinus tracts. The nodules are tender to palpation and express a

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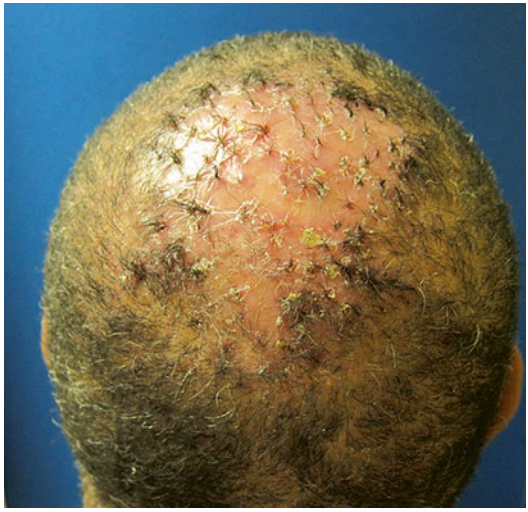

FIGURE 5.1 Dissecting cellulitis. Scattered erythematous papules and pustules are noted on the vertex with alopecia and tufted hairs

thick, white exudate. There are areas of hair loss over the nodules.

Clinical Differential Diagnosis

The patient's presentation is most consistent with dissecting cellulitis of the scalp (DCS). Other conditions to be considered in the differential diagnosis included acne keloidalis nuchae, tinea capitis or kerion, folliculitis decalvans, and cutis verticis gyrata. Unlike DCS, acne keloidalis does not present with sinus tracts, suppurative nodules, or cicatricial alopecia. A KOH preparation or positive fungal culture can help differentiate DCS from tinea capitis. Folliculitis decalvans can present with cicatricial alopecia like DCS, but does not present with sinus tracts or nodules. It is sometimes categorized as a more superficial variant of DCS. Cutis verticis gyrata is usually

asymptomatic and does not present with sinus tracts or suppurative nodules (Madu and Kundu 2014; Ross et al. 2005).

Histopathology

A biopsy was not performed in this case because the history and physical exam were felt to be sufficient for diagnosis. When biopsy of DCS is performed, histopathology reveals distention of the follicular infundibulum with perifollicular, mixed neutrophilic and lymphoplasmacytic inflammation. The inflammatory process involves the lower dermis and subcutaneous junction. Scarring and fibrosis can be seen in chronic lesions (Sperling 2001).

Diagnosis

Dissecting cellulitis of the scalp (DCS)

Case Treatment

The nature of the diagnosis of DCS was reviewed with the patient. Treatment options including oral antibiotics, oral or intralesional corticosteroids, oral isotretinoin, laser treatments, and tumor necrosis factor alpha (TNF-α) inhibitors were discussed. After a discussion of the risks and benefits of each treatment, the patient elected to start oral isotretinoin given the extensive presentation of his disease and the desire to reduce the development of further scarring alopecia. The patient was started on 1 mg/kg/day of oral isotretinoin until clinical remission of the disease was achieved 3 months later, followed by a maintenance dose of 0.75 mg/kg/day for 4 months afterwards. His cumulative dose was 180 mg/kg. Upon completion of the treatment, the patient had satisfactory partial hair regrowth in areas of previous hair loss and did not have recurrence of the disease at 1-year follow-up.

Discussion

Dissecting cellulitis of the scalp is a chronic inflammatory condition of the follicles of the scalp characterized by fluctuant nodules, cysts, draining sinus tracts, and secondary scarring alopecia (Madu and Kundu 2014). At least 80 % of all cases of dissecting cellulitis of the scalp occur in black men between the ages of 18–40. It has been less frequently reported in white males (10 % of cases), in women, and in children (Ross et al. 2005).

DCS follows a chronic and relapsing course (Ross et al. 2005). It initially presents as a follicular pustule (folliculitis) at the scalp vertex or occiput, which then transforms into a painful nodule. Multiple similar and contiguous papules and nodules occur shortly thereafter, giving the scalp a cerebriform appearance. During periods of waning, hypertrophic or atrophic scarring of the scalp remains and a pattern of cerebriform folds and furrows mimicking cutis verticus gyrata may occur (Coley and Alexis 2009). The condition does not usually involve the entire scalp. Purulent or keratinaceous discharge may be expressed from the lesions spontaneously or with applied pressure. Due to the interconnecting sinus tracts, pressure applied on one nodule/abscess can lead to expression of purulent material from an interconnected nodule. An unpleasant odor can be associated with the disease due to the presence of secondary infection. Early disease can present with a nonscarring alopecia. Long-standing disease can lead to cicatricial alopecia. The inflammatory nature of the disease can lead to the development of post-inflammatory hyperpigmentation.

The precise mechanism for the development of DCS is unknown but is thought to involve follicular occlusion. Keratin debris can occlude the pilosebaceous unit leading to follicular expansion, subsequent inflammation, and dilation (Madu and Kundu 2014). Secondary bacterial infection of the follicle with either *Staphylococcus aureus, Pseudomonas aeruginosa*, or anaerobic bacteria leads to a folliculitis or perifolliculitis (Coley and Alexis 2009). When these inflamed follicles rupture they release keratin and bacteria, which

precipitates a localized neutrophilic and granulomatous response leading to abscess formation. Abscesses can then expand and coalesce to form interconnecting abscesses and sinus tracts (Coley and Alexis 2009). The presence of hair follicles is necessary for the disease process; when follicles are eliminated, such as by laser hair removal or scalpectomy, the disease improves (Coley and Alexis 2009).

On trichoscopy of DCS, early findings can mimic non-scarring alopecia with empty follicular openings, yellow dots, and black dots. With progression of disease, dermoscopy reveals yellow structureless areas and dystrophic hair shafts with overlying yellow dots that have a "three-dimensional" structure. Dermoscopy of long-standing disease will reflect scar formation and reveal confluent, ivory-white areas lacking follicular openings (Mubki et al. 2014).

Biopsy may or may not be necessary to make a diagnosis of DCS, depending on the extent of the disease and the phase of disease that the patient presents in. Before undertaking biopsy, the physician should consider the risk of hypertrophic scarring and keloid formation, which occur at higher rates in patients with ethnic skin (Robles and Berg 2007). Cosmesis should be considered when choosing a biopsy site on the scalp. Intralesional corticosteroid injection can be considered to minimize the risk of keloid formation in patients with a known keloid diathesis.

DCS is associated with hidradenitis suppurativa and acne conglobata, collectively referred to as the follicular occlusion triad or, when seen in conjunction with pilonidal cysts, a tetrad. All of these disorders share pathogenesis related to follicular occlusion, secondary infection, and deep inflammation (Ross et al. 2005). Hidradenitis suppurativa is the development of deep-seated painful nodules, abscesses, draining sinuses, and scarring in intertriginous areas. Acne conglobata is a nodulocystic form of acne vulgaris that presents with comedones, papules, pustules, nodules, abscesses, and draining sinus tracts on the face, chest, back, and buttocks. Pilonidal cysts present as painful cyst near the intergluteal cleft that can lead to the development of an abscess or draining sinus tracts.

One-third of patients presenting with DCS may concurrently present with another condition of the follicular occlusion triad. The co-occurrence of two or more follicular occlusion triad conditions is a risk factor for the development of HLA-B27-negative spondyloarthropathy in black males, characterized by an asymmetric peripheral and axial joint arthritis. Other associated clinical conditions include sternoclavicular hyperostosis with polyarticular arthritis, SAPHO syndrome (synovitis, acne, palmoplantar pustulosis, hyperostosis, osteitis), and marginal keratitis. Squamous cell carcinoma can arise in the setting of DCS, and relapsing cases of DCS increase the risk of development of *Staphylococcus aureus* scalp osteomyelitis (Jerome et al. 2014).

Treatment

Data on the treatment of DCS are limited to case reports and small case series; there are no large clinical trials. Mild cases can sometimes be managed with antiseptics, topical antibiotics, lesional aspiration, and corticosteroid injections (Jerome et al. 2014). Treatment for more severe cases of DCS can be further categorized as medical, destructive, or surgical.

First-line medical therapy for severe cases of DCS is oral isotretinoin. Treatment with oral isotretinoin has a multifactorial effect on the pilosebaceous unit including changing the keratinization of the follicle, suppressing sebaceous gland activity, and exerting an anti-inflammatory effect (Plewig et al. 1982). A long course of isotretinoin is usually needed, with cumulative dosing around 170–180 mg/kg to see improvement (Khaled et al. 2007). The isotretinoin course is also prolonged several months after clinical remission in order to decrease the risk of relapse. A recent review article recommended an initial dose of 1 mg/kg/day followed by a maintenance dose of 0.75 mg/kg/day for at least 4 months after clinical control of the disorder was achieved (Mundi et al. 2012). Case reports using similar dosage guidelines illustrate the disease course during treatment with oral

isotretinoin: remission was achieved by month 2–4, hair regrowth by month 6, treatment was stopped at month 9–12, and there was no evidence of recurrence at 3–6 month follow-up (Khaled et al. 2007; Koca et al. 2002). Similarly, a retrospective study of seven cases of DCS showed complete healing and regrowth following oral isotretinoin administration at 0.75 mg/kg/day for 9–12 months (Koudoukpo et al. 2014). Another case series of four patients reported the use of rifampin 300 mg twice daily for 4 months to stop progression of DCS, followed by oral isotretinoin at 0.5 mg/kg/day for 3–4 months to induce complete remission; no recurrence was noted in 10–12 month follow-up (Georgala et al. 2008). One case report demonstrated remission with topical isotretinoin (Karpouzis et al. 2003).

Oral and intralesional corticosteroids may also be used for their anti-inflammatory effect. However, intralesional corticosteroids do not induce long-term remission of the disease and are used only as a temporizing measure for symptom management. Oral antibiotics including fluoroquinolones, tetracyclines, and dapsone have shown efficacy in effecting DCS remission, most likely due to anti-inflammatory effects. Numerous case reports indicate success in the treatment of long-standing, recalcitrant disease with the use of tumor necrosis factor alpha inhibitors including adalimumab and infliximab, though further study is needed to fully evaluate the efficacy and safety of TNF-α-inhibitors in DCS. Colchicine and oral zinc may also be used to help curb the disease (Madu and Kundu 2014; Ross et al. 2005).

Selective follicular destruction using laser and radiation beams has been reported to be an effective definitive therapy for DCS. It is non-invasive and has less recovery time when compared to surgical therapy. Case reports indicate success with the use of an 800nm pulsed diode laser, 1064nm long-pulsed Nd:YAG laser, electron beam radiation, and X-ray radiation (Madu and Kundu 2014; Ross et al. 2005).

Intractable cases of DCS can be addressed with scalpectomy of the affected area of the scalp followed by split thickness grafting. Several case reports have demonstrated success

in achieving remission and possible cure of the disease using this method, though recovery can be an arduous process (Jerome et al. 2014).

Key Points

- DCS is a chronic inflammatory condition of the follicles of the scalp.
- The classic presentation of DCS includes inflammatory perifollicular pustules progressing to fluctuant nodules, cysts, draining sinus tracts, and secondary scarring alopecia.
- The differential diagnosis of DCS includes acne keloidalis nuchae, tinea capitis or kerion, folliculitis decalvans, and cutis verticis gyrata.
- Treatment should focus on gaining timely control of the disease to avoid extensive scarring alopecia and post-inflammatory hyperpigmentation. First-line treatment for DCS is oral isotretinoin.
- Successful treatment and remission of the disease is often associated with regrowth of hair in areas of previous alopecia.

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Chapter 6
Hidradenitis Suppurativa

Cindy Ojevwe and Roopal V. Kundu

History

A 34 year old African American female presents with a 3-year history of intermittent tender subcutaneous nodules that rupture, drain and form abscesses in her axilla and groin. These are uncomfortable, have a foul odor, and often cause embarrassing leaks. Past use of topical neosporin have provided little relief.

Physical Examination

On examination, the axilla and groin reveal tender erythematous papules and nodules, double-ended comedones, and sinus tracts with pustular drainage upon compression.

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Clinical Differential Diagnosis

The presence of sinus tracts in addition to tender, red papules, nodules and double comedones in the *groin and axilla* strongly suggest a diagnosis of hidradenitis suppurativa. However, the following should be considered in the differential diagnosis: acne vulgaris or folliculitis, furuncles or carbuncles, epidermal or pilonidal cysts, or rarely Crohn's disease when localized to the perianal and groin area.

Although acne can present with comedones, these typically present in areas with large hormonally sensitive sebaceous glands, such as the face, neck, upper chest, and back. Furuncles, carbuncles, and cysts are often more isolated and not clustered in the axilla or groin.

Histopathology

A biopsy was not performed in this case as the diagnosis was made clinically. However, if a biopsy is done, the histopathologic picture of HS tends to differ depending on the stage of the lesions biopsied. In early lesions, a biopsy may show follicular hyperkeratosis, follicular plugging, follicular dilation, and lymphocytic perifolliculitis. Psoriasiform hyperplasia of the interfollicular epithelium and a dense inflammatory infiltrate in the lower part of the dermis and subcutaneous tissue may also be present. Later, there may be chronic abscesses (as seen in Crohns disease) and sinus tracts that are lined with stratified squamous epithelium. Granulation tissue, sometimes with the formation of foreign body giant cells can also be seen (Margesson and Danby 2015).

Diagnosis

Hidradenitis Suppurativa (HS)

Case Treatment

The diagnosis of HS was discussed with the patient including suspected predisposing factors, the clinical course of the disease as well as potential treatments. She was further evaluated for symptoms consistent with the other 3 disorders that form the "follicular occlusion tetrad", specifically for the presence of pilonidal cysts, dissecting cellulitis of the scalp and acne conglobata. There was also an assessment of the patient's emotional status as it related to the disease and necessary general measures to reduce the emotional impact of the disease were suggested. A culture was taken from a pustule to assess for potential secondary infection, which was negative. The patient was started on a benzoyl peroxide 5 % wash to use in the shower to the affected areas daily along with clindamycin 1 % lotion after bathing. In-office intralesional triamcinolone 5 mg/ml injections were performed to inflamed subcutaneous nodules.

Discussion

Hidradenitis suppurativa (HS) is a chronic and relapsing cutaneous disorder of the follicular epithelium in apocrine gland-bearing skin such as the axilla, inframammary region, and groin (Fig. 6.1). HS affects all races and ethnicities. Historically, it is considered a disease that is more common in those of African descent but published epidemiological data have provided no conclusive evidence (Reeder et al. 2014; Alikhan et al. 2009). With varying population prevalence rates reported of up to 4 %, HS is known to affect females more than males. However, discussions exist as to whether certain body sites are more affected in a certain gender. For example, it appears that perianal HS has a predilection for males. The disease has also been shown to affect mostly postpubertal individuals in their twenties and thirties.

The pathogenesis of hidradenitis suppurativa involves an interplay of genetics, hormones, infection, and social,

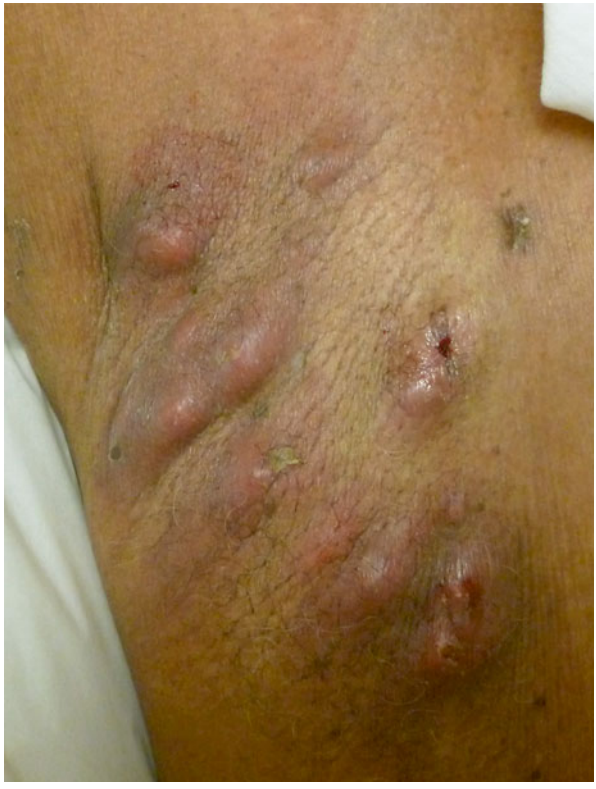

FIGURE 6.1 Hidradenitis suppurativa. Tender erythematous nodules and sinus tracts with pustular drainage along the axilla

immunological and mechanical factors. In terms of genetics, no single gene has been associated with the disease. However, familial occurrences of HS resembling an autosomal dominant-like inheritance pattern have been reported. As a result of the hormonal role, post-pubertal individuals seem to be mostly affected. There is a correlation between the disease in females and the onset of menarche. It is rarely seen before puberty or after menopause. Also, HS flares correlate with menstruation and are associated with an increased organ sensitivity to low levels of androgens, as there is no increased androgen production in

HS. Antiandrogen methods of therapy have been shown to be effective forms of treatment in HS in both males and females (Margesson and Danby 2014).

Historically, bacterial infections were thought to be the cause of HS but there is now a general consensus that infection plays a limited role. It appears to have a role solely in the development of relapsing lesions as a secondary infection (Margesson and Danby 2015). If there is an acute worsening of HS or lack of usual response to therapy, a bacterial culture may be performed to evaluate for secondary infection.

HS, classified as a follicular disorder, involves the plugging/occlusion of the folliculopilosebaceous units in the skin. Immunologically, this leads to activation of the innate immune system. After the follicles are clogged, they rupture into the dermis with the contents released causing an inflammatory response. This response leads to abscess formation and may also allow secondary bacterial infection. As the abscesses heal and recur, fistulous tracts may form.

As a follicular disorder, HS is often associated with other follicular disorders in what is termed the "follicular occlusion tetrad." Pilonidal cyst, dissecting cellulitis of the scalp and acne conglobata have established associations with HS and form the other three parts of the tetrad of follicular occlusion disorders. A patient with HS will typically have two of these disorders. It is also important to note that HS also carries an association with acne vulgaris as well as obesity and smoking.

The folliculopilosebaceous units are weak structurally in HS and are prone to rupture by trauma. This further contributes to the disease as a mechanical factor that accounts for the location of lesions in intertriginous areas. Social factors such as smoking, diet and the use of the drug lithium also contribute to HS by increasing follicular clogging. Obesity and nicotine have also been implicated specifically (Margesson and Danby 2015).

Treatment

There are varying forms of treatment for HS. These include general measures, pharmacy and surgical procedures. As a first step, general measures are encouraged to help reduce

the severity as well as the emotional impact caused by the disease. These general measures include education and support, good hygiene practices, proper wound dressings, avoidance of skin trauma, smoking cessation and weight management.

In terms of education and support, the patient should be evaluated for signs of depression. Resources should be provided if additional support is needed. Also, reassurance that the disease is not contagious or the result of poor hygiene is a necessary part of counseling.

Despite providing reassurance that the condition is not the result of uncleanliness, proper hygiene techniques should be encouraged: cleaning the affected area gently with antibacterial cleansers to minimize bad odor and secondary bacterial infection (Margesson and Danby 2015).

The patient should also be encouraged to avoid skin trauma by wearing light and loose clothing and to use dressings that minimize trauma to the area. The latter would likely take the form of gauze with a generous amount of petroleum jelly to prevent sticking of the gauze to the wounds.

Smoking is often associated with HS but unlikely is a causative agent. Existing literature mainly contends that smoking cessation has been known to cause improvement in HS symptoms. This, in combination with the fact that smoking has other adverse effects on health makes it prudent to counsel on smoking cessation.

Weight management is another option as it appears that skin shearing, increased presence of insulin and other hormonal changes associated with excess weight might have a contributory role in the development and exacerbation of HS.

In addition pharmacological methods may also be employed. For mild HS, which is termed Hurley Stage I, local therapy is indicated. These include topical clindamycin and resorcinol as well as punch debridement which can also be classified as a surgical procedure. Clindamycin's benefit in HS is likely as an antimicrobial agent that prevents secondary infection while resorcinol acts as a keratolytic

and anti-inflammatory agent that helps heal lesions and reduce pain.

Systemic pharmacological therapy is also used in the treatment of HS and is used for Hurly Stage II patients who have sinus tracts and scarring. This includes systemic antibiotics such as doxycycline, minocycline and clindamycin and systemic hormonal therapy that targets androgens. The latter includes drugs like cyproterone (not available in the US), finasteride, and anecdotal support of drospirenone-containing oral contraceptives and spironolactone. Clinically refractory cases of HS have been shown to be responsive to TNF-alpha inhibitors such as infliximab, adalimumab and etanercept. Of note, in 2015, the biologic therapy adalimumab became the first FDA-approved treatment for HS in adults who have moderate (Hurley stage II) or severe (Hurley stage III) HS.

Surgery is used at any stage of HS. It can vary from the punch debridement mentioned above which is a local "unroofing" of nodules and sinus tracts, to wide excisions which are reserved for very severe cases of HS. However, it is imperative that general and pharmacological measures be employed in conjunction with surgery, as surgery does not treat the underlying disease but instead only existing lesions.

Laser treatment is another option for HS that has some benefit. Carbon dioxide lasers and long-pulsed 1064nm Nd:YAG lasers have specifically been shown to decrease severity of disease. It is hypothesized that the latter works by disrupting inflammation (Margesson and Danby 2015).

Key Points

- The typical presentation of hidradenitis suppurativa is the intermittent presence of tender subcutaneous nodules that rupture, drain and form abscesses in the axilla, inframammary region and groin, with double comedones.
- HS has historically been associated with people of African descent but current literature is less

conclusive. However, females tend to be more affected than males, with males having a higher incidence of perianal HS.

- HS, classified as a follicular disorder involves the plugging/occlusion of the folliculopilosebaceous units in the skin.
- The follicular occlusion tetrad consists of hidradenitis suppurativa, pilonidal cysts, dissecting cellulitis of the scalp, and acne conglobata.
- Treatment is aimed at preventing the formation of nodules, sinuses and abscesses as well as treating existing lesions.
- Prevention is done via general measures such as good hygiene practices, proper wound care, avoidance of skin trauma, along with smoking cessation and weight management.

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Part II
Inflammatory Conditions

Chapter 7
Atopic Dermatitis

Parul Kathuria and Roopal V. Kundu

History

A 5-month-old African American female presented with a 2-week history of an oozing rash on her forehead and cheeks. Her parents reported increased irritability since the rash began and more nighttime awakenings. Cleaning the skin with soap worsened the rash. Her family history was notable for asthma in her father and allergic rhinitis in her mother.

Physical Examination

Scaly, fissured plaques with micropapules were noted on both the forehead and cheeks, along with hyperpigmented scaly plaques at the knees and ankles (Figs. 7.1 and 7.2). Erythema was not perceptible. Honey-colored crusting was noted over the cheeks.

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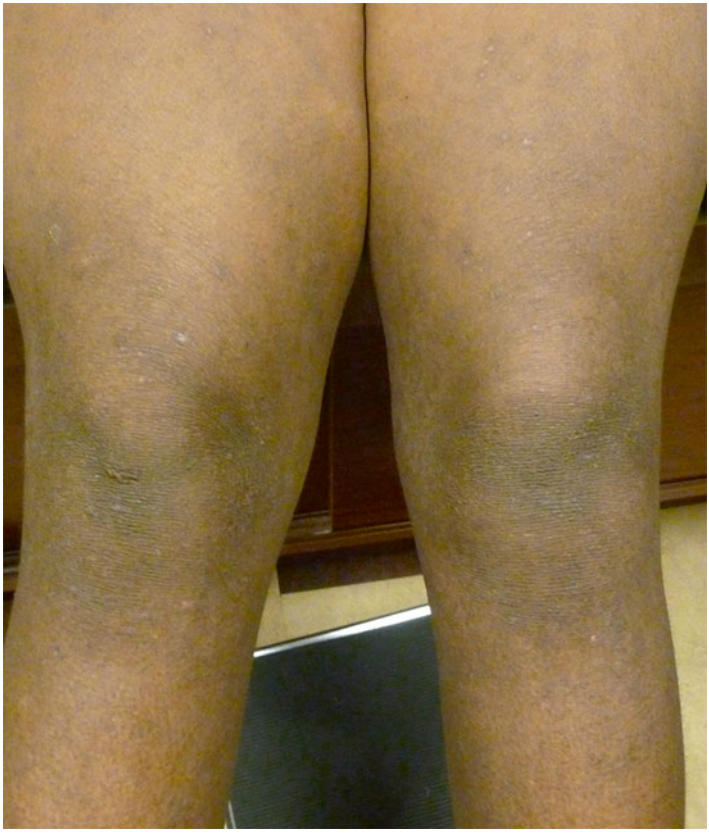

FIGURE 7.1 Atopic Dermatitis. Hyperpigmented scaly patches at the knees bilaterally

Differential Diagnosis

Based on age and clinical exam, atopic dermatitis was highest on the differential. Other forms of dermatitis such as contact dermatitis and seborrheic dermatitis were considered (Spergel and Paller 2003). Wiskott-Aldrich syndrome and hyperimmunoglobulin E syndrome are rare clinical entities but may also present with eczematous skin changes and were

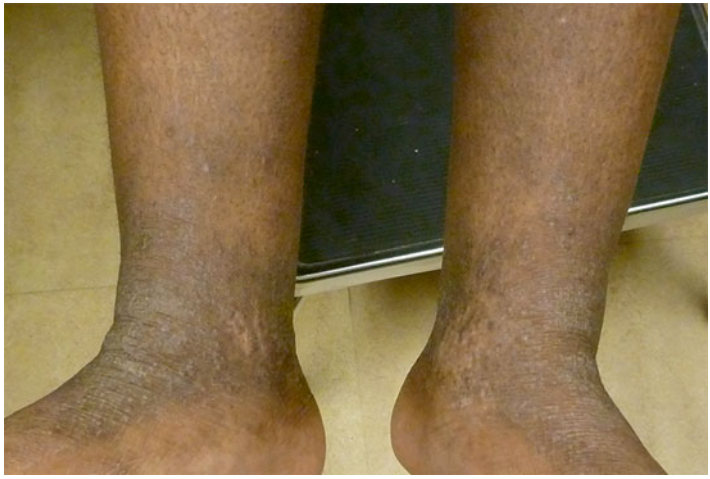

FIGURE 7.2 Atopic Dermatitis. Hyperpigmented scaly plaques at the ankles bilaterally

thus also considered, although in this case the appropriate constellation of symptoms were lacking (Dermatology atlas for skin of color 2014).

Histopathology

A biopsy was not performed in this case, as atopic dermatitis is a clinical diagnosis. Rarely, when a biopsy is performed, epidermal spongiosis and a superficial perivascular lymphocytic infiltrate with some eosinophils and melanophages is seen (Dermatology atlas for skin of color 2014; Vachiramon et al. 2012).

Diagnosis

Atopic dermatitis

Case Treatment

The diagnosis of atopic dermatitis was discussed with the patient's family, including the characteristic locations of infantile atopic dermatitis and the potential for postinflammatory hypo- or hyperpigmentation. Various treatment options were discussed, including skin hydration, topical corticosteroids, and/or topical immunomodulators. Given that this infant's lesions were located primarily on the face, hydrocortisone 2.5 % ointment twice daily was prescribed for a 2-week course (Eichenfield et al. 2014). The family was told that should this treatment fail to provide symptomatic relief, a stronger corticosteroid could be prescribed. For maintenance, transition to a topical immunomodulator, such as pimecrolimus or tacrolimus, could be given. The family was also instructed to apply moisturizers immediately after bathing for better skin hydration.

Discussion

Atopic dermatitis (AD/eczema) is one of the most common skin disorders seen in infants and children, with the prevalence in the United States population estimated to be approximately 17.2 % (Spergel and Paller 2003). Epidemiologic studies have reported that atopic dermatitis is a condition that disproportionately affects individuals of color. Based on data collected between 1993 and 2009 from the National Ambulatory Medical Care Survey, a sampling of ambulatory care visits to U.S. physicians, showed that AD was among the top ten diagnoses for both African Americans and Asian/Pacific Islanders but was not among the top ten diagnoses for Caucasians (Davis et al. 2012). Other studies have shown that African American children are much more likely than Caucasian children to have severe atopic dermatitis, potentially due to poor access to care or delayed diagnosis (Vachiramon et al. 2012). Of note, the word 'eczema' is pronounced differently around the world, and amongst individu-

als with skin of color. Three variations can be heard; "\ig-'zē-mə, 'eg-zə-mə, 'ek-sə-\" (www.meriam-webster.com).

The pathophysiology of atopic dermatitis is poorly defined but the main hypothesis relates to epithelial barrier and immune dysfunction. Mutations in the gene coding for filaggrin, a protein that helps to replace the plasma membrane in anucleated stratum corneum cells, are thought to be a factor, as filaggrin keeps the stratum corneum cohesive and affects epithelial cytokines (Dermatology atlas for skin of color 2014).

Atopic dermatitis classically appears in three sequential phases: infantile, childhood, and adult. The infantile phase is characterized by pruritic, erythematous patches and plaques that are generally located on the forehead and cheeks. The trunk or extensor surfaces may become involved with scattered, symmetrical, ill-defined patches. Affected areas tend to be edematous and fissured, often leading to secondary crusting. Pruritus is often severe, resulting in a disturbed sleep patterns. In children who are over 1 year of age, nummular lesions may accompany the erythematous patches of AD (Spergel and Paller 2003). In individuals with skin of color, erythema can be difficult to assess and thus should not be extensively relied upon. Instead, edema, warmth of the skin, and scaling in these particular distributions can help to correctly diagnose AD (Dermatology atlas for skin of color 2014).

The childhood phase of atopic dermatitis generally occurs from 2 years of age to puberty. Lesions are less likely to be exudative and are more likely to display lichenified papules and plaques more indicative of chronic disease. In children, lesions are classically seen in the hands, antecubital region, wrists, popliteal region, ankles, and feet (Spergel and Paller 2003). In African American children, a distinct clinical presentation is often seen with micropapules and perifollicular accentuation, leading to the development of monomorphic follicular papules coalescing into plaques on the trunk and extensors (Dermatology atlas for skin of color 2014; Vachiramon et al. 2012). These lesions must be distinguished from lichen nitidus, although lichen nitidus is typically located on the trunk, flexors, and genitalia and is less pruritic.

In African Americans, AD lesions can also closely resemble lichen planus, although the distribution of AD lesions (extensor surfaces with limited genital and mucosal involvement) helps to distinguish (Vachiramon et al. 2012).

The adult phase of AD begins at puberty and continues into adulthood. Lesions typically appear on the face, neck, upper arms and back, flexural folds, and dorsa of the hands, feet, fingers, and toes. Lesions are scaly, erythematous papules and plaques with large, lichenified plaques forming with chronic disease. Weeping, crusting, and exudation are less common but may occur with secondary staphylococcal infection (Spergel and Paller 2003).

Chronic atopic dermatitis may lead to postinflammatory hypopigmentation or hyperpigmentation. Hyperpigmentation is most visible at sites of lichenification, as the thickened epidermis contains a great deal of epidermal melanin pigment. This is especially prominent in children with skin of color. Such changes in pigmentation can be improved with treatment of the underlying inflammation (Spergel and Paller 2003). However, post-inflammatory hypo- or hyper-pigmentation can remain for months to years. Other changes seen in chronic atopic dermatitis include diffuse xerosis, prominent skin folds of the lower eyelids, and palmar hyperlinearity (Dermatology atlas for skin of color 2014).

Major and minor criteria for the diagnosis of atopic dermatitis have been established. Major criteria include chronicity, pruritus, and eczematous changes. Minor criteria include palmar hyperlinearity, periorbital involvement, perifollicular accentuation, keratosis pilaris, and ichthyosis vulgaris (Dermatology atlas for skin of color 2014).

Additionally, patients with AD are at elevated risk for secondary infections including *Staphyloccoccus aureus,* herpes simplex, and molluscum contagiosum. *S. aureus* in particular can be cultured from lesions in 93% of patients and contributes to exacerbations of AD, as the bacteria itself is a trigger due to heightened IgE and T-cell responses to the bacterial antigens (Spergel and Paller 2003).

Finally, the “atopic march” is a term used to describe the sequential development of different allergic diseases that

may occur in association with AD. Beginning with atopic dermatitis in infancy and childhood, followed by allergic rhinitis in later childhood, and then asthma during adolescence. Approximately a third of AD patients may develop asthma or allergic rhinitis.

Treatment

Topical corticosteroids are the mainstay of treatment for atopic dermatitis, as they have proven to be effective for both acute and chronic disease. Corticosteroids help to reduce inflammation and pruritus. The least potent corticosteroid that is effective should be used twice daily, and an amount adequate enough to cover the affected area should be prescribed. Fluticasone proprionate cream has been shown to be safe in infants as young as 3 months (Boguniewicz et al. 2003). Given that topical corticosteroids are associated with concerns about adverse side effects such as striae, telangiectasia, skin thinning, perioral dermatitis, acneiform eruptions, and suppression of the hypothalamic-pituitary-adrenal axis, educating the patient (or family) with a specific plan for acute flares and maintenance is important.

Given the potential side effects associated with topical corticosteroids, topical calcineurin inhibitors such as tacrolimus and pimecrolimus have come to play an increasingly important role in the treatment of AD. These drugs work by inhibiting the transcription of inflammatory cytokines and have been shown to display clinical efficacy. In subjects with moderate to severe AD, an average of 2.2 g of 0.1 % tacrolimus ointment was applied twice per day, leading to a 61 % improvement over baseline at 3 months and 71 % improvement at 1 year (Boguniewicz et al. 2003).

Skin hydration and moisturizers are also an important aspect of treatment for AD. As many patients with AD have a compromised epidermal barrier, atopic skin often displays enhanced transepidermal water loss and a greater susceptibility to colonization by *S. aureus*. Skin hydration can be accomplished by

soaking baths with rice starch added to the bath water or by taking bleach baths, with one quarter to one half cup of bleach in a half-full or full bathtub respectively. Patients should immediately apply moisturizers containing ceramides, petroleum, and urea after these baths. Together, these two treatments help to rebuild the stratum corneum (Dermatology atlas for skin of color 2014; Boguniewicz et al. 2003).

Avoiding irritants such as soaps, detergents, chlorine, and tight-fitting clothing is also important, as patients with AD generally have a low threshold for such irritants. For the subset of AD patients who have food allergies, avoidance of food allergens (usually milk, egg, peanut, soy, wheat, and fish) can help reduce clinical symptoms (Boguniewicz et al. 2003).

When determining treatment plans for patients with AD, assessing use of complementary and alternative medicines (CAMs) is important. Among individuals with skin of color, Asians are more likely than Hispanics and African Americans to use CAMs. Use of these treatments is also prevalent among non-Hispanic whites. Among children with eczema, the alternative medicines most frequently used include herbal therapy, vitamins, naturopathy, traditional healing, homeopathy, and Ayurveda. Many of these treatments, however, can be harmful to patients with AD, as their ingredients can include contact allergens and irritants that trigger an eczematous reaction. Asking about the use of these treatments is thus key when treating patients with skin of color (Silverberg et al. 2014).

A few differences regarding the treatment of skin of color individuals are important. African Americans have a lower ceramide-to-cholesterol ratio in the stratum corneum compared to Caucasians, leading to higher transepidermal water loss and skin dryness. Therefore, hydration therapy is recommended for general skin care; higher-potency topical corticosteroids and/or occlusive therapy such as polythene occlusion and wet wraps are recommended. Metabolism of oral cyclosporine, which can be given for severe, refractory AD, is influenced by the activity of the CYP3A5 enzyme. In African Americans, CYP3A5 is more frequently expressed, and the oral bioavailability of cyclosporine is 20–50% lower than in Caucasians. African American

patients may thus need higher doses of oral cyclosporine to maintain therapeutic concentrations, and monitoring of cyclosporine levels and troughs may be considered if patients are not appropriately responsive. Azathioprine, an immunosuppressant used as an alternative treatment for AD, is metabolized partially via the thiopurine methyltransferase (TPMT) enzyme. TMPT enzyme deficiencies are more common in African Americans than Caucasians; African Americans are thus at higher risk for azathioprine toxicity and require more frequent dose adjustments and monitoring (Vachiramon et al. 2012). Lastly, phototherapy such as narrow-band UVB phototherapy has also been found to be a useful adjunctive therapy for AD (Boguniewicz et al. 2003). Compared to lighter skinned individuals, darker skinned individuals often require a higher dose of narrow-band UVB (Vachiramon et al. 2012). However, patients with atopic dermatitis often need extensive phototherapy treatments at lower doses, and treating patients with skin of color with longer treatments may lead to a build-up of heat and a worsening of AD (Syed and Hamzavi 2011).

Key Points

- Atopic dermatitis (AD/eczema) is a condition that disproportionately affects individuals with skin of color.
- AD typically occurs in three phases: infantile, childhood, and adult. Each of these phases is most prominent in different parts of the body. Chronic AD may lead to postinflammatory hypo- or hyperpigmentation, particularly in individuals with skin of color.
- Topical corticosteroids are the first-line treatment for AD, although improved skin hydration, topical calcineurin inhibitors, and phototherapy all play a role.
- A number of differences between African Americans and Caucasians are necessary to keep in mind when seeing patients with AD.

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Chapter 8
Psoriasis

Nirali J. Shah and Roopal V. Kundu

History

An otherwise healthy 25 year old Chinese male presents with a rash over the elbows, knees and scalp that had been present for 4–6 months. The eruption is asymptomatic. He also notes tiny dots in his nails. He does not have any associated illnesses, myalgias or arthralgias. He had tried several over the counter moisturizers and shampoos without improvement.

Physical Examination

Well-demarcated erythematous scaly plaques with micaceous scale limited to the elbows, knees and scalp were seen. Fingernails reveal pitting, without oil spots or onycholysis (Figs. 8.1 and 8.2).

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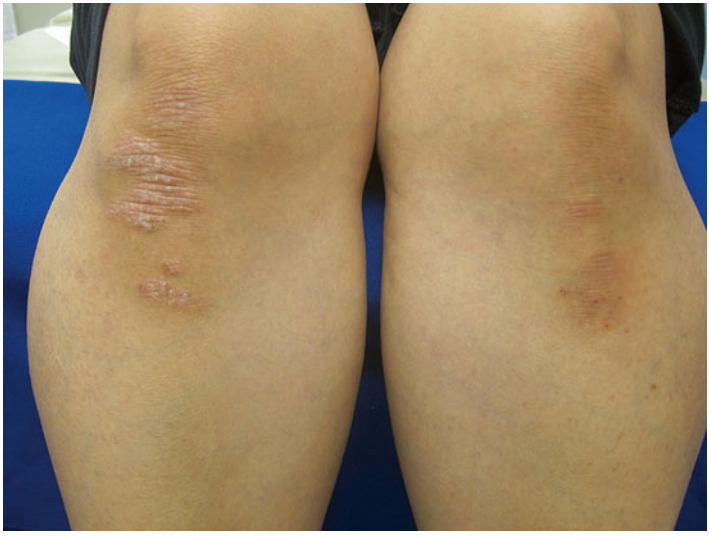

FIGURE 8.1 Plaque psoriasis. Well-demarcated erythematous scaly plaques with micaceous scale on the knees

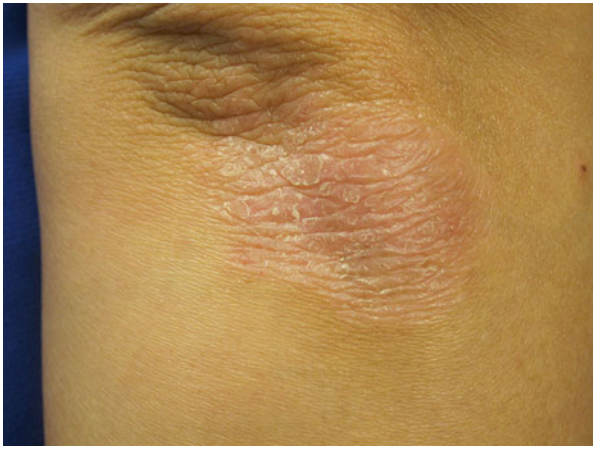

FIGURE 8.2 Plaque psoriasis. Close up of a well-demarcated erythematous scaly plaque with micaceous scale on the right elbow

Clinical Differential Diagnosis

The characteristic presentation is most consistent with psoriasis. However, other diagnostic possibilities include seborrheic dermatitis, eczema, lichen planus, and lichen simplex chronicus (Alexis and Blackcloud 2014). Seborrheic dermatitis is localized to the scalp and sometimes face. Eczema is characterized by pruritic patches and plaquess with fine scaling. Lichen planus presents with localized or widespread flat-topped violaceous to hyperpigmented papules with white lines running through them (Wickham's striae). The most common locations for lichen planus are the wrists, lower back, and ankles. Lichen simplex chronicus is the consequence of chronic localized irritation that leads to skin thickening and a leather-like plaque. The location of scaling over extensor surfaces and micaceous scale make these diagnoses less likely.

Histopathology

Psoriasis is often a clinical diagnosis but biopsy may be performed to confirm in less common presentations. The microscopic changes of psoriasis include regular acanthosis, parakeratosis, loss of the granular cell layer. Dermal edema, dilation of vessels of the papillary dermis and perivascular infiltration of lymphocytes and dendritic cells can be seen (Ragaz and Ackerman 1979). Neutrophilic microabscesses can aggregate in the epidermis (Munro microabscesses). Dilation of vessels helps further migration of immune cells into the affected areas of skin (Bowcock and Krueger 2005; Schon and Boehncke 2005).

Diagnosis

Psoriasis

Case Treatment

The clinical diagnosis of psoriasis was discussed, including the characteristic locations on the scalp and extensor surfaces. The potential for nail and joint involvement was also reviewed, with discussion of monitoring for morning stiffness. The increased risk of cardiometabolic comorbidities such as hypertension, hyperlipidemia, glucose intolerance and increased risk for cardiovascular events was reviewed with the patient. The patient was also encouraged to avoid smoking and follow regularly with his primary care physician. Various treatment options were discussed, including topical corticosteroids, topical vitamin D analogues and phototherapy. Given the localized presentation, triamcinolone 0.1 % ointment BID to the body and fluocinonide 0.05 % scalp solution was prescribed for a 2-week course (Eichenfield et al. 2014), with a goal to transition to pulsed treatment on weekends as needed.

Discussion

Psoriasis is a chronic inflammatory multisystem disorder. It occurs worldwide and is slightly more common in women than in men. Although it can present at any age, psoriasis is most commonly seen around age 20 or between 50 and 60 years old (Sabat et al. 2007). Psoriasis is rapidly becoming more prevalent in the non-Caucasian population. In a 2009–2010 National Health and Nutrition Examination Survey (NHANES), the prevalence of psoriasis in the US population of color was 1.6 % in Hispanics and 1.9 % in African Americans, which is much higher than the previously reported NHANES data from 1996 (Rachakonda et al. 2014). The wide variation in prevalence worldwide is multifactorial, ranging from differences in sun exposure and climate to dietary intake (Parisi et al. 2013; Mr 2004) Genetics also play a role in susceptibility to psoriasis. Genes such as HLA-Cw6, which plays a role in adaptive immune response, is amongst

one of the strongly associated susceptibility genes for psoriasis (Nair et al. 2006; Marsh et al. 2000) The prevalence of this allele is 15.09 % in Africans. The PSORS1 major histocompatibility complex (MHC) region may also be associated with psoriasis (Bowcock and Krueger 2005).

The pathogenesis of psoriasis is not completely understood. Influenced by genetic and immune-mediated factors, psoriasis involves immune dysregulation and hyperproliferation of the epidermal keratinocytes and increased epidermal cell turnover. Environmental factors such as infections (ie staphylococcal, streptococcal, and HIV), alcohol, and medications (beta-blockers, steroid withdrawal, lithium, antimalarials) are often associated with psoriasis.

In darker skin types, the impact of psoriasis is often more severe compared to Caucasian patients (Shah et al. 2011). Psoriasis can present diagnostic challenges due to its overlapping features with other papulosquamous disorders and decreased ability to identify erythema (Alexis and Blackcloud 2014).

Psoriasis has a great impairment on quality-of-life in patients with skin of color. Using the Dermatology Life Quality Index (DLQI), subjects impacted by the disease are also treated for pruritus and pain as well as psychosocial impacts of embarrassment and interference with work and studying (Shah et al. 2011). The psychosocial factor of psoriasis may be related to cultural variations in perceptions of skin disorders, and the impact of dyspigmentation following psoriasis treatment seen in skin of color. The quality-of-life concerns included: feelings of self-consciousness, embarrassment, anger, frustration, and helplessness.

Recent studies show an association between psoriasis and an adverse cardiometabolic profile. Although a causal relationship has not been determined, patients with psoriasis may have decreased adiponectin and leptin levels independent of their risk of metabolic disease. Adipokines leptin and adiponectin are key inflammatory mediators secreted by adipose tissue, and have downstream effects including regulation of insulin sensitivity, inflammation and immunity. The cardiometabolic comorbidities reported in psoriasis

suggest that systemic inflammation may be associated with adipose tissue inflammation similar to that seen in obesity (Li RC et al. 2014).

Treatment

There are several different treatment options available for psoriasis depending on the characteristics of the rash and extent of disease. For mild to moderate localized disease, topical treatments such as corticosteroids, vitamin D derivatives, calcineurin inhibitors, retinoids, anthralin, and tar-based formulations are considered first line (Feely et al. 2015). Combination treatments are often prescribed, such as vitamin D analogs and corticosteroids (Lambert et al. 2014). Topical treatments may be available in a variety of vehicles (cream, gel, solution, foam, or ointment) and can be prescribed based on patient preference.

Moderate to severe disease can be treated with phototherapy (narrow band UVB preferred) or systemic agents including retinoids, methotrexate, cyclosporine, or biologic immune modifying agents. Biologic agents include, but are not limited to: targeted therapies, anti-cytokine therapies (anti-tumor necrosis factor [TNF] therapies), and a monoclonal antibody against interleukin IL-12 and IL-23 (Papoutsaki and Costanzo 2013). Widespread disease with joint involvement (psoriatic arthritis) can be treated with biologic therapy or traditional systemic agents like methotrexate, which is a folate antagonist (De Eusebio et al. 2014). The risks of immunosuppressive systemic treatment include infections such as pneumonia and cellulitis, which were reported in approximately 1 % of patients in a large multi-center cohort. Increased risk of infection is associated with age, diabetes mellitus, smoking, infection history, infliximab exposure, and adalimumab exposure (Kalb et al. 2015). Although phototherapy is an extremely effective treatment option, the risk of increased pigmentation (tanning) and post-inflammatory hyperpigmentation is greater for a psoriatic patient of color (Talakoub and Wesley 2009).

Key Factors

- The incidence of psoriasis in patients with skin of color is rising.
- The classic presentation of psoriasis are scaly plaques over the extensor surfaces including the scalp. Myalgias and arthralgias representative of psoriatic arthritis may be associated.
- Psoriasis may have an adverse effect on cardiometabolic profile, with recommended counseling about increased risks for hypertension, hyperlipidemia and glucose intolerance.
- Skin of color patients are more susceptible to post-inflammatory dyspigmentation.

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Chapter 9
Pityriasis Rosea

Michael W. Pelster and Roopal V. Kundu

History

A 21-year-old African-American female presented with 2 weeks of an eruption on her chest, abdomen, and back. There was minimal involvement of the proximal extremities. She endorsed moderate pruritus. She noted one larger lesion on her left lower abdomen that preceded the rest of the rash by a few days. There was no history of a similar eruption. She denied sick contacts. For treatment, she had tried shea butter without improvement. Review of systems was otherwise negative.

Physical Examination

Numerous erythematous to subtly violaceous scaly papules and thin ovoid plaques were found in a "fir tree" distribution involving the chest, abdomen, back, and the proximal legs and arms (Figs. 9.1 and 9.2). The largest plaque measured approxi-

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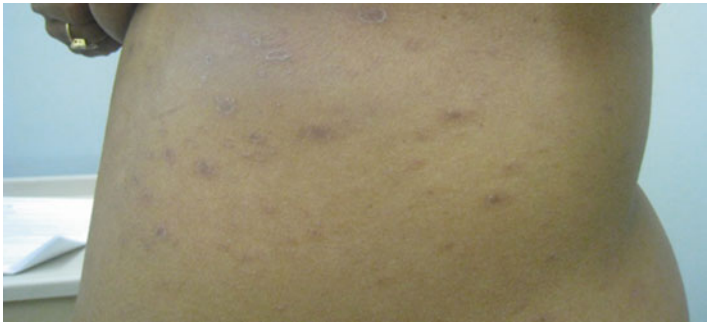

FIGURE 9.1 Pityriasis rosea. Numerous erythematous to violaceous and hyperpigmented ovoid scaly papules on the trunk

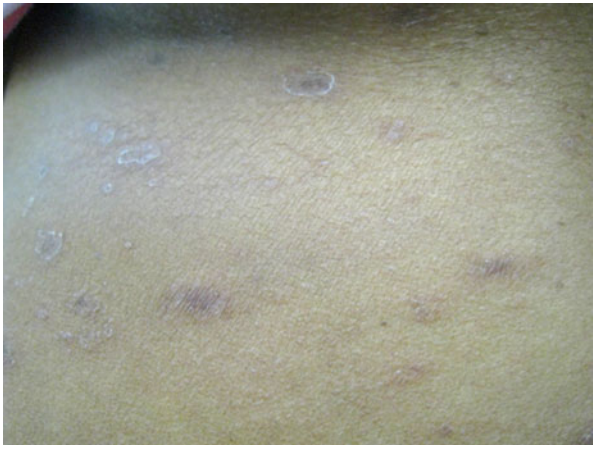

FIGURE 9.2 Pityriasis rosea. Close up. Erythematous to violaceous and hyperpigmented ovoid papules on the trunk with fine collarettes of scale

mately 5 cm in its longest dimension and was found on the left lower abdomen. There was no involvement of the palms, soles, or genitals. No nail or hair changes were identified.

Clinical Differential Diagnosis

The rash was felt to be most consistent with pityriasis rosea. However, other diagnostic possibilities included nummular eczema and secondary syphilis. A complete differential diagnosis of pityriasis rosea also includes guttate psoriasis, pityriasis lichenoides chronica, tinea versicolor, tinea corporis, HIV acute seroconversion illness, Lyme disease, and drug eruption (Goldstein et al. 2015).

Histopathology

A biopsy was not undertaken in this case because the history and physical examination were felt to be diagnostic. When a biopsy is performed, histopathologic evaluation is often nonspecific. Generally, there is subacute spongiotic dermatitis in the setting of a superficial perivascular lymphohistiocytic infiltrate. Other features include erythrocyte extravasation and subsequent transepidermal elimination. Non-herald patch lesions also frequently show a leading spongiosis with trailing parakeratosis, a feature also seen in erythema annulare centrifugum (Elston 2009). Notably, the finding of plasma cells favors a diagnosis of secondary syphilis.

Diagnosis

Pityriasis rosea (PR)

Case Treatment

The nature of the diagnosis of pityriasis rosea was reviewed with the patient, including the possible sequela of post-inflammatory hyperpigmentation (PIH). Treatment options

were discussed, including observation, topical corticosteroids, acyclovir, erythromycin, and/or phototherapy. Given her pruritus, triamcinolone 0.1 % ointment BID was prescribed for a 4-week course, and the patient was instructed to contact the clinic for consideration of phototherapy if she did not experience a significant improvement in pruritus. In addition, after a discussion of the risks and benefits and relatively limited data for acyclovir, the patient opted for a 1-week course of acyclovir 800 mg five times daily. Finally, after a discussion of the clinical similarities between pityriasis rosea and secondary syphilis, the patient agreed to a serum rapid plasma reagin (RPR) with prozone, which was non-reactive.

Discussion

Pityriasis rosea is an acute, self-limited, papulosquamous eruption that involves the trunk and proximal extremities of healthy adolescents and young adults, generally between the ages of 10 and 35 (Chuang et al. 1982). The disease is more common in females than males, but individuals of all races and ethnicities are affected equally. The rash generally clears within 2 months but occasionally can last somewhat longer. Lesions that persist longer than 5 months should prompt consideration of pityriasis lichenoides chronica. A viral etiology for pityriasis rosea has long been postulated. A recent review article of the existing data concludes that there is strong evidence for an association between a "reactive response" to HHV-7 and to a lesser extent HHV-6 and development of pityriasis rosea (Drago et al. 2009). Less robust evidence exists to support an association with HHV-8 and influenza A (H1N1).

Clinically, the classic presentation of PR is a "herald patch" (a pink- to salmon-colored scaly patch or thin plaque) that gradually enlarges with central clearing and the development of a "collarette" of scale over several days. In people of color, this patch can appear brown or hyperpigmented. Of note, the presence of the "herald patch" exists in a majority of cases but is not required for diagnosis. Subsequently, there is a more

diffuse eruption of smaller but morphologically similar papules and small plaques that involve the trunk and proximal extremities. Lesions tend to be distributed along skin cleavage lines (Langer's lines), leading to the characteristic description of a "fir tree" or "Christmas tree" pattern on the trunk. Importantly, in skin of color, the subsequent lesions tend to be more papular, monomorphic, and folliculocentric, and larger lesions sometimes have central hyperpigmentation with a papular border; this is conceptually similar to the papular eczema variant of atopic dermatitis in ethnic skin. There is also more frequent involvement of the face and scalp (Amer et al. 2007) and rarely, the oral cavity (Jacyk 1980). Additionally, post-inflammatory hyperpigmentation may be significant and prolonged, especially in skin of color (Amer et al. 2007).

A prodrome of headache, malaise, and/or pharyngitis is present in a small minority of patients. Pruritus occurs in approximately 25 % of patients and ranges in severity (Hartley 1999; Allen et al. 1995). There is also a well-described inverse variant of pityriasis rosea, which affects the axillae, groin, distal extremities, and rarely the face. This subtype of PR is thought to be more common in younger children (Trager 2007). Additional less common variants that have been described include pustular, purpuric, vesicular, urticarial, and erythema multiforme-like.

Biopsy is typically not necessary for the diagnosis of pityriasis rosea. However, if undertaken, the clinician should consider the risk of hypertrophic scarring and keloid formation. Keloids are known to occur at high rates in patients of Hispanic and African ancestry (Robles and Berg 2007). He or she should discuss this risk with patients, especially in those with a history of keloids, and the clinician should be sensitive to cosmesis while choosing a site if biopsy is indicated. Furthermore, the physician could consider intralesional corticosteroid injection or other peri-procedural therapies to minimize the risk of keloid formation in patients with a known keloidal diathesis.

Dermoscopy can also be a useful tool in the diagnosis of pityriasis rosea and in discriminating among inflammatory dermatoses in general. In one large study investigating the

dermoscopic features of plaque psoriasis, dermatitis, lichen planus, and pityriasis rosea, dermoscopy was found to be both sensitive and specific for detecting pityriasis rosea. PR was found to be significantly associated with the following features: yellowish background color, dotted vessels, patchy vascular distribution, and white peripheral scale (the "collarette" of scale). Of note, the dotted vessels seen in PR are also seen in psoriasis and dermatitis, although they are much more abundant in the latter conditions (Lallas et al. 2012). Unfortunately, the population studied largely consisted of white Europeans, so further investigations are needed to validate these dermoscopic findings in ethnic skin.

One of the most common dermatoses to mimic pityriasis rosea is secondary syphilis. Frequently, the two can be distinguished clinically, as syphilis will present with red-brown macules on the palms or soles or the history of a primary chancre, but there are many cases of clinical overlap. Therefore, serologic testing for syphilis, or immunohistochemistry on a biopsy specimen if performed, may be indicated to rule out syphilis in cases of suspected PR. In the United States, the incidence of syphilis is substantially higher in African-American and Hispanic populations, (Patton et al. 2014) so an increased pre-test probability in those populations may sway the risk/benefit analysis toward testing. More rarely, pityriasis rosea can appear similar to the acute exanthem of HIV seroconversion, so testing for HIV in the appropriate clinical setting may also be useful. Other diagnostic considerations include tinea corporis, tinea versicolor, nummular eczema, guttate psoriasis, Lyme disease, and PR-like drug eruptions. In-office KOH examination for fungal hyphae or spores and short, stubby hyphae ("spaghetti and meatballs") can be utilized to rule out tinea corporis and tinea versicolor, respectively. In nummular eczema, the pruritus is generally more severe than in pityriasis rosea, and there is more extensive involvement of the extremities. Guttate psoriasis presents with the coarser micaceous scale more classically associated with psoriasis, in contrast to the fine scale of PR, and is frequently preceded by pharyngeal streptotoccal infection. As

noted previously, a persistent PR-like eruption should prompt consideration of biopsy to evaluate for pityriasis lichenoides chronica. The most commonly associated medication with the development of a pityriasis rosea-like drug eruption is therapeutic gold, but a variety of other possible causative agents have been described as well (Goldstein et al. 2015).

Treatment

Frequently, therapy can consist only of monitoring and reassurance given the often benign, self-resolving course of PR. Specifically, patients can be told that the vast majority of cases clear within 2–3 months, and they should be advised to seek evaluation if their rash persists beyond this time frame. Pregnant patients should be educated that there are some limited data linking development of pityriasis rosea to spontaneous abortion, especially in the first trimester (Drago et al. 2014). In cases with pruritus, medium-potency topical corticosteroids or other topical anti-pruritic agents containing ingredients such as pramoxine or menthol can be utilized. Oral antihistamines can also be used for pruritus (Browning 2009) Additionally, several studies suggest a clear, clinical response to treatment with acyclovir compared to placebo, including a recent, large, randomized control trial from India which found benefit independent of the time of initiation of therapy (Ganguly 2014). Antiviral therapy may be especially beneficial in patients with ethnic skin, as decreasing the duration and/or severity of inflammation should theoretically minimize post-inflammatory hyperpigmentation. Although the evidence is less compelling, phototherapy (specifically broadband UVB and low-dose UVA1) has been demonstrated to be effective in clearing the eruption (Lim et al. 2009). There are mixed data regarding the utility of erythromycin in hastening the resolution of the cutaneous eruption of PR. Therefore, especially given the frequency of gastrointestinal side effects with macrolides, expert opinion generally suggests against using erythromycin (Goldstein et al. 2015).

Key Factors

- The classic presentation of pityriasis is a "herald patch" followed by a diffuse eruption of smaller but morphologically similar papules and small plaques that involve the trunk and proximal extremities, often along skin cleavage lines.
- In skin of color, the subsequent lesions tend to be more papular, monomorphic, and folliculocentric, and larger lesions sometimes have central hyperpigmentation with a papular border.
- Clinical mimics of PR include secondary syphilis and the acute exanthem of HIV, so serologic testing should be considered if the patient has risk factors or if the morphology or distribution of the rash are not entirely typical.
- As with other inflammatory dermatoses, pityriasis rosea can cause significant PIH, especially in patients with ethnic skin.
- Treatment should focus on controlling pruritus and minimizing the risk of PIH. Options include topical corticosteroids, oral antihistamines, acyclovir, and less frequently, phototherapy.

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Chapter 10
Lichen Planus

Amita Goyal and Roopal V. Kundu

History

A 51-year old South Asian female presents with a 6-month history of an itchy scaling rash that started on her anterior shins. She also has asymptomatic lesions inside her mouth that she noticed while brushing. She does not recall a history of any similar eruption. She denies any sick contacts or past medical history. She has used petroleum jelly over the lesions without improvement. Review of systems was positive only for fatigue in the last 3 months.

Physical Examination

On examination, scattered hypertrophic, flat topped, violaceous plaques were noted on the bilateral anterior lower legs (Figs. 10.1 and 10.2). Lace-like white reticulated striations

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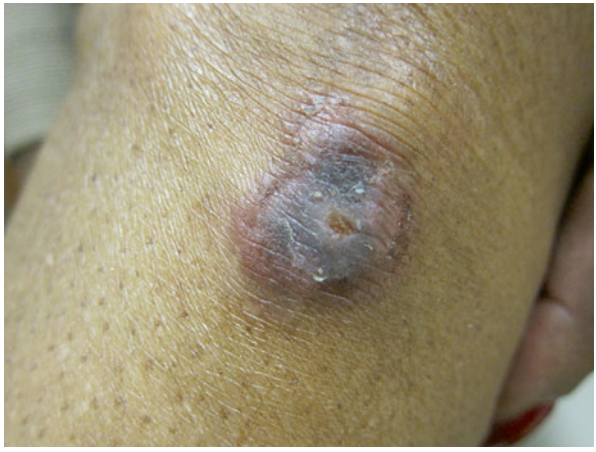

FIGURE 10.1 Hypertrophic lichen planus. Scattered hypertrophic, flat topped, violaceous plaques were noted on the bilateral anterior lower legs

were noted on bilateral buccal mucosa. Nail fissuring was noted on 2nd digit of the right hand.

Clinical Differential Diagnosis

The cutaneous disease in combination with oral mucosal lesions was most consistent with lichen planus. However, the differential for the cutaneous disease includes pityriasis rosea, guttate psoriasis, lichen simplex chronicus, and lichenoid drug eruption. The differential for oral lesions includes leukoplakia, candidiasis, oropharyngeal cancer, and syphilis.

Histopathology

A biopsy was undertaken in this case to ensure correct clinical diagnosis. Histologic features included a saw-tooth pattern of epidermal hyperplasia, orthokeratosis, beaded

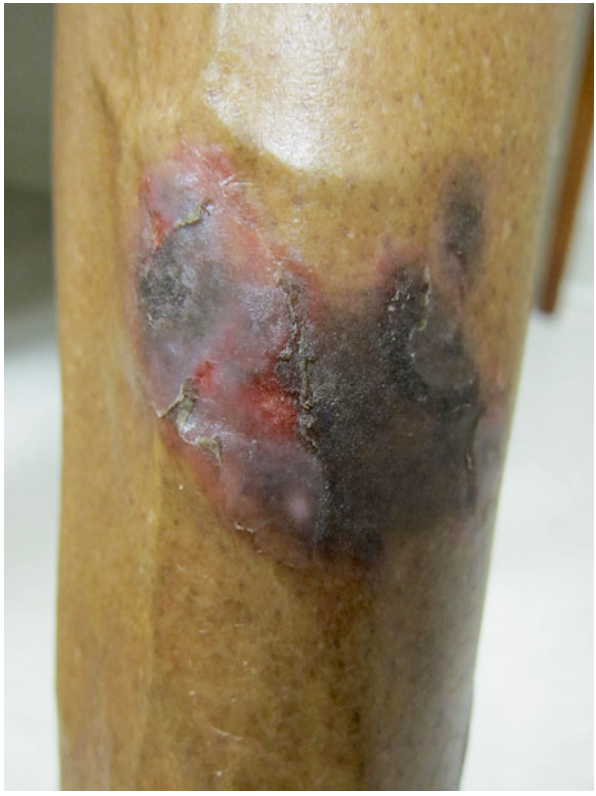

FIGURE 10.2 Hypertrophic lichen planus – close up. Scattered hypertrophic, flat topped, violaceous plaques were noted on the bilateral anterior lower legs

hypergranulosis and destruction of the basal layer, which is typical of lichen planus. Other common findings include a dense, bandlike infiltrate composed of lymphocytes and melanophages in the superficial dermis, civatte bodies (necrotic keratinocytes) in the superficial dermis, and epidermal hyperplasia in hypertrophic cases (James et al. 2011).

Dignosis

Lichen Planus (LP)

Case Treatment

The nature of the diagnosis of LP was discussed with the patient. Treatment options were discussed, including topical or systemic corticosteroids for cutaneous lesions and topical corticosteroids, topical immunomodulators, or intralesional steroids for oral lesions. Given the presence of both cutaneous and oral disease, topical triamcinolone 0.1 % gel for the buccal mucosa and clobetasol 0.05 % ointment to the shins was prescribed twice daily for a 3-week course. She was instructed to contact the clinic should lesions worsen or fail to respond. The possibility of post-inflammatory hyperpigmentation despite treatment was reviewed. The importance of close follow-up was also emphasized, especially given the presence of oral lesions and the known correlation with squamous cell carcinoma. Because of the patient's history of recent fatigue and finding of oral lesions, screening hepatitis panel was sent, which was negative for hepatitis C.

Discussion

Lichen planus is a common disorder that has an estimated prevalence of about 1 % of the general population (Boyd and Neldner 1991). Though there seems to be no racial predilection for the disease itself, the age at which the disorder appears varies. In patients of European descent, the peak incidence is between 40 and 70 years. It is generally rare for individuals under the age of 20 to have the disorder. However, in the Indian subcontinent, Arab countries, and Mexico, childhood lichen planus can account for more than 10 % of all cases (James et al. 2011).

LP is an idiopathic disorder. As caspase-3 is often found to be elevated in cutaneous and oral lesions, it is suspected that apoptosis of basal keratinocytes as mediated by cytotoxic T-cells is involved (Goldsmith and Fitzpatrick 2012). T-cells may be activated through an autoimmune mechanism or with an outside source including viruses, medications, and stress (Taylor SC. Treatments for skin of color 2011). LP has been shown to be correlated with a variety of diseases: hepatitis C, hepatitis B, and primary biliary cirrhosis. Studies have showed a higher prevalence of serum autoantibodies in Chinese patients with oral LP, higher rate of HBsAG in Nigerian patients with cutaneous LP, and a strong correlation between presence of hepatitis C virus and LP in Japanese and Mediterranean populations (Taylor SC. Treatments for skin of color 2011). However, the extent to the correlation and any causal relationship remains controversial. A recent study of Chinese patients with oral LP showed that HCV antibodies were detected to be positive at a lower rate than the control group (Zhou et al. 2010). In patients that have widespread and severe disease, and particularly oral disease, screening for hepatitis should be considered. Another possible etiology includes medication induced disease, which causes clinically and histologically similar lesions to LP. The mechanism of injury is still unknown, but the most common medications implicated are ACE-inhibitors, beta blockers, antimalarials, TNF-α inhibitors, and thiazide diuretics (Shiohara and Kano 2012). Contact allergens have also been associated with the eruption of oral LP. Specifically, prolonged exposure to dental amalgam fillings have been implicated. Most patients have regression of disease with removal of the metal. Interestingly, many of these patients have negative patch tests (Shiohara and Kano 2012).

Classically, LP in skin of color is characterized as a cutaneous disease with pruritic, flat topped, polygonal, dark violet or slate blue papules and plaques with fine scale on the wrists, flexural surfaces of arms, genitalia, and mucous membranes. The site of involvement may differ by ethnicity,

as shown in a study of African children where lower limbs were most affected (Nnoruka 2007). Because other inflammatory papular eruptions may also have a violet hue in patients with Fitzpatrick skin types III-V, the waxy characteristic of the papules in LP can often help to differentiate (Abdel-Naser et al. 2005). In addition, the surface of the papules/plaques is often covered in gray puncta or streaks, called Wickham striae.

The most common variant after classic LP is hypertrophic as seen in a study of African children (Nnoruka 2007). Other variants of cutaneous disease include linear, bullous, annular, atrophic, actinic, lichen planopilaris, and lichen planus pigmentosus. Actinic LP is more common in skin of color, almost exclusively affecting a younger population in the Middle East, Egypt, Tunisia, and India. This form is unique with non-pruritic photodistributed eruption of hyperpigmented patches (Sharma et al. 2013). Lichen planopilaris is a variant of LP that typically involves the scalp. Lesions often appear as perifollicular keratotic plugs with surrounding erythema, often leading to cicatricial alopecia. It may occur independently of LP or with classic oral and/or cutaneous lesions (Shiohara and Kano 2012). A rare variant of LP is the Graham-Little-Piccardi-Lassueur Syndrome, which is characterized by the triad of non-scarring hair loss in the inguinal and axillary regions, typical cutaneous or oral LP, and scarring alopecia of the scalp (Antonio et al. 2014). Nail changes occur in 5–10 % of patients with LP and appear as longitudinal ridging and splitting, often with onycholysis. More common in other ethnic groups, the Asian population rarely has nail changes (Taylor SC. Treatments for skin of color 2011).

Oral LP, compared to cutaneous LP, is characterized more by symmetric white striations on the buccal mucosa, tongue, and gingiva. Papules, plaques, erythematous patches, and erosions may also be present. Oral LP comes in a variety of forms, including reticular, atrophic, and erosive. As opposed to the pruritic nature of cutaneous disease, oral LP is often painful, especially in the erosive form (Le Cleach and Chosidow 2012). Mucosal LP has been found to be present in up to 75 % of patients with cutaneous disease. Oral LP is

considered a premalignant condition with about 1 % of patients developing squamous cell carcinoma, a risk that is altered by other risk factors such as alcohol and smoking (Le Cleach and Chosidow 2012). The erythematous and ulcerative subtypes of oral LP are the most at risk with the lateral border of the tongue being the most common site of squamous cell carcinoma development (James et al. 2011; Carbone et al. 2009). Along with oral LP, hypertrophic lichen planus also has an increased risk of malignant transformation to squamous cell carcinoma (Tong et al. 2015).

Clinical findings in anogenital LP are largely similar to cutaneous and oral LP. The erosive form is the most severe, leading to vulvar scarring, vaginal stenosis, and phimosis. Studies have shown a higher prevalence of a history of genital disease as compared to cutaneous disease in patients presenting with oral LP (Le Cleach and Chosidow 2012). Because the diagnosis of LP is difficult in the ethnic population, this crucial piece of history can aid in the differential.

Lesions in cutaneous LP often spontaneously regress within 18 months. It must be noted, though, that ethnic patients often present with concern for the post-inflammatory hyperpigmentation (PIH) that is typically more dramatic in skin of color. Oral LP tends to have a typical lifespan of about 5 years (Taylor SC. Treatments for skin of color 2011).

Treatment

Treatment of LP is difficult and typically must be individualized, especially in patients with skin of color who run the risk of significant post-inflammatory hyperpigmentation.

For cutaneous disease, localized lesions are treated first-line with topical corticosteroids. Trials have shown potent topical corticosteroids to be effective in treating early disease over the course of 2–3 weeks, especially when occlusion is used. If patients present with a lesion that is refractory to topical treatment or the lesion is more hyperkeratotic, intralesional corticosteroids may be used.

Widespread cutaneous disease is often treated with systemic corticosteroids. The recommended dose is 30–60 mg daily prednisone for 4–6 weeks, though the optimal dose and duration for treatment is unclear (Taylor SC. Treatments for skin of color 2011). Some patients have noticed a relapse in disease during the taper of the corticosteroid. For this reason, dermatologists in India often elect for monthly pulse dosing (James et al. 2011).

In patients that do not have remission with systemic corticosteroids, second-line therapy includes retinoids, sulfasalazine, and phototherapy. Both acitretin and isotretinoin have been shown to be effective. Therapeutic dosing is 30 mg/day of acitretin for 8 weeks or 10 mg of isotretinoin BID for 8 weeks (Shiohara and Kano 2012; Lebwohl MG. 2014). A benefit of these medications is that the patient is able to avoid long-term complications of systemic corticosteroids. In addition, systemic retinoids have been found to be more effective in patients with the hypertrophic subset of LP (James et al. 2011). Sulfasalazine at 1.5–3.0 g/day for 4 weeks has also been beneficial (Shiohara and Kano 2012). A study of patients in Spain showed a good response in corticosteroid and retinoid-resistant disease. The study showed that the effect was only to cutaneous lesions, however, with no change in mucosal disease (Bauza et al. 2005). For more resistant or diffuse involvement, phototherapy can also be considered. Numerous studies have shown its success, including one in an Israeli population (Pavlotsky et al. 2008). Treatment with phototherapy also seems to cause longer-term remission. Psoralen + ultraviolet A has also been seen to be comparable to UVB. Finally, metronidazole 500 mg twice daily for 20–60 days has been used (Shiohara and Kano 2012) based on its potential antimicrobial and immunomodulatory activity (Taylor SC. Treatments for skin of color 2011).

Third line therapy for refractory cutaneous disease includes thalidomide, low molecular weight heparin,

griseofulvin, cyclosporine, dapsone, hydroxychloroquine, and mycophenolate mofetil. In those with difficult to control disease, it is important to consider an underlying medical condition that may have exacerbating effects, such as hepatitis C virus.

Treatment of oral LP is generally more difficult as there is no definite therapeutic ladder, but more of a pool of possible interventions. Typically, initial treatment paradigms begin with topical corticosteroids (in Orabase or gel form), topical immunomodulators, topical retinoids, or intralesional steroids. Patients may also use combination elixirs containing diphenhydramine elixir, aluminum, magnesium hydroxide, and viscous lidocaine in equal proportions. Next line therapy include topical cyclosporine, griseofulvin, systemic corticosteroids, antimalarials, systemic retinoids, methotrexate, or PUVA. Finally, there has been more recent research into the use of laser therapy, which preliminary shows promising results when compared to high potency topical corticosteroids (Taylor SC. Treatments for skin of color 2011).

Key Points

- Cutaneous lichen planus in skin of color may be difficult to diagnose clinically.
- Lichen planus often heals with long-lasting post-inflammatory hyperpigmentation.
- Severe and refractory lichen planus may be a sign of an underlying medical etiology, such as hepatitis C.
- Treatment generally follows a therapeutic ladder and is individualized to the patient.

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Part III
Infectious Disorders

Chapter 11
Tinea Versicolor

Jennifer C. Li and Roopal V. Kundu

History

A 15-year old African American male presents with 3 months of hypopigmented spots localized to his chest and back. The discoloration became more noticeable at the end of summer. He is asymptomatic.

Physical Examination

On examination, multiple well-marginated hypopigmented round to oval macules, with fine dust-like scaling, on the chest and back were noted. Few isolated macules are noted on the proximal arms, and abdomen. The macules on the back have coalesced to larger patches (Figs. 11.1 and 11.2).

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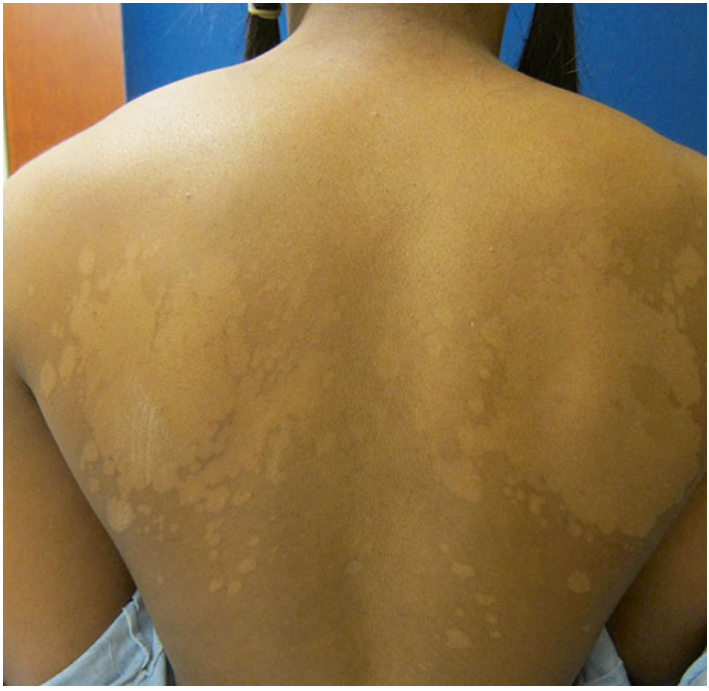

FIGURE 11.1 Tinea versicolor. Multiple well-marginated hypopigmented round to oval macules, with fine dust-like scaling, on the back

Clinical Differential Diagnosis

Diagnosis is typically based on clinical exam. The ultraviolet black light (Wood's light) may be supportive, revealing coppery-orange fluorescence. The diagnosis can be confirmed by in-office potassium hydroxide (KOH) preparation, which demonstrates the classic "spaghetti and meatballs" of short, cigar butt hyphae and spores.

Diseases of pigmentation common among people with skin of color can also include vitiligo, pityriasis alba, pityriasis rosea, seborrheic dermatitis, erythasma, and hypopigmented mycosis fungoides, which may be considered in the differential diagnoses.

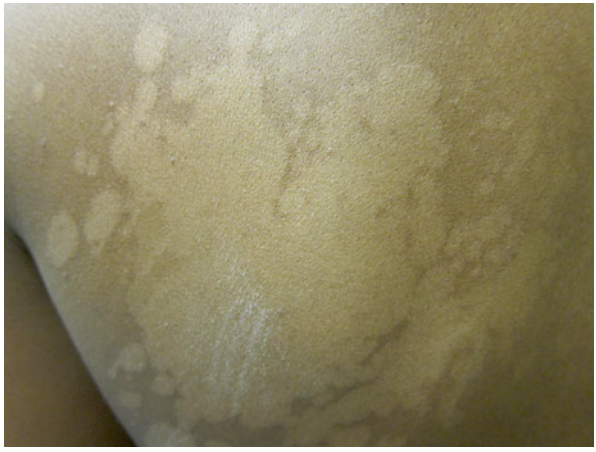

FIGURE 11.2 Tinea versicolor. Close up. Hypopigmented macules on the back have coalesced to larger patches with inducible scale (with #15 blade)

Histopathology

Although biopsy is not usually performed, histologic findings of the hypopigmented macules would show slight hyperkeratosis and acanthosis, minimal inflammatory infiltrate, and most notably positive Periodic acid-Schiff (PAS) stain revealing hyphae or yeast forms in the straum corneum.

Diagnosis

Tinea versicolor

Case Treatment

The diagnosis of tinea versicolor was discussed with the patient. Even though the patient was asymptomatic, the presence of the rash caused emotional distress due to the clinical appearance and the patient opted for treatment.

Since secondary postinflmmatory pigmentary changes is common in people of color, a more aggressive treatment regimen was chosen. Econazole 1 % cream once daily × 4 weeks was prescribed. It was explained to the patient that reoccurrence of tinea versicolor was very common. Prophylactic therapy including weekly application of ketoconazole 2 % shampoo as a body wash for 3 months following treatment and during warmer months was recommended to help prevent recurrence.

Discussion

Diagnosing tinea versicolor in patients with skin of color may pose challenges, including unique cultural implications and differing clinical presentations. Tinea versicolor has been shown to be especially common in dark-skinned individuals. If untreated, tinea versicolor could last for years.

In the United States from 1990 to 1999, tinea versicolor was diagnosed in 110 office visits per 100,000 population per year on average. However, people with skin of color accounted for higher frequencies than average, with 140 visits for black patients, 150 visits for Native Americans/Eskimos, and 40 visits for Asians/Pacific Islanders, respectively; while Caucasians accounted for 110 visits per 100,000 per year (Mellen et al. 2004). Similarly, a study conducted in southeastern London demonstrated that tinea veriscolor was statistically more common in those of darker skin, with 48 % of tinea versicolor diagnoses in the study in blacks versus 35 % in whites and 17 % in other races, including those of Asian and Arabic origin (Child et al. 1999). The reasons for these frequencies may vary; dark-skinned individuals may be more prone to infection by tinea versicolor or have greater health care utilization due to more concern about the dyspigmentation.

No differences in the causative species of tinea versicolor between dark-skinned or light-skinned patients have been identified. Tinea versicolor is caused by the dimorphic,

lipophilic organism of the *Malassezia spp.* (formerly known as *Pityrosporum*). The two most common species in tinea versicolor are *M globosa* and *M furfur*. The main predisposing factors of tinea versicolor involve having fatty acids on the skin, such as in adolescence where sex hormones increase leading to skin lipid production. Additional contributing factors include corticosteroid administration, application of oily preparations, exposure to sunlight, warm and humid climates, genetic predisposition, malnutrition, immunosuppression, and hyperhidrosis. Since humidity (which contributes to hyperhidrosis) and sunlight are key factors, populations living in tropical regions are most affected by tinea versicolor.

Dark-skinned individuals with tinea versicolor or those that have tanned are likely to present with secondary dyspigmentation. There is controversy on whether hypopigmentation versus hyperpigmentation are truly more common among people with skin of color. Several studies have shown that hypopigmentation is more common among patients with tinea versicolor in India, with 81.8 % hypopigmentation among patients in Kolkata, India (Ghosh et al. 2008). A study in Brazil demonstrated that most of the subjects of the mulatto race (brown skin) showed a higher frequency of hypopigmentation (Morais et al., 2010). However, according to a study on patients of Fitzpatrick skin types IV and V in Saudi Arabia, only 55 % of patients presented with only hypopigmentation as well as 33 % with only hyperpigmentation, which was concluded as not being statistically significant (Aljabre et al. 2001). The differences in climate between Saudi Arabia and India may have led to these opposing results, as hyperhidrosis is more associated with hyperpigmentation.

Tinea versicolor may have atypical presentations in skin of color. In general, tinea versicolor primarily affects the trunk and proximal arms even though it can occur in other atypical locations. Inverse tinea versicolor, commonly seen in skin of color, is a follicular variant with macules/patches localized to the face, flexural regions, and extremities, and can have

varying degrees of pruritus. In the study conducted in the Central African Republic, the majority of patients had tinea versicolor affecting the face (49.3 %) and secondarily on the upper trunk (48.6 %) (Bélec et al. 1991). Even after the active infection is treated, the hypo- or hyperpigmentation in inverse tinea versicolor can last for months. Another variant, tinea versicolor alba, has been especially noted in black patients (Thoma et al. 2005). In most patients, the macules/patches of tinea versicolor become depigmented or hypopigmented after a period of hyperpigmentation, either spontaneously or with UV light exposure. However, tinea versicolor alba is characterized by depigmented or hypopigmented macules/patches without a hyperperigmentation stage in the seborrheic areas. Furthermore, atrophying tinea versicolor, an atypical form of tinea versicolor associated with cutaneous atropy, has been recently reported in Korea, and may be a concern for patients of color (Yang et al. 2010).

Tinea versicolor has cultural implications in the black American community. "Acid skin" has been documented as an idiom from black American folklore used to describe hypopigmented patches on the upper trunk characteristic of tinea versicolor infections. This term is not restricted to a particular geographic region, and arises from the mistaken belief that overeating acidic foods, including citrus fruits and carbonated beverages, leads to this condition (VanDersarl and Arnold 1983). Patients should be counseled that an acidic diet does not predispose one to tinea versicolor, and that antifungal treatments are effective in eradicating this disease.

Treatment

Since tinea versicolor is caused by a fungus normally present on the skin surface, it is not contagious. There is no permanent scarring or pigmentary changes. However, dyspigmentation can take 3–4 months or more to improve. Treatment of tinea versicolor for people with skin of color involves selecting from a variety of antifungal topical and systemic agents, with careful consideration that recurrence is common despite clearance of

the disease. In addition to following standard treatment guidelines, it is further recommended that skin of color patients are given more aggressive treatment due to the secondary postinflammatory pigmentary changes. Postinflammatory dyspigmentation can last several months even with successful treatment, so detection of whether the condition is new or continuing should be conducted by KOH preparation.

In practice, topical treatment is commonly the first-line intervention. Common treatments include zinc pyrithione, selenium sulfide, sodium sulfacetamide, ciclopirox, and azole antifungals, such as econazole. Various regimens can be used. For zinc pyrthione, selenium sulfide, and sodium sulfacetamide, topical short contact application for 10 min to affected areas daily for 2 weeks prior to being washed off can be used. Topical azole antifungals can be applied daily for 2 weeks. The topical treatments are effective and generally safe, with a low chance of minor skin irritation and contact dermatitis.

Overall, topical therapy is preferred and recommended. However, systemic treatment may be used for patients that do not respond to topical treatments, have extensive involvement, have multiple relapses, or for ease of use. Systemic treatments for tinea versicolor are oral azole antifungals. Various dosing regimens have been used. Recommendations for these treatments are the following: itraconazole, 200 mg/day for 5 days (typically prescribed) or 7 days (for more severe cases) or fluconazole, 150 or 300 mg/week doses for 2–4 weeks (Gupta et al. 2014). Systemic ketoconazole is generally avoided due to the black box warning of hepatotoxicity. The treatment regimens are based on efficacy and safety concerns. Since the treatment durations of the recommended regimens are short, adverse events of these treatment regimens are infrequent (Gupta et al. 2014).

Since recurrence is common, prophylactic therapy may help reduce the high rate of recurrence. Recurrence can be as common as 60 % in the first year, increasing to 80 % in the second year. Weekly applications of any of the topical treatment options for 2–3 months following treatment and then during susceptible times such as warm, humid months may help prevent recurrence.

Key Points

- Tinea versicolor is a common infection among people with skin of color.
- Dark-skinned individuals may be more likely to present with hypopigmentation, though presenting with hyperpigmentation or a combination of both is not uncommon.
- Alternate variants of tinea versicolor, such as inverse tinea versicolor and tinea versicolor alba, have been seen in patients of color.
- "Acid skin" is a black American cultural term used to typically describe macules characteristic of tinea versicolor, and arise from the mistaken belief that these macules arise from an overly acidic diet.
- Patients with skin of color should be considered to be treated more aggressively than standard treatment recommendations, since they are more likely to experience postinflammatory pigmentary changes.

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Chapter 12
Tinea Capitis

Giselle Rodriguez and Roopal V. Kundu

History

A 10-year old African American boy presents with an oval patch of hair loss on his occipital scalp. He has had the patch for about a month. He also has dandruff. The patient's mother is concerned that this hairloss is permanent as she recalls her mother had alopecia. Review of systems is otherwise negative.

Physical Examination

On physical examination, there is a 2 × 3 cm oval patch of alopecia with short hair ends and black dots (Fig. 12.1). Scaling is seen throughout the scalp. Posterior cervical lymphadenopathy was noted. Dermoscopy of the patch

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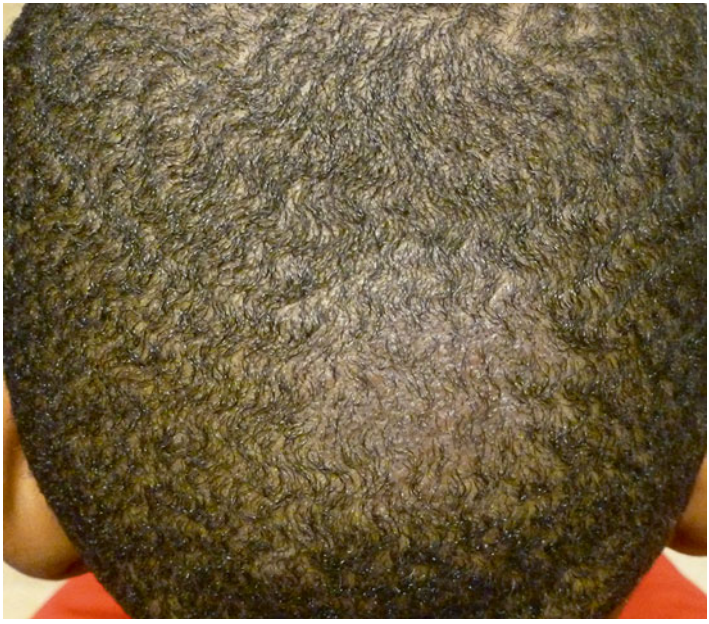

FIGURE 12.1 Tinea capitis. A 2 × 3 cm oval patch of alopecia with short hair ends and *black dots*

shows: greasy scales, perifollicular white macules, and bent hairs. Wood's lamp does not show any areas of fluorescence.

Clinical Differential Diagnosis

The physical examination and clinical history is most consistent with tinea capitis. However, other diagnostic possibilities include alopecia areata, seborrheic dermatitis, and atopic dermatitis. A complete differential diagnosis of tinea capitis also includes psoriasis, trichotillomania, systemic lupus erythematosus, pityriasis amiantacea, and folliculitis. It is imperative to distinguish tinea capitis from other possible superficial fungal infections caused by *Candida* spp and *Malassezia* spp.

Histopathology

Fungal culture to determine the causative organism is preferred but biopsy may be performed in unclear cases. Dermatophytes are hyaline fungi requiring GMS or PAS stain for adequate visualization in H&E preparations. Dermatophytes as branched, septate hyphae and/or spores are seen. Kerions might demonstrate a brisk neutrophilic infiltrate or Majocci's granuloma formation (follicular involvement of the fungal organism) (Guarner & Brandt 2011).

Diagnosis

Tinea Capitis

Case Treatment

Lesion scrapings were obtained, prepped with potassium hydroxide (KOH), and viewed under the light microscope, revealing branching hyphae. A fungal culture of involved hair was performed in order to identify the causative organism.

The diagnosis of tinea capitis, as well as the nature of this fungal infection, was discussed with the patient and family. Treatment options were reviewed including the need for oral antifungal medication as topical medications are often ineffective. The patient was immediately started on micronized griseofulvin 25 mg/kg daily for 8 weeks while cultures were pending. Topical antifungal shampoo with selenium sulfide was prescribed for the patient and close contacts to use. Precautions to rid fomites (hair brushes, pillowcases, and sheets) of fungal spores were discussed to prevent spread and reinfection. Possible sequelae of tinea capitis, including persistent alopecia and post-inflammatory dyspigmentation were discussed although they are rare. The patient was given a follow up appointment in 2 months to

assess for resolution of symptoms. Parents were told to come into clinic if symptoms worsen or if features of superimposed infection occur.

Discussion

Tinea capitis, commonly known as scalp ringworm, is a common cutaneous dermatophyte fungal infection of the scalp and hair follicles most commonly affecting children, especially of African American and Hispanic descent. Tinea capitis has a prevalence of 13 % in US school children (Silverberg et al. 2002). Rates continue to increase in African American children. Risk for tinea capitis is increased in crowded living conditions. Adults can be carriers of the pathogens in the scalp with African American women in particular having the most reported adult cases of tinea capitis (Silverberg et al. 2002).

Trichophyton tonsurans is the most common pathogen causing tinea capitis in the United States. Other species include *Microsporu*m spp, including *Microsporum canis* which is the most common worldwide pathogen. Human to human spread occurs most frequently but animals and plants can be reservoirs for dermatophytes. The method of spread depends on the type of fungal pathogen.

Signs of tinea capitis include: hair loss with broken hairs or black dots on the scalp, scaling, erythema, edematous boggy plaques often studded with pustules called kerions, tenderness, and scarring. Cervical lymphadenopathy may occur as well as low-grade fevers. There can also be associated pruritus of the affected scalp. Significant seborrheic dermatitis is less common in children; the presence of scaling in a child should trigger examination for tinea capitis. In Caucasian children, scalp hyperkeratosis of childhood is most often associated with atopic and seborrheic dermatitis, however research has shown that in African American and Hispanic children hyperkeratosis of childhood is most often associated with tinea capitis (Coley et al. 2011).

Diagnosis of tinea capitis is based on clinical exam and supported by confirmatory diagnostic tests. Potassium hydroxide (KOH) microscopy of infected hairs allows for diagnosis of tinea capitis in the office setting. A culture may be obtained by gently rubbing the involved area with a moist gauze pad or scraping gently with the end of a glass slide or blunt scalpel to obtain affected hair and scalp scale. A few plucked hairs can also be obtained from the affected area. A scalp culture should be considered in adults, especially African American women, when working up alopecia or papulosquamous disease (Silverberg et al. 2002). Since there is potential for false negative KOH examinations and fungal cultures may take several weeks to show growth, treatment is initiated if clinical suspicion is high. Wood's lamp examination will display a blue-green fluorescence with *Microsporum* spp; however *Trichophyton tonsurans* will not fluoresce. Dermoscopy evaluation of tinea capitis lesions shows greasy scales, perifollicular white macules, and bent hairs (Shim et al. 2014).

Treatment

Treatment of tinea capitis differs from other cutaneous fungal infections in that an oral antifungal therapy must be used. The infection often invades hairshafts and goes beyond superficial skin involvement, thus topical treatment is ineffective. Systemic medication is given for 8 weeks, but this may vary according to organism, treatment type, and severity of infection. Mainstay of treatment is micronized griseofulvin, given at 20–25 mg/kg daily for a minimum of 8 weeks. Oral terbinafine and itraconazole may be appropriate alternatives due to shorter length of treatment required and in cases of recurrent infection after griseofulvin. Children with refractory cases of tinea capitis may require crushed griseofulvin, terbinafine sprinkles, itraconazole, or fluconazole treatment. These alternatives have been shown to be effective in children with skin of color with tinea capitis (Bhanusali et al. 2012). In adults receiving treatment with

itraconazole or terbinafine, monitoring of liver function tests is important. Topical antifungal shampoos with selenium sulfide, zinc pyrithione, or ketoconazole, are used as conjunctive therapy in order to decrease shedding of viable fungal spores. Hair brushes, combs, hats, and pillowcases should be disinfected or thrown away to prevent spread and reinfection. Affected hairs, once shed, can carry viable organisms for over a year. There is also a role for screening household contacts for disease and treating any potential asymptomatic carriers.

Dermatophytid reaction, also known as an "id" reaction, is a common inflammatory reaction secondary to tinea infection and occurs at sites other than the primary infection site. The most common manifestation is a pruritic eczematous eruption that can be subtle, which can progress to vesicles or pustules (Cheng et al. 2011). Palms, soles and fingers can be affected. Reactions may occur either before or after starting systemic antifungal treatment. Culture or KOH prep of lesions will not show fungal forms. Antifungal therapy will typically lead to resolution of symptoms, however topical corticosteroid therapy can be considered. Importantly, this eruption does not indicate an allergic medication reaction and appropriate antifungal therapy should be continued.

Inflammatory forms of tinea capitis (i.e. kerion) can lead to scarring and permanent alopecia. Oral steroid preparations may be prescribed to prevent subsequent alopecia (Moriarty et al. 2012). However, steroids are not considered routine care and do not necessarily decrease healing time. Other complications of tinea capitis infection include superimposed bacterial infection (impetigo) and post-inflammatory dyspigmentation. Patients with skin of color are more prone to post-inflammatory hyperpigmentation (PIH) as the skin heals after an inflammatory trauma. There is an increase in the production of melanin or an increase in the release of melanin, which manifests as macules or patches of hyperpigmentation in the area of the lesion. Overall, treatment is typically effective and overall prognosis is very good after tinea capitis infection.

Key Points

- Tinea capitis is most prevalent amongst African American and Hispanic children. In adults, African American women have the highest incidence.
- Diagnosis is clinical but fungal culture may confirm species.
- Oral antifungal therapy is mainstay of treatment.
- Id reactions are not allergic and therapy should be continued.
- Tinea capitis can lead to scarring and alopecia, thus early effective treatment is imperative.
- Refractory cases of tinea capitis may require changes in oral antifungal therapy.
- Topical antifungals and disinfection of fomites can prevent reinfection and spread of infection.

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Part IV
Disorders of Hyperpigmentation

Chapter 13
Postinflammatory Hyperpigmentation

Marie Stoddard, Adekemi Akingboye, and Marcelyn Coley

History

A 30-year old African American woman presented to the office for evaluation of a 15-year history of persistent dark marks on chest with no other areas of involvement. Dark marks appeared after resolution of acne lesions on the chest and are not associated with any symptoms. Acne is still pres-

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ent but has abated in severity over the past 5 years, initially involving the face and back but persisting on the chest. Treatment with over the counter hydroquinone 2 % cream twice a day for 4 months has been ineffective.

Physical Examination

Skin examination revealed several scattered ill-defined hyperpigmented macules and patches localized to the chest along with 3 scattered erythematous papules (Fig. 13.1).

Clinical Differential Diagnosis

In this particular case of scattered macules and patches involving the chest, one may consider diagnoses such as pityriasis versicolor, postinflammatory hyperpigmentation (PIH) or erythema dyschromicum perstans. The former tends to present with surface scale, while the latter may have a component of erythema and a more widespread distribution. The differential diagnosis of hyperpigmentation can be vast and depends on the clinical presentation. Preceding inflammation may be subclinical in some instances, which may further complicate diagnosis. History, morphology and distribution can help narrow down potential inciting factors.

Histopathology

Hyperpigmentation on histology can be epidermal, dermal or mixed, where an excess of melanin is present in both the epidermis and dermis (Ortonne and Passeron 2005). Most cases of post-inflammatory hyperpigmentation will show increased pigmentation in basal epidermal keratinocytes; however,

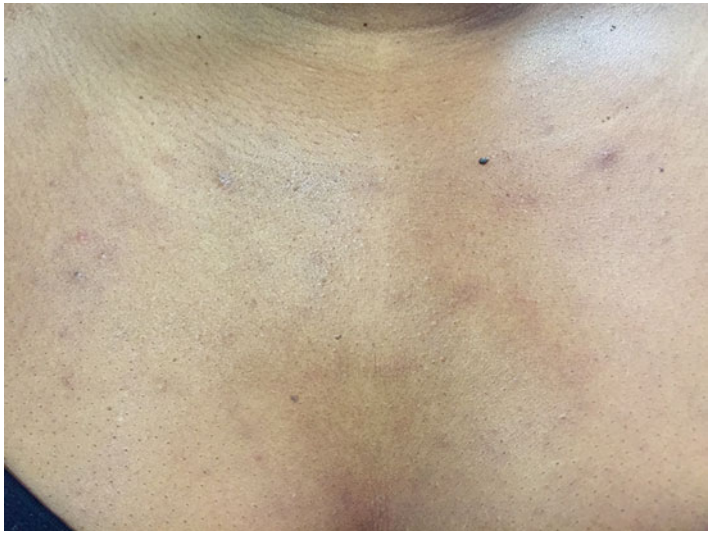

FIGURE 13.1 Postinflammatory hyperpigmentation. 30 year-old African-American woman with ill-defined hyperpigmented macules and patches on the chest

there may also be a dermal component, showing melanophages. Clinically, brown and blue hyperpigmentation are caused by excessive amounts of melanin within the epidermis or dermis, respectively. Focal deposition of melanin is mainly seen in PIH, which can occur after a burn, laceration, acne or any inflammation inducing insult to the skin (Davis and Callender 2010).

Diagnosis

Postinflammatory hyperpigmentation (PIH) secondary to acne vulgaris.

Case Treatment

As aforementioned, the patient did not note improvement with 4 months of twice a day use of over-the-counter hydroquinone 2 % cream. Hydroquinone 4 % cream twice a day to affected areas, along with daily broad spectrum sunscreen with at least sun protection factor 30 were recommended. In addition to addressing treatment of hyperpigmentation, the underlying causative condition, acne vulgaris, was also treated with benzoyl peroxide 4 % wash followed by topical clindamycin 1 % lotion every morning. Three months of this treatment regimen caused significant clinical improvement of hyperpigmentation.

Discussion

Hyperpigmentation is an umbrella term for a group of conditions that cause dark discoloration of the skin and includes melasma, PIH and medication-induced hyperpigmentation. Hyperpigmentation most commonly affects patients with Fitzpatrick skin phototypes IV-VI who are often patients of African, Asian, Hispanic, Pacific Islander, and/or Native Hawaiian backgrounds. There is no gender or age predilection. Considering dyschromia is one of the top five skin diagnoses in African-American patients, keen knowledge of pathogenesis, diagnosis and available treatment options for hyperpigmentation is of vital importance (Alexis et al. 2007). While considered cosmetic by some standards, dyschromias, such as PIH may have lasting psychosocial effects.

Acne-induced PIH is a particularly common occurrence in patients of color (Fig. 13.2). In a 2002 study that evaluated acne in skin of color, 65.3 % of African-American (N = 239), 52.7 % of Hispanic (N = 55), and 47.4 % of Asian (N = 19) patients acquired acne-induced PIH (Taylor et al. 2002). Atopic dermatitis, a chronic inflammatory dermatosis,

has a prevalence of 10.7 % in the US, with a significantly higher prevalence seen in both the African-American populations. A common sequela is PIH (Vachiramon et al. 2012).

The etiology of PIH has not been fully elucidated, however, it is hypothesized to involve inflammatory mediators, including prostaglandins (PGE2) and leukotrienes (LTC4 and LTD4). These mediators go on to stimulate epidermal melanocytes, causing an increase in melanin synthesis in the basal layer of the epidermis or release of melanin from labile melanocytes into the dermis. Elevation of melanin in the dermis in turn activates dermal macrophages (Desai 2014).

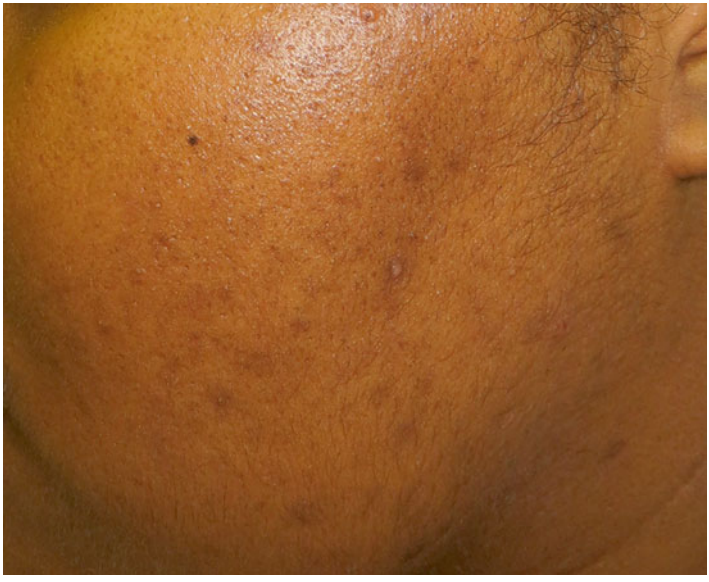

FIGURE 13.2 Acne induced postinflammatory hyperpigmentation. A young African-American woman with hyperpigmented macules on the cheek as a result of mild inflammatory acne vulgaris

Treatment

The initial approach to treating PIH begins with identifying and treating the underlying dermatosis. Once this is achieved, the resulting hyperpigmentation may then be targeted. A crucial element in the treatment of hyperpigmentation is the use of photoprotection. Use of a broad spectrum sunscreen with a sun protection factor of 30 or higher every two hours during sun-exposure will effectively prevent the worsening of hyperpigmentation (Desai 2014). After any possible inciting causes and photoprotection are addressed, it is then reasonable to initiate topical skin lightening agents. Such agents, alone or in combination, include: hydroquinone (HQ), mequinol, azelaic acid, kojic acid, retinoids, and soy.

HQ is a potent inhibitor of melanin production by competitively inhibiting tyrosinase, the key regulatory enzyme in the conversion of amino acid tyrosine to melanin within melanocytes. By decreasing the production of melanin, HQ once or twice daily effectively lightens the skin. It is important to know that at higher concentrations (4 % or higher), HQ can pose a strong irritant effect (e.g. contact dermatitis). Any strength of hydroquinone can cause a paradoxical hypermelanosis termed exogeneous ochronosis with prolonged unmonitored use (Ortonne and Passeron 2005). Although the exact amount of time required to cause ochronosis has not been delineated, clinical monitoring of patients using HQ and limiting refills can be preventative. Mequinol (4-hydroxyanisole) also functions as a competitive inhibitor of tyrosinase and is a less irritating derivative of HQ, which can be used as an alternative in patients who are particularly sensitive to HQ (Davis and Callender 2010).

Azelaic acid is a naturally occurring dicarboxylic acid produced by yeast, *malassezia furfur* that live on the skin. Dicarboxylic acid functions to inhibit tyrosinase, thereby, reducing the production of melanin. In addition, azelaic acid, 15 or 20 % is used to treat both comedonal and inflammatory acne by decreasing the bacterial load and keratin on the skin. In fact, a randomized controlled trial performed on 52

Fitzpatrick skin types IV-VI patients who presented with facial hyperpigmentation showed a visible decrease of pigment intensity after 24 weeks of treatment with 20 % azelaic acid cream (Davis and Callender 2010). Reported adverse effects include desquamation, pruritus, transient erythema, and irritation; all of which are usually mild and resolve within a few weeks (Alexis and Blackcloud 2013).

Kojic acid, a fungal metabolite, is yet another potent inhibitor of tyrosinase that can be compounded with other lightening agents, like HQ, to increase its effectiveness at reducing hyperpigmentation. However, there is a paucity of data showing its efficacy in the treatment of PIH. Common side effects of kojic acid are contact dermatitis and increased skin sensitization, which can also lead to PIH in patients of color (Alexis and Blackcloud 2013).

Functioning as derivatives of vitamin A, topical retinoids (e.g. tretinoin) are effective alone or combined with other topicals, including HQ, to treat hyperpigmentation in patients with darker complexions. Through several biologic effects that include the interference of melanogenesis and enhancement of both keratinocyte proliferation and epidermal cell turnover, tretinoin improves acne-induced PIH in patients of color. Potential adverse effects include erythema, desquamation, dryness, pruritus, and PIH.

Soy, formulated alone or with other agents like retinol, functions as an inhibitor of protease-activated receptor 2 (PAR-2) that are found on keratinocytes and mediate the transfer of melanosomes from melanocytes to the surrounding keratinocytes (Alexis and Blackcloud 2013). As a result, the phagocytosis of melanosomes into keratinocytes is reduced, triggering a reversible skin lightening effect in patients with acne-induced PIH. Although soy products are well tolerated, there is a need for more large-scale clinical trials in patients with skin of color (Ortonne and Passeron 2005; Davis and Callender 2010).

Adjunctive therapy with chemexfoliation (i.e. chemical peels) may be added once first line topical therapies, like HQ, have been initiated. Chemical peels are common, nonsurgical procedures that may aid in the reversal of various dyschro-

mias and are safe in patients of color when used properly. Chemical peels, with a peeling agent such as glycolic acid (20–70 %), are well tolerated and work superficially by penetrating the papillary dermis and inducing epidermolysis, which causes the dispersal of basal layer melanin and increases dermal collagen synthesis. In patients with darker skin, salicylic acid peels have also been shown to improve the dyschromia seen in acne-associated PIH in addition to the concomitant acne (due to its comedolytic effect). Efficacy may be achieved with applications at 2–4 week intervals, with concentrations ranging between 20 and 30 % (Grimes 1999). In addition, pretreatment with 4 % hydroquinone may improve results. Trichloroacetic acid (TCA) is another peeling agent used for treating dyschromias, but research data to support its use in Fitzpatrick skin types IV to VI is lacking. Regardless of the acid used, it is important to treat initially with the lowest concentration to avoid irritation, which can potentially worsen PIH or lead to new areas of dyspigmentation, hypertrophic scarring, or even keloid formation. Common side effects include burning sensation, superficial desquamation, and ery-

Key Points

- PIH is a common condition that most dermatologists will face in practice.
- Identification and treatment of the underlying cause of the PIH is the key to successfully treating this disorder.
- Sun protection is an important adjunct to treatment of dyschromias.
- Skin lightening agents such as hydroquinone are effective and safe when used properly.
- Being mindful of the diagnostic and therapeutic nuances of dyschromias in patients of color will help to guide the approach to treatment.

thema. Likewise, the use of photoprotection is essential to prevent worsening PIH after chemical peeling.

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Chapter 14
Melasma

Jasmine S. McNair and Porcia B. Love

Case Presentation

A 36-year-old Latina female presents for evaluation of brown spots on her left and right upper cheekbones. She began to notice brown spots on her cheeks a year ago but they have recently started to form into patches. The brown patches are not painful and do not itch, but they are not cosmetically appealing and have caused severe distress. She has a history of birth control pill use during her twenties and has two children. She noticed the brown spots worsening during pregnancy. She wears a moisturizer daily, but does not wear sunscreen. She is an avid gardener.

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Physican Examination

There are scattered, hyperpigmented macules coalescing into reticular patches on her forehead, cheeks, nose, and upper lip (Fig. 14.1).

Differential Diagnosis

The patient's clinical presentation was most consistent with melasma. Postinflammatory hyperpigmentation may present with brown macules and associated erythema, scale, and pruritus secondary to photosensitivity reactions or irritant contact dermatitis. Solar lentigines are secondary to ultraviolet radiation and present as round, flat, well-circumscribed macules in sun exposed sites. Drug-induced photosensitivity due to thiazides or tetracyclines may present as irregularly shaped hyperpigmentation. Actinic lichen planus often presents on the temples and may involve the neck and intertriginous sites. Exogenous ochronosis presents with hyperpigmentation followed by progressive darkening with superimposed pigmented papules. Acquired bilateral nevus of Ota-like macules (Hori's nevi) presents with multiple brown to gray to blue macules, primarily on the malar region. It is usually more common in Asian females (Chung 2008).

Wood's Lamp Examination

Wood's lamp examination (365 nm) shows accentuation or darkening of the hyperpigmented patches.

Histopathology

Melasma is typically a clinical diagnosis; however, if a biopsy were performed, pathology would show epidermal melanin in basal and suprabasal keratinocytes. The number of melanocytes

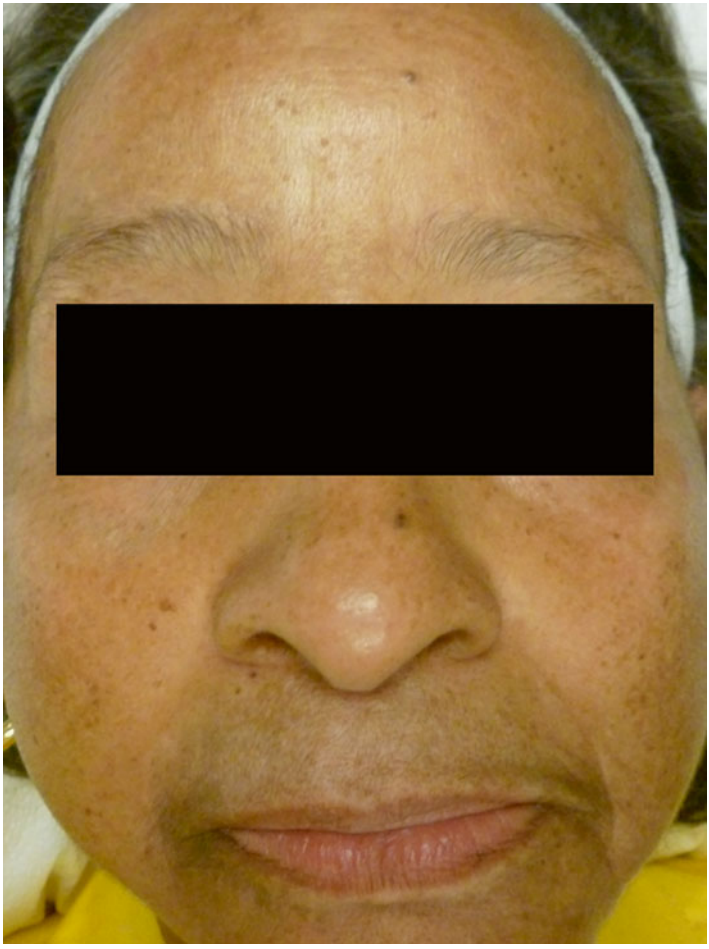

FIGURE 14.1 Centrofacial melasma. Brown, reticular patches are noted on the forehead, cheeks, upper lip, nose, and chin

is not increased; however, the melanocytes that are present are larger, more dendritic, and more active. Inflammation is typically absent (Chung 2008).

Diagnosis

Epidermal melasma

Case Treatment

The likely etiology of melasma, including her oral contraceptive usage, pregnancy, and sun exposure was discussed. A triple combination compound consisting of hydroquinone 6 % + tretinoin 0.025 % + fluocinolone 0.01 % cream was started every other night to the dark areas only. The patient was recommended to increase the cream to nightly after 1 week if she had no burning or irritation. A broad spectrum sunscreen with an SPF of 30 was recommended daily. Daily use of Polypodium leucotomos was recommended as a supplement. A 3 month follow-up was recommended. After mild improvement was seen, she was started on a series of three 35 % glycolic acid peels every 4 weeks in addition to her topical regimen.

Discussion

Melasma is a common acquired disorder of hyperpigmentation that is found mostly in Latina, Southeast Asian, and African American women with Fitzpatrick skin types III-V. Women are more prone to developing the disease than men, especially after the woman has experienced childbirth—leading to the common term, "the mask of pregnancy." Melasma is worsened by excess exposure to the sun; therefore, it is more common in those living in areas with intense ultraviolet radiation exposure (Sheth and Pandya 2011a). A recent multicenter survey from nine countries found that 41 % of women had onset of the disorder after pregnancy but before menopause. Only 8 % noted spontaneous remission, and 25 % had onset after starting their contraceptive (Ortonne et al. 2009).

The exact cause of melasma is unknown. The high incidence among family members suggest a genetic component,

and various surveys from around the world report 10–70 % of family members being involved (Ortonne et al. 2009). Sun exposure is likely an exacerbating factor because of the ultraviolet induced upregulation of melanocyte proliferation, migration, and melanogenesis (Sheth and Pandya 2011a). While melasma is known to occur with hormonal changes, clinical evidence to date does not clearly associate serum hormone levels to melasma. Perez et al examined the link between circulating hormones and found that nulligravid women with melasma had significantly higher serum levels of luteinizing hormone and lower levels of estradiol than their counterpart controls, though further research is needed (Perez et al. 1983). Several studies have noted the onset of melasma with oral contraceptive use and pregnancy. Therefore, it is recommended that patients who develop melasma while taking an oral contraceptive should stop the medication and avoid future use of such drugs when possible (Sheth and Pandya 2011a). However, stopping the culprit oral contraceptive will not necessarily reverse melasma. Some studies have suggested that mild abnormalities in thyroid function are associated with oral contraceptive or pregnancy related melasma; therefore, it is reasonable to consider checking thyroid function tests in melasma patients (Lutfi et al. 1985).

Melasma presents as symmetrically distributed hyperpigmented macules that coalesce into reticular patches. There are three distribution patterns. Centrofacial melasma, the most common pattern, involves the forehead, cheeks, upper lip, nose, and chin (Fig. 14.1). The malar pattern is limited to the cheeks and the nose (Fig. 14.2), and the mandibular pattern is specific to the jawline. Histologically, melasma may be divided into three subtypes. In epidermal melasma, melanin is increased in the epidermis, and patients present with tan to brown hyperpigmentation. In dermal melasma, melanin is found in superficial and mid dermal macrophages, which often congregate around small, dilated vessels, and patients present with a bluish discoloration (Fig. 14.3). Dermal melasma is typically harder to treat. In mixed melasma, mela-

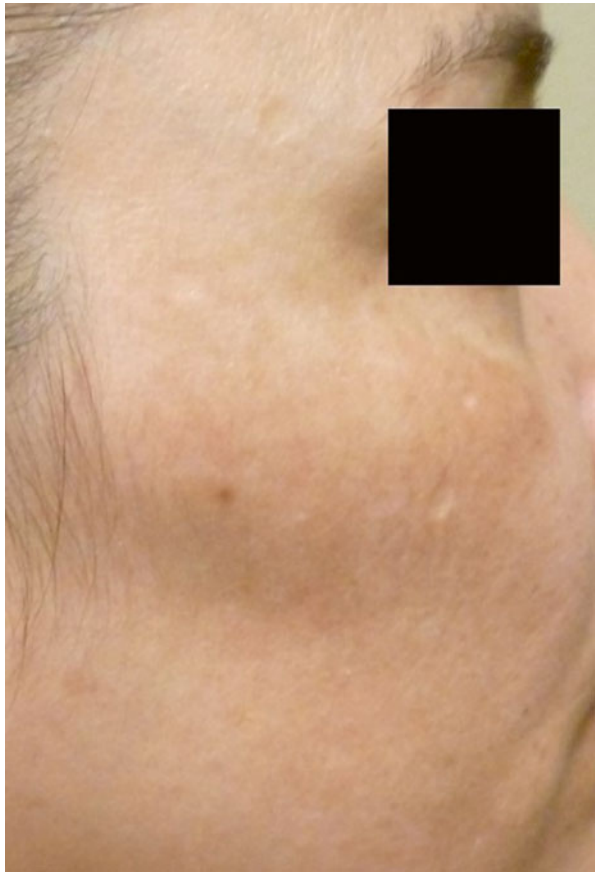

FIGURE 14.2 Malar melasma. Brown, reticular patches are noted on the medial cheeks and nose

nin is found in both the epidermis and the dermis. In most cases, the number of melanocytes is not increased, yet the melanocytes that are present are larger, more dendritic, and more active. Inflammation is sparse or absent (Kang et al. 2002).

The excess melanin can be visually localized to the epidermis or the dermis by use of a Wood's lamp. Epidermal pigment

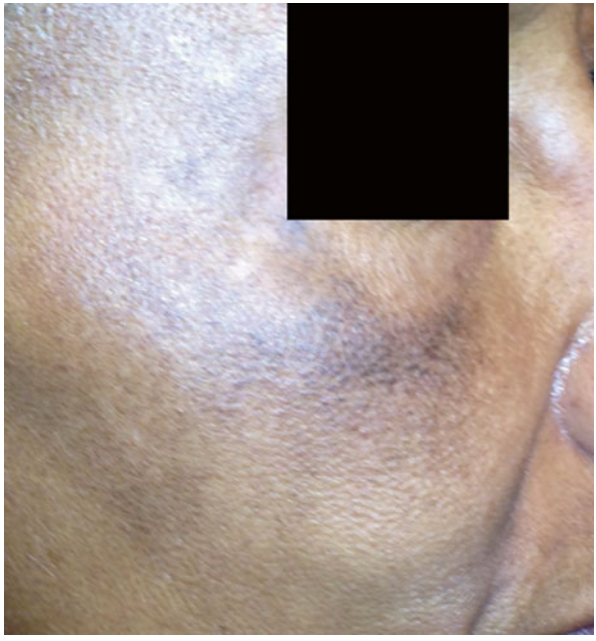

FIGURE 14.3 Dermal melasma. Brown-bluish discoloration is noted on the bilateral malar cheeks

is enhanced during examination with a Wood's light, whereas, dermal pigment is not. Lesions that have both enhancing and nonenhancing areas have a mixed pattern.

Treatment

Melasma is often difficult to treat and has a significant negative impact on patients' quality of life. The ultimate goal of melasma management is to lighten the affected area enough so that it is even with the rest of the skin. This can be difficult when treating patients with skin of color.

First line therapy involves topical compounds that affect the pigment production pathway. Topical hydroquinone is the

most common topical treatment used for melasma. Hydroquinone is a tyrosinase inhibitor, which primarily leads to decreased melanin production, along with altered melanosome formation and increased melanosome destruction (Jimbow et al. 1974). Ennes et al found that 38 % of patients treated with 4 % hydroquinone cream once daily for 12 weeks had a complete clinical response compared to only 8 % in the placebo group (Ennes et al. 2000). There is some controversy over the use of hydroquinone. Although rare in the United States, there have been several reports of exogenous ochronosis, a bluish-gray discoloration, after the use of hydroquinone cream, especially in South African blacks (Sheth and Pandya 2011b). One explanation for the high incidence in South Africans is that patients outside of the United States have uncontrolled access to over the counter high concentrations of hydroquinone (Olumide et al. 2008), often mixed with topical steroids, and used for long periods of time

Topical tretinoin cream is also an effective treatment, but often causes irritation and usually requires months to show improvement as monotherapy. The combination of hydroquinone, a retinoid, and a topical steroid appear to be highly effective for the treatment of melasma, with the Kligman-Willis Formula – 5 % hydroquinone, 0.1 % tretinoin, 0.1 % dexamethasone, and a hydrophilic ointment being the originally studied combination (Kligman and Willis 1975). The theory behind the effectiveness is that tretinoin prevents the oxidation of hydroquinone and improves epidermal penetration while the steroid reduces the irritation side effect of both. Side effects include erythema, desquamation, burning, and pruritus. Because irritation may lead to post inflammatory hyperpigmentation in patients with darker skin types, there are other topical agents that are available. These include azelaic acid, kojic acid, and ascorbic acid (vitamin C), all which may be less efficacious than hydroquinone but typically have less irritation.

Because ultraviolet and visible light can induce melanin formation, regular use of a broad spectrum sunscreen is effective both in preventing melasma and in enhancing the efficacy

of other topical therapies once melasma has developed. It is recommended that all patients with melasma use a UVA and UVB protective sunscreen with an SPF of at least 30 preferentially with a physical blocker, such as titanium dioxide or zinc oxide. Patients should also wear wide brimmed hats and protective clothing when outdoors. Many patients also use camouflage make-ups, with the most common brands being Dermablend (Vichy Laboratories, Paris, France), Covermark/CM Beauty (CM Beauty, Northvale, NJ), and Cover FX (Cover FX, Skin Care, Toronto, Ontario, Canada) (Sheth and Pandya 2011b).

Chemical peels can also improve melasma by removing unwanted melanin. However, they must be used with caution in skin of color, as they can cause irritation which can lead to postinflammatory hyperpigmentation. Glycolic acid peels are alpha hydroxyl acids that lead to epidermal remodeling, accelerated desquamation and pigment dispersion, along with inhibition of tyrosinase. When used in combination with a modified Kligman-Willis formula (5 % hydroquinone + 0.05 % tretinoin + 1 % hydrocortisone acetate), there was a decrease in the melasma area and severity index (MASI) by 79.9 % (Sarkar et al. 2002). Salicylic acid peels, which are beta hydroxyl acids, have also been used for melasma, especially in Fitzpatrick skin types V and VI (Grimes 1999).

The use of lasers have inconsistent results and is challenging because damage to surrounding tissue and subsequent inflammation can lead to postinflammatory hyperpigmentation. Fractional resurfacing is the only laser approved by the FDA for treatment of melasma. The microthermal zones of injury limit the area of skin that is damaged with each treatment, which may decrease the risk of postinflammatory hyperpigmentation. Studies have been limited to Fitzpatrick skin types III-IV (Rokhsar and Fitzpatrick 2005; Goldberg et al. 2008). Q-switched Nd:YAG lasers appear to have an increased risk of hyperpigmentation and a very high rate of relapse following treatment. Intense pulsed light therapy has been shown to be effective in improving melasma but is also characterized by a high relapse rate. In general, laser

and light therapies show the best response in lighter-skinned individuals and should be used very carefully, particularly in dark-skinned patients (Rivas and Pandya 2013). The use of lasers for melasma should be restricted to cases unresponsive to topical therapy or chemical peels. Appropriate maintenance therapy should be selected to avoid relapse (Arora et al. 2012).

Recently, orally administered Polypodium leucotomos has been shown to be beneficial for the prevention and potential treatment of several aesthetically relevant conditions, including melasma, due to the presence of its antioxidant and photoprotective properties. In a randomized, placebo-controlled study by Ahmed et al, the oral administration of Polypodium leucotomos as an adjunct to sunscreen improved the severity of melasma in women after 12 weeks. No adverse events have been associated with the use of Polypodium leucotomos. Therefore, Polypodium leucotomos appears to provide adjunctive benefits in treating melasma; however, more data with larger sample sizes are needed (Ahmed et al. 2013).

Key Points

- Melasma is worsened by exposure to ultraviolet radiation, oral contraceptives, and pregnancy.
- Regular use of a broad spectrum sunscreen is effective both in preventing melasma and in enhancing the efficacy of other topical therapies once melasma has developed.
- First line therapy involves topical compounds that affect the pigment production pathway, including hydroquinone and tretinoin.
- In general, laser and light therapies show the best response in lighter-skinned individuals and should be used carefully in dark-skinned patients.

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Chapter 15
Erythema Dyschromicum Perstans

Porcia B. Love

Case Presentation

A 35 year old Latina female presented with a several year history of discoloration of her chest, upper back, and arms. The discoloration began on her chest and slowly progressed to her arms and upper back. She has tried over the counter fade creams without success. There is minimal pruritus. She notes some improvement when she goes on vacation at the beach. She has no other associated systemic symptoms.

Physical Examination

The chest, anterior neck, upper back, and antecubital fossa have numerous 0.5–3 cm slate gray to bluish brown oval, annular coalescing patches. The lesions are nontender, and there is no associated scale (Fig. 15.1a, b).

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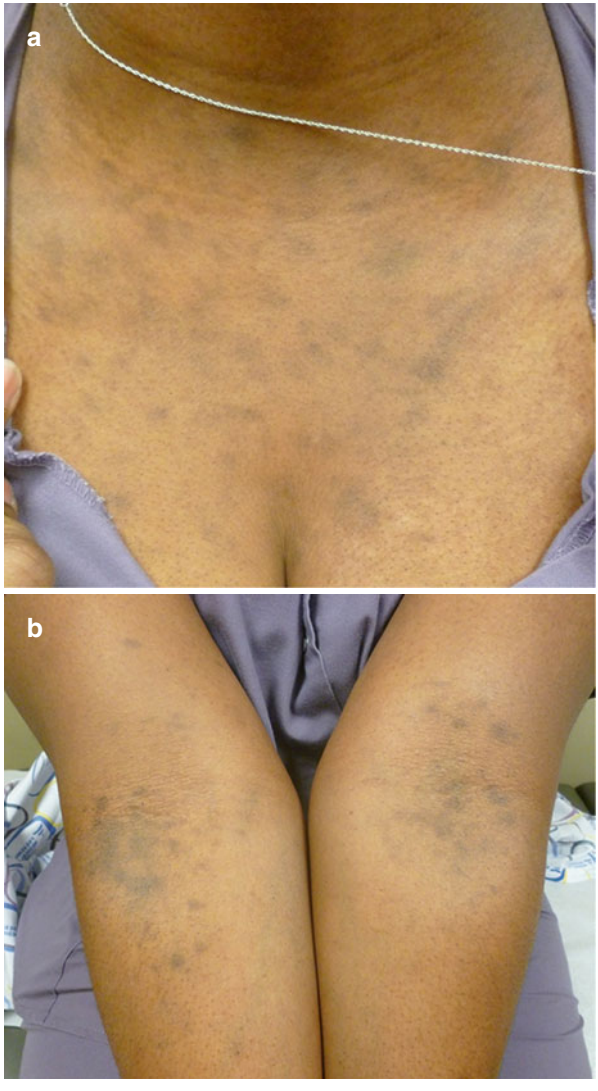

Figure 15.1 Erythema dyschromicum perstans. Ash-like, slate gray to blue, oval macules and patches are noted on the chest (**a**) and antecubital fossa (**b**)

Differential Diagnosis

The differential diagnosis of this disorder is broad. The most frequent cause of confusion and controversy is with lichen planus pigmentosus, which is characterized by hyperpigmented dark-brown macules with no active border and a noncharacteristic distribution that predominates in sun exposed areas and flexor folds. Its course is characterized by exacerbations and remissions and occasionally accompanied by pruritus. Lichenoid drug eruptions often involve trunk and limbs symmetrically and are photodistributed. Atrophic lichen planus can occur anywhere, but favors the flexor wrists, trunk, medial thighs, shins, dorsal hands, and lower back. Postinflammatory hyperpigmentation is characterized by brown discoloration. Idiopathic eruptive macular pigmentation is characterized by asymptomatic, hyperpigmented pigmented macules involving the neck, trunk, and proximal extremities. Pityriasis rosea typically begins with a solitary patch, and then progresses to a generalized exanthem of bilateral and symmetric macules with a collarette of scale oriented within the long axes along cleavage lines. Patients with hemochromatosis present with diffuse hyperpigmentation, but usually have cirrhosis and diabetes mellitus. Macular urticarial pigmentosum presents with widespread yellow tan to red brown macules and usually involves the trunk more than the extremities. Treponemal eruptions, such as secondary syphilis, may also resemble erythema dyschromicum perstans. Therefore, serological testing for treponemes is appropriate when encountering this type of outbreak (Bahadir et al. 2004).

Histopathology

A punch biopsy was performed on the border of an active macule on the antecubital fossa. Hyperkeratosis, a thinned epidermis, focal vacuolar changes in the basal layer of the

epidermis, superficial perivascular lymphohistiocytic infiltration, and pigment incontinence were present (Elder 2009).

Laboratory Studies

A complete blood count and comprehensive metabolic panel were normal. A human immunodeficiency virus test and rapid plasma reagin test were negative.

Diagnosis

Erythema dyschromicum perstans (EDP)

Case Treatment

The diagnosis of the disorder was discussed with the patient, along with its difficulty in treatment. Treatment options were discussed including hydroquinone, clofazimine, dapsone, and phototherapy. The patient declined clofazimine and dapsone due to the side effects of the medications. She was started on hydroquinone 4 % cream twice daily to affected areas. She also underwent narrowband UVB phototherapy three times a week. A broad spectrum sunscreen with an SPF of 30 was recommended for use daily. At 2 month follow-up, she noted mild improvement.

Discussion

Erythema dyschromicum perstans (EDP) or "ashy dermatosis" was first described in 1957 by Ramirez in Salvadorans as an "asymptomatic, ash-colored, macular hyperpigmentation that is slowly progressive and leaves a permanent discoloration" (Ramirez 1957). EDP is characterized by ash-like, slate gray, oval macules and patches with erythem-

atous borders that range in diameter from 0.5 cm to very large confluent patches. Individual lesions can be oval, irregular, or polycyclic in shape and continue to grow slowly. Lesions initially appear on the trunk and spread centrifugally to the extremities (Figs. 15.1 and 15.2). The scalp, palms, soles, and mucous membranes are rarely affected. As the lesions extend, the erythematous border eventually disappears within several months, so it may no longer be evident when the patient is examined. EDP has traditionally been characterized by its poor response to medication and its tendency to persist indefinitely in adult patients (Chun et al. 2009).

Erythema dyschromicum perstans usually occurs in the second or third decade of life and is most common in individuals from Central and South America, although cases have been described from different parts of the world. It is somewhat more common in women. EDP usually appears in adults, but some isolated cases and a small series of eight cases have been reported in prepubertal children (Silverberg et al. 2003).

The cause of EDP is unclear. Many consider EDP to be a variant of lichen planus actinus (Naidorf and Cohen 1982).

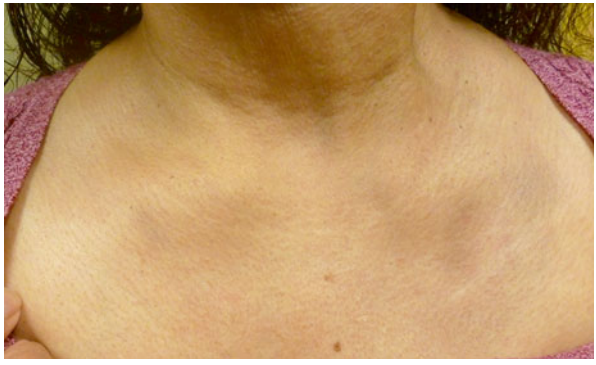

Figure 15.2 Erythema dyschromicum perstans. Ash-like, hyperpigmented patches are noted on the chest

Infections, such as whipworm, HIV (Nelson et al. 1992), exposure to environmental toxins, such as pesticides, ammonium nitrate, cobalt, radiocontrast media, and fungicides, and medications, such as oral antibiotics and benzodiazepines, have all been implicated in the etiology of EDP (Silverberg et al. 2003). Systemic conditions such as thyroid disease and chronic hepatitis (Kontochristopoulos et al. 2001) have also been implicated.

Although many factors may be involved in the pathogenesis of EDP, an important genetic susceptibility appears to be conferred by genes located within the major histocompatibility complex region. HLA-DR association with the genetic susceptibility to develop EDP in Mexican Mestizo patients was analyzed in 23 patients with EDP. The most frequent allele was HLA-DR4 subtype *0407 (65 %), compared with 23 % in controls (Correa et al. 2007).

Treatment

There is no definitive treatment for erythema dyschromicum perstans. A number of treatment modalities have been attempted, including antibiotics, topical corticosteroids, keratinolytic agents, isoniazid, chloroquine, and griseofulvin; however, all have had poor responses (Bahadir et al. 2004). Although EDP is unlikely to resolve in adults, most prepubertal children have a course of spontaneous slow resolution within 2–3 years. Therefore, in children, the use of sun protection to avoid lesional prominence while awaiting spontaneous resolution is recommended (Silverberg et al. 2003).

Recently, clofazimine has been used with some success in adults, apparently because of its anti-inflammatory and immunomodulating effects. It is not clear, however, if clofazimine produces improvement by reducing the inflammatory infiltrate and postinflammatory hyperpigmentation or simply by masking the lesions with its characteristic yellow discoloration of the skin (Silverberg et al. 2003). In one series of eight patients, seven had a good or excellent response to clofazimine administered either 100 mg every other day to patients weighing less

than 40 kg or 100 mg every day to patients weighing more than 40 kg. This medication was continued for 3 months, then reduced to 200 mg/week and 400 mg/week, respectively. The one remaining patient had only a marginal response (Piquero-Martin et al. 1989). This medication seems to have a valuable effect on the inflammatory phase of erythema dyschromicum perstans. Side effects of clofazimine include a temporary orange discoloration of the skin and the eye (i.e., cornea, conjunctivae); it also may produce ichthyosis. Its most serious adverse effect is crystal deposition in the intestines, producing a potentially fatal enteropathy. This rare complication is associated with months of high-dose (>100 mg/day) therapy. Nausea and diarrhea are more common. Splenic infarction and eosinophilic enteritis are also rare adverse effects (Piquero-Martin et al. 1989).

A successful response to dapsone in one patient from Turkey has also been reported. Besides its antimicrobial potency, dapsone is effective in polymorphonuclear-rich dermatoses, as well as lymphocyte-rich dermatoses. It also has been shown to suppress neutrophil migration and the respiratory burst by interfering with T-cell immunity. Dapsone possibly plays a role in the regulation of immune responses involved in the pathogenesis of EDP. Nevertheless, more reports and studies are necessary (Bahadir et al. 2004).

The use of narrow-band UVB phototherapy has been successful in a few patients with EDP (Tlougan et al. 2010). By suppressing immune function and reducing pro-inflammatory cytokines, the photo-immunologic effects of UVB phototherapy assist in EDP treatment by exerting potent anti-inflammatory effects. UVB phototherapy also provides camouflages the dermal pigmentation by stimulating pigment production. Additionally, UVB phototherapy induces thickening of the stratum corneum and apoptosis of T lymphocytes, which causes a decrease in the lichenoid inflammatory infiltrate that often is observed in active areas of EDP. Narrowband UVB phototherapy has also been used recently in the treatment of other lichenoid pigmentary disorders with success. Thus, UV light may be a viable treatment option for patients with EDP (Tlougan et al. 2010).

Key Points

- Erythema dyschromicum perstans usually occurs in the second or third decade of life and is most common in individuals from Central and South America, although cases have been described from different parts of the world.
- Erythema dyschromicum perstans has traditionally been characterized by its poor response to medication and its tendency to persist indefinitely in adult patients.
- Erythema dyschromicum perstans is very difficult to treat; however, clofazimine and dapsone have shown success in a small group of patients.
- The use of narrow-band UVB phototherapy has also been successful in a few patients.

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Part V
Disorders of Hypopigmentation

Chapter 16
Vitiligo

Shalini B. Reddy and Neelam A. Vashi

History

A 28-year-old Hispanic male presented with a 3 year history of asymptomatic white spots around his lips and on the back of his hands and fingers that had slowly increased in size over time. He had previously tried treatment with an over-the-counter antifungal cream for 2 months without improvement. Family history was positive for hypothyroidism in his mother.

Physical Examination

On examination, well-demarcated, depigmented patches and macules were noted on periorificial skin and bilateral dorsal hands and fingers. Under Wood's lamp examination, all lesions appeared more pronounced (Figs. 16.1, 16.2, and 16.3).

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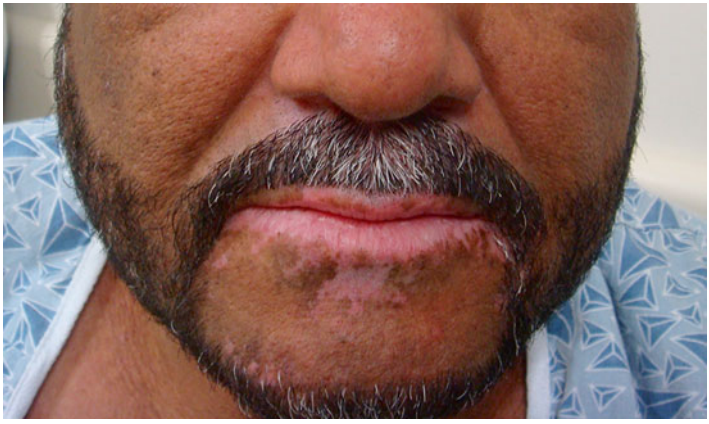

Figure 16.1 Depigmented patches on the cutaneous lips and perioral skin

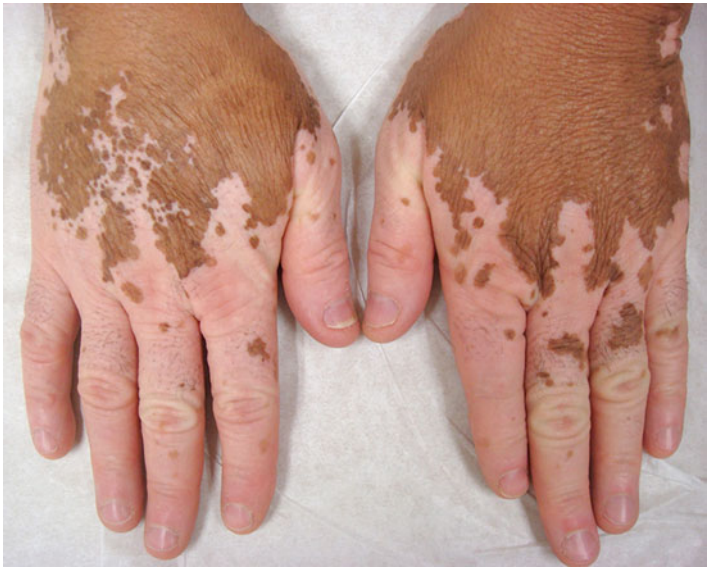

Figure 16.2 Depigmented patches on the bilateral dorsal hands

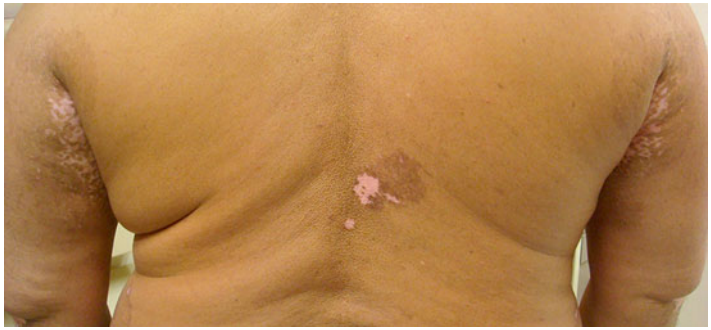

FIGURE 16.3 Depigmented patches on the mid-back and bilateral axilla with evidence of repigmentation

Clinical Differential Diagnosis

Based on the clinical findings, vitiligo was felt to be the most likely diagnosis. The differential diagnosis also included chemical leukoderma (occupational/exposure related), leukoderma associated with scleroderma, piebaldism, and post-inflammatory hypopigmentation. Depending on the distribution and the percentage of body surface area involved, the differential diagnosis for vitiligo can also include nevus anemicus, nevus depigmentosus, infections (such as tinea versicolor, leprosy, onchocerciasis), leukoderma associated with melanoma, idiopathic guttate hypomelanosis, and hypopigmented mycosis fungoides (Alikhan et al. 2011; Taieb and Picardo 2009).

Histopathology

Vitiligo is often a clinical diagnosis; however, in difficult cases, histopathology can help differentiate vitiligo from other pigmentary disorders. Biopsy of a vitiligo lesion typically reveals few or no melanocytes and loss of melanin pigment within the epidermis. In chronic, stable lesions, the rest of the skin typically appears intact and unremarkable. However, degenerative

changes in cutaneous nerves and adnexal structures in chronic lesions have been reported. In contrast, a lymphocytic lichenoid inflammatory infiltrate may be seen at the margins of newer lesions (Alikhan et al. 2011; Taieb and Picardo 2009).

Diagnosis

Vitiligo

Case Treatment

The nature and course of vitiligo was reviewed with the patient. Treatment options were discussed, including observation, topical corticosteroids, topical calcineurin inhibitors, and/or phototherapy. The patient opted for a combination of topical corticosteroids and narrowband ultraviolet B (NB-UVB) phototherapy. Triamcinolone 0.1 % ointment twice daily was prescribed for a 2-month course to his hands and fingers in a pulsed fashion. In addition, NB-UVB phototherapy three times weekly was initiated. A serum thyroid-stimulating hormone (TSH) was sent to screen for thyroid disease, which was within normal limits.

Discussion

Vitiligo is an acquired pigmentary skin disorder that affects individuals of all races and ethnicities. It is characterized by asymptomatic, well-demarcated, depigmented macules or patches that are surrounded by normal skin. The natural progression of the disease varies, ranging from insidious to rapid onset. It occurs in males and females equally and typically first presents between 10 and 30 years of age (Alikhan et al. 2011; Taieb and Picardo 2009).

Vitiligo affects nearly 0.5–1 % of the world population; however, prevalence varies based on region. The highest

reported prevalence is in Gujarat, India, where the disease affects up to 8.8 % of the population. One study in the French West Indies concluded that the disease prevalence in the black population is the same as or slightly less than in the white population (Alikhan et al. 2011). Overall, reporting rates likely vary greatly based on social stigma and the more obvious nature of disease in skin of color.

Diagnosis is usually made clinically. Use of a Wood's lamp, which is a handheld ultraviolet A (UVA) emitting device, can aid in diagnosis. The classic depigmented lesions of vitiligo give a white fluorescence and tend to be more pronounced under illumination compared to hypopigmented lesions (Alikhan et al. 2011; Taieb and Picardo 2009).

There are three main types of vitiligo: localized, generalized, and universal. Generalized vitiligo is the most common type, which is further subtyped into acrofacial, vulgaris, or mixed. Localized vitiligo can be focal, segmental, or mucosal in nature. Universal vitiligo involves more than 80 % of the body surface area. While any part of the body can be affected, initial lesions are most frequently found on the dorsal surface of hands, forearms, feet, face, and around facial orifices (eyes, nose, mouth). There are several clinical variants including: vitiligo ponctué, trichrome vitiligo, quadrichrome vitiligo, blue vitiligo, and inflammatory vitiligo. Quadrichrome vitiligo, which is defined by a tan zone between normal and depigmented skin and marginal or perifollicular hyperpigmentation, is more common in darker skin types (Alikhan et al. 2011).

The exact etiology of vitiligo is not clearly understood. Several theories have been postulated to explain the pathogenesis of vitiligo, the most common including autoimmune, neurohumoral, and autocytotoxic theories. The current accepted theory is that the etiology of vitiligo is multifactorial, with a combination of genetics, stress, autoimmunity, altered cellular environment, and impaired melanocyte migration all contributing to pathogenesis. Genetics play a varying role in disease pathogenesis depending on ethnicity, with a higher frequency of vitiligo in first-degree relatives in white, Indo-Pakistani, and Hispanic populations (Alikhan et al. 2011).

Several studies have supported the autoimmune theory by demonstrating an immune-mediated destruction of melanocytes. In addition, vitiligo may be associated with other autoimmune disorders, including diabetes mellitus, pernicious anemia, alopecia areata, and, most commonly, autoimmune thyroid disease (hyper- or hypothyroidism). In new onset vitiligo patients, thyroid screening with serum TSH is recommended (Alikhan et al. 2011; Taieb and Picardo 2009).

Although vitiligo generally is an asymptomatic disease, the cosmetic and psychological impact of the disease should be taken into consideration when deciding on treatment. Many societies have a poor understanding of vitiligo, and because it typically occurs on exposed areas, it can have devastating psychological effects, impacting patients' self-esteem and quality of life. These effects are particularly pronounced in patients with skin of color given the marked contrast between normal and affected skin. The goals of treatment are to halt the progression of disease and furthermore, induce repigmentation.

Treatment

First line therapy includes topical corticosteroids and topical calcineurin inhibitors (Taieb and Picardo 2009; Felsten et al. 2011; Taieb et al. 2013). Topical corticosteroids are the most clinically effective topical therapy. A study showed that when combined with UVA light therapy, topical fluticasone produced repigmentation rates three times greater than either as monotherapy (Felsten et al. 2011; Taieb et al. 2013).

Topical calcineurin inhibitors, such as tacrolimus and pimecrolimus, are good alternatives to topical steroids because they have immunomodulatory effects without the side effects of prolonged steroid use (Felsten et al. 2011; Taieb et al. 2013). Topical tacrolimus has been shown to be especially effective in the treatment of patients with skin of color, showing higher rates of repigmentation of body lesions and faster results compared to white patients (Silverberg and Silverberg 2011). Calcineurin inhibitors are most effective for lesions on the head and neck compared to those on the body and extremities

in all races (Silverberg and Silverberg 2011). Calcineurin inhibitors are often preferred over topical corticosteroids in the periocular and genital areas. They have also been shown to enhance the effect of phototherapy or laser therapy when used in combination (Felsten et al. 2011; Taieb et al. 2013).

NB-UVB phototherapy induces repigmentation in many patients and should be reserved for patients who fail topical therapy or with widespread disease. Vitamin D_3 analogs, such as calcipotriene, can be used in combination with phototherapy or topical corticosteroids. Psoralen plus UVA phototherapy (PUVA) can be used in generalized vitiligo, but it has lower efficacy rates than NB-UVB and may increase incidence of melanoma and nonmelanoma skin cancer (Felsten et al. 2011; Taieb et al. 2013).

The monochromatic excimer laser (308 nm) is a treatment modality that emits light in the UV range and allows for targeted treatment of specific lesions. It particularly works well in patients with skin of color compared to conventional phototherapy (Felsten et al. 2011). However, some patients will report an unappealing peripheral hyperpigmentation with this treatment.

A short course of systemic corticosteroids may be considered in rapidly progressive vitiligo as it can effectively halt disease progression, but guidelines on optimal dosing parameters and safety profiles have yet to be established (Felsten et al. 2011).

Surgical therapy can be considered for patients with stable, recalcitrant lesions who are unable to obtain desirable results with nonsurgical methods. Surgical treatment includes epidermal grafting (suction blister, split-thickness, and punch grafting) and autologous melanocyte suspension transplant. Risks and adverse effects include scarring, graft failure, koebnerization, infection, cobblestoning, and variegated pigmentation (Felsten et al. 2011; Taieb et al. 2013).

Depigmentation with topical monobenzone may be beneficial for extensive vitiligo in darkly pigmented patients who fail repigmentation therapy (Felsten et al. 2011; Taieb et al. 2013).

In patients with skin of color, providers should have a lower threshold to advance treatment to prevent further progression of disease. Response to treatment is slow and

psychological support and counseling may be necessary. Temporary or permanent camouflage with makeup or tattoo can be used at all stages of treatment. Sunless tanning products with dihydroxyacetone can be suggested as well. Patients should be counseled on sun protection strategies, including avoidance and use of sunscreen so as not to enhance the contrast between pigmented and nonpigmented areas (Taieb and Picardo 2009; Felsten et al. 2011; Taieb et al. 2013). Sun protective measures alone can be the treatment of choice in lightly pigmented persons.

Alternative, less studied, treatments have been used with variable efficacy including pseudocatalase and ginkgo biloba. Other treatments currently in trials include oral simvastatin and afamelanotide, a synthetic analog of the naturally occurring melanocortin peptide hormone alpha-melanocyte stimulating hormone. Lastly, clinicians should familiarize themselves with local and national resources that can offer support to those with this often psychologically devastating disease.

Key Points

- The cosmetic and psychosocial effects of vitiligo on patients with skin of color are particularly pronounced.
- The overall goal of vitiligo management is to minimize areas of depigmentation. In patients with skin of color, treatment should be started early, and providers should have a low threshold to advance treatment.
- Topical corticosteroids and topical calcineurin inhibitors (particularly topical tacrolimus) are first line therapy for limited disease in patients with skin of color.
- Depigmentation and surgical therapy are reserved for widespread and recalcitrant disease that is unresponsive to conventional treatment, respectively.

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Chapter 17
Pityriasis Alba

Yunyoung Claire Chang and Neelam A. Vashi

History

A 15-year-old Fitzpatrick Skin Type (FST) IV female with a history of atopic dermatitis and allergic rhinitis presented with light spots on her bilateral cheeks since childhood, worse in the summer, with occasional associated pruritus.

Physical Examination

Close examination demonstrated multiple ill-defined hypopigmented patches with irregular borders and fine scale on bilateral cheeks. The remainder of her skin demonstrated diffuse xerosis (Fig. 17.1).

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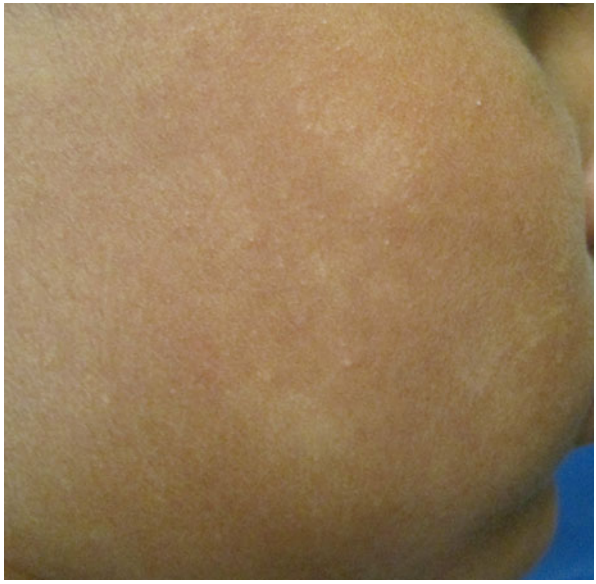

FIGURE 17.1 Ill-defined, hypopigmented slightly scaly patches on the right cheek

Clinical Differential Diagnosis

The findings were thought to be most consistent with pityriasis alba. The differential diagnosis for pityriasis alba includes tinea versicolor, nevus depigmentosus, vitiligo, nummular dermatitis, hypopigmented mycosis fungoides, tuberous sclerosis, and leprosy (Table 17.1).

Histopathology

A biopsy was not performed in this case because the physical examination was felt to be diagnostic. Pityriasis alba (PA) is typically nonspecific on histopathology, with early lesions demonstrating spongiosis, follicular plugging, focal parakeratosis

Table 17.1 Differential diagnosis

Diagnosis	Distinguishing features
Tinea versicolor	More extensive with more evident scale
	Common location: on trunk
Nevus depigmentosus	Usually a persistent, solitary, and hypopigmented patch with scalloped borders
	Present at birth or before age 3
	Common location: on trunk
Vitiligo	Completely depigmented and very well demarcated macules/patches
	Accentuated by Wood's lamp
Nummular dermatitis	Usually more well-defined, raised plaques with more prominent scale
	Associated with intense pruritus
Hypopigmented mycosis fungoides	Rare condition
	Common location: on trunk
Tuberous sclerosis	Present at or around birth
	Associated with other systemic manifestations
	Common location: on trunk
Leprosy	May have associated anesthesia/hypoesthesia with nerve involvement on histology

and acanthosis, atrophic sebaceous glands, superficial perivascular lymphocytic infiltrate, and dermal edema. Late lesions show nonspecific changes of hyperkeratosis, focal parakeratosis, and spongiosis. There is a variable reduction of melanin in the basal layer but no significant difference in melanocyte count (In et al. 2009).

Diagnosis

Pityriasis Alba

Case Treatment

The nature and course of this condition was discussed with the patient as well as treatment options, including monitoring and topical therapies. Hydrocortisone 1 % cream daily 1 week on, 1 week off as needed for pruritus was prescribed. In addition, the importance of dry skin care, including frequent emollient use, and sun protection was emphasized.

Discussion

Pityriasis alba (PA) is a common skin disorder in all skin types and ethnicities (In et al. 2009). It is characterized by asymptomatic or mildly pruritic hypopigmented ill-defined irregular patches covered with fine scale located primarily on the face but can also involve the trunk and limbs when diffusely involved. Epidemiologic studies have demonstrated that PA is the most common hypopigmentary disorder in children. It most frequently affects children 3–16 years of age but may occur in adulthood as well (In et al. 2009). It has a higher prevalence in individuals with darker skin (FST III-VI), with one study demonstrating 98.1 % of PA patients within these skin types (Blessmann Weber et al. 2002). This may be because the lesions are more apparent in darker skin types who tan more easily except in the areas with PA lesions (Blessmann Weber et al. 2002). In addition, lesions may be more cosmetically bothersome to patients with darker complexions, making them more likely to seek treatment.

Although it has been studied since the nineteenth century, the etiology of PA is not well established. The most consistently associated condition with PA is atopic dermatitis (AD) and is thought by some to be a low-grade or subclinical mani-

festation of AD. Like AD, external and personal factors that cause xerosis, including higher frequency and time spent in showers and higher water temperature, are associated with higher incidence of PA and may be a pathogenic factor (Blessmann Weber et al. 2002). Excessive and unprotected sun exposure is also closely related to onset of PA, which may explain the higher frequency of onset during the summer months. This has been postulated to be due to the direct action of UV radiation on decreasing melanocyte number and activity leading to hypomelanosis (Blessmann Weber et al. 2002). Other environmental influences have been implicated, including temperature variations, relative air humidity, altitude, and excessive sun light exposure. Microorganisms, such as *Pityrosporum*, *Streptococcus*, *Aspergillus*, and *Staphylococcus*, have been suggested as etiologic sources but not confirmed by studies (In et al. 2009; Blessmann Weber et al. 2002).

PA generally has a benign, chronic course with hypopigmentation persisting for years. Spontaneous resolution eventually occurs before adulthood for the majority of patients, but persistence into and onset in adulthood have been rarely reported (Jadotte and Janniger 2011).

Treatment

Although treatment is not necessary, the chronic course and visible localization of PA lesions on exposed areas, especially in darker skin types, make the desire for safe and effective treatment important to this population. Treatment in darker skin types is often frustrating due to the fact that the lesions may be more cosmetically apparent and existing treatment options are limited. Treatment begins with good general skin care and reassurance of young patients and their parents about the benign and generally self-limited nature of the disorder. Emollients and moisturizing skin care routines are important. Gentle cleansers or moisturizing soaps are recommended. In addition, sun protection

methods are essential because normal skin will darken, making the PA lesions seem even lighter. This must be emphasized in patients of skin of color given many patients of darker skin types less frequently endorse sun protective habits. Pharmacologic therapy is often unnecessary. Low potency, class 5 and 6, topical steroids (i.e. hydrocortisone 1 %, desonide 0.05 %) is considered first-line treatment and may help with erythema and pruritus associated with early lesions and may accelerate repigmentation of existing lesions with variable efficacy (Al-Mutairi and Hadad 2012). Topical steroid use should be limited and with frequent breaks to avoid long-term skin atrophy as well as potential worsening of hypopigmentation, especially on facial skin. A suggested regimen is an alternating 1 week on, 1 week off as needed.

Topical tacrolimus 0.1 % ointment and pimecrolimus 1 % cream are steroid-sparing agents that have demonstrated effectiveness in improving hypopigmentation and scaling when used twice daily for 9 weeks and 12 weeks, respectively, in darker skin types (Rigopoulos et al. 2006). The ointment formulation may be preferred as it better treats the background xerosis. The major disadvantages of this treatment are high cost and side effects of transient local irritation. Topical calcitriol 0.003 % twice daily for 8 weeks was also shown in one study to be effective treatment in darker skin types (FST IV-V) (Moreno-Cruz et al. 2012). Psoralen plus ultraviolet light A (PUVA) photochemotherapy may be used to help with repigmentation in extensive cases, but recurrence rate is high after treatment is stopped. An alternative is therapy with the 308-nm excimer laser twice a week for 12 weeks, which may deliver more localized treatment than PUVA (Al-Mutairi and Hadad 2012). Finally, cosmetic camouflage may be needed in skin of color patients alone or in adjunct to these treatments. Cosmetic camouflage is the application of creams, liquids, or powders with the goal of blending or concealing color or contour irregularities on the skin. It has been shown to significantly improve the quality of life in those with pigmentary disorders (Ramien et al. 2014).

Key Points

- Pityriasis alba (PA) is a common pigmentary disorder in all races and skin types, occurring more frequently in those with darker skin types.
- PA is characterized by asymptomatic or mildly pruritic hypopigmented ill-defined irregular macules and patches covered with fine scale that occur predominantly on the face.
- Atopic dermatitis and xerosis have been associated with PA.
- Dry skin care, including emollient use, and sun protection should be emphasized as treatment of PA in skin of color patients.
- Low-potency topical steroids are first-line treatment for PA but should be used with caution in darker skin types given the risk of dyspigmentation.
- Steroid-sparing topical agents, i.e. tacrolimus and pimecrolimus, have been studied to be effective in PA and are options for chronic treatment in darker skin types.

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Chapter 18
Progressive Macular Hypomelanosis

Mayra Buainain de Castro Maymone and Neelam A. Vashi

Case Presentation

A 21-year-old African American female presented with a 6 year history of asymptomatic light colored lesions on the chest, flanks, and back. She had tried numerous over-the-counter treatments, including topical clotrimazole and selenium sulfide shampoo without improvement (Figs. 18.1 and 18.2).

Physical Examination

On examination, multiple ill-defined, non-scaly hypopigmented macules were seen on the back, flanks, and chest. Lesions coalesced into patches over the midline back. Wood's lamp examination revealed red perifollicular fluorescence. Skin scrapings on potassium hydroxide (KOH) microscopic examination did not show evidence of spores or hyphae.

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Clinical Differential Diagnosis

The hypopigmentation was felt to be most consistent with progressive macular hypomelanosis (PMH). This disorder is often mistaken for other common conditions seen in darkly pigmented patients, e.g. tinea versicolor, pityriasis alba, vitiligo, and post-inflammatory hypopigmentation. PMH can be distinguished from tinea versicolor and pityriasis alba by its non-pruritic nature and failure to respond to anti-fungal or anti-inflammatory therapy, respectively. In addition, tinea versicolor can often be confirmed by microscopic examination with KOH that will show evidence of fungus. Vitiligo appears depigmented and will illuminate under Wood's lamp examination. Patients with post-inflammatory hypopigmentation will give a

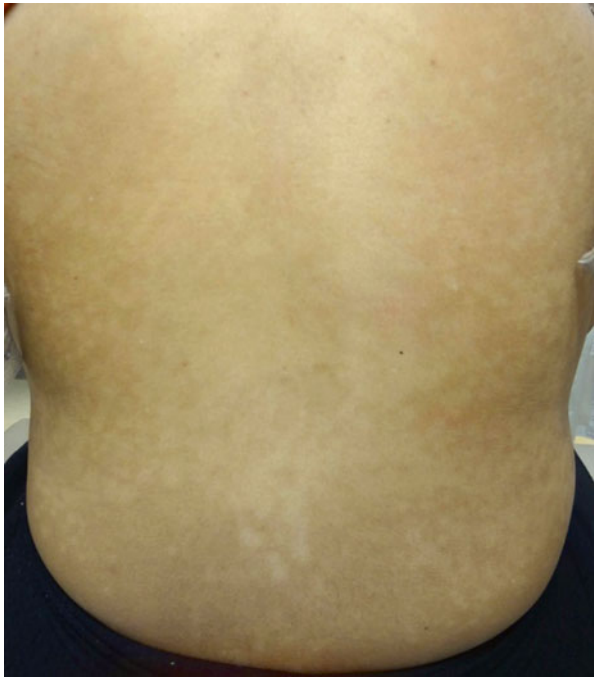

Figure 18.1 Non-scaly hypopigmented macules and patches on the back of a woman

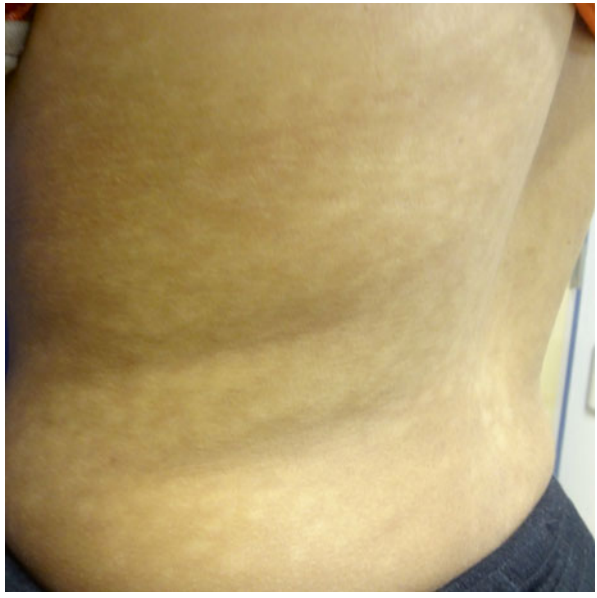

FIGURE 18.2 Non-scaly hypopigmented macules and patches on the left flank and back of a woman

history of a primary skin eruption and a shorter clinical course. Infectious processes and cutaneous lymphoma should be considered in select populations. Rarer infectious etiologies of hypopigmentation should be especially considered if the patient is from an endemic area of leprosy, leishmaniasis, and/or pinta. If asymmetric, atrophic hypopigmented macules and patches with fine scales on the trunk, chest, and sun-protected areas are seen, one should consider the diagnosis of hypopigmented mycosis fungoides (Relyveld et al. 2007; Elmariah and Kundu 2011).

Histopathology

Two biopsies were performed from lesional and non-lesional skin on a follow up visit due to minimal response to initial treatment. The biopsy results were non-diagnostic which is often the case in PMH. Skin biopsy of the affected area

revealed a normal number of melanocytes with reduced content of epidermal melanin when compared to unaffected skin. The dermis appeared normal. PAS stain was negative for fungal organisms.

Diagnosis

Progressive macular hypomelanosis (PMH)

Case Treatment

The nature of the diagnosis, disease course, and treatment expectations were discussed. The patient was prescribed benzoyl peroxide 5 % wash twice daily with clindamycin lotion 1 % twice daily. The patient had minimal response to this treatment and agreed to a biopsy as above. After exclusion of other entities, treatment was further optimized with narrowband ultraviolet B (NBUVB) three times weekly in adjunct to topical antimicrobials.

Discussion

Progressive macular hypomelanosis is a common yet underdiagnosed skin disorder. Authors worldwide have used several names to describe this entity including cutis trunci variata, dyschromia creole, progressive and confluent hypomelanosis of the melanodermic metis, nummular and confluent hypomelanosis, progressive macular confluent hypomelanosis, and idiopathic multiple large macule hypomelanosis (Elmariah and Kundu 2011; Westerhof et al. 2004). Although there are recent reports of PMH in individuals of lighter skin types, this condition continues to be more prevalent in patients with more richly pigmented skin (Relyveld et al. 2007; Westerhof et al. 2004). PMH is characterized by multiple ill-defined round to oval, non-scaly

hypopigmented macules and patches that occur on the trunk and that occasionally extend to the neck, face, and proximal extremities. Lesions are asymptomatic with no prior history of inflammation. PMH typically affects young adults, with a female predominance. The clinical course is variable, usually starting in adolescence. It may resolve spontaneously, within 2–5 years, or slowly progress over time (Relyveld et al. 2007; Elmariah and Kundu 2011).

The pathogenesis of PMH is not fully understood. Recently, Westholf et al. proposed a novel hypothesis based on the finding of red fluorescence under Wood's light examination in affected skin as opposed to normal skin which showed no fluorescence. Authors have attributed this red follicular fluorescence to porphyrin production. In the original studies, cultures from lesional skin but not from unaffected skin isolated *Propionibacterium acnes* (*P. acnes*), leading to the thought that *P. acnes* produces a depigmenting agent that interferes with melanin production, resulting in the hypopigmented macules observed clinically. Additional investigation, performed by the same group of investigators in 2010, demonstrated that the *Propionibacterium* bacteria found in PMH may be a different species than that found in acne patients (Relyveld et al. 2007; Westerhof et al. 2004; Relyveld et al. 2010). This is supported by observations that patients with acne are not at increased risk for the development of PMH and vice versa.

The diagnosis of PMH is made based on history, clinical features, red follicular fluorescence under Wood's lamp examination, and seldom a skin biopsy. Histology examination of PMH is non-diagnostic, and when performed, skin biopsies should be obtained from both lesional and normal skin. A blinded study conducted in a Chinese population confirmed no overall difference in number of S-100+melanocytes. Using electron microscopy, it was observed that lesional skin had a higher ratio of immature melanosomes (stage II and III-light) in contrast with normal skin. This supports the impression that hypopigmention seen in PMH may be due to impaired melanosome maturation (Relyveld et al. 2007; Wu et al. 2010; Kumarasinghe et al. 2006).

Treatment

The treatment of PMH is challenging and oftentimes delayed, which can be particularly disappointing in those with skin of color in which dyschromia is significantly more evident. There is no first line or single effective treatment for PMH. Given the presumptive bacterial etiology, antimicrobial therapy is the cornerstone of therapy, with many reported cases of successful treatment with oral and topical antimicrobials. Cultures obtained from species show sensitivity to several antibiotics and resistance to metronidazole (Westerhof et al. 2004). A randomized study of 45 patients showed that benzoyl peroxide 5 % hydrogel/clindamycin 1 % lotion in combination with UVA irradiation led to better repigmentation than fluticasone 0.05 % cream in combination with UVA (Relyveld et al. 2006). Another study aimed to compare the effectiveness of narrow-band ultraviolet B (NBUVB) monotherapy with NBUVB combined with antimicrobial therapy. A randomized left-right comparison study was conducted and found that significant repigmentation was observed in all 10 subjects over an 8 week treatment trial, with no significant difference between treated sides at all evaluation time points (Sim et al. 2011).

Wu et al. performed a small retrospective analysis of 6 patients with PMH who were treated with an average of 27 sessions of narrow-band ultraviolet B and reported improvement of hypopigmentation in 6 weeks. Unfortunately, improvement was transient with recurrence noticed as soon as 4 weeks (Wu et al. 2010). NBUVB appears to be a safe treatment option. The alleged mechanism of action is stimulation of melanogenesis along with the antimicrobial effects of UVB phototherapy (Sim et al. 2011).

A treatment algorithm was proposed by Elmariah and Kundu, where oral tetracycline, doxycycline, or minocycline with topical benzoyl peroxide and/or clindamycin are used for a minimum of 6 weeks. If no clinical improvement is observed, the authors recommend discontinuing oral antibiotics, and starting NBUVB phototherapy for a minimum of 25–30 treatment sessions in adjunct to topical antimicrobials. In cases of non-response to above-mentioned therapies, a

short course of PUVA may be considered. Other less reported treatments can also be considered. One author reported incidental improvement in PMH when oral isotretinoin at 10 mg daily was given for rosacea (Kim et al. 2012). In addition, in theory, alternative therapies like blue light as is used for acne may be a possible treatment option, but more research is needed.

Key Points

- Progressive macular hypomelanosis (PMH) is a relatively common yet under-recognized and misdiagnosed disorder.
- It is often misdiagnosed as tinea versicolor, pityriasis alba, post-inflammatory hypopigmentation, and/or vitiligo.
- Patients with skin of color are preferentially affected by this not infrequent pigmentary disorder, and the condition is particularly more noticeable in darker skin types.
- Early recognition and counseling is important to avoid unnecessary treatments and provide patients the necessary information in regards to their skin disorder.
- Pathogenesis appears to be related to a putative species of *Propionibacterium*.
- Proper treatment includes the use of antibacterial agents and phototherapy.

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