

Pityriasis Alba—Common Disease, Enigmatic Entity: Up-to-Date Review of the Literature

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Abstract: Pityriasis alba (PA) is a skin disorder that affects children and adolescents. Although it is common worldwide, its incidence is markedly higher in darker skin phototypes. Its characteristic features include an extended, multistage course and spontaneous remissions and recurrences. Preceded by erythematous changes, patches of hypopigmented skin of up to a few centimeters in diameter appear on the upper body. Pruritus may accompany it. Even though its etiology is unknown, possible reported triggering factors include sunlight, beauty treatments, and microorganisms, among others. Calcineurin inhibitors play the most crucial role in PA pharmacotherapy. PA often coexists with atopic dermatitis and is considered one of its milder forms.

Pityriasis alba (PA) is a mild skin condition reported all around the world. It most frequently affects children ages 3 to 16 years (1–3). The incidence of PA in children ranges from 1.9% to 5.2%, but is higher in populations with darker skin phototypes (4–8). The role of sex in its incidence has not been established (5,8–10). PA is a long-term, multistage disease with frequent, spontaneous remissions. Erythematous, clearly defined lesions that subside, leaving areas of skin depigmentation with scaling edges, are the predominant clinical presentation. Skin changes occur on the upper parts of the body, typically on the face (3,4,11–14). The incidence of PA in patients with a history of atopic lesions is significantly higher than in the general population, and it is one of the minor forms of atopic dermatitis (AD) (15–18). This information might be useful when

establishing a diagnosis, which, because of a nonspecific PA clinical picture, is a challenge. In spite of numerous hypotheses, no certain etiologic factor for PA has been determined (2,19,20). In the literature, PA is referred to as pityriasis streptogenes, pityriasis simplex faciei, pseudoleucoderma atopicum, erythema streptogenes, impetigo furfuracea, impetigo pityroides, impetigo sicca, pityriasis maculata, and Kleinflechte (20–22).

TRIGGERING FACTORS, ETIOLOGY, AND PATHOGENESIS

The major PA risk factors are young age, dark skin phototype, and AD. Because of the location of dermal lesions—typically in areas exposed to sunlight—PA has repeatedly been associated with overexposure to

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light. The aforementioned findings were confirmed in 54 patients diagnosed with PA (9,19). In addition, a positive correlation between some personal hygiene habits and PA has been recorded. Long, frequent baths, mechanical exfoliation, and other similar treatments may reduce the level of defensins and skin-protecting factors, contributing to the development of lesions (2,19). In view of the above, reports of a higher frequency of PA in patients with low socioeconomic status seem counterintuitive (2,19,23). Low levels of serum copper related to dietary deficiencies may account for the seeming paradox. Copper is indispensable to activate the tyrosinase in melanocytes, which is critical to melanin production. Galadari et al (24) demonstrated a markedly lower level of the microelement in the blood serum of individuals with PA than in a control group ($p < 0.001$). No differences were recorded in zinc, manganese, carotenes, or lead concentration between the two study groups. Azelaic acid, oxalic acid, and other metabolites of *Malassezia furfur* yeasts that normally colonize healthy skin may also cause tyrosinase inhibition (19). A lot of attention was paid to other microbiologic factors (*Staphylococcus aureus*, *Propionibacterium acnes*) and parasitic factors (*Ascaris*) as potential pathogenic elements in PA, but no relationship has been found, although dermal lesions (particularly during the first stage of the disease) favor infection development (25).

CLINICAL PRESENTATION AND COURSE OF THE DISEASE

PA is a long-term, multistage condition. The primary, early disease stage presents with erythematous changes with uplifted edges and typically lasts several weeks. During the following stage, erythema subsides, leaving smooth scales. Patients generally report to outpatient clinics at the third and final stage. Clearly defined areas of depigmentation 0.5 to 5 cm in diameter and scaling off at the edges are observed at this stage. Pruritus may accompany the condition. Lesions persist for several months to a few years and resolve spontaneously; skin changes occasionally recur (2,20).

CLINICAL VARIANTS

There are three clinical variants of PA: classic (CPA), extensive (EPA), and pigmenting (PPA) (2) (Table 1). The first two variants occur in all skin phototypes. The pigmenting variant is typical of non-Caucasian populations from the Republic of South Africa (Cape coloreds) and the Middle East (26,27).

CPA is the most common form of disease and affects primary schoolchildren of both sexes (13). The areas of depigmentation with scaling margins are typically found around the lips, on the chin and cheeks. Plaques are well defined and numerous and have a diameter ranging from 0.5 to 2 cm. An

TABLE 1. *Clinical Variants of Pityriasis Alba*

Clinical variant	Classic		Extensive	
	Endemic	Atopy related	Idiopathic	Pigmenting
Description of lesions	Numerous, well-defined, 0.5- to 2-cm-diameter areas of depigmentation with scaling margins		Single, symmetric, areas of depigmentation >2 cm in diameter with scaling margins	Numerous, bluish, 1.5 cm in diameter, surrounded by halo of depigmented skin
Age	Primary school-age children (related to poor socioeconomic conditions)		Teenagers and young adults	Children and adolescents
Sex	Female = male		Female > male	Female > male
Localization	Face: perioral region, chin, cheeks		Trunk, shoulders, neck, surface of the upper limb extensor muscles	Face: forehead, cheeks
Frequency	Most common		Less common	Least common
Erythematous stage	+		—	—
Length of course	Short		Longer	Often with the mycotic infections (65%): tinea capitis, tinea faciale, classic variant (33%)
Response to treatment	Good		Weak	Fairly good

erythematous stage may precede them (2,13). CPA has the shortest course and the best response to treatment of the three variants (28).

Two forms of CPA have been described: endemic, related to poor socioeconomic conditions, and another type related to atopy (2).

EPA is a less common disease variant. It affects teenagers and young adults, more often females, and consists of single, symmetric lesions that are larger than in the other variants (diameter >2 cm). EPA is not limited to the face but involves the neck, trunk, shoulders, and surface of the upper limb extensor muscles (29,30). The treatment period is longer than for CPA (28).

Similar to CPA, it has two subcategories: idiopathic and atopic (2,31).

The least common variant is PPA. No cases of PPA have been recorded in a Caucasian population. It affects children and adolescents, usually females. Typical lesions are bluish, form from melanin deposits, and are surrounded by a halo of depigmented skin. Numerous lesions, typically 1.5 cm in diameter, are located on the forehead and cheeks (11,26,32). PPA often coexists with CPA and mycotic infections (26). Response to treatment is relatively good (27).

HISTOPATHOLOGIC PRESENTATION

Even though PA is widespread, there have been few studies including a histologic account of dermal lesions, although some researchers indicate that histopathologic analysis is helpful in establishing the correct diagnosis (29,33,34).

Vargas-Ocampo (33) presented results of biopsies conducted in 39 individuals with EPA. Keratotic aggregates blocking hair follicles (43% of cases), sebaceous gland atrophy (86%), and irregular pigmentation by melanin of the basal layer of epidermis and follicular spongiosis (71%) were observed in the early lesions.

Irregular pigmentation in the late stage has been recorded in all patients and is thus considered to be characteristic of PA. Regression of keratotic aggregates in hair follicles from the previous stage was noted, although compact built-up areas of keratin were found around sweat glands. Mild acanthosis was observed in the stratum spinosum, slight spongiosis around hair follicles, and epidermal exocytosis. Sebaceous gland atrophy affected 60% of patients, and in some case, the glands were almost completely absent. A slight swelling was observed surrounding hair follicles related to inflammatory infiltration dominated by lymphocytes and histiocytes. Melanophages

were recorded rarely, most typically in the papillary dermis (33).

In et al (34) performed histologic and immunochemical analyses of 59 fine-needle biopsies conducted in South Korea between 2000 and 2006. Fontana–Masson staining and S-100, MART-1, and NK1/beteb antibodies were used to evaluate pigmentation and melanocyte count. The amount of melanin in the pathologic epidermis was found to be significantly lower than in the nonaffected epidermis. The melanocyte count was nonsignificantly higher; no correlation with inflammation was observed (34).

DIFFERENTIAL DIAGNOSIS

In view of the many clinical variants of PA and varied lesion presentation at various disease stages, when differentiating the condition from other disorders, one must consider numerous, markedly dissimilar disease entities (1–4,31) (Table 2).

Vitiligo is a common condition of unknown etiology in which melanocytes are absent in involved areas (35). Areas of depigmentation usually appear on the face and acral parts of the limbs. Lesions are well defined and may keep a hyperchromic halo. In contrast to PA, no epidermal scaling or pruritus is

TABLE 2. *Differential Diagnosis of Pityriasis Alba*

Vitiligo	No scaling or peeling Complete loss of melanocytes observed under Wood's lamp
Tinea versicolor	In older children On back and trunk Hyphae and spores seen on potassium hydroxide test Yellow fluorescence seen under Wood's lamp
Hypomelanosis of Ito	Occurs at age 1 year Has irregular margins Coexistence of epileptic seizures
Fitzpatrick patches (ash-leaf spots)	Present at tuberous sclerosis Typically present at birth
Nevus depigmentosus = nevus achromicus	Congenital, usually more distinct at age 3 years Dermatome structure Involves trunk, back, and buttocks
Nevus anemicus	Nonpigmented congenital lesion formed as a result of enhanced vascularization around a seemingly lighter area Blood redistribution at diascopy
Mycosis fungoides	Rarely in the form of depigmentation More often in population >20 years of age and of darker skin Nonpeeling, nonscaling lesions on trunk and limbs Excess CD4 ⁺ T-cells in epidermis
Psoriasis	More pronounced and less smooth lesions Positive Auspitz sign

observed. Wood's lamp examination accentuates the chalk white patches as a result of complete depigmentation (2,28,36).

Tinea versicolor is a common inflammation caused by *Malassezia furfur* yeast. When ultraviolet (UV) light is applied to changes, yeast lesions lose color, whereas the surrounding skin increases in color. The above phenomenon may resemble PA. When conducting a differential diagnosis of the two diseases, one should focus on the patient's age and the location of changes. Tinea versicolor affects older children and eruptions are located on the trunk. Potassium hydroxide preparation reveals spores and hyphae of mycelium. Wood's lamp examination shows yellow fluorescence (2,28,37).

Psoriasis is a chronic condition that tends to remit and relapse. Like many other inflammatory conditions, it may resolve, leaving hypopigmented lesions. Inflammatory mediators (interleukin [IL]-6 and IL-7, tumor necrosis factor [TNF]- α and - β) increase the number of intercellular adhesion molecules 1 on the surface of melanocytes. There is an intensification of leukocyte infiltration and melanocyte phagocytosis. Disease differentiation in this case is based on patient history and the presence of typical papules manifested in psoriasis (1,38,39).

Hypomelanosis of Ito (incontinentia pigmenti achromians) is one of the phakomatoses. A Japanese dermatologist, Minor Ito, first described it in the 1950s (40). It is characterized by skin depigmentation following the lines of Blaschko. Loss of pigment may coexist with epileptic seizures and developmental anomalies of the bones and central nervous system (41).

Granuloma fungoides (mycosis fungoides) is the most common type of cutaneous T-cell lymphoma (42). Lesions are erythematous and infiltrative. Areas of depigmentation on the trunk and limbs may rarely manifest mycosis fungoides, but in contrast with PA, there is no epidermal flaking. Disease onset is typically observed at age 50 to 60 years (28,43).

Nevus depigmentosus is manifested by depigmented maculae, which are often present at birth and usually become more visible at the age of 3 years. They may affect the whole body and often follow dermatomes (2).

Nevus anemicus is a congenital nonpigmentary problem. Areas of locally high epidermal vascularization, which may cause the lesion to seem faded, surround the unaffected skin. Diascopy, a method associated with applying pressure to the skin lesion, leads to blood redistribution and makes nevus anemicus indistinguishable from the surrounding skin.

The differential diagnosis should also account for leprosy, scleroderma, hypopigmentary lesions formed in the course of inflammatory skin conditions, the effect of chemical and physical factors, and iatrogenic lesions (2,28).

TREATMENT

The primary objective of treatment is to limit the potential triggering factor. One needs to reduce exposure to sunlight, apply sunscreen daily, and in some patients decrease the frequency of baths or beauty treatments (3). The first attempts to treat PA were based on emollient creams. The effectiveness of emollient therapy is difficult to evaluate because of coexisting AD, for which PA is an identification criterion. Resolution of lesions may then be indicative of primary disease therapy efficacy rather than a response to PA treatment (3,12,20,21). Topical glucocorticoids have limited efficacy in individuals with CPA, although long-term treatment, lesions located on the face, and extensive PA limit their application (20,21,38). Positive effects were also observed with topical administration of hydrocortisone 0.5% and diiodohydroxyquinoline in children (44). Furthermore, the beneficial effects of topical tretinoin and UVA light therapy after photosensitization with psoralen were recorded (11,13,33).

Topical tacrolimus 1%, a macrolide immunosuppressant inhibiting the catalytic function of calcineurin, is reported to be effective. Tacrolimus binds to FKBP12, a cytoplasm molecule, inhibiting B-lymphocyte signal transduction. Consequently, TNF- α , interferon gamma, IL-2 and other cytokines responsible for humoral and cellular response are not produced. In addition, tacrolimus reduces the number of inflammatory mediators that mast cells, basophils, and eosinophils release. Antiinflammatory drugs are of particular importance in the first two stages of the disease. In *in vitro* experiments with human melanocytes, an activating effect of tacrolimus on tyrosinase and enhancement of melanin biosynthesis were demonstrated, despite cell growth suppression. Moreover, migration of cells treated with tacrolimus is markedly increased (45). Thanks to the effect on melanin synthesis, tacrolimus is effective when applied to hypopigmented areas in the third stage of disease (46). Pimecrolimus, another calcineurin inhibitor, has a comparable effect. Topical application of 1% cream significantly reduces itching, peeling, and extension of hypopigmented areas (47). Both products are safe and should be used instead of glucocorticoids, particularly in the case of long-lasting lesions on the face.

Pimecrolimus therapy is preferred because of a rarely reported burning sensation with tacrolimus application. Even though no clear relationship between the two drugs and skin infections has been demonstrated, viral infections need to be kept in mind. Few cases of molluscum contagiosum and herpes have been reported during treatment (lesions appeared more often when tacrolimus was used) (48).

Calcitriol therapy (0.0003%) also provides promising results. Its efficacy is comparable to that of tacrolimus (49).

Profound improvement of PA was observed after 308-nm excimer laser phototherapy, with no significant side effects (50).

CONCLUSIONS

Although PA is common, it remains enigmatic. It is understudied in northern latitudes because of its rarity in light-skinned individuals. This creates the risk of an underestimation of disease incidence, and in the long run, extends time to diagnosis. In addition, implementation of effective treatment may be delayed due to nonspecific, often only somewhat bothersome symptoms, which may go unnoticed until PA recurrence.

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