Juvenile pityriasis rubra pilaris: a case report with immunohistochemical and electromicroscopic studies

Jeng-Feng Chen¹, Hong-Wei Gao², Wei-Ming Wang¹*

¹Department of Dermatology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan
²Department of Pathology, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Case report

A 5-year-old male child was brought to our clinic with itchy hyperkeratotic scaly eruptions on the palms and soles which appeared 2 months ago. He was otherwise healthy and born full term by an uneventful vaginal delivery. Subsequently, similar skin lesions developed on his face, ears and scalp. The cephalocaudal spreading of hyperkeratotic lesions to his elbows, sacral area, lower abdomen, groins and knees was noted in the following 2 months. In addition, he was also found to have palmoplantar hyperhidrosis. His parents were non-consanguineous; they were a Taiwanese father and a Vietnamese mother. There was no similar skin manifestation disclosed in his family.

Dermatologic examination revealed multiple discrete erythematous hyperkeratotic papules on the forehead, bilateral cheeks and ears. These papules showed a tendency to coalesce into large hyperkeratotic plaques covered with fine and powdery scales in some areas (Figure 1A). Furfuraceous scaling of the scalp was prominent (Figure 1A). There were also several large well-circumscribed erythematous scaling plaques with many keratotic follicular papules around the margins on bilateral elbows and knees (Figure 1B). In addition, there were scattered erythematous scaly follicular and/or perifollicular papules with a prominent central keratotic plug affecting the lower abdomen and bilateral inguinal areas. Similar skin lesions were identified on the buttock. There were also diffuse reddish to orange palmoplantar keratoderma extending to the lateral and dorsal aspect of the hands and feet (Figures 1C and 1D). All the skin lesions exhibited a characteristic orange hue, which was most pronounced on the palms and soles.

The child's developmental and neurological evaluations were normal. Results from other laboratory examinations including complete blood count, biochemistry, level of immunoglobulin E and urine analysis were within normal limits. Examination of skin scrapings from both the scalp and elbow lesions (dissolved in 10% potassium hydroxide solution) did not reveal presence of spores or hyphae.

Histopathologic findings of the specimen obtained from right knee showed psoriasiform hyperplasia of the epidermis with alternating orthokeratosis and parakeratosis in both vertical and horizontal directions (Figures 2A and 2B). In addition, focal hypergranulosis, thick suprapapillary plates, broad rete ridges and sparse superficial perivascular infiltration were also observed (Figure 2A). Immunohistochemical results of the lesional skin for Ki-67 showed positive immunoreactivity of basal keratinocytes and many scattered suprabasal keratinocytes (Figure 2C). The normal basal staining pattern of Ki-67 without suprabasal staining was noted in the adjacent unaffected skin (Figure 2D).

Electron microscope results showed a decreased number of tonofilaments and desmosomes, but enlarged intercellular spaces. Interestingly, we noticed some abnormalities at the level of upper spinous and granular layer of the epidermis. Some membrane-bound lamellar structures were seen in the cytoplasm of the keratinocytes (Figure 3A) as well as the intercellular spaces. These abnormal lamellar entities were variable both in size and shape (Figure 3B). At higher magnification, heterogeneous shapes of these vesicles from empty to soccer ball-like or concentric onion-skin-like configurations were more clearly demonstrated (Figures 3C and 3D).

According to the clinicopathologic presentation, the child was diagnosed as type III juvenile pityriasis rubra pilaris
Juvenile pityriasis rubra pilaris

staining of Ki-67. Electron microscopic examination was also performed to evaluate any possible altered ultrastructure which may have contributed to the pathogenesis of PRP.

The underlying pathoetiology of PRP has not been fully elucidated. Several familial occurrences have led investigators to consider the genetic basis for this disorder. Genetic background may be important in a subset of patients; however, most cases seem to be sporadic with no definitive gene mutations identified. The derangement of vitamin A metabolism or deficiency of vitamin A as the cause of PRP has been an area of debate for decades. The good response of PRP patients to treatment with either systemic or topical retinoids suggested a possible role of vitamin A metabolism in the etiology of PRP.1 A preceding infection such as gastroenteritis or upper respiratory tract infection has been repeatedly reported to occur in juvenile PRP.1 These cases imply that bacterial antigens may trigger the manifestation of juvenile PRP. Several autoimmune disorders such as isolated IgA or hypogammaglobulinemia have also been recorded in association with juvenile PRP.1

(PRP). He was treated with topical hydrocortisone and 5% salicylic acid ointment to achieve moderate symptomatic relief.

Discussion

PRP, an uncommon papulosquamous dermatosis in children, has been categorized into different types. Although we report a case of type III juvenile PRP, the type IV juvenile circumscribed form has been described as the most common juvenile PRP in a large Taiwanese series.3 The majority of the reported cases were sporadic. Familial occurrence is rare; it was not until 1910 that the first familial case of PRP was reported. Most familial cases reported later showed an autosomal dominant inheritance with variable penetrance. Diagnosis is based on distinctive clinical features with supplemental histopathologic findings. Here we report a clinically and pathologically typical case of juvenile PRP. In addition, we attempt to investigate the nature of the affected epidermis using immunohistochemical staining of Ki-67. Electron microscopic examination was also performed to evaluate any possible altered ultrastructure which may have contributed to the pathogenesis of PRP.

The underlying pathoetiology of PRP has not been fully elucidated. Several familial occurrences have led investigators to consider the genetic basis for this disorder. Genetic background may be important in a subset of patients; however, most cases seem to be sporadic with no definitive gene mutations identified. The derangement of vitamin A metabolism or deficiency of vitamin A as the cause of PRP has been an area of debate for decades. The good response of PRP patients to treatment with either systemic or topical retinoids suggested a possible role of vitamin A metabolism in the etiology of PRP.2 A preceding infection such as gastroenteritis or upper respiratory tract infection has been repeatedly reported to occur in juvenile PRP.1 These cases imply that bacterial antigens may trigger the manifestation of juvenile PRP. Several autoimmune disorders such as isolated IgA or hypogammaglobulinemia have also been recorded in association with juvenile PRP.1

Figure 1  (A) Several discrete erythematous hyperkeratotic papules were noted on the forehead, cheek and ear, and coalesced into large hyperkeratotic plaques in some areas. Bran-like scaling of the scalp was also evident. (B) Large circumscribed erythematous hyperkeratotic plaques with satellite follicular hyperkeratotic papules were found on bilateral elbows and knees. (C,D) Diffuse palmoplantar keratoderma (not shown here) extend to the lateral and dorsal aspect of the hands and feet with an orange hue.
Our result is thus in line with previous cell kinetic studies, which support the view that PRP results from a hyperproliferative disorder of the epidermal keratinocytes. Immunohistochemical staining with a widely available marker, Ki-67 is shown to be a more convenient and economic way to evaluate the skin of suspected PRP cases.

In the electron microscopic investigation, we found a decreased number of tonofilaments and desmosomes, but enlarged intercellular spaces. Moreover, there was an increased number of membrane-bound lamellar structures in the cytoplasm and the intercellular area. Their concurrent presence both intracellularly and extracellularly indicated that these lamellar structures are altered keratinosomes and keratinosome-derived entities. Keratinosomes, which are synonymous to lamellar granules, are membrane-bound vesicular structures in the upper spinous layer and found most abundantly in the upper granular layer. Recently, a growing body of evidence has shown that these structures were found to play an important role in the transportation of various secretory molecules such as lipids, proteases, protease inhibitors and structural proteins. Keratinosomes can fuse with the cell membrane and expel the contents into the

suggested that a subset of patients may have underlying immunologic abnormality.

Whereas the relationship between PRP and psoriasis is not clear, both conditions are similar clinically and pathologically. In 1976, Niemi et al. studied 31 PRP patients using tritiated thymidine autoradiography, and found that the labeling index was raised in the lesional sites in comparison to the normal epidermis. Furthermore, the epidermal cell kinetic study conducted by Ralfs et al. also showed apparently elevated proliferative indices among PRP patients.

Ki-67 is a nuclear non-histone protein first described in 1983. It was originally defined by the prototype monoclonal antibody Ki-67, which was generated by immunizing mice with nuclei of the Hodgkin lymphoma cell line L428. The Ki-67 revealed no homology to any known polypeptide, and the function of the protein remained unclear. It is universally expressed in proliferating cells, but not detectable in resting cells. In normal human skin, Ki-67 expression is often restricted to the basal layer, where there is a high proliferative activity. In our case, we demonstrated an upregulation of Ki-67 expression in the PRP lesional epidermis in comparison to the adjacent non-affected skin.

Our result is thus in line with previous cell kinetic studies, which support the view that PRP results from a hyperproliferative disorder of the epidermal keratinocytes. Immunohistochemical staining with a widely available marker, Ki-67 is shown to be a more convenient and economic way to evaluate the skin of suspected PRP cases.

In the electron microscopic investigation, we found a decreased number of tonofilaments and desmosomes, but enlarged intercellular spaces. Moreover, there was an increased number of membrane-bound lamellar structures in the cytoplasm and the intercellular area. Their concurrent presence both intracellularly and extracellularly indicated that these lamellar structures are altered keratinosomes and keratinosome-derived entities. Keratinosomes, which are synonymous to lamellar granules, are membrane-bound vesicular structures in the upper spinous layer and found most abundantly in the upper granular layer. Recently, a growing body of evidence has shown that these structures were found to play an important role in the transportation of various secretory molecules such as lipids, proteases, protease inhibitors and structural proteins. Keratinosomes can fuse with the cell membrane and expel the contents into the

Figure 2  (A) Microscopic examination showed hyperkeratosis with psoriasiform hyperplasia, focal hypergranulosis, thick suprapapillary plates, broad rete ridges, narrow dermal papillae and sparse superficial perivascular infiltration (H&E, 200×). (B) Higher-power field highlighted the alternating orthokeratosis and parakeratosis in both vertical and horizontal directions (H&E, 400×). (C) Immunohistochemical stain of the specimen with Ki-67 revealed positive immunoreactivity of the basal as well as many suprabasal keratinocytes (200×). (D) The normal basal staining pattern of Ki-67 without suprabasal staining was noted in the adjacent unaffected skin (200×).
extracellular space, making them crucial in the formation of the protective, water-impermeable stratum corneum. Interestingly, studies focusing on ultrastructures of PRP and psoriasis revealed that keratinosomes seem to be increased in PRP but decreased in psoriasis. Abnormalities of the keratinosome and its related components have also been recently reported to result in several other distinct skin diseases. Our current study suggests that the identified altered keratinosomes might contribute to the pathogenesis of PRP. However, the precise mechanism resulting in the disease phenotype requires further investigation.

In conclusion, juvenile PRP is an uncommon papulosquamous disorder with an unclear pathophysiology. We report a typical case with an identified hyperproliferative activity shown in the lesional epidermis using the proliferation marker, Ki-67. In addition, we also describe some altered electron microscopic features. The formation of many abnormal keratinosomes indicates a disturbance which may have occurred during the process of keratinization. Although the current report is confined to a solitary case, it still potentially sheds light for further investigation on the pathogenesis of this disorder.

References


Figure 3  (A) Electron micrograph showed intracytoplasmic membrane-bound lamellated keratinosomes (arrow; 25,000×). (B) There are many variably-sized and shaped intercellular vesicular structures in the upper spinous layer of affected epidermis (arrows; 25,000×). (C,D) At higher magnification, heterogeneous shapes of these vesicles from soccer ball-like (35,000×) to concentric onion-skin-like configurations (60,000×) were more clearly resolved.

