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Circumscribed Juvenile-Onset Pityriasis Rubra Pilaris With Hypoparathyroidism and Brachyonychia

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Circumscribed juvenile-onset pityriasis rubra pilaris (PRP) manifests as well-defined erythematous scaly plaques with follicular keratosis mainly over the elbows and knees. There are several reports of the association of PRP with other conditions. We report a boy with scattered erythematosquamous skin lesions and follicular hyperkeratotic papules since he was 6 years old. Results of a skin biopsy were compatible with PRP. The patient also had hypoparathyroidism and brachyonychia. To our knowledge, this association has not been reported to date, though minor disturbances of calcium and vitamin D metabolism have been mentioned in some disorders of keratinization. We further discuss the epidemiologic, clinical, and pathologic features of PRP; review the conditions associated with brachyonychia; and give a brief discussion about the possible role of calcium metabolism in disorders of keratinization.

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Pityriasis rubra pilaris (PRP) refers to a heterogeneous group of idiopathic erythematosquamous diseases characterized in their classic forms by circumscribed follicular keratosis, palmoplantar keratoderma, and erythroderma.[1] Griffith[2] has classified the disease into 5 groups, among which types III to V occur in children. Type IV (circumscribed juvenile-onset PRP) presents with well-defined involvement, frequently of the knees and elbows. There also are other classifications.[3-5]

PRP has been associated with several cutaneous and noncutaneous conditions.[6-16] We report a constellation of PRP, hypoparathyroidism, and brachyonychia in a 10-year-old boy and discuss the clinicopathologic features of the disease and its associated conditions.

Case Report

A 10-year-old Iranian boy presented to our dermatology clinic with nonpruritic, slightly erythematous, scaly skin lesions affecting the face, trunk, and limbs since 4 years prior. The lesions had started insidiously and progressed over time. The boy's parents had not sought medical advice for the lesions. The patient also had a short, wide left thumbnail. His medical history was unremarkable except for infrequent episodes of muscle spasm. He did not have any history of atopic state. The patient took no medications. His parents were not consanguineous. The family medical history revealed primary hypoparathyroidism in his mother and 2 sisters, but his father and the only brother were healthy. There was no family history of skin diseases or brachyonychia.

On examination, the patient's blood pressure level was 105/75 mm Hg. The Trousseau sign (precipitation of carpopedal spasm by inflation of a blood pressure cuff applied to the forearm to 20 mm Hg above the systolic blood pressure level for 3 minutes) and Chvostek sign (involuntary twitching of the facial muscles by light tapping of the facial nerve just anterior to the external auditory meatus) were positive. These 2 signs, which are manifestations of latent tetany, prompted us to order laboratory tests for probable concealed hypocalcemia. The results of

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laboratory investigations are shown in the Table. Results of a dermatologic examination revealed discrete, well-defined, slightly erythematous and sometimes flesh-colored plaques with fine follicular scale distributed predominantly over the upper eyelid and the upper back and forearms, with prominent flesh-colored hyperkeratotic follicular papules on both elbows and knees. There also was moderate palmoplantar thickening with exaggeration of palmar creases. The patient had left thumb brachyonychia (Figures 1 and 2); the other nails were normal. There were no mucosal lesions. The clinical impression at that time included psoriasis and circumscribed juvenile-onset PRP as potential diagnoses.

The patient was treated with topical steroids and coal tar shampoo. He also was given oral calcium (1500 mg/d) and vitamin D (50,000 U/d). His skin lesions markedly improved in 6 months except for hyperkeratotic follicular papules on the elbows and knees.

One year after his initial presentation, the patient returned with exaggerated elbow and knee lesions after he discontinued steroid therapy (Figure 3). He had no lesions elsewhere. A skin biopsy from his left elbow revealed severe acanthosis with alternate orthokeratosis and parakeratosis, dense horny follicular plugging, focal hypergranulosis, and scanty dermal lymphocytic infiltrate (Figure 4). There was no spongiosis, thinning of the epidermis over dermal papillae, or polymorphonuclear cell exocytosis into the epidermis. The whole clinicopathologic feature was consistent with circumscribed juvenile-onset PRP (type IV, Griffith[2]).

Biochemical Values in the Patient Described

Variable	Value (Reference Range)
Total serum calcium, mg/dL	8.2 (8.6–10.6)
Serum inorganic phosphate, mg/dL	8.6 (≤6 for children)
Parathyroid hormone, pg/dL	9.1 (13–16)
Serum alkaline phosphatase, U/L	331 (45–450 [<17 y])
Serum magnesium, mg/dL	2 (1.7–2.1)

Comment

PRP was first described by Claudius Tarrel in 1835. The condition occurs equally in both sexes and has a bimodal age distribution with peaks in the first and fifth to sixth decades.[1] According to the Griffith classification,[2] type I (classic adult) and type III (classic juvenile) present with cephalocaudal eruption of follicular hyperkeratotic papules that coalesce into large, scaly, erythematous plaques with characteristic islands of sparing and palmoplantar keratoderma. Type II (atypical adult) and type V

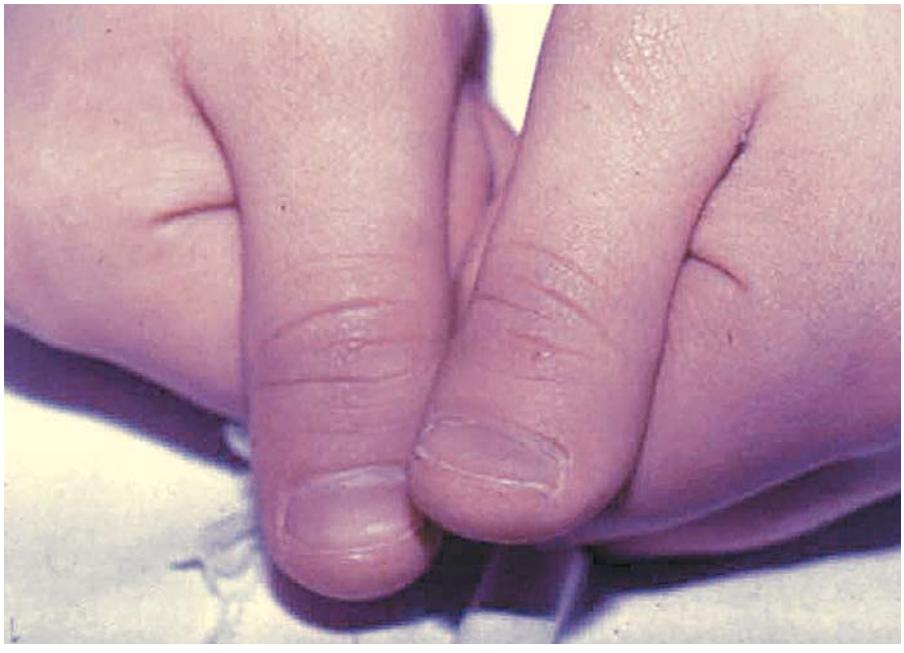

Figure 1. Left thumb brachyonychia.

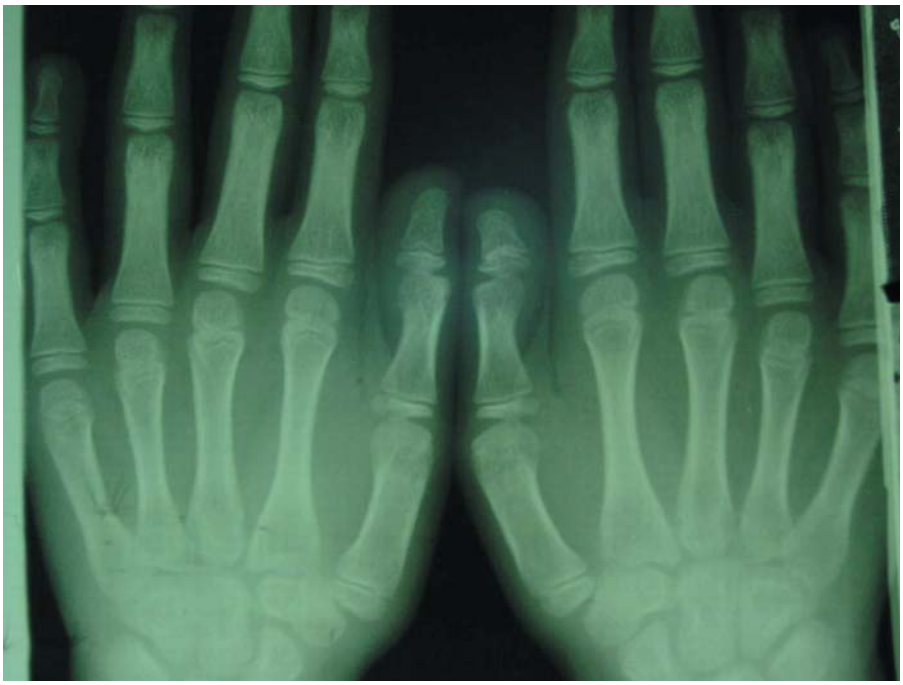

Figure 2. Radiograph of the hands showing a short distal phalanx in the left thumb.

(atypical juvenile) have atypical morphologic features, such as ichthyosiform scale, lamellar scaling of the palms and soles, and sclerodermatous changes of the fingers in type V. Type IV (circumscribed juvenile onset) is the most prevalent type of the disease in children,[1,3] though in one study it comprised only 33% of the childhood cases and ranked after type III.[17] The most frequent sites of involvement in type IV are elbows, palms, soles, knees, and nails.[17] There also may be a few scattered erythematosquamous patches on the trunk or scalp.[2] It does not progress to classic PRP; however, changes from type III to type IV have been reported.[5] In our patient, scattered erythematous lesions suggested psoriasis at first glance. Later, the prominent follicular hyperkeratosis of elbows and knees suggested PRP, which was confirmed by biopsy.

There also is a high incidence of palmoplantar involvement with erythematous thick plaques in juvenile PRP,[5] which has been reported as the second most common diagnostic feature of the disease,[3] though it is less common in the circumscribed form than in the other types.[5] Our patient showed only slight palmar thickening with exaggeration of palmar creases, which might be considered mild involvement.

Some kind of nail involvement occurs in 25% to 50% of cases of type IV PRP.[3,17] Nail changes in PRP include subungual hyperkeratosis, nail plate thickening, yellow-brown discoloration, and splinter hemorrhage. Onycholysis, salmon patches, small pits, and larger indentations of the nail plate occur less frequently and favor the diagnosis of psoriasis.[18] Brachyonychia as seen in our patient is not known to be a feature of PRP.

Racket nail (brachyonychia) is usually an autosomal-dominant trait with frequent thumb involvement.[19] Acquired forms occur in nail biters, patients with hyperparathyroidism with bone resorption, and patients with psoriatic arthropathy. It is also a feature of pseudohypoparathyroidism.[20] Our patient had neither a positive family history nor any of the

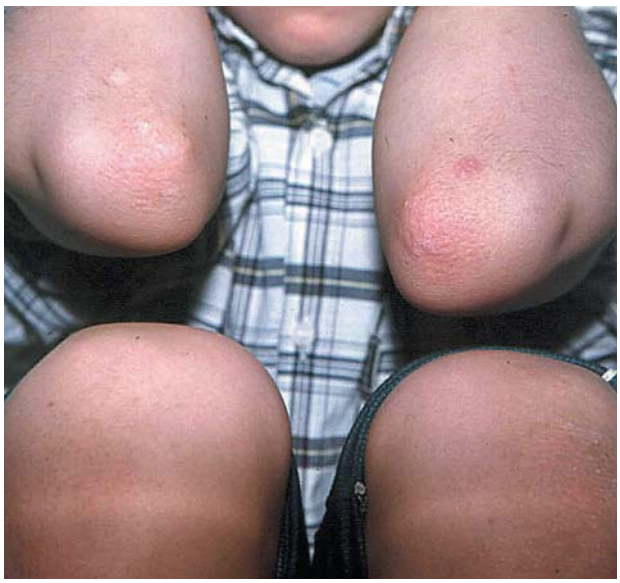

Figure 3. Follicular hyperkeratotic lesions on both elbows and knees.

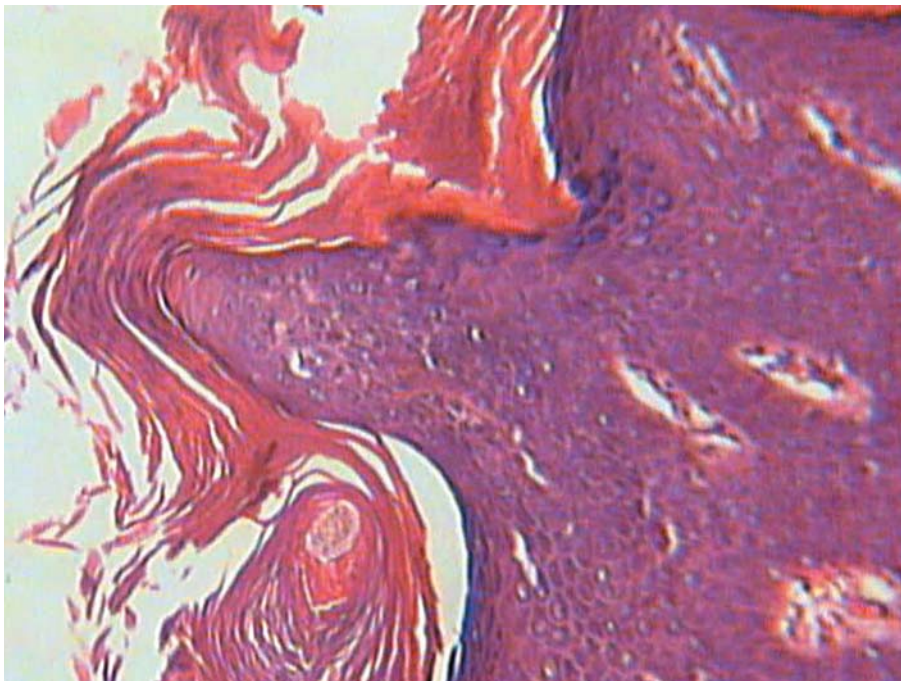

Figure 4. A skin biopsy from left elbow showing acanthosis, alternating orthokeratosis and parakeratosis, and focal hypergranulosis (H&E, original magnification ×200).

previously mentioned causes. This seems to be a sporadic case of isolated racquet thumbnail, which might be the result of a new mutation or variable penetration of a gene.

Histologic features of PRP include alternating orthokeratosis and parakeratosis; focal or confluent hypergranulosis; thick suprapapillary plates; broad rete ridges and narrow dermal papillae; small superficial, dermal lymphocytic infiltrate; and follicular plugging, which only is seen in clinically follicular hyperkeratotic lesions.[21] Some patients show acantholytic dyskeratosis. Type I appears more psoriasiform with less acanthosis and hypergranulosis.[1] We ruled out the diagnosis of psoriasis because there was neither thinning of the suprapapillary epidermis nor polymorphonuclear cell exocytosis into the epidermis.

PRP has been associated with myasthenia gravis[8]; hypothyroidism[9]; celiac sprue[10]; and malignancies, such as metastatic adenocarcinoma,[13] multiple cutaneous squamous cell carcinoma and Merkel cell carcinoma,[14] hepatocellular carcinoma,[15] and leukemia.[16] Type IV PRP has been associated with Down syndrome and vitiligo.[6,7] Types I, II, and V have been associated with seronegative arthropathy.[11,12] There is a single report of elevated parathyroid hormone in PRP secondary to hypocalcemia.[22] In this study, hypocalcemia was attributed to extensive loss of calcium or lower vitamin D synthesis through the diseased skin, and it was not a primary phenomenon.[22]

Can primary abnormalities of calcium metabolism play a role in the pathogenesis of disorders of keratinization? The answer is not clear yet, but there are some leading points in this area. It has been shown that calcium, which is present only in the lowest layers of normal stratum corneum, counteracts the effect of cholesterol sulfate in stabilizing stratum corneum lipid organization.[23] In the model systems of stratum corneum vesicles, calcium neutralizes the fatty acids in the lipid bilayer of these vesicles and causes intervesicle lipid mixing followed by vesicle fusion and lysis—an effect that is prevented by the addition of cholesterol sulfate.[24] Knowing that a drop in cholesterol sulfate levels in the superficial layers of the stratum corneum causes destabilization of the lipid lamellar phases and facilitates the desquamation process, one might consider that abnormally low concentrations of extracellular calcium may enhance the activity of cholesterol sulfate and impede the normal desquamation process, possibly leading to the hyperkeratosis and follicular plugging seen in PRP. Our patient had familial hypoparathyroidism, which to our knowledge has not been reported to be associated with PRP. Currently, we have no explanation for this association. Further investigations might reveal in-depth information about the role of abnormalities of calcium metabolism in disorders of keratinization.

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