Progressive symmetric erythrokeratodermia with delayed intellectual milestones and convulsions

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ABSTRACT

Progressive symmetric erythrokeratoderma is an uncommon genodermatosis and is thought to arise due to mutations in the *connexin* gene, however, genetic heterogenicity has been described. Very few cases of neurological involvement have been described in this unusual entity. We report a case of progressive symmetric erythrokeratoderma, with convulsions and delayed intellectual milestones.

Key words: Convulsions, loricrin, progressive symmetric erythrokeratoderma

INTRODUCTION

A 10-year-old child was brought by his parents for a symmetrical thickening and scaling on its hands, feet, and knees. The child had a history suggestive of erythroderma in its first week of birth, which gradually developed into symmetrical lesions that had progressed until the present time. They were non-migratory in nature. He also had delayed intellectual milestones and had a history of convulsions, which on evaluation, had not been explained sufficiently. We report an unusual case of progressive symmetric erythroderma (PSEK) with neurological involvement.

CASE REPORT

A 10-year-old boy was brought to this clinic (SV) by his parents who were concerned about the rough, dry, and scaly skin over both his hands and feet, which always seemed worse during winters. The boy was born by normal vaginal delivery, had neonatal jaundice at birth, and was given phototherapy. The parents said that they had noticed scaly, wrinkled, and reddish skin, which the child shed when about a week old, and this was followed by wrinkled, thickened, scaly, and reddish skin in very well-demarcated areas of the hands and feet in a couple of weeks after birth. He also had profuse scaling of the scalp and had no hair at the time of birth. The obstetrician had told the parents that he may be a mongoloid child and that he should be followed up. Three weeks after birth the child started shedding skin all over the body and was treated with simple emollients. There were no vesicles or bullae, no infections or any systemic abnormalities. The hyperkeratotic areas increased gradually for the first two-to-three years of life and then became static.

On examination the skin over both his hands and forearms was scaly and thickened in a well-demarcated manner, almost like gloves and socks, with the hyperkeratosis and scaling extending along the medial aspect of the forearm up to the elbows, where it abruptly ended [Figures 1-3]. Similarly he had thickened scaly skin over the dorsa of both feet, extending about 4 cm above the malleoli in the socks area. Erythema was not appreciated in the lesions, except until he was two-to-three years old. The palms and soles were mildly thickened, but there was no fissuring or scaling. The trunk, neck, proximal extremities, scalp, and face were normal. His nails, hair and teeth were normal. The child was a slow learner and was withdrawn. He had undergone neuropsychiatric evaluation twice and was found to be two years younger than his chronological age, however, exact documentation was not available and a suggestion to get a re-evaluation done was taken negatively by the parents. He had generalized convulsions for the first time when he was two-and-a-half years of age and was put on sodium

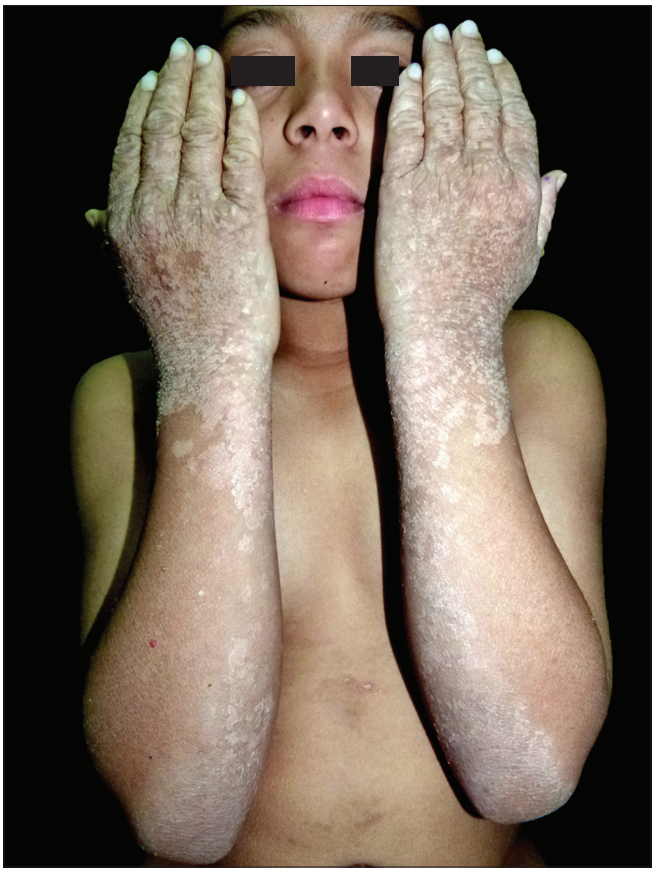

Figure 1: Symmetrical hyperkeratosis with scaling over both hands extending medially up to the elbows

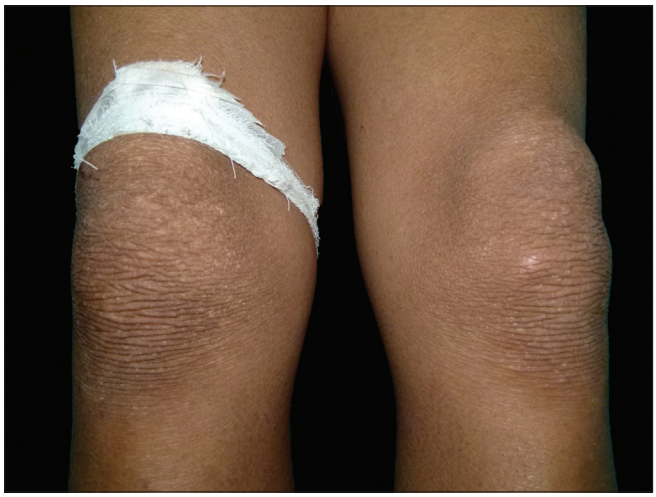

Figure 3: Symmetrical hyperkeratosis with accentuated creases over both knees

valproate. Magnetic resonance imaging (MRI) of the brain was normal. He had convulsions about once a year, and it was invariably when the parents tried to wean him off sodium valproate. No explanation was been given by anyone for this phenomenon. A biopsy of the lesion on his hand showed sparse superficial perivascular lymphocytic infiltrate in the dermis, with slight epidermal hyperplasia. The epidermis

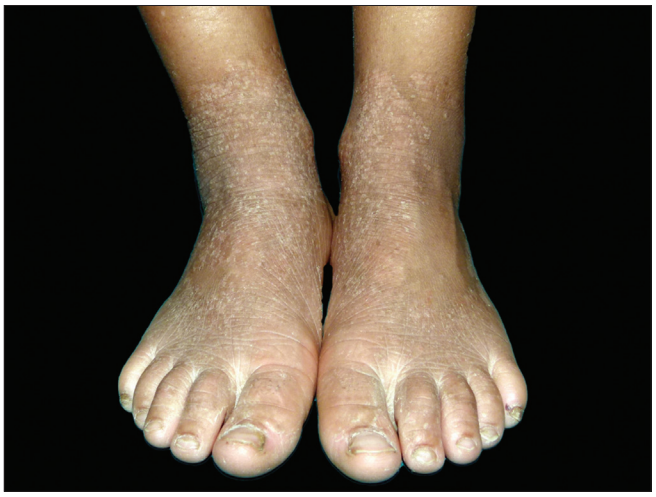

Figure 2: Symmetrical hyperkeratosis with fine scales over both feet, up to the ankle, in the 'socks' area

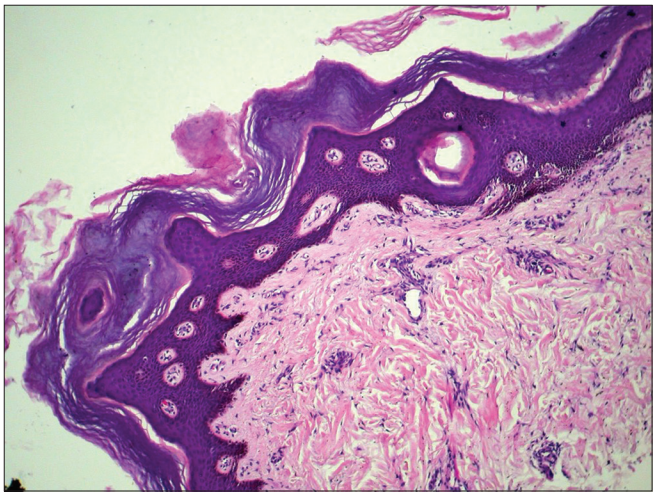

Figure 4: Lamellated hyperkeratosis, intact granular layer, acanthosis, and mild spongiosis, with mild perivascular lymphocytic infiltrate

showed acanthosis in some areas, mild focal spongiosis with an intact granular layer and a moderately thickened stratum corneum showing lamellated hyperkeratosis, with parakeratosis being visible only in some fields [Figure 4]. On the basis of the clinicopathological correlation, a diagnosis of progressive symmetric erythrokeratoderma (PSEK) was made.

He is under treatment with salicylic acid ointment and a urea-based cream, with marginal improvement. Taking his young age into consideration the parents did not allow administration of oral retinoids.

DISCUSSION

Progressive symmetric erythrokeratoderma is a rare type of erythrokeratodermia inherited in an autosomal dominant fashion in about 50% of the cases. The entity is characterized by non-migratory, erythematous or hyperpigmented,

symmetric plaques that are usually distributed on the extremities, buttocks, and sometimes the face. The histology is nonspecific in PSEK. Orthokeratosis, orthohyperkeratosis with focal parakeratosis, a well-preserved granular layer, psoriasiform hyperplasia without thinned suprapapillary plates, and a perivascular infiltrate of lymphocytes in the upper part of the dermis, have all been reported.[1-4] Associated neurological abnormalities, including deafness, have been described rarely, as seen in this case.[5]

Progressive symmetric erythrokeratoderma is clinically different from erythrokeratoderma variabilis (EKV) first described by Mendes da Costa) its closest differential diagnosis, by well-demarcated *non-migratory* erythematous plaques in contrast to the migratory plaques seen in the latter.[6] The erythema component of the erythrokeratoderma seems not to be relevant to populations with Type IV – VI skin, as the erythema is not easily appreciated on dark skin, as is evident from many other dermatoses in these populations.

The candidate gene for EK-related mutation is *connexin* (*CON*).[7-10] CON mutations result in disturbed cell–cell communication due to faulty gap junctions. CON mutations have been identified in both the PSEK and EKV families, including CON 31 (GJB3) and CON 30.3 (GJB4).[10] On the other hand, some families have no CON mutations at all.[11] The available data suggest some genetic heterogeneity of PSEK. A 27-year-old female PSEK patient from Japan and her family were analyzed for loricrin (LOR) mutations. Loricrin is a major constituent of the epidermal cornified cell envelope. Indeed, the authors could detect a single-base-pair insertion of a C following nucleotide 709 leading to a frame shift into the missense amino acids and the addition of further 65 amino acids to the molecule.[6] Recent investigations suggested that the LOR mutation in the case described above might be due to the occurrence of the Vohwinkel's syndrome in the same family, and PSEK was not associated with the LOR mutations at all.[7]

We are unable to explain the delayed milestones, learning disability, and convulsions in this case, although there are only scattered reports of neurological involvement in the erythrokeratodermas.[1-5] Therefore, the occurrence of neurological symptoms may just be a coincidence. Further studies are needed to come to a final conclusion.

Topical emollients and salicylic acid ointment, along with urea, was the recommended treatment, but was only of marginal benefit in the present patient.[12] Etretinate and acetretin had been tried too, with varying success.[13]

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