

## Bilateral verruciform lesions: A new CHILD syndrome presentation

Dear Editor,

CHILD syndrome (congenital hemidyplasia with ichthyosiform nevus and limb defects syndrome) is a rare X-linked dominant disorder which is lethal in hemizygous males. Unilateral congenital hemidyplasia with ichthyosiform erythroderma and ipsilateral limb defects characterize this condition. A large proportion of patients with this condition have unilateral ichthyosiform erythroderma lesions, with a few having verrucous xanthoma-like symptoms. A rare case of CHILD syndrome with bilateral verruciform lesions is described.

A 30-year-old Chinese woman presented with keratotic papules on her left and right extremities which had been present since birth. Following a Blaschko linear distribution, the skin lesions had steadily increased with age. Lesions

appeared on the left jaw as well. In addition, the left leg and spine of the patient were shorter than the right. There were no signs of cognitive impairment in the patient. There were no other serious diseases in the past. Ten years ago, patient had a bacterial infection of the skin lesions over the left ankle joint which was treated surgically leaving behind scars. There was nothing significant in the family history.

The patient was 130 cm tall and weighed 36 kg. Her left lower limb was shorter than her right one. Dermatological examination revealed verruciform lesions over the left mandible and bilaterally over hands and feet [Figure 1]. Hyperkeratosis and parakeratosis in the epidermis, as well as dense histiocytic infiltrates and foamy cells in the dermis were found on histopathological examination [Figure 2]. The routine blood and urine tests revealed nothing unusual. X-ray



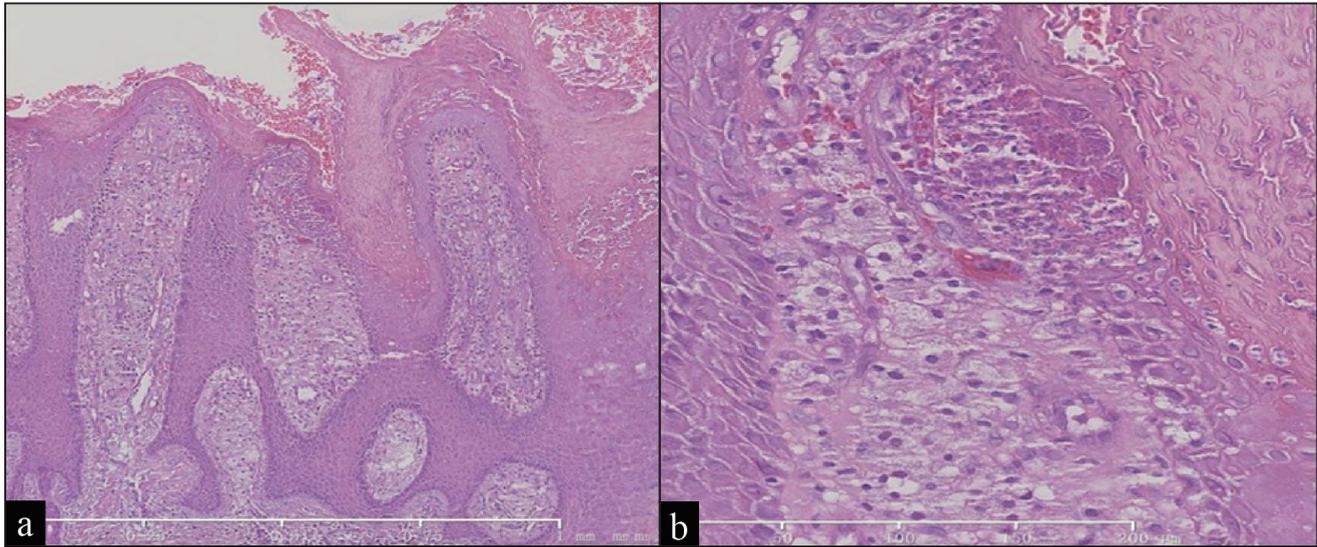
**Figure 1:** A dermatological examination revealed verrucous papules and plaques that were distributed in the left mandible, hands, and feet in a linear pattern. Figure 1e is an enlarged image of the localized skin lesion in Figure 1f

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**Figure 2:** Histopathological examination revealed epidermis hyperkeratosis and parakeratosis, as well as dense histiocytic infiltrates and foamy cells in the dermis (a, haematoxylin and eosin,  $\times 25$ ; b, haematoxylin and eosin,  $\times 200$ )



**Figure 3:** An X-ray examination revealed that the spine was twisted to the left. The left tibia was shorter and thinner than the right tibia, and the fifth toe was missing; (a) arrows point to the leftward curvature of the spine, (b-c) arrows point to the left tibia, (d-e) arrows point to the stumped fifth toe.

examination of spine showed scoliosis to the left [Figure 3]. The left tibia was shorter and thinner than the right, and fifth toe on the left foot was missing (white arrow).

Genetic sequencing revealed c.766C>T nonsense mutations in the nicotinamide adenine dinucleotide phosphate-dependent steroid dehydrogenase-like genes. This was linked to the dependent steroid dehydrogenase-like gene's p.R256X amino acids, which hindered protein activity. Gene sequencing of the enhancer-binding proteins produced negative results.

The patient was diagnosed with CHILD syndrome based on her clinical symptoms and gene alterations.

Happle and colleagues initially characterized the CHILD syndrome in 1980.<sup>1</sup> The right side of the body is usually affected by CHILD syndrome lesions. On the right side of the body, almost two-thirds of patients have a clear midline delineation. Right-sided lesions affect about a third of the patients.<sup>2</sup> There have only been two occurrences of bilateral involvement documented.<sup>3,4</sup> More than 60 patients with

CHILD syndrome have been previously reported, but only 12 of them had verruciform lesions. The remaining patients had ichthyosiform erythroderma. Our patient did not have erythematous lesion. To the best of our knowledge, our patient might be the first case of CHILD syndrome to develop bilateral verrucous lesions.

The clinical history, histopathology and congenital history can help distinguish CHILD syndrome from other similar conditions. A histopathological examination should be used to differentiate the verruciform lesions of CHILD syndrome from other linear keratinized diseases, such as inflammatory linear verrucous epidermal nevus. CHILD syndrome has histopathological findings that are similar to xanthomatous diseases. Hence it should be distinguished from conditions like Simple verrucous xanthoma, clinically. Furthermore, some congenital skin diseases with bone dysplasia have clinical manifestations similar to CHILD syndrome. Hence, histopathological examination and genetic screening should be performed to rule out conditions like X-linked dominant chondrodysplasia punctata type 2, which is an X-linked dominant disorder caused by mutations in the gene encoding enhancer-binding proteins.<sup>5</sup>

There is currently no specific treatment for CHILD syndrome. Verruciform lesions are treated in the same way as that of ichthyosis, with topical application of keratolytics, lubricants, and corticosteroids. These methods only provide temporary relief from dermatologic symptoms, have limited therapeutic efficacy and are often poorly tolerated by patients. Based on the abnormal lipid metabolism in the pathogenesis, there are a few reports of successful treatment of skin lesions of CHILD syndrome with simvastatin ointment. However, the efficacy and safety of these drugs are yet to be confirmed in larger clinical trials. It has been found that verruciform lesions in CHILD syndrome have a favorable prognosis. Malignant tumors were not found in any of the 12 previously reported cases.

The phenotype and genotype of this disease were not found to be correlated in the literature. Our patient's dependent steroid dehydrogenase-like gene had a c.766C > T (p.R256X) mutation in exon8. Only one of the previously discovered mutation sites agreed with our findings, but this patient had ichthyosiform erythroderma lesions on the left side.<sup>6</sup> This Hence it is assumed that a link between the site of gene mutation and phenotype is unlikely.

While genetic testing accurately diagnosed the disease, clinical manifestations vary greatly, making it difficult to choose which gene to screen. Our case serves as a reminder to clinicians to test for the dependent steroid dehydrogenase-like gene in patients who have congenital bilateral verruciform lesions.

#### Declaration of patient consent

Patient consent is not required as the patient's identity is not disclosed or compromised.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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