Vitamin D deficiency rickets in a child with xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a rare autosomal recessive genetic disorder of DNA repair characterized by an extreme sensitivity to ultraviolet (UV) rays from sunlight and an inability to repair damage caused by UV light [1]. It is a genetically heterogeneous genodermatosis and is classified into several groups based on the genes involved [2]. Till date, mutations of nine genes have been found to be associated with this disorder [3]. The most common form is related to the mutations in XP, complementation (XPC) gene (XPC Group C) located on chromosome 3 [3]. The incidence of XP appears to be low in India as compared to several other countries such as Pakistan, Egypt, and Nigeria where the rates of consanguinity are high [2].

In patients with XP, sun exposure causes severe sunburn, and most of the children develop freckling of the skin in sun-exposed areas by 2 years of age. The exposure to sunlight also results in dry skin and changes in skin pigmentation. Patients may also develop the ocular surface disease, oral lesions, and neurological problems [1,2]. There is no cure available for these patients except avoiding the sun exposure. In addition, patients with XP need to avoid the high-intensity light sources such as energy saving fluorescent lamps which emit high levels of UV radiation [2]. The lack of ability to repair the UV-mediated DNA damage increases the risk of skin cancers [1]. Due to such drastic effects of sun exposure, patients with XP are advised strict photoprotection which often hampers the cutaneous synthesis of Vitamin D and results in Vitamin D deficiency (VDD) if adequate oral Vitamin D supplementation is not provided.

A 9-year-old boy presented with progressive lateral bowing of legs for the past 2 years. Since infancy, he had dryness and scaling of skin along with increased pigmentation and severe photosensitivity forcing parents to avoid sun exposure. There were no systemic complaints and no family history of a similar disorder. Skin examination revealed dry, scaly and hyperpigmented skin with interspersed hypopigmented areas, and actinic keratosis over the back suggesting a diagnosis of XP (Fig. 1a). Physical examination revealed signs of rickets including rachitic rosary, widening of wrists and genu valgum (Fig. 1b). Ocular, neurological and systemic examinations were unremarkable.

Biochemical investigations revealed normal serum calcium (8.9 mg/dL, normal range 8.8–10.2 mg/dL), low normal serum phosphate (4.0 mg/dL, normal range 3.6–5.8 mg/dL), and markedly elevated alkaline phosphatase (1325 U/L, normal range 86–315 U/L). Serum 25 - dihydroxyvitamin D was very low (<3 ng/mL, normal >20 ng/mL) while serum parathyroid hormone was elevated (484.4 pg/mL, normal range 15–65 pg/mL). Radiographs revealed splaying and fraying of metaphyseal ends of femur and tibia along with valgus deformity (Fig. 1c). A diagnosis of VDD rickets was made, and the patient was given cholecalciferol (60000 IU/day for 10 days followed by 1000 IU/day). Repeat laboratory evaluation 4 weeks later showed normal biochemical parameters. Lifelong oral cholecalciferol supplementation (1000 IU/day) was advised.

Several skin disorders which require photoprotection to avoid exacerbation of symptoms predispose patients to VDD [4]. XP is one such disorder characterized by defective repair of UV irradiation-induced DNA damage and >10,000-fold higher risk to develop sunlight-induced skin cancer [5]. Patients are advised strict photoprotection to prevent UV-induced DNA damage [1,5]. Such rigorous photoprotection often results in VDD manifesting as rickets or osteomalacia as cutaneous production of Vitamin D is also UV-mediated [6]. VDD is indeed common in XP patients who do not receive adequate oral Vitamin D. In a recent study from Japan, all the 21 patients with XP had Vitamin D levels <20 ng/mL; 76% had levels as low as <10 ng/mL [5]. The authors recommended lifelong Vitamin D supplementation (1000 IU/day) to avoid unfavorable skeletal consequences in patients with XP [5].

Furthermore, improving the Vitamin D status would be beneficial for patients with XP as recent epidemiological data suggest that higher Vitamin D levels are associated with reduced risk and improved survival of patients with skin cancers [7]. Our case highlights the need for oral Vitamin D supplementation in patients with XP and the deleterious skeletal consequences if the same is not provided. In our country, the comprehensive care of children with XP does not often include provision of Vitamin D supplements probably due to focus on the more troublesome disease complications [2] or lack of realization of VDD and its consequences [8,9]. Furthermore, physicians often avoid using larger supplementation doses of Vitamin D in children due to fear of hypervitaminosis D; although this complication occurs only if there is an underlying condition such as a granulomatous disease-causing overproduction of 1,25 dihydroxyvitamin D [10].

Current evidence supports the provision of at least 1000 IU/day of Vitamin D in patients with XP; although the requirements in Indian children may be higher due to several factors [5,9]. The treating physicians should routinely prescribe oral Vitamin D as part of the standard care of patients with XP.

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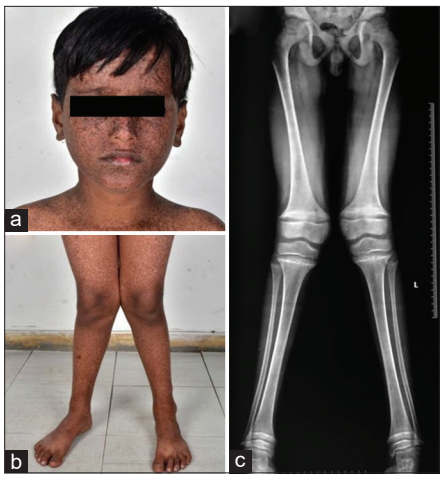

Figure 1: Photograph showing dry, scaly and hyperpigmented skin (a), genu valgum (b) and changes of rickets in the metaphyses of femur and tibia (c)

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