Acute and chronic UV exposure is an important risk factor leading to photocarcinogenesis, photoimmunosuppression and photoaging (1, 2). Patients with Gorlin syndrome (GS) harbour a hereditary predisposition to develop basal cell carcinomas (BCC) and are, therefore, advised that effective sun protection is essential and can help reduce skin cancer risk (1–4). On the other hand, adherence to strict sun-protection habits can result in vitamin D deficiency, which has been demonstrated in many patients with GS (2, 3). Vitamin D deficiency is associated with an increased risk of osteomalacia, bone fractures, autoimmune diseases, cancer and cardiovascular disease (1).

CASE REPORT

Here, we report a 54-year-old man with GS who was admitted to our hospital for surgical treatment of multiple BCC (Fig. 1). Characteristic features of GS were present in the form of multiple BCC since youth, palmoplantar pits, an odontogenic cyst, calcification of the falx cerebri, and positive family history (5). DNA analysis by multiplex ligation-dependent probe amplification revealed a novel heterozygous deletion of exons 11 and 12 within the PTCH1 gene, leading to a frame shift and premature termination codon. Moreover, the patient’s medical history revealed that within the past decades, multiple bone fractures had occurred after minimal trauma, suggesting a bone calcification disorder. The patient reported of his strict photoprotection habits by daily textile and cosmetic sun protection measures as well as trying to avoid sun exposure. Laboratory work-up including parameters of bone turnover and metabolism showed serum 25(OH)D levels of < 4 ng/ml, far below the normal range (30–70 ng/ml), elevated alkaline phosphatase and low serum phosphate concentrations. Serum calcium, parathyroid hormone and vitamin A, E and K concentrations were within normal ranges. Dual-energy X-ray absorptiometry (DEXA) was consistent with severe osteoporosis according to the WHO classification, with a mean T-score of −3.6 measured from the hip (Fig. 2). Based on these observations, we concluded that the patient suffered from a disorder of bone mineralisation caused by vitamin D deficiency. Substitution therapy was initiated with a single dose of intramuscularly administered vitamin D3 derivative (cholecalciferol 100,000 IU) followed by long-term daily oral substitution of 2,000 IU of vitamin D3. The 25(OH)D level was within the normal range 3 months after initiation of therapy.

Vitamin D deficiency has been described in GS patients and is thought to be related to strict sun protection habits (1–3). The time of vitamin D measurement in our patient was spring (April), where probands usually have higher vitamin D levels than during winter (2), but they were still below the detection limit of the laboratory test. Normal serum levels of the other lipophilic vitamins (vitamins A, E, K) argue against an intestinal malabsorption disorder or an imbalanced overall nutritional vitamin supply in our patient. There were no signs of renal or hepatic insufficiency which could have influenced vitamin D metabolism (6).

DISCUSSION

Vitamin D deficiency is well-known in GS patients (3), but no data have so far been available regarding the clinical relevance (2). Our patient experienced multiple bone fractures due to insufficient bone mineralisation and had a high need for vitamin D substitution.

The present case shows that strict photoprotection habits of GS patients are a double-edged sword.
Therefore, we strongly support the plea for analysis of vitamin D levels in GS patients (3). Moreover, a thorough screening for clinical features heralding a vitamin D deficiency is recommended. Interestingly, in vitamin D receptor deficient mice (serving as model of vitamin D deficiency), BCC development was shown after UV exposure and was attributed to overactivation of the hedgehog signalling pathway, which is also the pathophysiological basis for BCC development in GS patients (7, 8). Hence, iatrogenic vitamin D deficiency of GS patients could even represent an environmental factor enhancing BCC development in these individuals.

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