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Varied, unprecedented dermatologic manifestations of hypovitaminosis D –A case series

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ABSTRACT

Vitamin D deficiency is endemic in India. Hypovitaminosis D not only results in musculoskeletal disorders but also affects extraskeletal systems. In this article, we describe three interesting patients suffering from hypovitaminosis D with dermatologic manifestations of erythema nodosum, heel fissures, and palmar hyperhidrosis. All the three cases responded well to treatment with vitamin D. Similar cases have not been reported earlier.

Key words: Hypovitaminosis D; Erythema nodosum; Heel fissures; Palmar hyperhidrosis

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INTRODUCTION

Vitamin D deficiency (hypovitaminosis D) is endemic in India, with a prevalence of around 70–100%.[1] Hypovitaminosis D deficiency is most underdiagnosed and undertreated nutritional deficiency in the world.[2-4] The source of vitamin D is primarily from skin through synthesis on exposure of ultraviolet –B rays. More time spent indoors with mobile phones or laptop in hand and less exposure to sunlight, cultural and social taboos dictating lifestyle patterns such as clothing, vegetarianism in most Indians, and reduced vitamin D synthesis in dark skinned people are the main reason for rising prevalence of hypovitaminosis D. Hypovitaminosis D not only results in musculoskeletal disorder but also affects extraskeletal system.[5,6] In this case series, we report three undescribed dermatogic manifestations of hypovitaminosis D.

PATIENT DETAILS

Patient 1

A 49-year-old female in government service was hospitalized in August 2016 with severe generalized muscle pain, vomiting, anorexia, fever, malaise, joint pain and multiple 1–2 cm, painful, and nodular swellings on the both sole of feet for 3–4 days. She had history of

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recurrent episodes of similar swellings in the past for 3 years preceding to this event and these swellings subsided each time with a course of antibiotics and analgesics, which was diagnosed as idiopathic erythema nodosum by treating physician. She was also complaining of recurrent headache in past, diagnosed as chronic tension headache and had relief with flunarizine. On examination, she was conscious, pulse 110/min, blood pressure 140/90 mm of Hg, and systemic examination did not reveal any abnormality. On investigation, complete blood count, kidney and liver function test, sugar (fasting), lipid profile, uric acid, calcium, phosphorus levels in blood, electrocardiogram, chest skiagram, and computerized tomographic scan of thorax were normal. The ultrasonography of whole abdomen showed cholelithiasis, thyroid stimulating hormone level was mildly raised (8.2 μIU/ml) with normal free T4 level, and serum vitamin D level was very low (10 ng/ml). She was treated during hospitalization with intravenous fluid, injection pantoprazole, ondansetron, paracetamol infusion, and amoxicillin-clavulanic acid. Cholecalciferol 60000 U orally once weekly was started and continued for 10 weeks followed by once monthly maintained for the past 6 years and her follow-up vitamin D level was normal during that period. She did not suffer from a single episode of erythema nodosum lesion during past 6 years until September 2022. She was also receiving levothyroxine 25 μg/day.

Patient 2

A 50-year-old female homemaker attended out-patient department with complaint of generalized aches and cracked heel in the month of December 2017. She observed that these cracked heel during winter months each year. On examination, her pulse was 84/min, blood pressure was 128/84 mm of Hg, and systemic examination did not reveal any abnormality. On investigation, complete blood count, sugar (F), lipid profile, kidney and liver function test, calcium and phosphorus, chest skiagram, electrocardiogram, and ultrasonography of whole abdomen were normal. Her vitamin D level was low (14 ng/ml). She received treatment with paracetamol 1000mg thrice daily and oral cholecalciferol 60000 U every week for 10 weeks followed by once monthly continued for the past 5 years to maintain the normal vitamin D level. On follow-up, she did not notice cracked heel during winter months during past 5 years.

Patient 3

A 22-year-old male student with complaint of multiple 1–3 mm pustulonodular lesions over face and upper trunk and excessive sweating over both palm in May 2019. On physical examination, no abnormality was detected. His complete blood count, sugar (F), kidney and liver function tests, and thyroid-stimulating hormone level were normal, but vitamin D level was below normal level (19 ng/ml). A course of oral doxycycline, topical retinoids, and oral cholecalciferol in a dose of 60000 U once weekly for 10 weeks was prescribed. Cholecalciferol was continued once monthly and excessive palmar sweating subsided.

DISCUSSION

Human beings obtain a adequate amount of vitamin D either from adequate exposure of the skin to sunlight or from their diet. Vitamin D exists in two forms, namely, vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol). Vitamin D_3 is produced in the skin on exposure to sunlight and is found in animal food sources, for example, fatty fish (e.g., salmon, mackerel, and tuna), cod liver oil, and milk. The source of Vitamin D_2 is from sun-exposed yeast and mushrooms. Vitamin D (both forms D_3 or D_2) is a prohormone which requires two hydroxylations. The first hydroxylation occurs in the liver to form 25-hydroxyvitamin D, also known as 25(OH) D or calcidiol. The second hydroxylation occurring primarily but not exclusively in the kidneys to form 1.25 $(OH)_2$ D, also known as calcitriol. This active form of vitamin D [1.25 $(OH)_2$ D] is released in blood, which reaches its target tissues to exert its endocrine functions through the vitamin D receptor (VDR). Vitamin D deficiency is defined as 25 (OH) D <20 ng/mL, insufficiency as 20–29 ng/mL, and sufficiency as ≥30 ng/mL[1].

Musculoskeletal pain, recurrent erythema nodosum, chronic tension headache, subclinical hypothyroidism, cholelithiasis, and vitamin D deficiency were the clinico-biochemical abnormality in first patient of this study. Chronic tension headache and musculoskeletal pain in vitamin D deficiency has been described in literature.[7,8] After the normalization of serum vitamin D levels, the patient has not suffered from even a single episodes of erythema nodosum lesion during past 6 years. Erythema nodosum is the most common form of panniculitis (inflammation of subcutaneous fat tissue) and occurs 3–5 times more often in females.[9] In this study, the patient was also a female. Typically, erythema nodosum appears as erythematous painful round nodules, located on the anterior surface of the leg, but can spread to other areas of body. Unlike this typical site of lesion, it was present on sole of both feet in patient of the present study. The episodes of erythema nodosum lesion may be accompanied by systemic symptoms such as fever, malaise, and arthralgia. All of these symptoms were present during last episode in patient of the present study. The lesions of

erythema nodosum usually resolve spontaneously within 2–8 weeks without leaving scars. The most common causes are infections (28–48%), sarcoidosis (11–25%), drugs (3–10%), pregnancy (2–5%), and enteropathies (1–4%).[9] However, in many cases, it is impossible to determine the cause (idiopathic).[10] The recurrent erythema nodosum with elevated markers of inflammation may be the only manifestation of vasculitis.[9] Vitamin D3, the active form of vitamin D, not only regulates calcium and bone metabolism but also plays an immunomodulatory role mediated through binding of its receptor, VDR in monocytes, macrophage, and activated lymphocytes.[11] It has also been observed that individual with a type 2 lepra reaction associated with neuritis and or erythema nodosum leprosum had very low VDR on RNA expression, along with low vitamin D levels in blood.[11] Hence, recurrent erythema nodosum in first patient of the present study was probably due to unregulated immune expression of hypovitaminosis D.

The second patient in the present study had the problem of cracked heel, also known as heel fissures and vitamin D deficiency. With correction of vitamin D deficiency, there was healing of heel fissures, and subsequently, it did not recur. Heel fissures are a common cosmetic problem. Dry and thick skin on the bottom, outer edge of the heel with increased pressure on the fat pad, results in skin to split that can manifest with pain and bleeding. The other factors for heel fissures are obesity, wearing open heel footwear such as sandals and exposure to cold weather. The active vitamin D locally produced in skin is involved in epidermal differentiation and proliferation, wound response and tumorigenesis.[12] The hypovitaminosis D in second patient of the present study could be a contributory factors in persistent and recurrent heel fissures.

The relief from the problem of palmar hyperhidrosis following correction of vitamin D deficiency was observed in third patient of the present study. Although direct relation of vitamin D and sweat production was not found after thorough literature search, the role of calcium as a important link in the process of stimulus – secretion coupling and stimulus permeability coupling has been demonstrated for a variety of exocrine glands.[13-15] Hence, there may be some indirect control over sweat production by vitamin D through calcium.

CONCLUSION

The erythema nodosum, heel fissures, and palmar hyperhidrosis in vitamin D deficiency have not been described in literature. The novelty of these findings in a common deficiency disorder of vitamin D inspired us to publish this article. Future large – scale studies are needed to establish these relations.

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