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Pseudo-hypoparathyroidism Coexistent with Systemic Sclerosis: A Rare Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Authors FAM, UK, SA, ABA and HA designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors FAM, AM and ABA managed the literature searches and analyses. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Systemic sclerosis is a chronic autoimmune inflammatory disease with wide-spread fibrosis of the skin and internal organs. The hypoparathyroidism associated with systemic sclerosis is infrequent and rarely reported in literature.
Case Report: A 48 year-old female patient applied to our clinic with headache, increasing pallor and bruising cold of the hands. Physical examination revealed sclerodactyly and hardening on the skin of forearms and face. Centromeric type anti-nuclear antibodies were detected in the serum, and the patient and was diagnosed with systemic sclerosis. The same woman had also been

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diagnosed as epilepsy and she had been subjected on anti-epileptic drug therapy for 14 years. We found that she had also hypocalcemia (4,6mg/dl). She was diagnosed as pseudohypoparathyroidism.

Conclusions: Pseudo-hypoparathyroidism associated with systemic sclerosis is a very rare entity. And pseudo-hypoparathyroidism should also be kept in mind in autoimmune disorders.

Keywords: Hypocalcemia; pseudohypoparathyroidism; systemic sclerosis.

1. BACKGROUND

Systemic sclerosis is a chronic auto-immune inflammatory disease characterized with skin and organ fibrosis [1]. Although the etiology of systemic sclerosis is not precisely known; this disorder has been proposed to be caused by factors with genetic, immunological and environmental nature [2]. Systemic sclerosis is divided into two sub-classes based on the clinical features on the skin: localized and diffuse. In patients with skin involvement, vasculopathy, auto-immunity evidence or clinical findings related to internal organ involvement are accompanied. Hypoparathyroidism, associated with systemic sclerosis is rarely reported in literature [3,4]. Hypocalcemia can occur on different bases and mechanisms according to age. Hypoalbuminemia, hypomagnesemia, hyperphosphatemia, surgery, parathyroid hormone (PTH) deficiency or resistance, vitamin D deficiency or resistance can be considered among the causes of hypocalcemia.

Hereby, we reported a patient who was followed- up with systemic sclerosis and who was diagnoed as a concomitant pseudohypoparathyroidism (PHP). She had two rare diseases appearing together.

2. CASE REPORT

Forty-eight year old female patient presented with headache and color change of the hands in cold weathers. Physical examination revealed fever of 36.9℃, blood pressure of 120/80 mmHg, pulse rate of 80 per minute, and respiratory rate of 20/min. Neurological examination revealed that she was conscious, cooperative, and oriented. Pupils were isochoric, direct and indirect light reflexes were normal. Motor examination revealed normal findings, chovestek and trousseau signs were negative. Sensory and cerebellar system examinations were normal. The patient had sclerodactily in both hands as well as stiffness on face and forearms. Other systemic examination findings were normal. The patient's blood tests and biochemical parameters were evaluated, and complete blood count, transaminases, gamma-glutamyl transferase, alkaline phosphatase, BUN (Blood urea nitrogen), and creatinine levels were in the normal ranges, besides sedimentation rate was 44 mm / h (0-20), anti-nuclear antibody (ANA) was 1 / 1000 dilution with a centromeric pattern. When the patient was questioned about the headache, it was learned that the patient had been diagnosed with epilepsy 14 years ago, and she had been on anti-epileptic therapy by 1x 400 mg carbamazepine treatment. Brain magnetic resonance imaging detected T2-hyperintense foci in bilateral centrum semiovale localization and it was thought to be a non-specific gliotic focus. The serum electrolyte levels were detected like that serum sodium, potassium levels were in the normal ranges, calcium was 4.6 mg / dL (8.4 to 10.2 mg / dL), and phosphorus was 6.2 mg / dL (2.5 to 4.5 mg / dL). Upon evaluation of hypocalcemia, 25-hydroxyvitamin D3 was measured 5.7 ng / ml (25 to 80 ng / ml), and parathyroid hormone was measured 120 pg / ml (15 to 65 pg / ml). The patient had vitamin D deficiency and severe hypocalcemia, so that intra-venous calcium replacement and oral vitamin D supplementation were provided in a controlled manner because of concomitant hyperphosphatemia. The patient was treated with a combination of 300 mg/day Acetylsalicylic acid and 30 mg /day Nifedipine for symptoms of Raynaud's syndrome appeared with systemic sclerosis. The patient had improvement on vitamin D and calcium levels, and she was monthly followed-up at out-patient clinic with oral calcium and vitamin D supplements.

3. DISCUSSION

Systemic sclerosis is a chronic connective tissue disease associated with fibrosis, inflammation and vascular changes. Our patient with Systemic Sclerosis patients presented here was diagnosed as concomitant hypocalcemia coincidentally. Calcium plays a critical role in cell function,

neural transmission, membrane stability, bone structure, blood coagulation and intra-cellular signaling. Hypocalcemia can be completely asymptomatic, but it may also be presented with acute hypocalcemic crisis, increased neuro-muscular irritability, tetany, convulsions, paresthesia around mouth and fingers, carpopedal spasm, spontaneous painful muscle cramps, bronchospasm, syncope, congestive heart failure, angina pectoris, laryngeal stridor, hypotension, and arrhythmia. Vitamin D deficiency is the most common cause of hypocalcemia, besides hypomagnesemia, hypoalbuminemia, hypoparathyroidism, and pseudo-hypoparathyroidism which are among the other well-known reasons. Our patient had systemic sclerosis in addition to vitamin D deficiency, hypocalcemia, hyperparathyroidism and hyperphosphatemia.

The most common endocrine disorders seen in systemic sclerosis are associated with the thyroid gland [5,6]; but other as osteoporosis, hyperprolactinemia and prolactinomas can also be seen frequently [6]. So far we know, rare cases of hypoparathyroidism, associated with systemic sclerosis, have been in the literature [3,4]. In the first case, the patient had progressive systemic sclerosis with a concomitant polymyositis. The first patient had also symptomatic hipoparathyroidy findings [3]. In the autopsy of the same patient, fibrosis of parathyroid glands has also been reported [3]. In the other case, the patient had skin thickening and centromeric type ANA positivity as in our case, but in the second patient seizures had also been established(4). It was also suggested that vitamin D deficiency may increase auto-immunity [7]. Vitamin D is believed to have significant effects on the immune system and also believed to contribute to the pathogenesis of autoimmune diseases [8,9]. Except hypocalcaemia, both hypophosphatemia and hyperparathyroidism can be seen in vitamin D deficiency. In patients with vitamin D deficiency who also have hyperparathyroidism and hyperphosphatemia, pseudohypoparathyroidism should also be kept in mind.

Pseudohypoparathyroidism is a rare syndrome characterized by the clinical hypoparathyroidism with normal parathyroid hormone secretion. The incidence has been reported as 3-4/million in the literature [10]. PHP is divided into sub-groups according to genetic defects, phenotypic and biochemical findings in hormone receptor-adenylyl cyclase system. PHP can be diagnosed with clinical symptoms and laboratory findings as normal kidney function with the biochemical examination of low-calcium, high phosphorus and PTH level. We diagnosed pseudohypoparathyroidism in our patient in search of asymptomatic hypocalcemia, and we arranged her treatment.

4. CONCLUSIONS

Rare cases of patients with systemic sclerosis, who also developed hypoparathyroidism, have been reported in the literature [3,4]. In searching the etiology of asymptomatic hypocalcemia in patients with auto-immune diseases such as systemic sclerosis, hypoparathyroidism and pseudohypoparathyroidism should always be kept in mind due to a rare possibility of co-existancy.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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