RHEUMATOLOGY RESEARCH JOURNAL

Vol. 7, No. 3, July 2022
Webpage: http://rheumres.org/
Email: rheumres@gmail.com
ISSN:2476-5856
doi: 10.32592/RR.2022.7.3.71

Case Report Open Access

Systemic lupus erythematosus as a rare cause of hypercalcemia: A case report

Hamidreza Bashiri[1], Hamidreza Soltani[2]*, Fatemeh Paksima[3]

[1]Rheumatology Department, Shahidsadoughi University of Medical Sciences, Yazd, Iran. [2]Rheumatology Department, Shahidsadoughi University of Medical Sciences, Yazd, Iran. [3]Rheumatology Department, Shahidsadoughi University of Medical Sciences, Yazd, Iran.

Hypercalcemia is a rare manifestation in systemic lupus erythematosus (SLE) patients. In this case report, a thirty-five-year-old woman with a 3-year-old history of lupus was reported. Our case had symptoms of SLE flare, including joint pain, hair loss, photosensitivity, high level of calcium and creatinine, and lymphadenopathy. In her brain magnetic resonance imaging, intracranial hemorrhage was detected. Given her high serum level of calcium and phosphorus, reduced parathyroid hormone, and normal level of vitamin D, her hypercalcemia was attributed to the presence of stimulating parathyroid hormone receptor autoantibody. Regarding the findings of this study, it is suggested to consider SLE as a rare but possible cause of severe hypercalcemia.

Keywords: Systemic lupus erythematosus; Autoimmune disease; Hypercalcemia; Parathyroid hormone

Introduction

Hypercalcemia is a possible manifestation of two condition, one primary hyperparathyroidism and the other neoplastic syndrome due to various malignancies [1, 2].

However, systemic lupus erythematosus (SLE) is an autoimmune disease, which manifest itself with the involvement of various organs and a wide range of symptoms. SLE can rarely be the cause of severe hypercalcemia. In the literature, the pathogenesis of hypercalcemia in SLE is described as a high level of parathyroid hormone-related protein (PTHrP) or the presence of stimulating autoantibodies against parathyroid hormone (PTH) receptor [3, 4]. In this case study, we reported a thirty-five-year-old women suffering from SLE since 3 years ago. Our patient was presented with lupus flare up, hypercalcemia, and intracerebral hemorrhage (ICH). The patient was treated with steroids and cyclophosphamide and was discharged after elimination of her symptoms and signs. Given the increase in her PTH serum level during steroid administration, the pathogenesis of hypercalcemia in the present case might bedue to the presence of stimulating autoantibodies against PTH receptor.

Case presentation

A thirty-five-year-old female suffering from SLE for three years was presented in this study. She had polyarthritis of sacroiliac, wrists, ankles, elbows, and shoulders, hair loss, photosensitivity, blurred vision, high level of calcium and creatinine (Cr), left pleural effusion and auxiliary, inguinal and cervical lymphadenopathy. She was under treatment with hydroxychloroquine and prednisolone that she discontinued in the past

*Corresponding Author: Rheumatology Department, Shahidsadoughi University of Medical Sciences, Yazd, Iran. Email: mailto:hr.soltan@yahoo.com

Received: 24 April 2022; **Accepted:**02 June 2022

months. It should be mentioned that a mild unjustifiable elevation of calcium level occurred during two previous flare-up of SLE but management of SLE had normalized the calcemia. The results ofher laboratory tests are shown in Table1.

Table1. Laboratory Data

Laboratory parameters	At the time of admission	After treatment
Urea	68 mg/dl	59 mg/dl
Creatinine	1.8 mg/dl	1.4 mg/dl
Iron	17 mg/dl	-
TIBC	231 mg/dl	-
Ferritin	255 mg/dl	-
RF	61	-
ESR	95	-
CRP	36.5	-
FANA	+1/200	-
Anti-ds DNA	+245.5	-
C3	49.33 (low)	-
C4	8.61(low)	-
Ca (normal range=8.6-10.3)	11.8 mg/dl	9.5 mg/dl
Albumin (normal range=3.5-5.2)	3.5 mg/dl	-
Phosphorus(normal range=3.9-7.7)	4.6 mg/dl	2.9 mg/dl
PTH (normal range=9-94)	8 mg/dl	12 mg/dl
vitamin D (normal range=30-70)	42 mg/dl	-
urine calcium 24hr (normal range=50-300)	334 mg/dl	700 mg/dl
urine protein 24hr (normal range=10-150)	285 mg/dl	522 mg/dl
urine Cr 24 hr (normal range= 0.6-1.8)	0.3 mg/dl	0.2 mg/dl

TIBC, total iron binding capacity; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ANA, anti- nuclear antibody; anti-ds DNA, anti-double stranded DNA; PTH, parathyroid hormone; Cr, creatinine

Electrocardiogram test suggested evidence of short QT (317 msec) syndrome. Due to hypercalcemia, the patient was transferred to coronary care unit (CCU). During cardiac monitoring, no arrhythmia occurred. After calcium adjustment through severe hydration andintravenous Furosemide 40Mg Bid, QT correction was done and the patient was transferred to general unit care.

Chest X-ray demonstrated evidence of left pleural effusion. Following soft tissue ultrasonographic evaluation, evidence of several lymph nodes with the largest size of 21×3 mm in right inguinal space, multiple lymph nodes with the largest size of 20×3 mm in left inguinal space, several lymph nodes with the largest size of 14×8 mm in left axillary fossa, several lymph nodes with the largest sizeof 8.4×3.7 mm in right carotid sheath, and several lymph nodes with the largest size of 12.2×4.6 in the left carotid sheath was observed. Abdominal ultrasonography demonstrated evidence of mild free fluid in Morrison's pouch and right sub-diaphragmatic area. No other pathologic findings were reported. In her brain MRI, mild diffuse parenchymal atrophy and cortical and subcortical abnormal high signal foci (flair/T1) in posterior parieto-occipital sulcuscontaining foci of gyral hemorrhage were reported.

The patient was treated with intravenous pulse (IV) of cyclophosphamide 700 mg in two divided doses one day apart because of intracerebral hemorrhage (ICH). In addition to cyclophosphamide, steroids and hydration were started for the patient. Due to proteinuria and hypercalcemia and the risk of lupus nephritis, the patient received IV pulses of methylprednisolone (Total 5 gr). After 7 days, according to laboratory data revealing a good general condition, symptom elimination, and normal level of calcium and PTH the patient was discharged and eight tablets of hydroxychloroquine 200 mg per week, five tablets of prednisolone 5 mg per day, five tablets of amlodipine 5mg per day, and cyclophosphamide for 6 times (75 g/m^2) were prescribed for her.

Discussion

Common causes of hypercalcemia include primary hyperparathyroidism and malignancies. Malignant hypercalcemia seems to be a common finding in cancer patients, affecting up to 44.1% of patients. It is also important to note that malignant hypercalcemia is especially common in advanced stages of cancer not in early ones. Patients with malignant hypercalcemia usually have a limited survival of several months, and it is unclear whether this poor prognosis is related to the advanced stage of hypercalcemia associated with malignancy or is simply a consequence of the cancer [5]. In other words, in malignancy-associated hypercalcemia, usually the symptoms of malignancy has already brought the patient to the physician and the hypercalcemia was discovered during following assessments, so the reason of this manifestation would be clear [6]. Patients with malignant hypercalcemia usually present with higher degrees of hypercalcemia in an ascending and continuous pattern and for a shorter duration, which is why these patients are usually more symptomatic than patients with other causes of hypercalcemia [5]. In the presented patient, treated and discontinuous episodes of mild hypercalcemia were observed, which did not match the afore-mentioned pattern. The less common causes of hypercalcemia are hyper-vitaminosis D, sarcoidosts and other granulomatous diseases. Among the causes of hypercalcemia, SLE is an extremely rare differential diagnosis. SLE is an autoimmune disease and has a wide range of symptoms since it can engage various organs. However, hypercalcemia has been reported as a rare manifestation in SLE [7, 8]. In these cases, calcium level returns to normal after controlling the active SLE through steroid administration and aggressive hydration [1]. As mentioned before, milder unjustifiable elevations of calcium level also occurred during the previous flare-up of SLE in this case but management of SLE had normalized the calcium level and no further intervention was needed. Pleural effusion in these patients is due to serosal inflammation which is common in SLE and does not require any intervention if it does not cause acute symptoms for the patient and improves after lupus control [1].

In the literature, three mechanisms were described for hypercalcemia in SLE, including increased PTHrP, presence of stimulating auto-antibodies against PTH receptor and stimulation of bone resorption by active cytokines in uncontrolled lupus [4]. It is assumed that in this patient, the autoantibodies against PTH have been probably inhibited by steroid administration. Although two other mechanisms can be involved in lupus-induced hypercalcemia, and the control of lupus may have led to their control. ICH might be accompanied by SLE [9] and as you know, there is an association between lower serum calcium level and the extent of bleeding in ICH patients [10] but simultaneous hypercalcemia and ICH has beenalso reported in a patient [10]. However, hypercalcemia and ICH were not reported simultaneously in a SLE case yet and the present case seems to bethe first report of this case. It should be mentioned that hypercalcemia and ICH might have a cause-and-effect association. In the present case, high level of calcium, suppressed PTH, normal vitamin D and phosphorus, and an increase in PTH level after steroid administration indicated that the cause of hypercalcemia was the presence of stimulating autoantibodies against PTH receptors. In addition, after starting steroid, elimination of these antibodies led to an improvement in PTH level and serum calcium level.

Conclusion

It is suggested that SLE be considered as a differential diagnosis in cases with unexplained severe hypercalcem

Acknowledgment

The authors would like to thank the staff of the Clinical Development Center of Shahid Sadoughi Hospital, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding

No funding.

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