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## An interesting case of systemic lupus erythematosus presenting with hypercalcemia: A diagnostic dilemma

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**Background:** Hypercalcemia is common in primary hyperparathyroidism malignancies and even in tuberculosis. Interestingly, systemic lupus erythematosus (SLE) rarely presents with hypercalcemia.

**Case Report:** We describe an interesting case of SLE in a patient who was otherwise thought to have either tuberculosis or a malignancy. The patient initially presented with feeling unwell, with generalized lymphadenopathy, bilateral pleural effusion, and bilateral corneal calcium deposits secondary to severe hypercalcemia. The diagnosis of SLE was made based on positivity of antinuclear antibodies (ANA) and anti-dsDNA, the presence of serositis, lymphadenopathy, autoimmune hemolytic anemia, and constitutional symptoms. She was treated with steroids, with tremendous improvement in her general well-being, resolution of lymphadenopathy and pleural effusion, and normalization of her hemoglobin and serum calcium. The atypical presentation of SLE with hypercalcemia with pleural effusion is discussed.

**Conclusions:** SLE should be one of the differential diagnoses in patients presenting with severe hypercalcemia.

**Key words:** **atypical presentation • hypercalcemia • systemic lupus erythematosus**

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## Background

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organs. The clinical manifestations include arthritis, dermatitis, involvement of the central nervous system, and the hematological and genitourinary tract systems [1]. SLE can present with atypical presentation, which makes diagnosis challenging. There are many causes of hypercalcemia, and SLE is a very rare cause of it. To the best of our knowledge, only 10 cases of SLE patients presenting with hypercalcemia had been reported in the literature. We report the case of a 27-year-old woman who presented with complaints of being unwell for the past 3 weeks, loss of appetite, and extreme lethargy. There was a strong familial history of connective tissue disease. We describe our experience in treating this unique case, initially thought to be tuberculosis or malignancy.

## Case Report

A 27-year-old woman reported she had been feeling sick for the past 3 weeks. She complained of loss of appetite, loss of weight, and extreme lethargy. There was no fever, no altered bowel habits, and no night sweats. There was minimal cough, with no sputum. She had a strong family history of connective tissue disease; her aunts had SLE and rheumatoid arthritis. She denied taking any medications or supplements.

Physical examination revealed generalized lymphadenopathy, hepatosplenomegaly, corneal calcium deposits, and bilateral pleural effusion. Her initial white blood cell count was  $12.4 \times 10^9/L$ , hemoglobin was 10.8 g/dl, and erythrocyte sedimentation rate (ESR) was 111 mm/h. She had severe hypercalcemia (corrected serum calcium 4.31 umol/L, serum phosphate 1.42 umol/L) with acute kidney injury (AKI) (serum creatinine 367 umol/L). Her chest radiograph showed bilateral pleural effusion, but results of investigations for infection and tuberculosis were negative. Initially, she was investigated for hyperparathyroidism, but intact parathyroid hormone level was low. Her serum calcium responded to intravenous pamidronate 60 mg, and the AKI resolved with hydration. With clinical features of generalized lymphadenopathy and hypercalcemia, a working diagnoses of lymphoma and tuberculosis were considered.

Her pleural fluid cytology was negative for malignant cells. CT scan thorax and abdomen revealed multiple enlarged mediastinal, axillary, paraaortic, iliac, and inguinal lymph nodes. Axillary lymph node biopsy was performed and reported as reactive lymphadenitis with no evidence of tuberculosis.

Because the patient had a strong family history of connective tissue disease and negative investigations for tuberculosis and lymphoma, she was also screened for connective tissue

disease. She had profound hypocomplementemia, with C3 of 0.89 mg/dl and C4 of 0.09 mg/dl, with positive antinuclear antibodies (1: 640 homogenous) and anti-double stranded DNA. Her Coombs' test result was positive, suggesting autoimmune hemolytic anemia secondary to SLE. With these findings, the patient was treated for SLE with intravenous steroid. She responded very well, with improvement of her symptoms, normalization of her serum calcium, and resolution of her bilateral pleural effusion and generalized lymphadenopathy.

## Discussion

Hypercalcemia is a common finding in primary hyperparathyroidism and other malignancies [1]. Other conditions (eg, milk alkali syndrome, Vitamin D hypervitaminosis, sarcoidosis, granulomatous, and endocrine diseases) may also give rise to hypercalcemia [1,2]. Tuberculosis is an important cause of hypercalcemia, especially in this endemic area. We have published a case report of a patient who presented with severe hypercalcemia needing regular hemodialysis secondary to tuberculosis [3].

In this presented case the patient did not have any other disease that may have resulted in hypercalcemia. Furthermore, the patient's serum calcium remained normal after the patient was treated for SLE. Deposition of calcium in the cornea secondary to hypercalcemia in SLE is rare. An earlier study reported electron microscopically visible and immunohistochemistry changes in the eyes which included swelling of the axons of the retinal fibre layer, degenerative changes in the pericytes and smooth muscle cells of blood vessels, and fibrin deposits in Bruch's membrane [4].

AKI in this patient was most probably secondary to severe hypercalcemia and it responded well with hydration. Serositis is common in SLE and the patient can present with pleural effusion.

There are many hypotheses explaining the cause of hypercalcemia in SLE patients. High levels of PTH-related protein and autoantibodies that might activate the PTH receptor were suggested in some cases [1,5,6]. Patient with active SLE also have elevated levels of certain cytokines that might stimulate osteoclastic bone resorption, leading to hypercalcemia [1]. These factors are believed to work together to cause severe hypercalcemia. In our case, serum calcium remained normal while the patient was on immunosuppressive medications.

## Conclusions

We conclude that SLE should be one of the differential diagnoses in patients presenting with severe hypercalcemia. Doctors should suspect SLE in patients with unexplained hypercalcemia.

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