HYPERCALCEMIA IN A PATIENT WITH SLE AND ANTIPHOSPHOLIPID ANTIBODY SYNDROME: A RARE CASE REPORT FROM BANGLADESH

Dewan G[1]

ABSTRACT

Association of hypercalcemia with SLE is very rare. Since initial report in 1991 only hand full cases have been described mainly in adult patients sporadically. Three pattern observed in this rare presentation. Commonly it is associated with serositis and lymphadenopathy or lymphedema known as hypercalcemia-lymphadenopathy SLE (HL-SLE) or hypercalcemia- lymphedema syndrome. Second group do not show this particular association. Concomitant primary hyperparathyroidism is responsible for third variety. This report describes a case of hypercalcemia associated with SLE from Bangladesh.

KEYWORDS: Systemic lupus erythematosus (SLE), Hypercalcemia, Serositis, Lymphedema, Lymphadenopathy

1. Consultant, Department of Internal Medicine, Rangamati General Hospital, Rangamati, Bangladesh

For Correspondence
Dr. Gourab Dewan
Consultant,
Department of Internal Medicine,
Rangamati General Hospital,
Rangamati, Bangladesh
E-mail: gourab.dewan@yahoo.com

INTRODUCTION

Systemic lupus erythematosus (SLE) is uncommon cause of hypercalcemia in practice. This rare clinical association in a SLE patient described here along with review of clinical features and management.

CASE REPORT

Patient was a 28 year old female from Rangamati district of Bangladesh. She was diagnosed of SLE with class II lupus nephropathy (WHO classification) and antiphospholipid antibody syndrome in 2001. Nephropathy was in remission since initial immunosuppressive treatment. She was irregularly treated and without follow up for last few years. Her last renal function report before current presentation was normal.

On September 2013 she presented with exertional dyspnoea, fatigue and polyuria. Clinical examination was unremarkable except marked pallor of body and conjunctiva and a resting tachycardia and mild dehydration. There was no history of abnormal blood loss.

Haemoglobin was 4.4 gm/dl, ESR 145 mm in 1st hour. WBC and platelet counts were normal. Serum creatinine was 2.5 mg/dl. Anti ds- DNA titer elevated and C3 was low. ECG showed sinus tachycardia. Electrolytes were normal but serum calcium was 12.4 mg/dl (8-10 mg/dl). Urine analysis, serum albumin, serum alkaline phosphatase, serum phosphate, chest x-ray and ultrasonogram of abdomen were normal. Parathyroid hormone (PTH) level was 60 pg/ml (10-80 pg/ml). Coombs test was negative. Her SLE DAI score was 4 (mild or moderate flare).

Anemia and dehydration corrected with repeated blood transfusion & normal saline respectively. Treatment for SLE started again with hydroxychloroquine & low dose prednisolone (20 mg/day). Subsequent calcium & creatinine level gradually came to normal over two weeks. On follow up Calcium level, C3 was normal and ESR & anti ds-DNA titer reduced.

DISCUSSION

Hypercalcemia in SLE was first described in 1991. Porto et al. made a review of all 12 hypercalcemia cases in SLE reported up to 2011.[1] To the best of knowledge three more such cases reported since then.[2-4] Three groups of patients may have hypercalcemia in SLE. One group has hypercalcemia with lymphadenopathy or lymphedema and serositis which was described as "hypercalcemia-lymphadenopathy (HL-SLE)" syndrome by Porto et al.[1] But the original report by Braude et al. and a subsequent report by Berar-Yanay et al. described this entity as "hypercalcemia-lymphedema" syndrome as their patient had lymphedema.[5-6] However case reports show lymphadenopathy is more common than lymphedema in this group. Lymphadenopathy can be localized or generalized. Bilateral pleural effusion is commonest presentation as serositis.[1]

Second group has no lymphatic abnormality or serositis; literatures described this group as simply case of "SLE".[1] Our patient falls in this category. First adult Asian patient of this group described in China in 2013.[4] However in 2008 a pediatric patient from India with non HL-SLE syndrome was described.[7] Unique feature of this child is that it remains to date the only recorded pediatric case manifesting hypercalcemia in SLE. Metastatic pulmonary calcification may be found in bone scan in this variety. If remain undiagnosed both variety can cause osteopenia or chest wall deformity.[1] This is important as SLE patients often require long term steroid and there is risk of iatrogenic osteoporosis.

The last group is where SLE is associated with primary hyperparathyroidism. This is incidental association. Exclusion of this variety leaves only 12 cases where hypercalcemia was a genuine association of SLE. More than 90% cases of hypercalcemia are associated with hyperparathyroidism & malignancy or granulomatous disease like sarcoidosis.[8] Possible secondary causes of hypercalcemia need exclusion as far as possible before attributing hypercalcemia to SLE. Because of paucity of cases no definite characterization of patients with these SLE variant are yet to be established firmly. All but one case were reported in adult population.[7] Majority patients were young female but also reported in late onset SLE cases.[1,4] Current patient from Bangladesh also complies with this observation.

Hypercalcemia was reported usually at the time of diagnosis of SLE in past cases, so rarely hypercalcemia can be sole presenting feature of SLE. Current patient differs from all past reported cases in that hypercalcemia was detected 13 year after establishing SLE diagnosis. Along with hypercalcemia wide range of system involvement as seen in SLE may be present. Calcium level is usually mild but severe hypercalcemic crisis may occur.[4] In some cases diagnosis of SLE may not be obvious. Previous case reports shows in many cases extensive search for malignancy was carried out at first as little was known regarding this SLE variety. Some cases may require confirmation by prolong follow up.

PTH level usually remain depressed in first two variant described. A low PTH suggests either peptide or PTH receptor

related antibody as underlying cause of hypercalcemia.[1,8] PTH is elevated in SLE cases associated with primary hyperparathyroidism. Some relates parathyroid hormone related protein (PTHrP) as possible explanation of hypercalcemia. But PTHrP is more commonly seen in malignant conditions. First reported case had high serum PTHrP.[5] Nonmalignant lymphoid tissue in SLE may produce PTHrP. Immunochemistry detected PTHrP expression in lymph node biopsy.[9] But serum PTHrP has been found to be normal or even negative in one but all subsequent patients after the original reporting in 1991.[1] Other postulates role of cytokines or anti PTH receptor antibody (stimulatory), anti FGF23 antibody as underlying cause.[1,4] Elevated PTHrP requires exclusion of concomitant malignancy meticulously. Tests for PTHrP are not available in Bangladesh so a conclusion cannot be drawn in this point.

Hypercalcemia might be marker of disease activity and it is suggested by the fact that management of SLE results in normalization of hypercalcemia.[1] No special treatment of hypercalcemia is usually required other than usual management of SLE.[1] Occasional hypercalcemic crisis requires bisphosphonate therapy or even dialysis.[10] Concomitant osteoporosis requires standard bisphosphonate, calcium & vitamin D. Our patient had class II nephritis in remission. As her most recent renal function reports were normal and present urine analysis unremarkable it was assumed the slight elevation in creatinine was due to hypercalcemia and it normalized as treatment of SLE restarted and calcium level normalized.

Though rare; in unexplained hypercalcemia cases SLE should be considered especially in young female. Calcium level should be checked in established SLE cases if symptoms are suggestive or show evidence of serositis with lymphadenopathy or lymphedema. And finally close follow up necessary to exclude any occult malignancy if PTHrP elevated.

REFERENCES

1. *Del Porto F, Proietta M, Koverech, Trappolini AM . Aliberti G. Hypercalcaemia in systemic lupus erythematosus. Lupus. 2011; 20: 75862. http://dx.doi.org/10.1177/0961203310387182 PMid:21282297*

2. *Hypercalcemic crisis due to primary hyperparathyroidism in systemic lupus erythematosus (SLE) . Lupus .2013; 22: 847-850. http://dx.doi.org/10.1177/0961203313491847 PMid:23753296*

3. *Gafor AHA, Cader RA, Das S, Masir N, Wahid FA. An interesting case of systemic lupus erythematosus presenting with hypercalcemia: A diagnostic dilemma Am J Case Rep. 2013; 14: 83-85. (DOI: 10.12659/AJCR.883849)*

4. *Zhang B, Yu X, Mao H, Xing C, Liu J. Late onset systemic lupus erythematosus with severe hypercalcaemia. West Indian Med J. 2013; 62(1):92-4. PMid:24171337*

5. *Braude S, Graham A, Mitchell D. Lymphoedema/hypercalcemia syndrome mediate by parathyroid-hormone related protein. Lancet .1991; 337: 140141. http://dx.doi.org/10.1016/0140-6736(91)90802-V*

6. *Berar-Yanay N, Weiner P, Magadle R. Hypercalcemia in systemic lupus erythematosus. Clin Rheumatol. 2001; 20: 147149. http://dx.doi.org/10.1007/s100670170088 PMid:11346230*

7. *Kohli U, Lodha R, Bagga A. Familial Systemic Lupus Erythematosus with Hypercalcemia. Ind J Pediatr. 2008; 75:855857.*

8. *Jacobs TP, Bilezikian JP. Clinical Review: Rare Causes of Hypercalcemia. J Clin Endocrinol Metab. 2005; 90(11):63166322. http://dx.doi.org/10.1210/jc.2005-0675 PMid:16131579*

9. *Deftos LJ, Burton DW, Baird SM, Terkeltaub RA. Hypercalcemia and systemic lupus erytematosus. Arthritis Rheum. 1996; 39:20662069. http://dx.doi.org/10.1002/art.1780391217 PMid:8961913*

10. *Erdozain JG, Egurbide MV, Ruiz-Irastorza G, Ojanguren J, Aguirre C. Systemic lupus erythematosus presenting as acute symptomatic hypercalcemia. Lupus. 2004; 13(2):132-4 http://dx.doi.org/10.1191/0961203304lu476cr PMid:14995007*