CASE REPORT

A case of idiopathic hypoparathyroidism with Systemic Lupus Erythematosus

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Abstract:

Hypoparathyroidism is a rare disease. The main cause of hypoparathyroidism is postsurgical hypoparathyroidism. However, cases of hypoparathyroidism in patients suffering from SLE exist although it is uncommon. We present the case of a woman suffering both from systemic lupus erythematosus and hypoparathyroidism. This reported association of hypoparathyroidism with lupus expands the spectrum of endocrine disorders seen in this disease. We suggest that there may be a common underlying pathophysiological process linking these diseases.

Case report:

We present a case of 50-year-old female resident of Madhya Pradesh, India who had chief complaint of seizures and generalised weakness. She is a known case hypothyroidism and systemic lupus erythematous for 15 years. Past history of repeated pericardial effusion. On admission, radiological findings on MRI (plain & contrast) were multiple lacunar infarcts in basal ganglia on both side and calcification in caudate nucleus, putamen, pulviener, internal capsule. Laboratory findings were total serum calcium – 4.5mg/dl, PTH – 2.02pg/ml, ionized calcium – 0.67mg/dL, 25-hydroxy vitamin-D – 70ng/ml. Hypercaliuria present. ANA; positive, Anti-ds DNA antibodies positive. All other laboratory findings are within normal limit. This association of hypoparathyroidism with SLE is a rare association.

Keywords: Hypoparathyroidism, SLE, Hypercalciuria, CaSR, Basal ganglion calcification, Hypothyroidism,

Introduction:

Hypoparathyroidism is rare disease. Broadly speaking, causes of hypoparathyroidism can be classified as PTH- deficient and PTH-sufficient (Psuedo hypoparathyroidism type 1 and type 2). Causes of PTH-deficient Hypoparathyroidism include post thyroid surgery, infiltration of parathyroid glands, neck radiation which impairs either PTH synthesis or secretion.[1]This can be caused by autoantibodies to parathyroid gland and related molecules.[2]Laboratory values of intact PTH, Serum Ionized calcium, 25 (OH) D levels, Serum Phosphate, Glomerular filtration rate (GFR), serum Magnesium and evaluation for relative hypercalciuria help to dissect out causes of Hypocalcaemia. Screening for autoimmune polyglandular syndrome helps to understand syndromal presentation of hypocalcaemia.[3]Here we report a case of PTH deficient hypoparathyroidism associated with hypothyroidism and SLE.

Case Report:

50-year-old female, presents with complaints of cough with yellow expectoration for 15 days. She has pedal oedema and generalised weakness and arthralgia on and off for 15 years. She has seizure disorder for 15 years and is treated with anti-seizure treatment. Additionally she has documented severe hypocalcaemia for 10 years (Range of hypocalcaemia is in between Total calcium=4 to 5 mg %). On examination, patient does not have any sign suggestive of neuromuscular irritability. Her laboratory values from recent encounter are presented in Table:

Haematological parameters:

Test	Value	Remark
Hb	11.6 Gm%	Slightly anaemic
MCV, MCH, MCHC, TLC, DLC, Platelets	97fl/31.8/32/10220/3.2 lakhs	Within Normal Limit
ESR	76mm/hr	Raised

Serum Chemistry:

Test	Value	Normal range	Comment
Sr. ALT	24 IU/L	4-10 IU/L	
Sr. AST	20 IU/L	4-14 IU/L	
Sr. ALP	90 IU/L	40-120 IU/L	
Sr. Total Protein:	8gm%	7.0-7.5 mg/dl	
Sr. Albumin	4.1gm%	3.5-5 mg/dl	
Sr. Urea	21 mg/dl	15-40 mg/L	
Sr. Creatinine	1.1mg/dl	0.9-1.1 mg/L	
Sr. Na	138 mEq/L	136-145 mEq/L	
Serum K	4.0 mEq/L	3.5-5.5 mEq/L	
Serum Cl	102 meq/L	95-105 mEq/L	
Serum Total Calcium	4.7 mg/dl	9-11 mg/dl	
Serum Ionized Calcium	0.67 mg/dl	4.5-5.5 mg/dl	**Severe Hypocalcaemia**
Serum Phosphorus	4.8 mg/dl	3.5-5.5 mg/dl	
Vit D (OH,25)	70 ng/ml	20-100 ng/ml	**Sufficient status**
Serum Mg	1.9 mg/L	1.8-2.0 mg/dl	Rules out Hypomagnesaemia
Serum PTH	2.02 pg/ml	10-65pg/ml	
Serum TSH	10.4 µIU/L	0.4-4.0 µIU/L	Diagnostic of Hypothyroidism
*Urinary Calcium	384 mg/24 hr	250-300 mg/24 hr	**Relative Hypercalciuria**
Urinary Ca/Cr	0.2	Less than 0.14	**Indicates Hypercalciuria**
eGFR	120 ml/min/1.73m2	110-120 ml/min	Rules Out Kidney failure
Sr ANA Level	Positive in 1:160 titre		**Sensitive for SLE**, These much high titres s/o SLE
Anti ds-DNA Ab	Positive		**Highly specific for SLE**

*Hypercalciuria is defined as urinary excretion of more than 250 mg of calcium per day in women or more than 275-300 mg of calcium per day in men while on a regular unrestricted diet.

MRI brain (plain & contrast) showed multiple lacunar infarct in basal ganglia bilaterally, calcification in caudate nucleus, putamen, pulvinar, internal capsule (Figure y). On Chest X-ray, pleural and pericardial effusion is seen.[4,5]

Family history and pedigree analysis was inconclusive in this patient.

Discussion:

This patient has hypoparathyroidism with deficient parathormone. There was no history of removal of parathyroid or surgical manipulation of thyroid which rules out inadvertent damage to parathyroid glands. In cases without such iatrogenic removal, age of presentation and accompanying illness can suggest the diagnosis.[3] Early age of presentation is associated with some genetic diseases like DiGeorge syndrome or HDR syndrome, a group of hypoparathyroidism associated with hypomagnesemia. In familial isolated hypoparathyroidism, there is activating mutation of CaSR. CaSR is expressed extracellularly on parathyroid gland and renal distal tubules. Free ionized calcium is the direct first messenger for these receptors.[6] Activating mutations of CaSR results in suppressed secretion of PTH. This results in hypercalciuria as activation in kidney tubular cells result in suppression of paracellular reabsorption of Ca and Mg ions resulting in hypocalcaemia and hypomagnesemia.[5,4]

Antibodies to CASR are shown to be responsible for hypoparathyroidism in autoimmune polyendocrine syndrome type 1 in one reported study.[7]Usually APS type 1 presents in childhood to adolescence. Addison's disease and type 1 diabetes are the associates in this syndrome.

Acquired hypoparathyroidism patients have antibodies reactive exclusive to CaSR as observed by the experiment done by Yangxin Li and et al which showed the presence of such antibodies. In this study, 8 female Patients were having associate hypothyroidism.[8]

Prevalence of hypothyroidism and presence of anti-thyroid antibodies (Anti-TPO, anti-thyroglobulin) is quite high in SLE.[9,10]

Known causes of Hypoparathyroidism due to Impaired PTH:

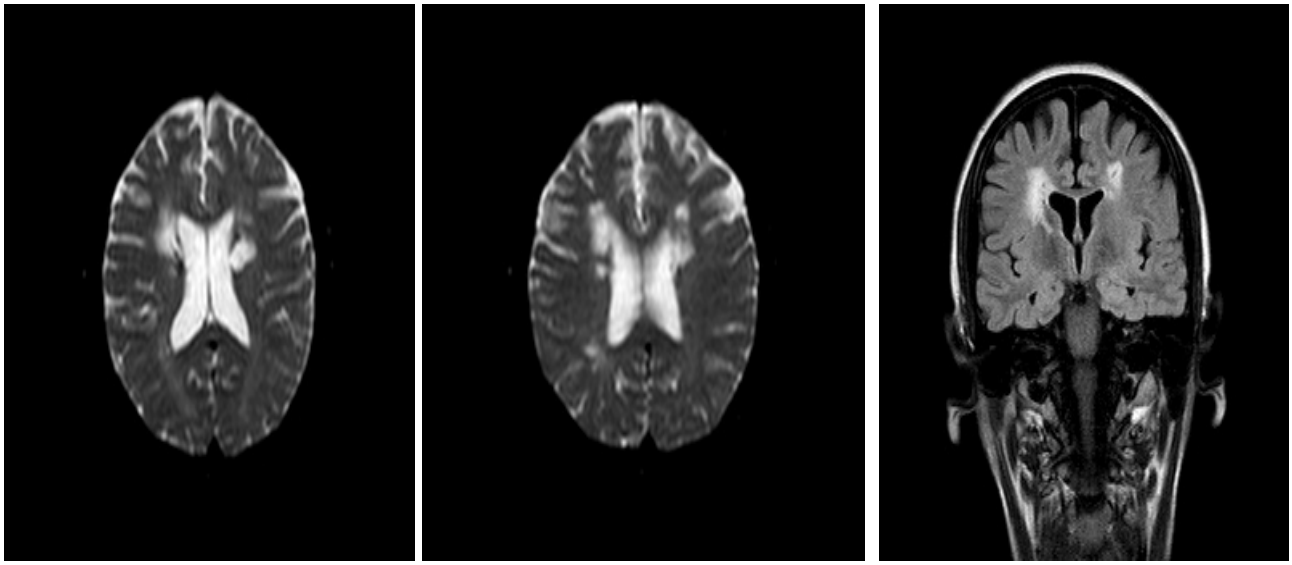
Known Syndrome or diagnosis	**Onset**	**Presentation and association with**	**Mechanism**
H/o Surgical removal of thyroid or parathyroid/ radiation/cancer metastasis/hemochromatosis	Hypocalcaemia persistent after 6 months of surgery		Damage to parathyroid glands
DiGeorge syndrome	Early onset,	facial dysmorphology, cardiac anomalies	Branchial arch dysmorphogenesis
HDR syndrome	Early Onset	Renal disease, sensorineural deafness	
Familial Hypoparathroidism with Hypomagnesemia	Neonatal/Infantile presentation	Associated with hypomagnesemia. Some are associated with Bartter's syndrome Family history. Can be autosomal recessive or dominant	Genetic diseases with Activating CaSR mutations/ defective Parathormone secretion
Autoimmune polyendocrine Neoplasis(APN) type 1	**Late onset/** Or Post partum.	Addison's disease. Type 1 Diabetes **Hypothyroidism,** Waxing and waning of disease.	Mutations in autoimmune regulator region. Few cases are seen with **autoantibodies against CaSR**
Acquired Hypoparathyroidism	**Late Onset**	In one of the study strongly associated **withhypothyroidism** and female gender	**Antibodies against CaSR receptors**

In this patient, SLE is diagnosed by criterion laid down by American College of Rheumatology as patient has evidence of pericardial effusion, arthralgia, history of Seizure disorder and positive anti ds-DNA and ANA. [(11)] She has hypothyroidism and hypoparathyroidism. She is a severe and long-standing case of hypocalcaemia with

symmetrical basal ganglion calcification and long history of seizure disorder (MRI Images attached). Similar pattern of calcification has been reported previously.[12-14] Despite severe deficiency of ionized calcium, patient did not show any signs of neuromuscular irritability or any ECG changes. She has signs of cardiac failure in terms of pedal oedema and signs of pericardial effusion. (Most likely disease process of SLE). She has laboratory evidence of hypothyroidism in terms of raised TSH. In spite of very low calcium, kidneys are excreting large amount of calcium suggest activation of CaSR receptors. (See table). We did not perform assay of anti CaSR antibody or mutation testing for the same.

Presence of hypoparathyroid dysfunction in SLE is very rare [2,11,15–17] though evidence of anti CaSR antibodies in SLE is not found in literature. We suggest that there may be a common underlying pathophysiological process linking these diseases which could be genetic or even autoimmunity.

So this is a case of late onset, female of SLE with hypothyroidism and PTH-deficient-hypoparathyroidism with severe hypocalcaemia and hypercalciuria and normomagnesemia.



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