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# SEVERE HYPOMAGNESEMIA, HYPOKALEMIA AND HYPOCALCEMIA ASSOCIATED WITH PULMONARY TUBERCULOSIS

Baskaran S., Gopi Manigandan, Arumugam Aashish

Department of General Medicine, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India

E-mail of Corresponding Author: lyfdiver@gmail.com

## ABSTRACT

We report a case of severe hypomagnesemia, hypokalemia and hypocalcemia in a 55-year-old lady who defaulted her treatment twice for pulmonary tuberculosis and presented with tetany to the emergency room. Hypocalcemia and hypokalemia persisted despite adequate correction and improved only after the correction of hypomagnesemia. The biochemical abnormalities were further complicated by streptomycin therapy necessitating to modify the anti-tuberculous regimen. The association of hypomagnesemia with tuberculosis is reported earlier and this association is attributed to renal magnesium wasting following aminoglycoside containing anti tuberculous regimen. However, hypomagnesemia contributing to hypocalcemia and hypokalemia, occurring as a primary abnormality in patients with tuberculosis is reported rarely. Here we report a case of active pulmonary tuberculosis who presented with such rare manifestations. This report emphasizes the need to maintain a high index of clinical suspicion of hypomagnesemia in patients with tuberculosis and in those receiving aminoglycoside as a part of their anti tuberculous therapy (ATT).

**Keywords**: hypomagnesemia, hypokalemia, hypocalcemia, pulmonary tuberculosis

## INTRODUCTION

Magnesium is the second most abundant intracellular cation after potassium and plays a significant role in neuromuscular function. Though magnesium depletion may contribute to increased morbidity and mortality in hospitalized patients, it is most under diagnosed electrolyte abnormality in current medical practice.[(1)] Magnesium deficiency is strongly associated with other electrolyte deficiencies especially potassium and calcium, although phosphate and sodium deficiencies are also described.[(2)] We report a case of active pulmonary tuberculosis presented to us with clinical manifestations of hypomagnesemia and associated biochemical abnormalities.

## CASE REPORT

A 55-year-old south Indian lady presented to the emergency room with numbness and paresthesia involving the extremities over the past two days and episodes of carpopedal spasm over the past twelve hours. She had no history of recent episodes of loose stools and vomiting. She reported occasional cough, poor appetite and undocumented weight loss over the past two years. Earlier, she was diagnosed to have pulmonary tuberculosis elsewhere and had defaulted her treatment twice within a period of two years. She had no history of diuretic or aminoglycoside use in the past. She had no other significant past, personal or family history. On examination, she was moderately built and poorly nourished. She was pale with pulse rate 96/min, BP 110/70mmHg and respiratory rate 18/min. Chevostek's and Trousseau's signs were present. Systemic examination revealed bronchial breath sound over the right axillary region.

Initial laboratory evaluation showed Haemoglobin 8.6g/dl, total leukocyte count 12900/cu.mm, differential leukocyte count N90%, L8%, E2%, platelet count 3.05 lakhs/cu.mm, erythrocyte sedimentation rate 96mm/hr, urea 31mg/dl, creatinine 1mg/dl, sodium 130meq/L, potassium 2meq/L. Arterial blood gas showed metabolic alkalosis (pH-7.65, HCO3-40meq/L, PCO2-41mmHg). Serum calcium was reported as 6.2mg/dl (NV : 8.7 – 10.2mg/dl). Her LFT including serum albumin was within normal limits. ECG showed QTc prolongation (Fig.1) and chest X-ray revealed a thin walled cavity over the right midzone and a small pleural effusion on the left. (fig.2) which was exudative but sterile on aspiration.

Correction of hypokalemia and hypocalcemia initiated with intravenous infusion of KCl and calcium gluconate at recommended doses. However serial electrolytes and biochemical tests revealed persisting hypokalemia and hypocalcemia despite adequate correction. Magnesium level was reported as low at 1mg/dl (NV:1.5-2.3 mg/dl). Patient was administered magnesium 8gm (64mEq) infusion for 24 hours followed by 4gm (32mEq) infusion for next five days with simultaneous potassium and calcium replacement with necessary precautions and frequent monitoring of the serum magnesium, potassium and calcium levels. Electrolyte abnormalities, calcium level and metabolic alkalosis gradually improved with reduction of patient's symptoms.

Her further investigations revealed urinary spot magnesium as 0.9mg/dl(NV:0.9-1.9mg/dl), urinary spot potassium 15meq/L, urinary spot creatinine 67mg/dl(NV:25-400mg/dl), serum osmolality-278.1 mOsmol/kg serum water (NV:275-295 mOsmol/kg serum water), urine osmolality-328.5 mOsmol/kg water(NV:500-800 mOsmol/kg serum water), 24 hrs urinary calcium 0.27g (NV:0.15-0.35g/d), 25 – hydroxyl - vitamin D 38.8 ng/ml (NV:30-100 ng / ml), PTH 16.41 pg / ml (NV:15-65 pg / ml).

She was found to be positive for sputum AFB, microcytic hypochromic picture on peripheral smear, low serum ferritin and no evidence of GI blood loss on stool examination and endoscopy. She was started on antituberculous treatment as per the WHO guidelines with isoniazid, rifampicin, pyrazinamide, ethambutol and Streptomycin. After five days of ATT, she again developed symptoms of tetany with carpopedal spasm and was found to have severe hypomagnesemia (0.8mg/dl), hypokalemia (3.2meq/L) and hypocalcemia (6.3mg/dl). Repeated urinary spot magnesium and creatinine showed 5.6mg/dl and 72mg/dl respectively. Streptomycin was discontinued. She was restarted on intravenous magnesium and calcium gluconate with continuing oral potassium. Patient improved symptomatically and biochemically and was discharged on modified ATT regimen including isoniazid, rifampicin, pyrazinamide, ethambutol and ofloxacin, oral magnesium, calcium and Iron supplements. One week later, she was reviewed in the OPD and was found to be doing better symptomatically. Her repeated values showed serum magnesium 1.4mg/dl, potassium 3.8meq/l and calcium 8.2mg/dl. Oral potassium was discontinued and was continued with ATT, magnesium and calcium supplementation. She was counselled for regular follow up.

## DISCUSSION

Hypomagnesemia, though infrequently looked for, is present in up to 12 % of hospitalised patients.[3] Hypomagnesemia may present clinically as fatigue, cramps, nausea, irritability, tetany, seizures, lethal cardiac arrhythmias and sudden death.[2] Symptomatic magnesium depletion is often associated with multiple biochemical abnormalities such as hypokalemia, hypocalcemia and metabolic alkalosis.[4]

Few studies[5,6, 7, 8] have documented the association of hypomagnesemia in patients with tuberculosis and is multifactorial in origin such as malnutrition, malabsorption, and therapy induced

renal loss. Hypomagnesemia occurring as a complication of anti tuberculous therapy is reported by few authors [7, 8, 9], however, hypomagnesemia occurring as a primary complication of pulmonary tuberculosis is reported rarely.

The above patient harbouring active pulmonary tuberculosis presented to us with symptoms of tetany secondary to hypomagnesemia and hypocalcemia. Hypomagnesemia contributed to Hypokalemia due to increased distal renal potassium secretion [10] as indicated by increased transtubular potassium gradient at 6.34. Hypocalcemia associated with hypomagnesemia is due to inappropriately low PTH level and PTH resistance [11, 12] which is consistent with the observations in our patient. Further, persistent hypocalcemia and hypokalemia despite adequate correction and had improved only after the correction of hypomagnesemia suggest that hypomagnesemia is the primary electrolyte abnormality contributing to other biochemical abnormalities in our patient. Hypomagnesemia in our patient prior to initiating antituberculous therapy in the absence of urinary magnesium wasting (fractional excretion of magnesium, FEMg<3%) is probably due to nutritional deficiency or malabsorption and is also supported by coexistence of iron deficiency anaemia.

However magnesium depletion of nutritional origin seldom occurs in the absence of alcoholism and parenteral feeding, as nearly all foods contain significant amount of magnesium and renal adaptation to conserve magnesium is very efficient.[13] This suggests that magnesium depletion in this case may be due to malabsorption of magnesium however the underlying mechanism of magnesium malabsorption in tuberculosis is not clear.

Recurrence of severe hypomagnesemia following streptomycin therapy in our patient was secondary to renal magnesium wasting as evidenced by increase in FEMg (value 13.89 %, NV: <3%). Increased urinary loss of magnesium and hypomagnesemia following aminoglycoside therapy is reported with the use of capreomycin [9] and gentamycin [14]. In our patient Streptomycin also caused similar effect on magnesium homeostasis, necessitating to modify the antituberculous regimen.

## CONCLUSION

We conclude that it is important to maintain a high index of suspicion of magnesium deficiency and its associated biochemical abnormalities in patients with tuberculosis. Streptomycin which is used as a first line anti tuberculous drug in patient with previously treated tuberculosis may further cause severe hypomagnesemia. Hence we recommend that streptomycin may be avoided in tuberculosis patients with pre existing hypomagnesemia and in patients receiving streptomycin, high index of clinical suspicion to be maintained to look for early signs and symptoms of hypomagnesemia.

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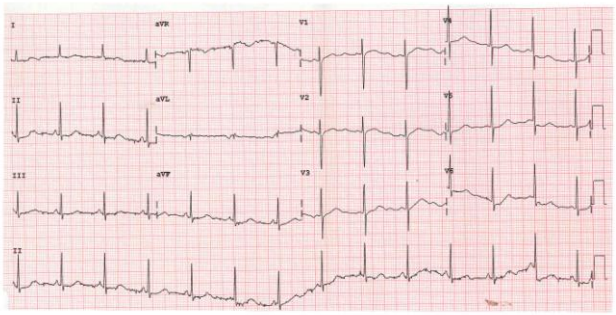

**Figure 1.ECG showing QTc prolongation (482 milli seconds)**

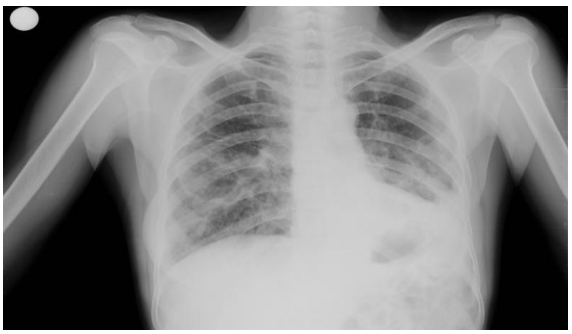

**Figure 2: Chest X ray PA view showing a thin wall cavity in the right mid zone and left sided pleural effusion.**