Refractory Hypokalemia: A Rare Presentation of Hypomagnesemia

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Abstract: We describe a case of refractory hypokalemia associated with hypomagnesemia and with other clinical features, characteristic ECG changes of ventricular bigeminy, prolonged PR interval, ‘U’ waves and associated laboratory features. Intravenous magnesium therapy reversed the Hypokalemia, ECG changes and led to improvement in clinical symptoms. A brief review of literature is also presented.

INTRODUCTION
Magnesium is fourth most common extracellular and second most common intracellular cation of the body. It is required for activation of various cellular enzymes and is responsible for neurotransmission, hormone receptor binding and postreceptor activation. It is also required for maintenance of calcium and potassium homeostasis. Severe magnesium deficiency thus results in varied manifestations ranging from ECG changes, neuromuscular abnormalities and defects in electrolyte and hormonal homeostasis. Hypomagnesemia though relatively common in clinical practice, esp. in ICU setting, is relatively infrequently diagnosed, mainly due to low index of suspicion. This article highlights the clinical findings of hypomagnesemia and stress the need for proactive treatment.

CASE REPORT
70 yr old female patient was referred to medical emergency with presenting complaints of protracted vomiting for last 15 days associated with generalized weakness and decreased appetite. Her vitals were stable and no complaint of chest pain or palpitation was present. No history suggesting any chronic illness could be elicited. On examination she was severely malnourished and CNS examination suggested decreased tone and decreased power (grade 2) of all 4 limbs with depressed reflexes. Other systemic examination showed transient prolonged PR interval, followed by persistent U waves. This prompted us to look for electrolyte imbalance as the underlying cause. Further investigations revealed low serum potassium of <2 mEq/L(3.5-5.5) and normal Serum sodium 133mEq/L.

Patient continued to have refractory hypokalemia even after adequate replacement with potassium chloride. A 24 hr urinary K+ level of 89mmol/24hrs (25-125) was found with metabolic acidosis. Serum Magnesium was 0.67 mg/dl (1.7-2.3) with 24 hr urine magnesium 8.0 mg/24hrs (75-125). Serum Ionized Ca+ was 0.98mmol/l (1.01-1.35) & S. Phosphorus 2.5 mg/dl(3.5-5). The patient’s potassium levels and symptoms improved remarkably after i.v. magnesium replacement. Subsequently raised parathyroid hormone (PTH) values of 201.50 pg/ml (15-68.30) and low normal 25- hydroxyl vitamin D (25-OHD) 30 ng/ml (11-70) were found. Also patient had low S. proteins. Liver and kidney functions and uric acid levels were unremarkable. Hypothyroidism was also documented with TSH > 100 IU/ml(0.5-5), Total T3- 20ng/dl (70-200) and Total T4- <1mg/dl(5.5-13.5).

DISCUSSION
Magnesium is the fourth most abundant extracellular cation and second most abundant intracellular cation after potassium. A normal adult contains about 25 mEq/kg magnesium with only 1% of this magnesium present in the extracellular compartment. The rest of magnesium being present in bone (67%), and cells (31%). Normal magnesium concentration is 1.7-2.1 mg/dl (0.7-0.9 mmol/l or 1.4-1.7 mEq/l). Unbound intracellular magnesium is an integral part of the energy metabolism and catalyses phosphatases that hydrolyze and transfer organic phosphate and reactions that involve adenosine triphosphate (ATP). Magnesium is required for conversion of ATP to cyclic AMP by the enzyme adenylyl cyclase. The substrate for adenylyl cyclase is Mg+-ATP and in addition, magnesium appears to have a catalytic effect on adenylyl cyclase activity. As ATP has a pivotal role in metabolism, magnesium deficiency has a potential to impair many critical cellular functions.

Proximal small bowel is the major site of magnesium absorption. Vitamin D may increase magnesium absorption. Renal excretion of magnesium occurs by glomerular filtration and tubular reabsorption, mainly in thick ascending limb (TAL) of the Loop of Henle(60-70%). Causes of hypomagnesemia can be due to gastrointestinal or renal losses.

In gastrointestinal causes prolonged nasogastric suction or vomiting, acute or chronic diarrhea, malabsorption syndromes and protein calorie malnutrition may be responsible. 24hr urine Mg+ excretion is generally less in gastrointestinal diseases. Renal loss occurs due to renal tubular acidosis, pylonephritis, Bartter’s & Gitelman’s syndrome, osmotic diuresis as present in diabetes, mannitol administration, and due to high urea levels. Also increased renal losses may be due to alcohol or metabolic acidosis. Normal urinary excretion of magnesium in the normal range in presence of hypomagnesemia suggests a renal leak. Endocrine disorders like hyperthyroidism, hypercalcemia, hyperaldosteronism, phosphate depletion may be responsible.

Hypomagnesemia may coexist with hypokalemia, hypocalcemia & hypophosphatemia. Potassium depletion in hypomagnesemia may be multifactorial e.g. due to kaliuresis, altered cell membrane permeability, decreased Na+-K+ ATPase activity, decreased inward rectification of K+ and decreased Na+-K+ cotransport. Thus Mg+ has a pivotal role in maintaining K+ homeostasis.

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Although, hypomagnesemia is usually associated with hypoparathyroidism, few cases with normal or high PTH values have been found in literature\(^1\). Our case has high PTH levels. In spite of high PTH levels, calcemic response of parathyroid hormone is not adequate. This may be due to End organ resistance to PTH at the level of bone and kidney. Due to low 25 hydroxy vitamin D, there is defective mineralization of osteoid tissue which leads to defective calcemic response of PTH. Even low magnesium levels are responsible for this end organ resistance. This may be explained by defective generation of cyclic AMP in kidney, bone and parathyroid gland resulting from magnesium deficiency as cyclic AMP is a mediator in the peripheral actions of PTH resulting in decreased renal and skeletal responsiveness to parathyroid hormone. In our case, there were low S. phosphorus levels, which may be due to low dietary phosphorus intake before admission and intravenous dextrose infusion given to patient after admission\(^4\). Hypothyroidism may be an isolated finding in this case. Thus prolonged protracted vomiting, led to loss of magnesium and low serum phosphorus levels were also responsible for low magnesium levels. Severe symptomatic hypomagnesemia should be treated with intravenous magnesium. It can take up to 3 to 7 days to replenish the intracellular stores. So after intravenous therapy, oral magnesium supplementation is required. Our patient achieved normal magnesium levels followed by normal potassium & calcium levels subsequent to intravenous replacement\(^6\). After about 2 months, magnesium was discontinued, and subsequent magnesium levels done are with in the normal levels. The presence of resistant hypokalemia & hypocalcemia should alert the physician to look for underlying hypomagnesemia as the cause.

**REFERENCES**