Tacrolimus-Induced Hypomagnesemia in A Kidney Transplant Recipient

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Introduction

- While several medications can cause hypomagnesemia in kidney transplant recipients (KTR).
- Calcineurin inhibitors (CNI) is one of the most common causes from early through late post-transplant periods.
- We report a case of KTR presenting with hypomagnesemia from renal magnesium (Mg) loss. Serum Mg was inversely related to a 12-hour tacrolimus trough level.
- Hypomagnesemia is resolved after the tacrolimus level was in the target range.

Case Description

- A 37-year-old man with ESKD secondary to primary FSGS had a LRKT that lasted for 11 years and failed due to recurrent FSGS 8 years ago.
- He underwent an uneventful DDKT one year ago with maintenance immunosuppressive medications including tacrolimus, mycophenolate sodium, and prednisolone.
- He also had GERD and had taken pantoprazole 40 m daily.
- He developed post-transplant hypomagnesemia with a serum Mg of 1.3–2.4 mg/dL requiring Mg replacement with magnesium chloride ($MgCl_2$) 64 mg oral daily.
- Five days prior to admission, he developed dizziness and generalized weakness. The workup revealed a dropped serum Mg of 1.1 mg/dL from 1.7 mg/dL 10 days ago. He also had diarrhea but denied taking diuretics.
- Physical exam showed no Chvostek sign.
- A 12-lead EKG showed normal sinus rhythm with left ventricular hypertrophy. He had normal corrected serum calcium of 8.82-9.98 mg/dL, ionized calcium of 1.03 mmol/L, serum potassium of 4.2–4.7 mmol/L, and TSH of 1.334 uIU/mL.
- The FE_{Mg} was elevated to 15.13%. He had normal serum phosphorus of 2.9–3.8 mg/dL and elevated PTH of 301 pg/mL while taking cinacalcet 30 mg daily.
- During this admission, serum Mg fluctuated with the lowest of 1.1 mg/dL and up to 2.4 mg/dL after Mg replacement with IV magnesium sulfate 6 g daily, $MgCl_2$ up to 128 mg oral three times daily, and magnesium oxide (MgOx) up to 800 mg oral three times daily.
- A 12-hour tacrolimus trough level had been elevated 9.6- 27.3 ng/mL (target level of 5-7 mg/mL) despite the lowest tacrolimus dose of 0.5 mg twice daily. Pantoprazole was discontinued.
- After a 1-week hospitalization, his symptoms including diarrhea were improved with a serum Mg of 1.6 mg/dL. He was discharged home with oral Mg. Follow-up serum Mg 1 week later was 1.8 mg/dL. A 12-hour tacrolimus trough level ranged 6-6.6 ng/mL (Figure 1).

Discussion

- Our patient presented with acute onset of symptomatic hypomagnesemia. Diarrhea and proton pump inhibitors are common causes of hypomagnesemia from GI loss.
- However, high FE_{Mg} indicates renal Mg wasting.
- Tacrolimus can cause hypomagnesemia from downregulating TRPM6, the major active transport protein at the apical membrane of the distal renal tubule epithelial cells requiring magnesium reabsorption.
- In our patient, there was a temporal correlation between elevated tacrolimus level and low serum magnesium.
- Cinacalcet may also contribute to renal Mg wasting in this patient since it activates calcium receptors in the thick ascending limb of loop of Henle resulting in decreased Mg reabsorption.

Conclusions

- CNI is a common medication used in KTR which well-known to induce post-transplant hypomagnesemia from immediate through late post-transplant period.
- Carefully reviewing the temporal relationship ofthe CNI level with the occurrence of hypomagnesemia and excluding other potential causes can guide transplant providers to lower the dose of CNI and mitigate the severity of hypomagnesemia.

Reference

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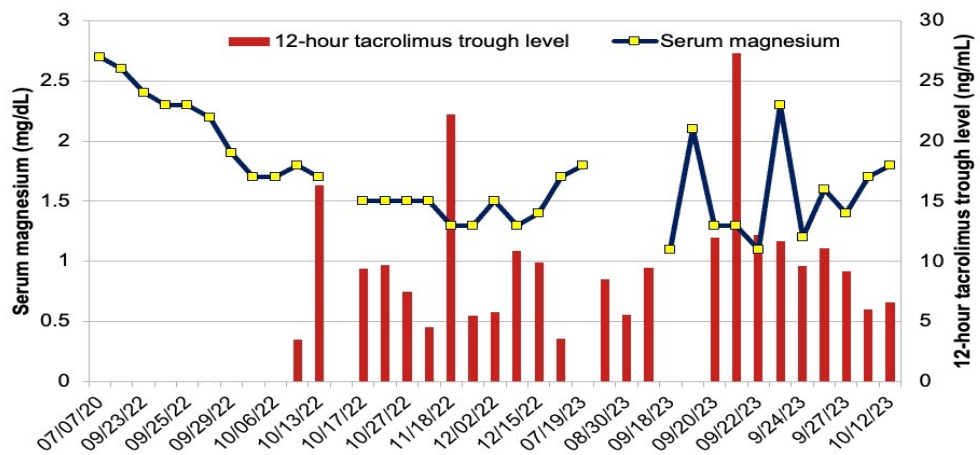

Figure 1: Clinical cause demonstrating temporal relationship between decreased serum magnesium and elevated tacrolimus level