Case Report: A Rare Life threatening Side Effect of Trimethoprim-Sulfamethoxazole

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ABSTRACT

Trimethoprim-Sulfamethoxazole (TMP-SMX) or Co-Trimazole is the treatment of choice for meliodosis. A 52-year-old man presented with generalized body weakness with reduced appetite. He had bradycardia on examination. After investigations, he was diagnosed as hyperkalaemia. He had life-threatening hyperkalaemia treated with Trimethoprim-Sulfamethoxazole (TMP-SMX) as part of the eradication therapy for Meliodosis. Urgent haemodialysis was done. There were changes done for his meliodosis treatment. This case wished to highlight the importance of considering hyperkalemia in patient treated with Trimethoprim-Sulfamethoxazole especially when risk factor for hyperkalaemia is present.

Keywords: Trimethoprim-Sulfamethoxazole, hyperkalaemia, meliodosis

INTRODUCTION

Trimethoprim-Sulfamethoxazole (TMP-SMX) or Co-Trimazole has been used as an antibiotic since 1974[1]. TMP-SMX is effective against a wide variety of aerobic gram positive and gram negative bacteria, P.jirovecii and some protozoa[2, 3]. In Meliodosis infection, TMP-SMX forms the 'back bone' of its treatment[4]. The efficacy of TMP-SMX in Meliodosis treatment has been well documented in literature[4,5, 6,7]. However, like other antibiotics, TMP-SMX is not free from side effects. One of the often overlook side effects of TMP-SMX is hyperkalemia that may be life threatening if not detected and treated promptly. The association between Trimethoprim-Sulfamethoxazole and hyperkalaemia has been well described in literature[8, 9].

CASE PRESENTATION

A 52-year-old man known case of diabetes mellitus, hypertension, chronic kidney disease and chronic liver disease due to Hepatitis B was seen in the medical outpatient clinic a month after his discharge. He had a recent long stay in the ward and treated for meliodosis with chronic osteomyelitis of left tibia and abdominal prostate abscess. He was discharged with oral Trimethoprim-Sulfamethoxazole as part of Meliodosis eradication therapy. The antibiotic supply was given until his clinic appointment date.

Two weeks after discharged, he was reviewed in the clinic. During clinic review, he complained of generalized body weakness with reduced appetite, other systemic review was unremarkable. He was compliance with his medication. He was neither on nephrotoxic drugs like ACEI or other diuretics nor traditional medication. In view of his significant past medical history and the possibility of meliodosis relapse, he was admitted to the ward for further clinical evaluation.

On examination, he was alert with intact cognition. He had stigmata of chronic liver disease but no asterixis or jaundice to suggest decompensation. There was a discharging sinus over the left anterior shin with minimal clear secretion. Vital sign revealed blood pressure of 130/79 mmHg; heart rate 37 beats/min, temperature 37°C, SpO2 97%. Cardiovascular system: S1 and S2 without murmur; Respiratory system: equal breath sound without added sound; Abdomen system: soft, non-tender without palpable liver/spleen.

In view of the unexplained bradycardia and background chronic kidney disease, we performed urgent serum potassium, venous blood gases and ECG (see Figure 1).

Venous Blood Gases (VBG): pH7.168, pCO2 19 mmHg, HCO3 6.7 mmol/L, urea 25.7 mmol/L, sodium 128 mmol/L, potassium 8.91 mmol/L, creatinine 487 µmol/L, creatinine clearance 12 ml/min, haemoglobin 8.8g/dl, total white cell 9.8x109/L, platelet 257 × 109/L. A month ago, his renal parameters were urea 17.6 mmol/L, sodium 132 mmol/L, potassium 3.73 mmol/L, creatinine 374 µmol/L; creatinine clearance 15.92 ml/min.

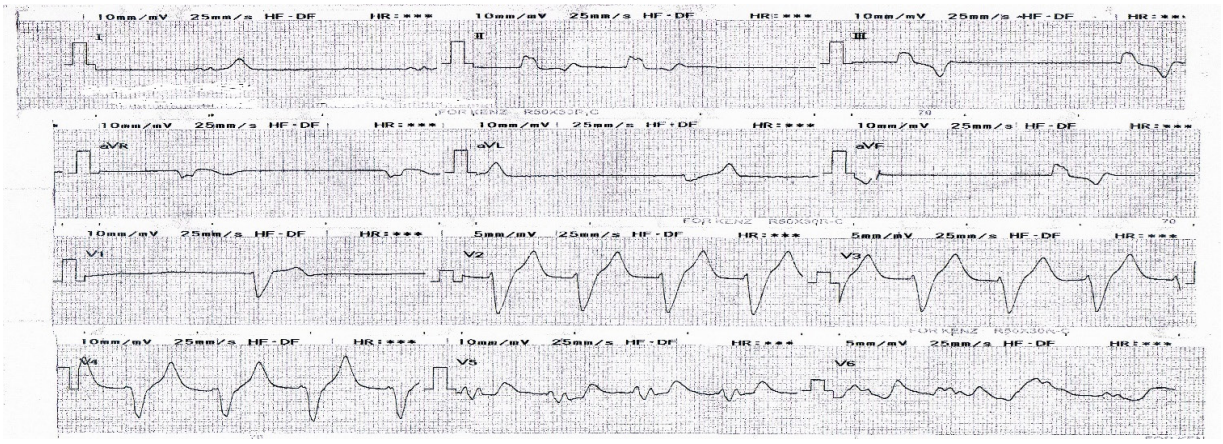

Figure 1 Sinus bradycardia with broad QRS complex and tall tented T-wave consistent with hyperkalaemia changes before haemodialysis

He was treated as life threatening hyperkalaemia secondary to Trimethoprim-Sulfamethoxazole. He was dialyzed urgently via a temporary femoral catheter. While waiting for haemodialysis, he was given two cycles of IV Calcium Gluconate 10% with IV Dextrose 50% and IV Insulin, twice Salbutamol 5 mg nebulization and immediate dose of powder calcium polystylene sulphonate (Kalimate) and Syrup Lactulose. During admission, he underwent twice haemodialysis session to lower down his potassium. Trimethoprim-Sulfamethoxazole was withheld and adverse drug reaction to this agent was notified to the pharmacy unit. Overtime, his serum potassium level reduced to normal range and the initial ECG changes had resolved as shown in Figure 2. His initial bradycardia had resolved once haemodialysis commenced and hyperkalaemia resolved. Upon discharge, his heart rate was in the range of 70 – 85 beats/min, regular with good volume.

He was discharged with oral amoxicillin-clavulanic acid and Doxycycline as an alternative eradication therapy for his meliodosis treatment. Both antibiotics were given for two weeks where he was seen again in clinic after that. His serum potassium has remained in the normal range ever since not on Trimethoprim-Sulfamethoxazole. Two months after discharge, he was admitted again in septic shock with relapse of meliodosis. Unfortunately he did not survive the second admission.

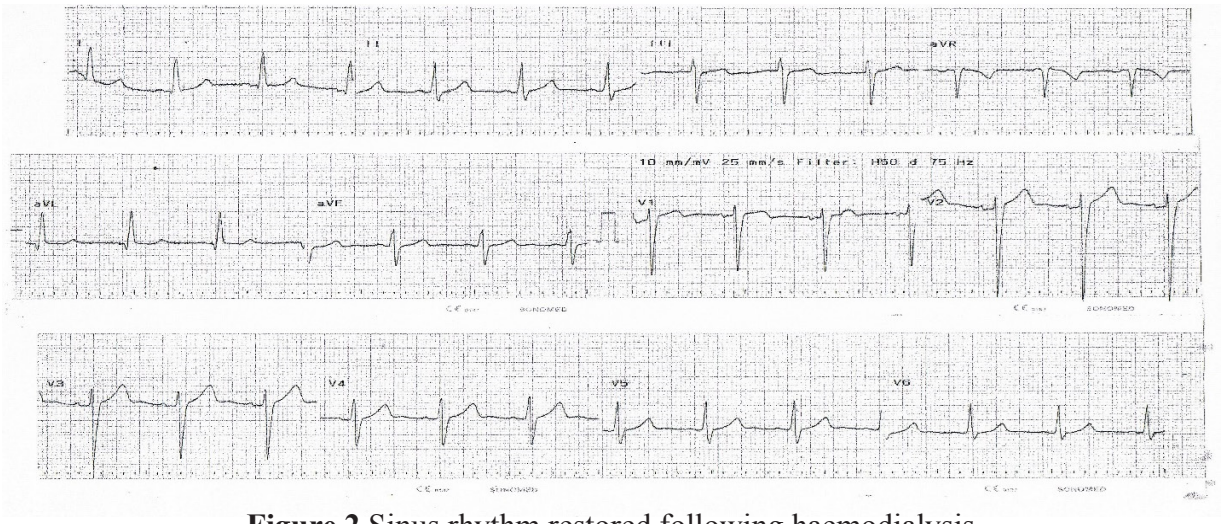

Figure 2 Sinus rhythm restored following haemodialysis

DISCUSSION

This case illustrates a rare yet important side effect of trimethoprim-sulfamethoxazole in causing life threatening hyperkalaemia especially in a chronic kidney disease patient. Often this side effect is overlooked in general practice, exposing patient to unnecessary risk that may threaten life.

The association between Trimethoprim-Sulfamethoxazole and hyperkalaemia has been well described in literature 8, 9. The risk factors for hyperkalaemia predisposition in patient taking Trimethoprim-Sulfamethoxazole include chronic kidney impairment, concurrent usage of angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), potassium sparing diuretic (i.e. spironolactone), underlying immune-compromised state 9, 10. Trimethoprim acts like Amiloride, a potassium sparing diuretics by inhibiting the apical membrane sodium channel of distal nephron. As a result, the transepithelial voltage is reduced causing potassium retention11. In our patient, he had baseline kidney impairment but he was not prescribed with any nephrotoxic medication.

Trimethoprim-Sulfamethoxazole forms the critical component meliodosis treatment4. This is more essential with the presence of deep-seated abscess and osteomyelitis like in our case. Literature review showed that other alternative for meliodosis therapy like Amoxicillin-Clavulanic Acid is less effective, associated with higher relapse rate as compare to regimen containing Trimethoprim-Sulfamethoxazole 7. Based on this finding, hence this patient was prescribed with Trimethoprim-Sulfamethoxazole despite having renal impairment as the benefit outweighs the harm. Duration of Trimethoprim-Sulfamethoxazole treatment is at least 5 months depending on clinical and radiological response.

We wished to emphasize that close monitoring of serum potassium and kidney function warranted once Trimethoprim-Sulfamethoxazole commenced for patient especially for those with high-risk factors 8, 9, 10. A deterioration of kidney function may need adjustment of dosage or even stopping the agent directly. The most serious manifestation of hyperkalaemia are muscle weakness, paralysis, cardiac arrhythmia and conduction abnormalities. Hyperkalaemia has many effects on the heart; the cardiac manifestation can varies from bradyarrhythmia at one end of spectrum to tachyarrhythmia at the other end. In our case, if the hyperkalaemia was not detected earlier and treated promptly, he might went into cardiac arrest due to cardio-toxic effect of hyperkalaemia. The association between sudden death and hyperkalaemia has been strongly supported by various literatures 8, 9. Yet some patient may be apparently well apart from some vague symptoms as shown in this case. Hence a strong clinical suspicion is necessary.

CONCLUSION

Life-threatening hyperkalaemia and sudden death are a known rare complication of Trimethoprim - Sulfamethoxazole treatment. High-risk patient for hyperkalaemia due to Trimethoprim - Sulfamethoxazole include chronic kidney impairment, concurrent usage of angiotensin converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), potassium sparing diuretic (i.e. spironolactone), underlying immune-compromised state like AIDS. Thus, close monitoring of serum potassium and kidney function warranted especially among the high-risk group patients.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

CONSENTS

Written informed consent was obtained from the patient to publish the case with its related pictures. A copy of the written consent is available for review by the Chief Editor of this journal.

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