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Case Report
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Use of Trimethoprim-Sulfamethoxazole in Patient with G6PD Deficiency for Treating Pneumocystis Jirovecii Pneumonia

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Abstract

Case Report: A fixed dose of Trimethoprim-Sulfamethoxazole (TMP/SMZ) is the treatment of choice for Pneumocystis Jirovecii Pneumonia (PJP) recommended by Infectious Diseases Society of America (IDSA). However, TMP/SMZ has been reported to cause hemolysis when administered to patients with deficiency. PJP might be fatal without receiving treatment. Therefore, there is a dilemma on the use of TMP/SMZ in G6PD deficient patients. Herein, we report a G6PD deficient patient with PJP treated successfully with 21 days of TMP/SMZ without any signs and symptoms of hemolysis.

Conclusion: It might be safe for the Southeast Asia population with a history of G6PD deficiency to administer TMP/SMZ under expert surveillance.

Keywords: Glucose-6-phosphate dehydrogenase deficiency; HIV; Pneumocystis pneumonia; Trimethoprim-sulfamethoxazole

Abbreviations

ALT: Alanine Amino Transferase; AST: Aspartate Transaminase; BUN: Blood Urea Nitrogen; CXR: Chest X-Ray; Cr: Creatinine; G6PD: Glucose-6-Phosphate Dehydrogenase; GGO: Ground-Glass Opacities; Hb: Hemoglobin; HRCT: High-Resolution Computed Tomography; IDSA: Infectious Diseases Society of America; OPD: Out-Patient Department; PJP: Pneumocystis Jirovecii Pneumonia; PCP: Pneumocystis Pneumonia TMP/SMZ: Trimethoprim-Sulfamethoxazole; RBC: Red Blood Cell; WBC: White Blood Cell; WHO: World Health Organization

Introduction

Pneumocystis Pneumonia (PCP) is an opportunistic and fatal infection caused by the fungus Pneumocystis jirovecii. As per guideline, Trimethoprim-Sulfamethoxazole (TMP/SMZ) is the recommended regimen for managing Pneumocystis Jirovecii Pneumonia (PJP) [1]. However, TMP/SMZ is associated with the serious side effect of drug induced hemolytic anemia associated with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency. Although substitute regiment does exist, the success rate of using those alternative regimens is below 80% except for the combination use of TMP and dapsone, which is also a medication contraindicated in patients with G6PD deficiency. Jennifer et al. [2] therefore suggested avoiding using TMP/SMZ in patient with the deficiency of G6PD. On the other hand, a literature reviews done by Youngster et al. [3] Suggested that TMP/SMZ is probably safe when given in usual therapeutic dose. Together with the inconclusive recommendations, there was also no real-world experience on the use of TMP/SMZ in G6PD deficiency patients in Taiwan. In this article, we reported a G6PD deficient patient whom recovered from PJP by administration of TMP/SMZ.

Case Presentation

A 31-year-old Han Taiwanese man with a history of G6PD deficiency was admitted due to fever, cough, fatigue, muscle soreness and occasional dyspnoea for 20 days. After admission, Chest X-Ray (CXR) revealed bilateral infiltration. The White Blood Cell (WBC) count was 5200 cells/mL, N-Seg 72.3%, lymph 19.2%, Hemoglobin (Hb) 13.2 g/dL, platelet 231,000/mL, Blood Urea Nitrogen (BUN) 16 mg/dL, Creatinine (Cr) 0.8 mg/dL, Sodium (Na) 136 mmol/L, Potassium (K) 3.6 mmol/L, Aspartate Transaminase (AST) 30 U/L, Alanine Amino Transferase (ALT) 21 U/L

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and total bilirubin 0.7 mg/dL. Blood and sputum acid fast satin, TB culture, pneumococcal and legionella urinary antigen test, *Mycoplasma* IgM, *Chlamydophila* IgM, Toxoplasma IgG all showed negative. High-Resolution Computed Tomography (HRCT) was arranged and showed diffuse Ground-Glass Opacities (GGO) and thickening of interlobular septum. PJP was then considered. HIV EIA and HIV western blot both showed positive result. CD4 counts were 50 cells/mm^3. HIV RNA (Ribonucleic Acid) load was 45588 copies/ml. Oxygen supplement was delivered and TMP/SMZ 240 mg/1200 mg intravenously was given every eight hours. At Day-13 of TMP/SMZ treatment, a review of medication was preformed and the issue of G6PD deficiency history was raised. The blood test was done immediately and Hb was 11.6 g/dL, total bilirubin was 0.7 mg/dL, direct bilirubin was 0.3 mg/dL. With no obvious sign and symptoms as well as episode of acute hemolytic, the TMP/ SMZ treatment was continued. At Day-16, under stable condition, the patient was discharged with oral TMP/SMZ 240 mg/1200 mg three times a day for five more days and an Out-Patient Department (OPD) appointment was arranged. After 21 days of PJP treatment completed, a prophylaxis dose of TMP/ SMZ 160 mg/800 mg once daily was given until CD4 reach 200 cells/mm^3. The G6PD enzyme activities were measured by quantitative fluorescence assay and showed a level of 0.6 U/g Hb (reference range: 6.4 U/g Hb to 12.9 U/g Hb) which was classified as severe enzyme activity deficiency by the definition defined by World Health Organization (WHO) [4].

Discussion

G6PD deficiency is the most commonly inherited Red Blood Cell (RBC) enzymatic defect, affecting around 400 million people worldwide [5]. About 7.5% of the world population carries one or two genes for G6PD deficiency. It is an X-linked genetic disorder with 187 known allelic mutations [6]. In Taiwan, G6PD deficiency prevalence between male and female were approximately 2.81% and 0.7% respectively [7].

TMP/SMZ is used in a variety of infectious diseases and is the recommended treatment option in current practice for managing PJP [8]; however, it is associated with hemolysis when administered to G6PD deficient patients. Chisholm-Burns et al. [9] demonstrated a case with of African ethnicity with G6PD deficiency that experienced hemolysis after administration of double strength of TMP/SMZ orally for eight days. Reinke et al. [10] also reported a black woman with HIV infection who received only one dose of TMP/SMZ intravenously for managing PJP which then resulted in acute hemolysis. On the contrary literature had reported challenging G6PD subjects with genetic variant alleles. A commonly observed in the African population, with TMP/SMZ at the dose of 320/1600 mg every 12 h. The level of hemoglobin did not decrease significantly nor did any hemolysis occur throughout the trial [11]. The possible explanation was that the regeneration rate of hemoglobin was faster than destruction of hemoglobin in G6PD A-variant population. However, the severity of hemolytic anemia varies among individuals with G6PD deficiency. Specific G6PD alleles are associated with G6PD variants with different enzyme activity and, therefore, result in different levels of disease severity [12]. In Southeast Asia, the most common variant alleles appear to be G6PD Kaiping and Canton, which are different from the western or African ethnicity [13]. To date, there is still insufficient evidence for the population in Taiwan to suggest a robust relationship between our G6PD variant alleles and the degree of disease severity with regards to the safety in the use of TMP/SMZ in G6PD deficiency [14].

Conclusion

The experience and evidence regarding safety in the use of TMP/SMZ in G6PD deficient HIV infected patients is not yet clear. Herein, we documented a case of a G6PD deficient HIV infected man successfully treated the PJP with high dose of TMP/SMZ without any signs and symptoms of hemolysis.

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