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Pneumocystis jirovecii pneumonia in a human immunodeficiency virus-infected patient with G6PD deficiency-successful treatment with anidulafungin

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Abstract. – CASE REPORT: We reported a HIV-infected patient, diagnosed as PJP with G6PD deficiency. *Pneumocystis jiroveci pneumonia* (PJP) is the most common opportunistic infection in subjects with human immunodeficiency virus (HIV) infection. Trimethoprim-sulfamethoxazole (TMP-SMX) is the first line regimen for *Pneumocystis jirovecii pneumonia*. However, patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency should avoid this agent to prevent hemolysis. Although there is evidence of echinocandins used successfully in animal studies, and few articles describing the clinical use of caspofungin, the clinical experience of anidulafungin as an alternative regimen to the treatment of PJP is rare in the HIV-infected patients.

CONCLUSIONS: The patient was successfully treated with anidulafungin for 3 weeks and was led to a successful outcome.

Key Words:
Pneumocystis jiroveci pneumonia, G6PD deficiency, HIV, Anidulafungin.

Introduction

Pneumocystis jiroveci pneumonia (PJP) is the most common opportunistic infection in subjects with human immunodeficiency virus (HIV) infection. Trimethoprim-sulfamethoxazole (TMP-SMX) is the first line regimen used for *Pneumocystis* pneumonia. However, patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency should avoid this agent to prevent hemolysis. Alternative regimen with caspofungin has been reported in the literature. Here, we present a patient diagnosed as having PJP and successfully treated with anidulafungin.

Case Report

A 19-year-old man with a history of glucose-6-phosphatase dehydrogenase (G6PD) deficiency was admitted due to dry cough for 1 month. Shortness of breath (SOB) was also noted when fast walking. At our Ordinary Patient Department (OPD), physical examination showed bilateral mild coarse, and chest roentgenography showed bilateral interstitial infiltration of lung fields (Figure 1A). The white blood cell (WBC) count was 5700 cells/mL, N-Seg 54.3%, lymph 35.1%, hemoglobin (Hb) 13.6 g/dL, platelet 170,000/mL, blood urea nitrogen (BUN) 8 mg/dL, creatinine (Cr) 0.95 mg/dL, sodium (Na) 139 mmol/L, potassium (K) 3.1 mmol/L, aspartate transaminase (AST) 26 U/L, alanine aminotransferase (ALT) 17 U/L. Blood and sputum acid fast satin, TB culture, pneumococcal and legionella urinary antigen test, Mycoplasma IgM, Chlamydophila IgM all showed negative. Computed tomography scans revealed extensive bilateral ground glass infiltrates (Figure 2). HIV ELISA test and syphilis test both showed positive. CD4 count was 44 cells/mm^3, and HIV RNA (ribonucleic acid) load was 572004 copies/ml. PJP-PCR (polymerase chain reaction) of sputum specimen showed positive. Due to the patient's G6PD deficiency history, we used second line medication for treating his PJP. Combination therapy with anidulafungin (200 mg IV loading then 100 mg IV qd) plus clindamycin (600 mg IV q8 h) was used

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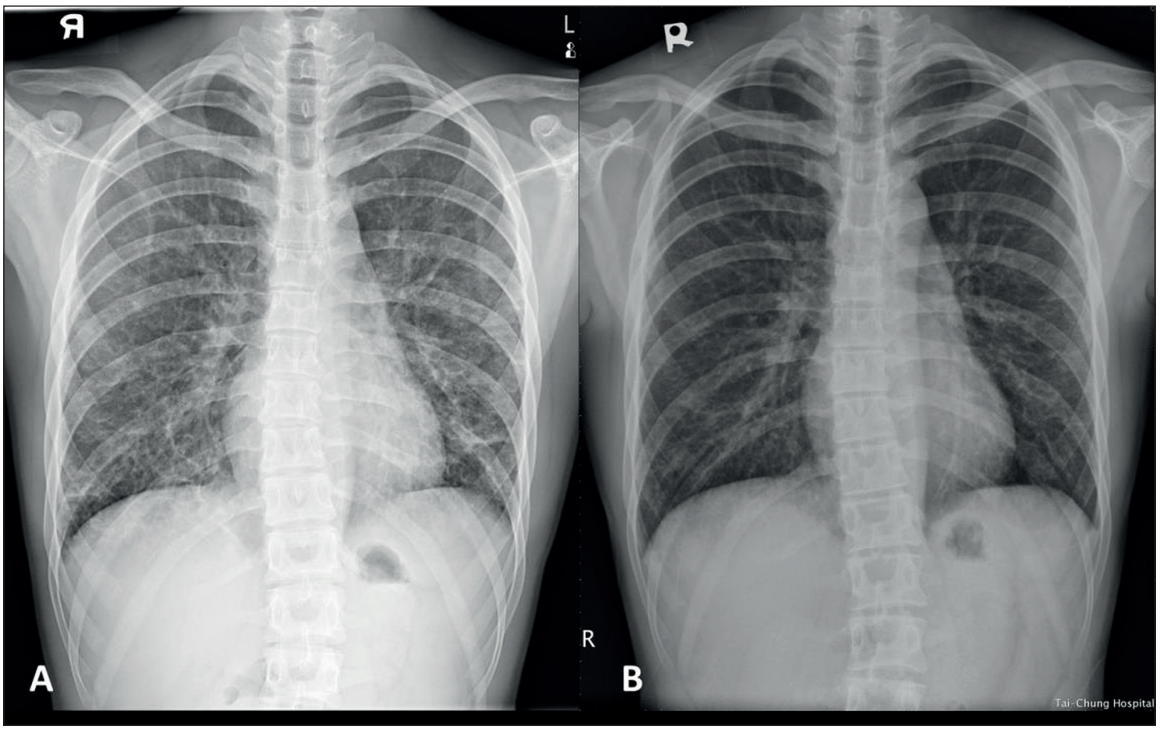

Figure 1. ***(A)*** Chest roentgenography revealed bilateral interstitial infiltration of lung fields on Day 1. ***(B)*** Chest roentgenography revealed significant improvement on Day 21.

on Day 2. Skin rash was observed over trunk and limbs on Day 5. We discontinued the use of clindamycin under the suspicion of drug allergy. At the same time diphenhydramine (30 mg IV q8 h) and hydrocortisone (100 mg IV q8 h) were given on Day 5-11. Skin rash improved after medication treatment. Fever subsided and dyspnea improved gradually. The patient underwent anidulafungin therapy for 21 days. The chest X-ray also showed a significant improvement on Day 21 (Figure 1B). The patient started highly active antiretroviral therapy (HAART) regimen with triumeq® 1 tablet (600/50/300 mg, ViiV Healthcare, GSK, UK) orally once daily, a combination of abacavir, dolutegravir, and lamivudine for the treatment of human immunodeficiency virus type 1 (HIV-1) since Day 15. No significant side effect was observed during the period of triumeq® treatment. The patient did not use PJP prophylaxis agent at discharge on Day 22 and keep triumeq® treatment home and OPD follow-up.

Discussion

The significant improvement in the mortality and morbidity rate of HIV-infected patients has been achieved with the increased use of HAART, which has made HIV disease become a chronic disease[1]. However, PJP is a potentially life-threatening pulmonary infection that occurs

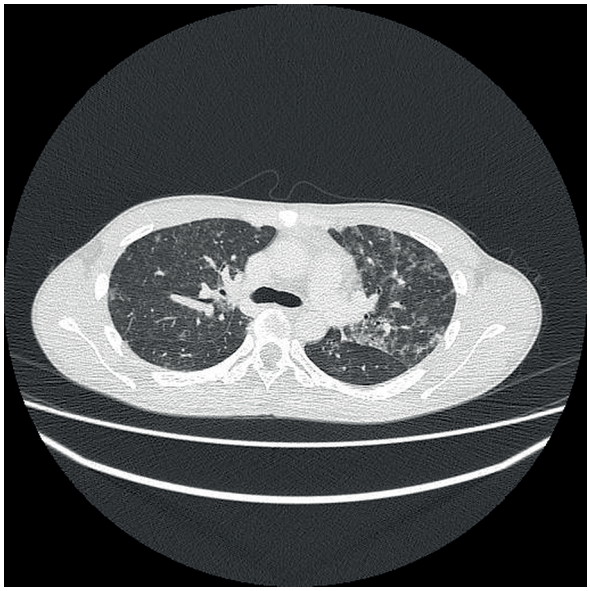

Figure 2. Computed tomography revealed bilateral ground glass infiltrates.

among HIV-infected patients with a low CD4 count. In Taiwan, a prospective observational multicenter study[2] showed that PJP was the most common cause of pulmonary complication (63%) in patients with HIV infection and CD4 count < 200 cells/mm^3. Currently, the first-line treatment regimens of PJP are sulfonamides, and fixed combination of TMP-SMX is the first choice. TMP-SMX synergistically blocks folic acid synthesis leading to bactericidal effect by inhibiting dihydrofolate reductase (DHFR) and dihydropteroic acid synthase (DHPS). However, patients with G6PD deficiency should avoid this agent to prevent hemolysis.

The clinical available alternative regimens include pentamidine, clindamycin plus primaquine, atovaquone or dapsone plus TMP. In a review article, the treatment success rate of pentamidine and clindamycin plus primaquine was 40-74% and 64-76% in patients with moderate-to-severe PJP infection, and the success rate of atovaquone and dapsone plus TMP was 57-80% and 88-93% in patients with mild-to-moderate infection[3]. However, primaquine, SMX, and dapsone are contraindicated in patients with G6PD deficiency to prevent hemolysis whilst atovaquone is relatively safety. Although there is evidence of echinocandins used successfully in animal studies, a few investigations[4-6] described the successful clinical use of caspofungin in HIV-infected patients. We treated the patient with anidulafungin due to the availability in our hospital. *Pneumocystis jirovecii* used to be classified as a protozoan but is now considered a fungus. Morphologically, *Pneumocystis jirovecii* exists in two forms: the cyst form and the trophic form. Echinocandins are antifungal agents that inhibit the synthesis of (1-3) -β-D-glucan (BDG) in fungal cells. The cyst form of *Pneumocystis jirovecii* also contains BDG, which might be sensitive to echinocandins, but not in trophic form.

In an animal study, Cushion et al[7] showed for that the treatment with echinocandins significantly reduced cyst burden within lung tissue, not trophic burden.

Ceballos et al[4] demonstrated a case of HIV infection with *Pneumocystis pneumonie*. TMP-SMX was initiated, but the patient had treatment failure after four weeks. Caspofungin was added to TMP-SMX. After 3 days of caspofungin initiation, the patient demonstrated a significant improvement[4]. Another case reported by Lee et al[5] showed that the patient was initially administered with TMP-SMX, leukopenia and skin rash developed after one week. TMP-SMX was discontinued, and the regimen was switched to caspofungin for two weeks with favorable outcome[5]. A 4-year retrospective analysis revealed that 10 HIV-infected patients received caspofungin as a part of salvage therapy after first-line treatment failure; mortality rate was 10%[6].

Caspofungin, micafungin and anidulafungin are three drugs of the echinocandin class of antifungals. Cushion et al[8] reported that echinocandins differ in their abilities to deplete the ATP (adenosine triphosphate) of *Pneumocystis* in both biofilms and suspension cultures and this variability mostly reflected the reported efficacies in animal models of infection. Anidulafungin had significant activity at 1 and 5% serum concentrations, and consistently reduced the ATP levels better than caspofungin or micafungin in either biofilms or suspension cultures assay system. Cushion et al[7] also showed that anidulafungin-treated mice failed to spread the infection, but regeneration of cyst forms happened after withdrawal of anidulafungin treatment.

Conclusions

Evidence of monotherapy with echinocandin has not been well established and the experience as alternative or rescue therapy for HIV-infected patients with PJP is limited. Here, we present a HIV-infected patient, diagnosed as PJP with G6PD deficiency, who was successfully treated with anidulafungin for 3 weeks and led to a successful outcome. Except for caspofungin, anidulafungin is another option of alternative regimens in treating PJP in HIV-infected patient.

Conflict of Interest

None to declare. Each author certifies that he or she has no financial organization (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article. There are no other conflicts of interest. The case described in the article was performed with funding from Taichung Hospital, Ministry of Health Welfare, Taichung, Taiwan, R.O.C.

Authorship

All authors meet the ICMJE authorship criteria

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