Journal of Microbiology, Immunology and Infection 57 (2024) 518—519

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com

Correspondence

Combination of trimethoprim-sulfamethoxazole and clindamycin in the treatment of relapsing toxoplasmic encephalitis

Dear Editor,

Toxoplasmic encephalitis (TE) in patients with acquired immunodeficiency syndrome (AIDS) almost exclusively results from reactivation of latent tissue cysts of *Toxoplasma gondii* because of progressively deteriorating cellular immunity in the hosts.[1] Current treatment guidelines for TE recommend pyrimethamine (PYR) plus sulfadiazine (SDZ) for initial therapy of choice, and PYR plus clindamycin (CLD) for patients intolerant of SDZ or who do not respond to PYR-SDZ, while trimethoprim-sulfamethoxazole (TMP-SMX) for an alternative.[1] Of note, PYR has higher side effects (especially hematologic toxicities) and higher price, and is not always readily accessible in many countries.[2] PYR is reportedly no longer available in retail pharmacies in the USA (https://clinicalinfo.hiv.gov/en/news/notice-availability-pyrimethamine). This underscore the importance of reports added to the not yet pooled enough cases to clarify the potential therapeutic role of TMP-SMX and TMP-SMX containing regimen against TE.

A 49-year-old woman with underlying AIDS and tetralogy of Fallot was poorly compliant to antiretroviral therapy (ART) and primary prophylaxis for *Pneumocystis jirovecii* pneumonia (PJP) with TMP-SMX (80—400 mg) per day. She first experienced severe headaches in September 2013 when her CD4-T lymphocyte count was 77 cells/μL. Brain computed tomography (CT) and magnetic resonance imaging (MRI) revealed ill-defined lesions in bilateral cerebrums, with a midline left shift (Fig. 1, A-C); her anti-toxoplasma immunoglobulin G (IgG) antibody was positive, and IgM negative. It was clinically and radiologically improving under treatment with TMP-SMX (5 mg/kg-25 mg/kg) per 12 h for 6 months. Treatment was then switched to secondary prophylaxis with TMP-SMX (80 mg—400 mg) per day. However, she was again poorly compliant to medication, and once declined follow-up serological evaluations.

On 2016/03/22, the patient was presented to our Emergency Services because of a 2-week sustained headache and progressively altered consciousness. Her CD4-T lymphocyte was 156 cells/μL, and HIV viral load 121,506 copies/mL. Brain CT (Fig. 1, D) and MRI (Fig. 1, E) disclosed an ill-defined mass lesion over the right basal ganglia with marked perifocal edema. Intravenous TMP-SMX (5 mg/kg-25 mg/kg) per 12 h and CLD 600 mg per 6 h were administered for an assumed relapsing TE. Mannitol and dexamethasone were tailored based on clinical responses. Her altered consciousness improved one week later with consistent findings in the follow-up brain CT (Fig. 1, F). The patient was released after a 3-week hospitalization, and oral-form TMP-SMX (5 mg/kg-25 mg/kg) per 12 h was prescribed for continuous treatment on an outpatient basis. Therapeutic TMP-SMX was switched to its secondary prophylactic dosage 4 months later. Follow-up brain CT at 21 months later indicated continuous regressive change, despite residual hypo-dense lesions over the right putamen and right temporal lobe (Fig. 1, G).

When last seen on 2023/8/31, the patient was clinically well, with CD4-T lymphocyte count of 396 cells/μL. This case suggests that TMP-SMX plus CLD be effectively treat acute TE. TMP-SMX alone was previously reported to be as effective as PYR plus SDZ in the treatment of acute TE in a randomized control trial with 77 patients included.[3] Focal subacute neurological deficits and ring-enhancing brain lesions in the basal ganglia are frequently encountered in TE[4]; the earlier the diagnosis of TE, the better the outcome is.[4] Unfortunately, small number HIV-infected patients suffering TE are seronegative for *T. gondii*.[1] Under these circumstance, multiplex polymerase chain reaction (PCR) assay targeting *T. gondii* may facilitate early diagnosis.[5]

When compared with PYR-containing regimens in treating TE, in addition to less side effects and thereby

https://doi.org/10.1016/j.jmii.2024.02.008

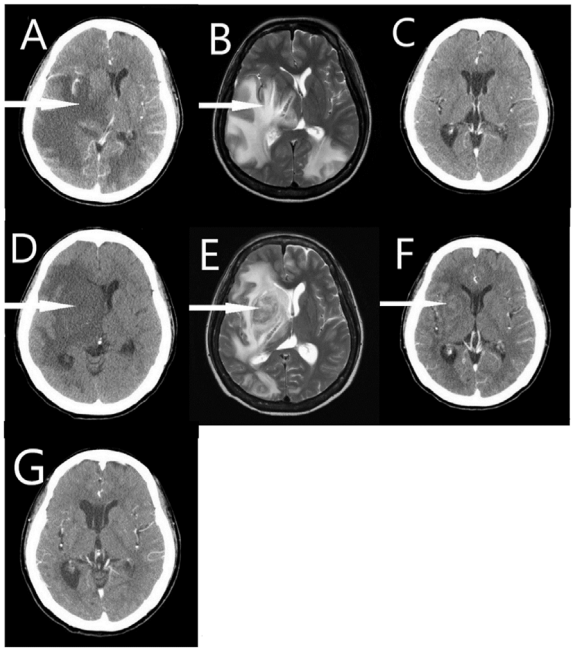

Figure 1. (A) Brain CT (2013/09/07) and (B) brain MRI (2013/09/09) showed huge ill-defined lesions in bilateral cerebrums (more prominent over the right one) with brain swelling and midline shift to the left; (C) regressive brain lesions in follow-up CT (2013/12/27). (D) Brain CT (2016/03/22) and (E) MRI (2016/03/24) showed an ill-defined mass (about 36 × 27 mm) over the right basal ganglia; (F) evolutionary brain CT imaging (2016/04/14) was found after 3-week antitoxoplasmic treatment, and (G) brain CT imaging (2018/01/05) found 21 months later.

possible more tolerability and higher drug compliance, lower drug cost, and easy accessibility, TMP-SMX with its parenteral formulation available for subsequent secondary prophylaxis, simultaneously offers cross-protection against PJP in such an immunocompromised patient.[1] This report suggests that TMP-SMX plus CLD merit a well-controlled clinical trial to consolidate evidence of the effectiveness of this antibiotic combination in the treatment of TE.

References

1. *Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV*. National Institutes of Health, Centers for Disease Control and Prevention, HIV Medicine Association, and Infectious Diseases Society of America; 2017. Available at, https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/toxoplasma-gondii. [Accessed 10 July 2023].
2. Hernandez AV, Thota P, Pellegrino D, Pasupuleti V, Benites-Zapata VA, Deshpande A, et al. A systematic review and meta-analysis of the relative efficacy and safety of treatment regimens for HIV-associated cerebral toxoplasmosis: is trimethoprim-sulfamethoxazole a real option? *HIV Med* 2017;**18**:115—24.
3. Torre D, Casari S, Speranza F, Donisi A, Gregis G, A Poggio A, et al. Randomized trial of trimethoprim-sulfamethoxazole versus pyrimethamine-sulfadiazine for therapy of toxoplasmic encephalitis in patients with AIDS. Italian Collaborative Study Group. *Antimicrob Agents Chemother* 1998;**42**:1346—9.
4. Vida JE. HIV-related cerebral toxoplasmosis revisited: Current concepts and controversies of an old disease. *J Int Assoc Phys AIDS Care* 2019;**18**:1—20.
5. Lin GY, Lin CY, Chi H, Huang DT, Huang CY, Chiu NC. The experience of using FilmArray Meningitis/Encephalitis Panel for the diagnosis of meningitis and encephalitis in pediatric patients. *J Microbiol Immunol Infect* 2022;**6**:1180—7.

Shih-Wen Ting
Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Jien-Wei Liu*
Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan
Chang Gung University College of Medicine, Taoyuan, Taiwan

*Corresponding author. No.123, Ta Pei Road, Niao Sung District, Kaohsiung 833, Taiwan.
E-mail address: 88b0@cgmh.org.tw (J.-W. Liu)

13 September 2023
Available online 28 February 2024