



Significant clinical outcome using pyrimethamine and clindamycin in cerebral toxoplasmosis with severe edema: a case report

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Introduction and Importance: Cerebral toxoplasmosis is a complication in HIV/AIDS patients that has recently increased in new cases due to increased HIV/AIDS incidents.

Case Presentation: An Indonesian male, 26-year old, complained of severe headache, left hemiparesis, and tremors. A brain computed tomography scan with contrast showed a large mass, extensive edema, and a significant midline shift resembling a brain tumor. The HIV test was positive, and CD4 decreased. The patient was treated with dexamethasone, mannitol, and pyrimethamine-clindamycin as therapy. After 2 weeks of treatment, the headache, hemiparesis, and tremor were clinically improved. Two months later, a brain computed tomography scan and MRI showed a good prognosis.

Clinical Discussion: The diagnosis of cerebral toxoplasmosis is based on a radiological examination and an HIV/AIDS test. Management of cerebral toxoplasmosis using pyrimethamine-clindamycin, while steroids are not recommended unless disproportionate cytotoxic edema is displayed and life-threatening.

Conclusion: A combination of pyrimethamine-clindamycin, and steroids can improve the prognosis of cerebral toxoplasmosis with severe edema.

Keywords: case report, cerebral toxoplasmosis, clindamycin, infectious disease, pyrimethamine

Introduction

Cerebral toxoplasmosis is a pathogenic parasite infecting one-third of the world's population. The parasite invades and resides in the infected host's central nervous system. The spread of these parasites is related to the patient's immune response, in hosts with a decreased immune system, the infection can reactivate so that it can cause manifestations in the central nervous system^[1]. Cerebral toxoplasmosis is often found in patients with acquired immune deficiency syndrome (AIDS)^[2,3]. This accounts for approximately 50-70% of all brain lesions in immunodeficient patients, clinical manifestations usually appear in the late stages of AIDS, when the CD4 level is below 200 cells/mm³, and patients

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HIGHLIGHTS

- The combination of pyrimethamine-clindamycin, and steroid shows a good prognosis in cerebral toxoplasmosis with severe edema.
- The diagnosis of cerebral toxoplasmosis is based on a radiological examination and an HIV test.
- Early management of cerebral toxoplasmosis increases the prognosis.

with CD4 below 50 cells/mm³ is at most significant risk^[4,5]. Cerebral toxoplasmosis in HIV/AIDS patients has a poor prognosis; 53% of patients die within 3 months of diagnosis. Management of cerebral toxoplasmosis-associated edema recommend specific anti-*Toxoplasma gondii* and supportive care, adjunctive steroids (dexamethasone), but data on steroid safety and efficacy are scarce^[6]. This study reported on an Indonesian male with cerebral toxoplasmosis and severe edema treated with combined pyrimethamine-clindamycin and steroids based on SCARE 2020 guidelines^[7].

Presentation of case

An Indonesian male, 26 years old, complained of severe headache, left-side weakness, and left-hand tremors. A stabbing headache in the back of the neck on the right side with a pain scale of 7–8 (numeric rating scale) 5 days ago. The pain scale increased (pain scale of 10) since yesterday, and the patient also vomited twice. The patient also experienced decreased motor skills in the left hand and leg since the first headache. He experienced tremors

since the pain scale was 10 and the Glasgow coma scale score was 13.

Neurological status revealed left hemiparesis with motor strength (arms of five and legs of four) and a simple kinetic tremor on the left hand. Brain computed tomography (CT) scan with contrast showed a brain tumor with hypodense lesions (35 HU), indistinct boundaries, irregular edges, a size of $5.6 \times 6.7 \times 7.9$ cm in the right corona radiata to the basal ganglia, and $1.5 \times 2.5 \times 1.2$ cm in the left frontal region, and an urgent mass was seen that caused a midline shift of 0.8 cm to the left side and dilation of the left lateral ventricle (Fig. 1). Laboratory examination showed abnormal potassium (3.3 mmol/l). The patient was declared HIV positive based on a rapid HIV test result of reactive, an immunoglobulin G antitoxoplasma of 19.52, HIV-3 of reactive, and CD4 of 125 cells/mm³.

The patients received pyrimethamine 200 mg followed by a dose of 25 mg every 8 h and clindamycin 600 mg every 6 h for 4–6 weeks, accompanied by folic acid and an analgesic (metamizole injection) related to headaches. There was a significant mass pressing effect, as indicated by a midline shift, and the patient's headaches worsened. Therefore, he was given an injection of dexamethasone at 5 mg every 6 h with a quick taper off and given an infusion of 200 mg of mannitol loading followed by 100 ml every 4 h of tapering off every day. On the sixth day, the headache decreased (pain scale of 2), left-side weakness improved, and specific kinetic tremor signs disappeared. The patient continued outpatient treatment after 8 days of treatment.

On the seventh day posthospitalization, there was no headache, left-sided weakness improved with motor values of all four upper and lower extremities (5/5), no tremor was found, and a Glasgow coma scale score of 15. On the first month, a CT scan of the contrast head evaluation was carried out for 1 month; the edema and the mass pressure effect improved, and no midline shift was found (Fig. 2). Pyrimethamine and clindamycin were continued for 4–6 weeks, and then the therapy was halved. In the eighth month, a brain MRI showed multiple lesions in the right lentiform nucleus, left frontal lobe cortical-subcortical, right

parietal lobe, left right occipital lobe, and left temporal with surrounding perifocal edema. The MRI results showed a significant reduction in the size of the lesion as well as a significant edema effect compared with the initial contrast head CT scan (Fig. 3).

Discussion

Cerebral toxoplasmosis is very rare, and the incidence is increasing in line with the increasing cases of HIV/AIDS^[8]. Typical features on CT scans and MRI of toxoplasmosis are multiple ring-enhancing basal ganglia (48%), frontal lobe (37%), and parietal lobe (37%) with surrounding edema^[3,9]. MRI images of toxoplasmosis show the presence of a 'target sign', described as an isointense core surrounded by a hypointense zone and hyperintense enhancing rim on T1 postcontrast^[8,10]. Lesions in cerebral toxoplasmosis are usually round and iso/hypointense at the grey-white matter junction. A presumptive diagnosis of cerebral toxoplasmosis can be established based on a combination of clinical symptoms, positive immunoglobulin G toxoplasma antibodies, and radiological imaging results of the brain, especially if the CD4 is below 200 cells/mm³. If it meets the criteria above 90%, it leads to cerebral toxoplasmosis^[4,10].

To reach the brain parenchyma through the brain's blood circulation, toxoplasma must adhere to the endothelium in the brain, especially in the capillaries^[1]. *T. gondii* can reach the blood–brain barrier through various mechanisms, namely by migrating directly to tight junctions on the endothelial surface, replicating in endothelial cells, which causes disruption of the blood–brain barrier and causes severe edema effects^[11]. The most effective therapy for cerebral toxoplasmosis is the administration of sulfadiazine and pyrimethamine. Administration of corticosteroids such as dexamethasone can reduce brain edema but can sometimes exacerbate the patient's immunosuppressed condition^[12]. Therefore, the administration of steroids is not recommended unless there is cytotoxic edema resulting from a large mass that threatens the patient^[13].



Figure 1. Brain computed tomography scan with contrast shows a hypodense intracranial lesion with ill-defined borders and irregular margins in the left frontal region and right corona radiata with edema causing a midline shift to the left side.

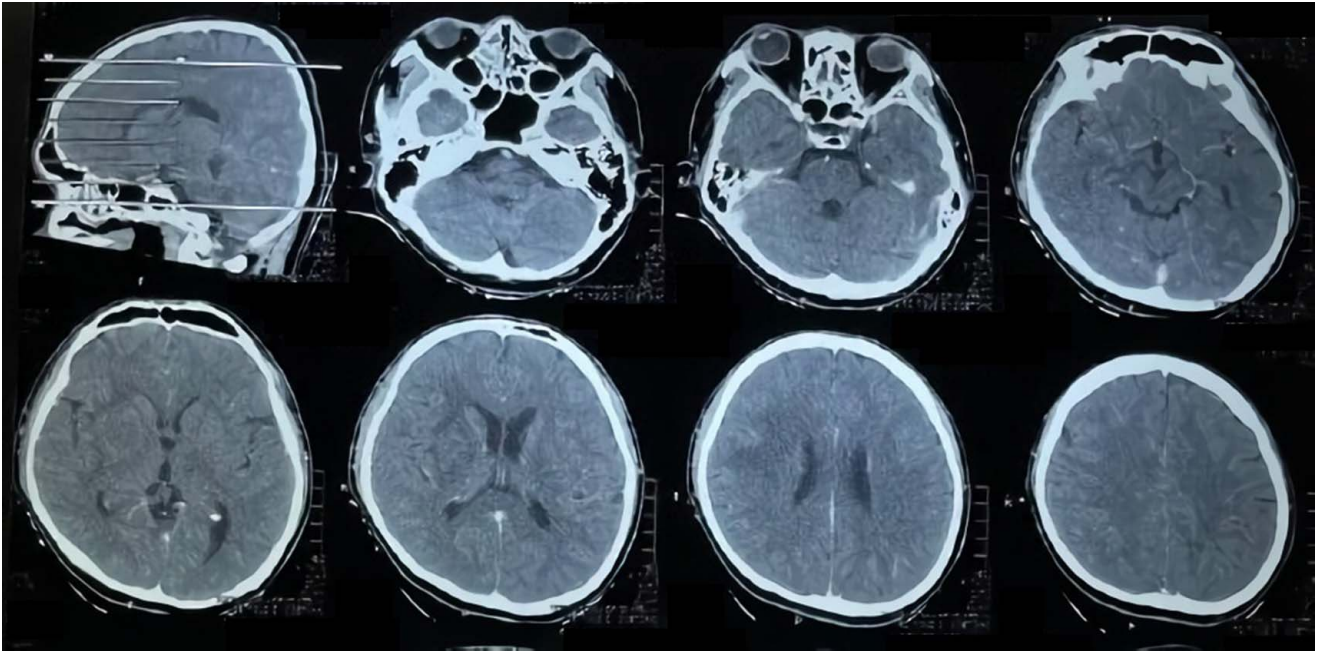


Figure 2. Brain computed tomography scan with contrast shows reduced edema and crowding effect after 1 month of pyrimethamine-clindamycin regimen.

Empirical therapy with pyrimethamine and sulfadiazine should be considered in patients with neurological symptoms and an intracranial mass, especially in immunodeficient patients^[4]. First-line therapy for cerebral toxoplasmosis combines pyrimethamine and sulfadiazine, or co-trimoxazole when sulfadiazine is not available. Clindamycin is used as second-line therapy^[8]. Toxoplasmosis therapy consists of a combination of two antimicrobials, namely dihydrofolate reductase

(pyrimethamine and trimethoprim) and dihydropteroate synthase (sulfonamides, such as sulfadiazine, sulfamethoxazole, and sulfadoxine) because the target of pyrimethamine is in the cytoplasm, where it can inhibit folic acid synthesis, leucovorin or folic acid can be given at a dose of 10–20 mg/day^[14].

Administration of a combination of pyrimethamine and sulfadiazine plays a role in the active stage of infection and is the gold standard in cases of toxoplasmosis. The role of clindamycin is to

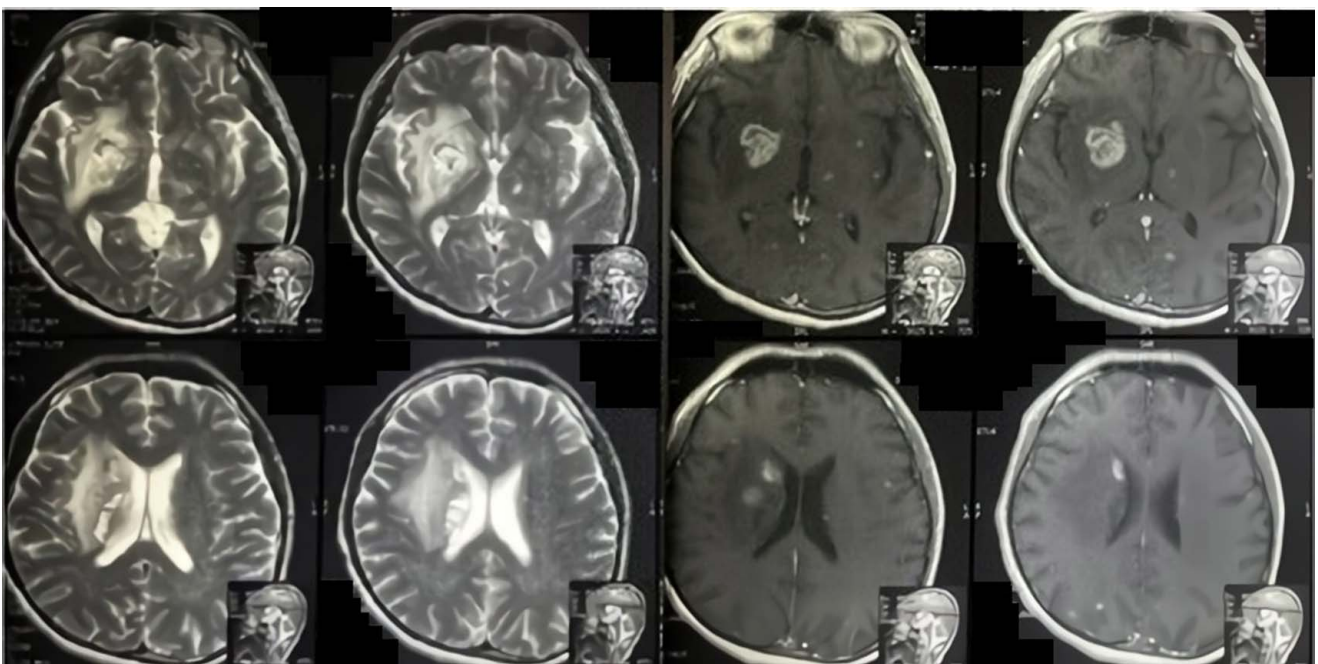


Figure 3. Computed tomography scan sequence T2 (left) and T1 (right) shows the reduced size of the lesion in the right lentiform nucleus (2.1 x 2.8 x 2.6 cm) and significantly reduced edema.

inhibit protein translation in toxoplasmosis^[14]. Based on previous studies, it was stated that the combination of pyrimethamine and clindamycin is more recommended because it has fewer drug side effects than the combination of pyrimethamine and sulfadiazine^[15]. In addition, in cerebral toxoplasmosis with poor conditions, it is recommended to use a combination of pyrimethamine and clindamycin^[16,17].

Steroids were permitted only for the management of intracranial hypertension or mass effect^[6], which steroids are the mainstay of therapy since they restore the blood–brain barrier, decrease T-cell activation, and prevent the influx of inflammatory cells^[9]. Steroid administration is recommended only when lesions due to toxoplasmosis have developed a significant mass effect or diffuse brain edema is seen. However, the significant benefit of adjunctive steroid therapy in mortality, even in the treatment of cerebral edema, has not been demonstrated in a large cohort^[13].

Conclusion

An Indonesian male, 26 years old, complained of severe headache, left-side weakness, and left-hand tremors. Brain CT scan and MRI results showed cerebral toxoplasmosis and severe edema, supported by a positive HIV test and low CD4. Management of cerebral toxoplasmosis and severe edema used a combination of pyrimethamine-clindamycin and steroids, which significantly improved the prognosis.

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

All authors contributed toward data analysis, drafting, and revising the paper, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

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All authors declare that they have no conflicts of interest.

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