LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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When to Start Prophylaxis? A HIV-infected Patient Presenting with Upper Extremity Weakness

Ne Zaman Profilaksi? Üst Ekstremitede Güç Kaybı Yakınması ile Başvuran HIV Sendromu Olgusu

Hüsnü PULLUKÇU[1], Hasip KAHRAMAN[2], Cenk ERASLAN[3], Oğuz Reşat SİPAHİ[1], Meltem IŞIKGÖZ TAŞBAKAN[1]

[1]Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, İzmir, Turkey
[2]Datça State Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Muğla, Turkey
[3]Ege University Faculty of Medicine, Department of Radiology, İzmir, Turkey

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Dear Editor,

Human immunodeficiency virus (HIV) infection is a major global health problem that affects 36.7 million people worldwide, with almost 2.1 million new cases each year[1]. Early diagnosis and the use of highly active antiretroviral therapy (ART) have reduced the incidence of opportunistic infections in HIV[2]. However, some patients develop various opportunistic infections despite normal CD4 T-cell counts. Herein, we discuss a HIV-infected patient who presented with loss of muscle strength in the upper extremities.

A 63-year-old man had presented with fever and been diagnosed with HIV at another center 20 days earlier. His CD4 T-cell count was 200 cells/mm^3 and HIV viral load was 160000 copies/ml. He was started on elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide therapy as well aa trimethoprim/sulfamethoxazole (TMP/SMX) and fluconazole prophylaxis. At the time of his admission to our outpatient clinic, he exhibited no signs of viral, parasitological, or sexually transmitted diseases (hepatitis A, hepatitis B, hepatitis C, syphilis) except for hepatitis A, B, and *Toxoplasma* immunoglobulin G (IgG) positivity due to past exposures. Kaposi's sarcoma lesions were noted on the dorsal parts of his feet. He was advised to continue TMP/SMX prophylaxis for another month, discontinue fluconazole, continue his current HIV treatment regimen, and return to the outpatient clinic for follow-up in three months. However, the patient presented approximately ten days before his scheduled appointment with complaints of loss of strength in his left arm and leg, as well as lisping during speech. He had no comorbidities other than coronary artery disease and hypertension. Upon physical examination, Kaposi's sarcoma lesions were observed on the dorsal parts of both feet, predominantly on the left side. Motor strength in his left arm was graded as 3/5, with no loss of sensation. No motor deficits were detected in his other extremities. Laboratory tests indicated white blood cell count: 5,500 cells/mm^3, lymphocyte count: 2260 cells/mm^3, hemoglobin level: 13.7 g/dl, C-reactive protein level: <0.03 mg/dl, erythrocyte sedimentation rate: 48 mm/hour, HIV-RNA: <40 k/ml, and CD4 count: 420 cells/mm^3. Kidney and liver function tests were normal. *Toxoplasma* IgM was negative, *Toxoplasma* IgG was positive, and avidity was 71%. Real-time

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Address for Correspondence/Yazışma Adresi: Hasip Kahraman MD, Datça State Hospital, Clinic of Infectious Diseases and Clinical Microbiology, Muğla, Turkey
Phone: +90 506 972 96 66 **E-mail:** hasipkahraman@gmail.com
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polymerase chain reaction analysis of a blood sample was negative for *Toxoplasma*. Tissue biopsy obtained from his foot lesion confirmed Kaposi's sarcoma. In contrast-enhanced cranial magnetic resonance imaging (MRI), supratentorial sections revealed lesions with peripheral contrast enhancement at the right corona radiata and thalamus level that were suggestive of cerebral toxoplasmosis (Figure 1). Perfusion MRI of the lesions was suggestive of lymphoma. Cerebrospinal fluid sampling could not be performed since lumbar puncture was considered to be contraindicated by the consulting neurologist. The neurosurgery department was consulted while a biopsy could not be performed due to the potential risks (the patient did not provide consent). Although it could not be confirmed microbiologically, treatment was initiated with oral TMP/SMX at a dose of 1600/320 mg 3 times daily for a diagnosis of probable toxoplasmosis. The patient was discharged with antiretroviral and TMP/SMX therapy. Cranial MRI performed three weeks later showed regression of the edema in the right hemisphere and surrounding tissues (Figure 2). The patient exhibited full clinical recovery and six-month MRI demonstrated complete recovery. Viral load was negative at all follow-up visits. CD4 cell count never fell below 400 cells/mm^3. The patient continued follow-up for Kaposi's sarcoma and received TMP/SMX prophylaxis for another six months, after which discontinuation was planned.

The incidence of AIDS-defining opportunistic infections has decreased since the introduction of effective ART combinations. Nevertheless, opportunistic infections are still among the main causes of hospitalization and mortality in HIV-infected patients[3].

Central nervous system (CNS) pathologies account for 5-7% of all case presentations[4]. CNS pathologies may develop in direct association with viral replication in the brain and spinal cord, or through opportunistic infections and tumors during any stage of HIV infection. Pathogens such as *Toxoplasma*, *Cryptococcus*, JC virus, Epstein-Barr virus, and cytomegalovirus are the opportunistic microorganisms most commonly associated with CNS involvement in HIV-infected individuals[5].

Cerebral toxoplasmosis is a parasitic disease caused by *Toxoplasma gondii*. Primary infection is rare, and signs usually emerge upon the reactivation of latent cysts. Clinical manifestations are rarely observed in patients with CD4 cell count >200 cells/mm^3. Those with CD4 cell count <50 cells/mm^3 are at highest risk of developing the disease. The most common clinical presentation is focal encephalitis with headache, confusion, motor weakness, and fever. Patients may also present with atypical headaches, psychiatric symptoms, and epileptic seizures[6].

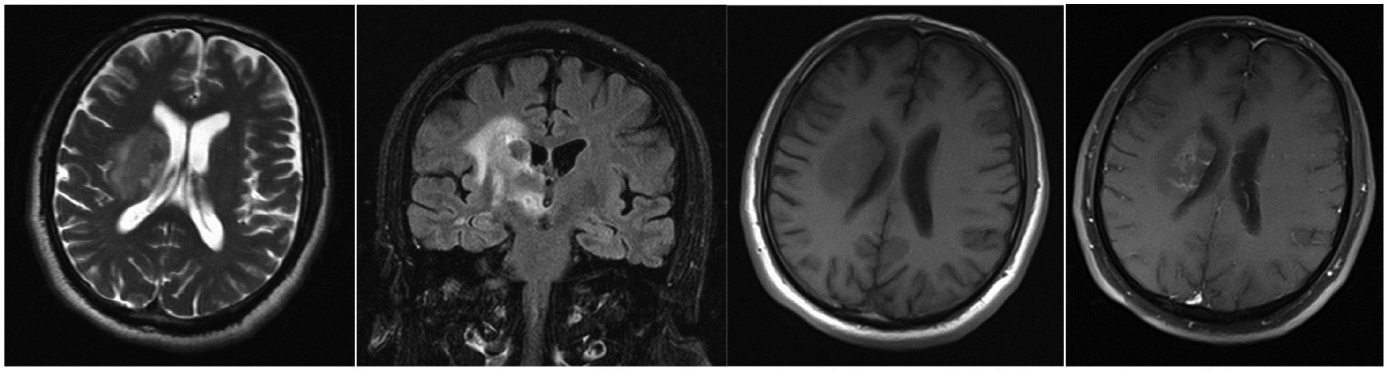

Figure 1. Pre-treatment magnetic resonance images of the patient. Left to right: T2 axial, flair coronal, T1 axial pre-contrast, T1 axial post-contrast

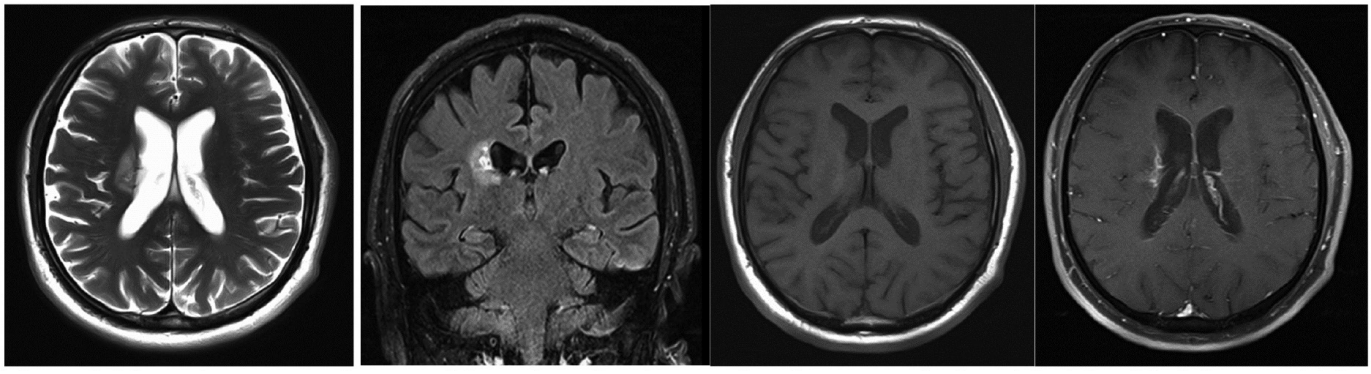

Figure 2. Magnetic resonance images of the patient after three weeks of treatment. Left to right: T2 axial, flair coronal, T1 axial pre-contrast, T1 axial post-contrast

Nearly all HIV-infected patients with cerebral toxoplasmosis exhibit anti-*Toxoplasma* IgG seropositivity. These patients are generally negative for IgM antibodies. Quantitative antibody assays do not contribute to the diagnosis. Definite diagnosis of *Toxoplasma* encephalitis is made in the presence of clinical symptoms as well as isolated or multiple mass lesions on cranial computed tomography (CT) or MRI and demonstration of the causative agent in clinical samples. MRI is superior to CT in identifying cranial lesions. Treatment should be initiated immediately in cases with clinical and radiologic evidence suggesting cerebral toxoplasmosis. If clinical response is not observed within two weeks of treatment, a brain biopsy should be performed as soon as possible[6]. In the present case, the contrast-enhancing area around the lesions raised suspicion of lymphoma. Since a biopsy could not be performed, initial treatment targeted *Toxoplasma*. The patient showed a dramatic response to this treatment.

A combination of pyrimethamine/sulfadiazine is recommended for primary treatment of cerebral toxoplasmosis. The combination of pyrimethamine/clindamycin and TMP/SMX are recommended as alternative therapies. Treatment duration is at least six weeks in cerebral toxoplasmosis patients who achieved clinical and radiological cure with acute treatment[6].

It should be kept in mind that in patients with AIDS-defining illnesses, a CD4 cell count around 200 cells/mm^3 may lead to problems in terms of opportunistic infections. In fact, as in the present case, we believe that a certain period of prophylactic therapy may be necessary for the management of toxoplasmosis in patients with signs of AIDS-defining illnesses, regardless of CD4 cell number.

Ethics

Informed Consent: Consent form was filled out by the presented case.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.P., H.K., C.E., O.R.S., M.I.T., Concept: H.P., H.K., C.E., O.R.S., M.I.T., Design: H.P., H.K., C.E., O.R.S., M.I.T., Data Collection or Processing: H.P., H.K., C.E., O.R.S., M.I.T., Analysis or Interpretation: H.P., H.K., C.E., O.R.S., M.I.T., Literature Search: H.P., H.K., C.E., O.R.S., M.I.T., Writing: H.P., H.K., C.E., O.R.S., M.I.T.

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