

Toxoplasmosis mimicking CMV chorioretinitis in newly diagnosed PLWH: a case report

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Article received 15 July 2023, accepted 31 July 2023

SUMMARY

Background: cytomegalovirus (CMV) retinitis, cerebral and ocular toxoplasmosis are common infections in patients with acquired immunodeficiency syndrome (AIDS). **Material and methods:** this is a case of a 46-year-old female with previous Kaposi's sarcoma, diagnosed with an HIV infection two weeks prior to hospitalization. Blood test at diagnosis showed a CD4+ count of 77 cell/ μ L and HIV-RNA 3.758.745 copies/mL. Therapy with bictegravir/emtricitabine/tenofovir alafenamide fumarate was started and clinical, viroimmunological and microbiological investigations were performed.

Results: the patient went to our hospital for the onset of left occipito-parietal headache and blurred vision. Brain CT and MRI were performed which did not show focal lesions or vascular alterations. Syphilis serology was negative, *Toxoplasma gondii* serology showed positive IgG and negative IgM, serum CMV-DNA was 31.184 IU/mL. Eye fundus evidenced intraretinal hemorrhages, fluorescein angiography and computed optical tomography documented cottony exudates, retinal hemorrhages and vitreous involvement. Therapy with valganciclovir was initiated for suspicion of CMV retinitis. About a month later, the patient reported blurred vision for which she was re-admitted. Ocular fundus showed a cottony lesion near the macula. Molecular test on vitreous body was positive for *Toxoplasma gon-*

dii, while on cerebrospinal fluid it was negative; in addition, an MRI of the brain with contrast medium was performed which showed an area of altered hyperintense signal compatible with a diagnosis of *Toxoplasma gondii* uveitis and neurotoxoplasmosis. Therapy with pyrimethamine and clindamycin (allergy for sulfonamide reported by the patient) was started. Allergy counseling was performed with the execution of allergy tests (patch test) with negative result; therefore the administration of clindamycin was replaced with sulfadiazine. A month following the start of anti-toxoplasma therapy, there was a clinical and radiological improvement.

Conclusions: despite progressive developments in the management of PLWH, in this case two different kind of opportunistic infection are found in a late-presenter patient. In particular, two aspects can be highlighted. The first one is that, in the setting of an highly impaired immune system, clinical presentation can be deceptive and more than one opportunistic infection can be observed together in the same patient. The second aspect is that after starting antiretroviral therapy, a rapid improvement of viro-immunologic parameters has been documented, probably leading to an immune reconstitution inflammatory syndrome (IRIS).

Keywords: Toxoplasmosis, CMV, chorioretinitis, PLWH.

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■ INTRODUCTION

Cytomegalovirus (CMV) is a ubiquitous DNA herpes virus that causes significant morbidity and mortality in immunocompromised individuals, specially person living with HIV (PLWH). CMV retinitis is a potentially cause of blindness commonly seen in advanced acquired immunodeficiency syndrome (AIDS) [1]. Central nervous system infection by *Toxoplasma gondii* is the most common cause of brain mass lesions in PLWH [2]. CMV retinitis, cerebral toxoplasmosis and ocular toxoplasmosis are common infections in patients with AIDS and usually occur in PLWH who have low CD4 T-cell count.

■ CASE PRESENTATION

This is a case of a 46-year-old female with history of anxious-depressive syndrome and anorexia nervosa. She was referred to our outpatient clinic after acquiring positivity for anti-HIV antibodies performed for the persistence of low-grade fever and weight loss for about two years. At the first visit, purplish-colored lesions consistent with Kaposi sarcoma were found on the nose and limbs. On 2022 August 23rd blood test showed a CD4+ count

of 77 cell/ μ L and HIV-RNA 3.758.745 copies/mL. For the onset of left occipito-parietal headache and blurred vision, she was admitted on 2022 August 30th to our Infectious Disease ward. During hospitalization, brain CT and brain MRI were performed which did not show focal lesions or vascular alterations (Figure 1A). Syphilis serology was negative, while *Toxoplasma gondii* serology showed positive IgG and negative IgM. Ophthalmological examination of the eye fundus showed evidence of intraretinal hemorrhages, fluorescein angiography and computed optical tomography documented cottony exudates, retinal hemorrhages and vitreous involvement. Serum CMV-DNA was performed with evidence of 31.184 IU/mL. Therefore therapy with valganciclovir was initiated for suspicion of CMV retinitis. The patient reported clinical improvement. She was discharged on 2022 September 19th with maintenance therapy. For HIV infection, therapy with bictegravir/emtricitabine/tenofovir alafenamide fumarate was started.

After the discharge, the patient maintained a good compliance to antiretroviral therapy, with a rapid drop of HIV-RNA and rising of CD4 count (on 2022 September 28th the tests showed HIV-RNA 674 copies/mL and CD4+ 200 cells/mm³; on 2022 October 22nd HIV-RNA 215 copies/mL

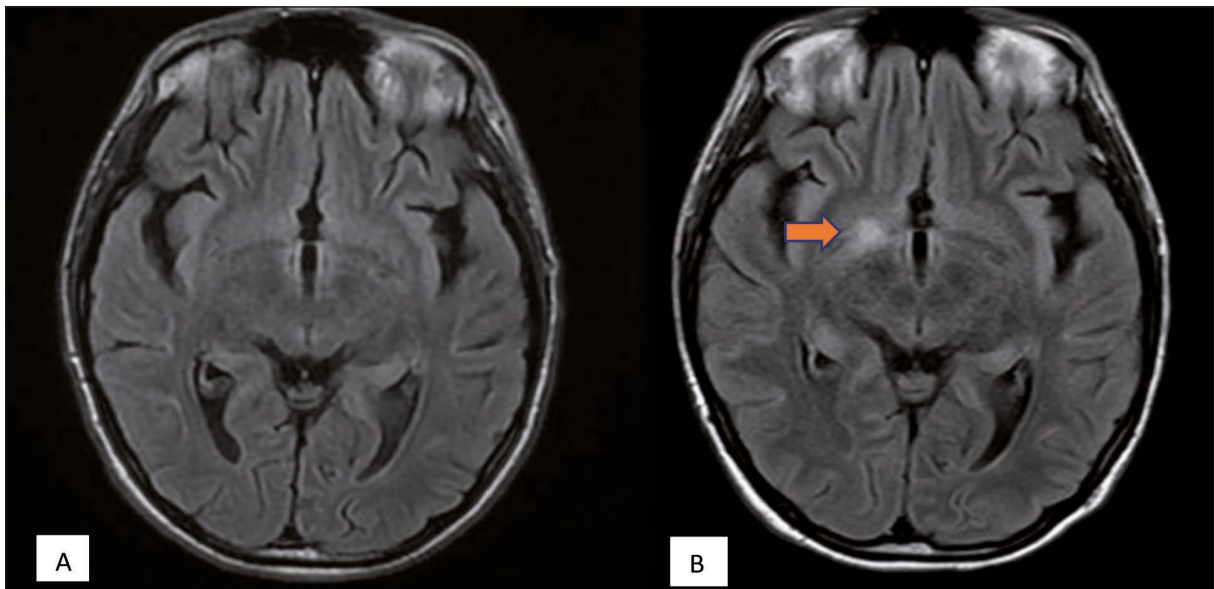


Figure 1 - A: absence of lesion. B: area of altered hyperintense signal in the right anterior perforated white matter on T2-weighted/FLAIR sequences, with marginal enhancement after administration of contrast agent, with a maximum axial diameter of 7 mm and minimal perilesional vasogenic edema.

and CD4+ 230 cells/mm³). At the end of October 2022, the patient reported onset of blurred vision again. For this reason, she underwent an ophthalmological examination of the ocular fundus that highlighted a cottony lesion near the macula. A vitrectomy was performed with samples sent for microbiological testing: the molecular test was positive for *Toxoplasma gondii*, negative for *Candida*, CMV, HZV e HSV. The patient was admitted to our ward for further investigations. A lumbar puncture was executed. The cerebrospinal fluid chemical examination showed only an augmented level of proteins (88 mg/dL) and the molecular test for *Toxoplasma gondii* resulted negative. In addition, MRI of the brain with contrast medium showed an area of altered hyperintense signal in the right anterior perforated white matter on T2-weighted/FLAIR sequences, with marginal enhancement after administration of contrast agent, with a maximum axial diameter of 7 mm and minimal perilesional vasogenic edema (Figure 1B). A diagnosis of *Toxoplasma gondii* uveitis and suspect neurotoxoplasmosis was made. Therapy with pyrimethamine and clindamycin (allergy for sulfonamides reported by the patient) was started. Allergy counseling was performed with the execution of allergy tests (patch test) with negative result; therefore the administration of clindamycin was replaced with sulfadiazine. A month following the start of anti-toxoplasma therapy, there was an improvement in visual symptoms, the fundus examination also showed dimensional reduction of the chorioretinitis focus and an MRI documented dimensional reduction of the area of the altered signal.

■ DISCUSSION

Despite progressive developments in the management of PLWH, here it is presented a case of AIDS where two different kind of opportunistic infection are found in a late-presenter patient. In particular, two aspects can be highlighted. The first one is that, in the setting of an highly impaired immune system, clinical presentation can be deceptive and more than one opportunistic infection can be found together in the same patient. In fact, it can be seen that after an initial improvement in symptoms, making us think that CMV chorioretinitis was the only disease, another worsening of the same symptoms led us to the di-

agnosis of toxoplasmosis uveitis and suspect neurotoxoplasmosis.

The second aspect is that after starting antiretroviral therapy, a rapid improvement of viro-immunologic parameters has been documented, probably leading to an immune reconstitution inflammatory syndrome (IRIS). IRIS is a dysregulated immune response against an infecting opportunistic pathogen and the host [3]. There are 2 types of IRIS: paradoxical and unmasking. The first manifests as a paradoxical worsening of symptoms during the antiretroviral therapy-induced immune reconstitution period, while the second refers to the flare-up of an underlying, previously undiagnosed infection, soon after antiretroviral therapy (ART) is started. In the above case, probably, unmasking IRIS occurred which allowed to make a diagnosis of toxoplasmosis.

Funding

This work was supported by internal funding.

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Fondazione Policlinico A. Gemelli (N0013332/16).

Informed consent statement

Informed consent was obtained from the subject involved in the study.

Conflicts of interest

A.C. received support for travel to meetings from ViiV Healthcare, A.B. received speakers' honoraria from ViiV Healthcare, and fees for attending advisory boards from Janssen-Cilag. S.D.G. was a paid consultant or member of advisory boards for Gilead Sciences, ViiV Healthcare, Janssen-Cilag, Merck Sharp & Dohme and Bristol-Myers Squibb. All other authors: none to declare.

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