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Case Report

Co-infection of progressive multifocal leucoencephalopathy and tuberculosis in a patient with acquired immunodeficiency syndrome: case report and literary review

Coinfección de leucoencefalopatía multifocal progresiva y tuberculosis en paciente con síndrome de inmunodeficiencia adquirida: reporte de caso y revisión literaria

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ABSTRACT

Introduction: we present a case of a 44-year-old male patient, diagnosed with both the human immunodeficiency syndrome (hiv) and progressive multifocal leukoencephalopathy, along with extrapulmonary tuberculosis. Progressive multifocal leukoencephalopathy is an opportunistic viral infection caused by the john cunningham virus, leading to multifocal involvement of the central nervous system. Antiretroviral treatment for hiv aims to restore the immune system and suppressing the john cunningham virus. Therapeutic non-adherence and/or hiv resistance to antiretrovirals predispose individuals to opportunistic infections such as progressive multifocal leukoencephalopathy and tuberculosis. **Objectives:** this study aims to address the co-infection of progressive multifocal leukoencephalopathy and extrapulmonary tuberculosis in the context of an individual with acquired immunodeficiency syndrome, supported by a literature review.**Materials and methods:** a bibliographic search was conducted in scielo and pubmed. The clinical case report includes the patient's clinical record. **Results:** patients with acquired immunodeficiency syndrome often experience opportunistic infections by pathogens considered harmless, such as the john cunningham virus, which manifests with severe symptoms. Antiretroviral treatment is essential. **Conclusion:** currently, initiating antiretroviral treatment promptly after diagnosis is crucial, irrespective of the cd4 count, to prevent the progression of immunosuppression and exposure to opportunistic germs. The use of complementary studies, guided by the patient's clinical history and physical examination, facilitated a correct and early diagnosis.

Keywords: progressive multifocal leukoencephalopathy, john cunningham virus, acquired immune deficiency syndrome, antiretrovirals, opportunistic infections, tuberculosis.

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RESUMEN

Introducción: Presentamos un paciente masculino de 44 años, portador del virus del síndrome de inmunodeficiencia adquirida, con diagnóstico de leucoencefalopatía multifocal progresiva y tuberculosis extrapulmonar. La leucoencefalopatía multifocal progresiva es una infección viral oportunista producida por el virus John Cunningham, presenta afección multifocal del sistema nervioso central. El tratamiento tiene como objetivo primario restaurar el sistema inmune y suprimir el virus John Cunningham. La no adherencia terapéutica y/o resistencia del virus de la inmunodeficiencia humana a antirretrovirales, predispone a infecciones oportunistas como la leucoencefalopatía multifocal progresiva y tuberculosis.**Objetivos:** Abordar un caso de coinfección de leucoencefalopatía multifocal progresiva y tuberculosis extrapulmonar en el contexto de un paciente con síndrome de la inmunodeficiencia adquirida y revisión literaria. **Materiales y métodos:** Búsqueda bibliográfica en Scielo y Pubmed. Relato de caso clínico con expediente clínico. **Resultados:** Frecuentemente hay infecciones oportunistas, en pacientes con síndrome de la inmunodeficiencia adquirida, por patógenos considerados inocuos, como el virus John Cunningham, que se manifiesta con cuadros graves. Siendo esencial el tratamiento antirretroviral. **Conclusión:** Para evitar la inmunodepresión y en consecuencia las infecciones oportunistas en pacientes con el síndrome de la inmunodeficiencia adquirida, el tratamiento antirretroviral debe ser en momento oportuno y hecho independientemente del valor de CD4. En este trabajo, debido a los estudios complementarios realizados con amparo de la historia clínica y examen físico, fue posible realizar un diagnóstico oportuno y correcto.

Palabras clave: Leucoencefalopatía Multifocal Progresiva, Virus John Cunningham, Síndrome Inmunodeficiencia Adquirida, Antirretrovirales, Infecciones oportunistas, Tuberculosis.

Introduction

Progressive multifocal leukoencephalopathy (PML) is a rare, debilitating, and frequently fatal demyelinating disease of the central nervous system (CNS). It is caused by human polyomavirus 2, also known as the John Cunningham virus (JC virus), which exhibits tropism for oligodendrocytes [1,2]. In most individuals, the JC virus presents as an asymptomatic, persistent, or latent lifelong infection [3]. However, in patients with long-term compromised cellular immunity, the virus can reactivate from latent sites and undergo sequential genomic rearrangements [4]. Intra-host viral evolution allows a typically benign virus to cause a lytic infection of CNS glial cells, leading to the progression of PML [5]. PML is characterized by demyelination, astrocytic and nuclear changes, and abnormal oligodendrocytes, whereas edema, lymphocytic infiltration, and blood-brain barrier disruption are typically absent [4,6].

Immunosuppressive therapy (for cancer, autoimmune diseases, or organ transplantation) and human immunodeficiency virus (HIV) infection are associated with the development of PML [6,7,8].

Prior to the HIV pandemic, PML was a rare complication in patients with immune-mediated lymphoproliferative diseases [9,10]. The first surge in PML cases occurred during the acquired immunodeficiency syndrome (AIDS) pandemic [8,11]. Although the introduction of effective antiretroviral therapy (ART) reduced its incidence in patients with AIDS, HIV remains the primary contributor to the total number of PML cases [12,13].

The immune status of untreated people living with HIV/AIDS (PLWHA) predisposes them to opportunistic infections (OIs) such as PML, tuberculosis, toxoplasmosis, cryptococcosis, and many other diseases that serve as markers

of advanced immunosuppression [14,15].

Although ART has significantly reduced the frequency of OIs worldwide, they remain a major issue for all HIV-positive patients with low CD4+ T-cell counts who are not receiving ART [16].

Tuberculosis and HIV co-infection is a major public health issue worldwide [15,16]. In the Americas, the World Health Organization (WHO) estimated that in 2021, 10.6 million people developed tuberculosis, resulting in approximately 1.6 million deaths, including 187,000 cases among PLHIV [17,18,19].

CASE PRESENTATION

A 44-year-old male patient was admitted with acute-onset dysarthria of ten days' duration, accompanied by dizziness associated with ambulation. The patient reported a prior consultation at the service, where a non-contrast brain computed tomography (CT) scan was performed; the report indicated unremarkable findings, with structures of normal dimensions and appearance.

Physical examination revealed expressive aphasia, bradyphasia, bradypsychia, myoclonus, and asterixis in the extremities. Upon ambulation, he presented with an ataxic gait. No alterations were observed in other systems.

No alterations were observed in X-ray studies and the electrocardiogram. In complementary studies, two samples were collected for a fourth-generation HIV rapid test, both yielding positive results; therefore, plasma HIV viral load measurement and CD4 T-lymphocyte count were requested, along with serologies for opportunistic infections.

Based on the results obtained, it was decided to initiate empiric treatment for cerebral toxoplasmosis.

The patient remained hospitalized for treatment, continuous monitoring, and diagnostic investigation. Due to the lack of significant abnormalities on the non-contrast brain CT, a lumbar puncture was performed for cerebrospinal fluid (CSF) analysis. Results showed: colorless appearance, clear supernatant, glucose 55 mg/dL (serum glucose 88 mg/dL), protein 37 mg/dL (reference range: <45 mg/dL), lactate 14.2 mg/dL (reference range: 10-22 mg/dL), non-reactive VDRL, leukocytes within range, no red blood cells observed, Gram stain negative for organisms, and India ink negative for fungal elements. With these CSF results, meningeal involvement was ruled out. A neurology consultation was requested, along with a brain magnetic resonance imaging (MRI), which reported findings consistent with PML.

After 10 days of empiric treatment for cerebral toxoplasmosis, the patient showed unfavorable progress; therefore, the decision was made to discontinue toxoplasmosis treatment, and diagnostic hypotheses of HIV-associated CNS vasculitis or extrapulmonary tuberculosis were considered.

New laboratory studies were requested, including bacterial blood cultures and cultures for fungi and mycobacteria, all yielding negative results. A urine TB-LAM test was requested; the result was positive, allowing for the diagnosis of extrapulmonary tuberculosis. Based on this finding, antitubercular treatment was initiated. Additionally, a CSF PCR for JC Virus was requested, returning positive with a viral load of 66,807 copies/µL.

After 2 weeks of antitubercular treatment, ART was initiated to prevent Immune Reconstitution Inflammatory Syndrome (IRIS). The patient showed a stationary clinical course, maintaining a Glasgow Coma Scale score of 10/15 due to verbal and motor impairment. He was discharged with instructions to complete the treatment initiated in the service with ART and antitubercular agents.

Discussion

Patients with AIDS have a higher probability of contracting OIs due to ineffective control and/or resistance to ART [20]. Factors such as alcohol use, illicit drug use, depression, low educational level, treatment non-adherence, lack of social support, inadequate access to healthcare, and social stigma contribute to the development of OIs, as seen in the presented case where the patient developed extrapulmonary tuberculosis [21,22].

Diseases such as PML and tuberculosis are associated with poor viral load control and low CD4+ T-cell counts, as patient recovery relies heavily on the immune response [23,24]. Given the high comorbidity and mortality associated with PML, there is a concern regarding timely diagnosis to improve the prognosis of these patients [25,26].

In many cases, PML is not considered in the differential diagnosis of other CNS opportunistic infections in immunocompetent patients or those without an AIDS diagnosis [26,27]. However, population studies indicate that between 63% and 65% of PML cases occur in the absence of evident immunosuppression [28]. This suggests a potential for PML cases without immunosuppression to occur more frequently than recorded, as it is not often considered in the differential diagnosis of progressive and symmetrical multifocal CNS lesions [27,28].

Thus, the spectrum of clinical and imaging presentations of PML highlights the need to develop a method to be included in the screening for AIDS-related OIs [4,7,25]. Currently, diagnosis is made through differential diagnosis with other neurological OIs such as cerebral toxoplasmosis, using two methods most accepted in the literature: first, histopathology evidencing the presence of the JC virus; and second, the combination of clinical and/or radiological characteristics with a positive JC virus PCR in CSF analysis [2,4,24,29,30]. In the absence of clinical or radiological features, even with a positive JC virus PCR in CSF, or when the diagnosis is based solely on clinical criteria, or when the JC virus cannot be demonstrated despite classic histopathological features, the diagnostic certainty of PML is reduced [2,4,29,30].

Conclusion

The early initiation of antiretroviral therapy (ART) in detected HIV/AIDS cases aims to prevent the progression of immunosuppression, a key risk factor for the development of opportunistic infections (OIs) such as tuberculosis and progressive multifocal leukoencephalopathy (PML) [12,13,26].

In the presented case, early treatment was made possible by a timely diagnosis based on clinical history, general and neurological physical examinations, and the use of diagnostic aids such as magnetic resonance imaging (MRI) and polymerase chain reaction (PCR) [29,30].

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