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Severe Neurological Manifestations and Medication Challenges in an Elderly Female Cancer Patient: a missed opportunity

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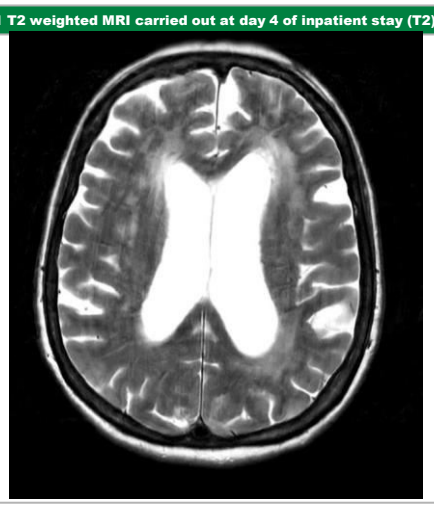
Introduction

Since the introduction of highly active antiretroviral therapy (HAART), there has been a significant decrease in the incidence of HIV-associated neurocognitive impairment (HNCI). This decline may have led to a decreased consideration of HNCI in the differential diagnosis of neurological syndromes resulting in unfavourable outcomes for patients.

Our case

A 65-year-old female presented to our hospital in Rome in December 2023 after developing prolonged fever and psychomotor slowing whilst undergoing chemotherapy for a breast tumour. Symptoms started August 2023 when attention memory deficits and apathy appeared (consistent with subcortical involvement), followed by gait disturbance and urinary incontinence. The patient was first seen as an outpatient by neurologists who determined the presentation to be consistent with the Hakim-Adams' triad. After being admitted to the neurology ward the patient soon developed severe encephalopathy, with stupor and muteness which progressed to a catatonic-like state, together with myoclonic jerks of the upper and lower limbs.

Figure 1 **T2 weighted MRI carried out at day 4 of inpatient stay (T2)**

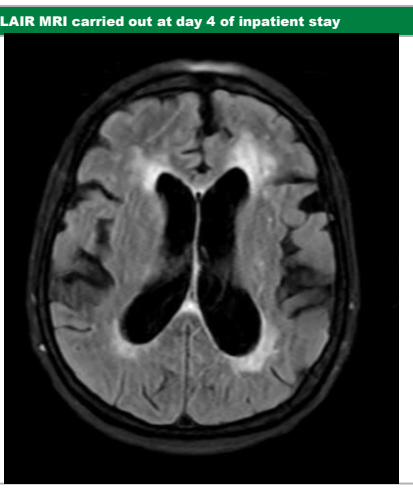


MRI images showed signs of trans-ependymal oedema and bilateral hyperintensities in the temporo-polar areas, compatible with communicating hydrocephalus.

CSF analysis showed mononuclear pleocytosis with normal protein and glucose. A viral PCR screen resulted positive for Cytomegalovirus (CMV) although attention initially focused on the presence of oligoclonal bands in the liquor (liquor>serum), suggesting acute CNS inflammation and supporting a diagnosis of paraneoplastic auto-immune encephalitis. However, following an infectious disease consult, at 5 months from symptom onset, an HIV test resulted positive.

Further testing quantified HIV RNA (9040 copies/ml) and CMV DNA (347 copies/ml) in the CSF with contextual viremias of 150000 copies/ml of HIV-RNA, and CMV-DNA of 931000 copies/ml and a nadir CD4 count of 28 cells/mm^3.

Figure 2 **T-2 FLAIR MRI carried out at day 4 of inpatient stay**



Unfortunately, the examination was interrupted due to the patient's persistent myoclonus, preventing the determination of periventricular contrast enhancement, an element the consulting radiologists had suspected.

HIV-associated CMV encephalitis manifesting as hydrocephalus with accompanying myoclonus was considered. Few such cases have been described in the literature [3].

At day 5 from diagnosis, after necessary testing, antiviral treatment was started with ganciclovir (at a loading dose of 325mg x 2) and bictegravir/emtricitabine/tenofovir alafenamide (50mg/200mg/25mg). Given the catatonic state and unavailability of liquid HAART, BIC/FTC/TAF was crushed and administered via a nasal gastric tube, raising concern for possible reduced drug absorbance. INSTI therapeutic drug monitoring was therefore carried out at day 20 of therapy (at 14hrs from the last pill administration) revealing a bictegravir plasma concentration of 1902 ng/ml. According to in vitro experiments revealing a minimum effective concentration of 162ng/ml [4], this value was considered optimal.

Indeed, the patient rapidly showed virological improvement: at 25 days of therapy, CSF analysis revealed a 1-log reduction in CMV DNA and a 6-fold reduction in HIV RNA with similar decreases in viremia in the plasma. Unfortunately, this was not matched with clinical improvement; the patient died for likely cardiac complications, at day 27 of therapy.

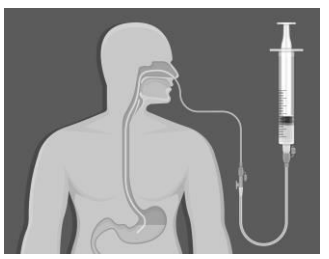


Figure 3 **Virological response at day 25 of antiviral treatment (with ganciclovir)**

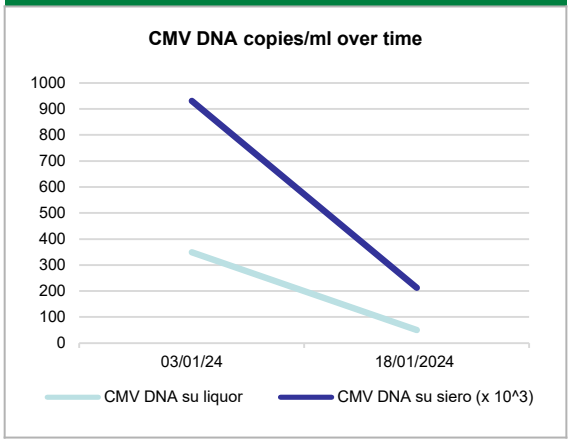
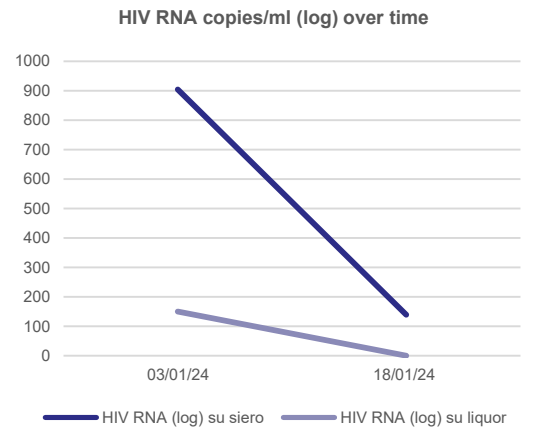


Figure 4 **Virological response at day 25 of antiviral treatment (with BIC/FTC/TAF)**



Key points and future objectives:

- Late HIV Diagnosis (CDC C3 stage) with the delay in testing being attributed to the absence of HIV risk factors and the atypical presentation of the opportunistic infection → **Increase HIV screening, including in patients without known risk factors, especially before oncology treatments and improve communication with other specialties.**
- Challenges in Neurological Differential Diagnosis → **Optimize the identification of neurological syndromes, considering the pathophysiological and clinical variations in HIV patients.**
- Lack of confidence in treating critically ill patients: → **Promote utilization of existing non-oral ART therapies (parenteral, intramuscular and syrup forms), even in cases where their administration is outside official guidelines. Examples are: lenacapavir for patients who are not heavily treatment-experienced, and long-acting cabotegravir/rilpivirine for patients who are not virologically suppressed.**

These measures should contribute to a decreased incidence of critically ill AIDs patients, and where prevention does not occur, they should help increase the efficacy and efficiency of case management.

References

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