A Complex Case of HIV mediated CD8+ Encephalitis

J Lowry[1], P Carey[2], J McGettigan[2], A Conway[2], S O'Connell[2]

[1,2]*Department of Infectious Diseases, University Hospital Limerick*

Background

The presentation of acute encephalopathy in the HIV-positive patient represents both diagnostic and therapeutic challenges. This is compounded by the possibility that these neurological manifestations may represent multiple pathologies in the immunosuppressed.

CD8 encephalitis is a severe form of HIV-related acute encephalopathy that with early commencement of high-dose-corticosteroids can provide promising outcomes **[1]**. We report the clinical and pathological features associated with this case of CD8 encephalitis to sensitize clinicians to its early recognition.

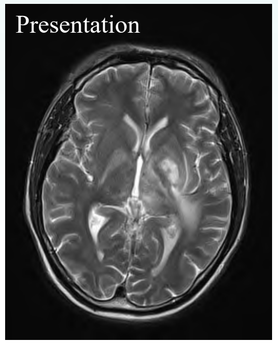


Image 1:
Multifocal ring enhancing lesions of left caudate, lentiform nucleus and left midbrain. Differential included Toxoplasmosis, TB, lymphoma

Case

We present the case of a forty-one-year-old male from Zimbabwe who presented with a three-week history of reduced power in the right upper and lower-limbs associated with expressive dysphasia. He was diagnosed with HIV ten years previously and had a complex social history with resultant disengagement from care and non-compliance with therapy. Once re-engaged in care, he was re-commenced on Tenofovir/Emtricitabine, Darunavir/Ritonavir.

On presentation, laboratory investigations revealed a viral-load of 78,929 and a CD4 count of 77. MRI-imaging of the brain displayed "multifocal T2 hyperintensities throughout the frontal and parietal lobes with hyperintensity of the left caudate nucleus." ***(Image 1)***. The decision was made to commence empiric cerebral toxoplasmosis treatment. Initial right-parietal biopsy (performed due to failure of lesions to respond to empiric treatment for toxoplasma) demonstrated non-specific inflammation alone, with PCR negative for bacteria, TB and fungi. CSF samples were equally non-specific revealing a lymphocytic predominance– with flow cytometry non-suggestive of lymphoma and culture/toxoplasma and JC virus PCR negative, HIV viral load in CSF was <200 copies/ml.

He continued to deteriorate with worsening hemiparesis and new-onset urinary retention despite initial treatment. Further imaging raised concern for lymphoma; and a second biopsy of the left-temporal-area demonstrated 'lymphocytic inflammation, microglial activation and astroglial reaction with CD8 predominant population' – hallmarks of CD8 encephalitis **[2]** ***(Images 5 & 6)***

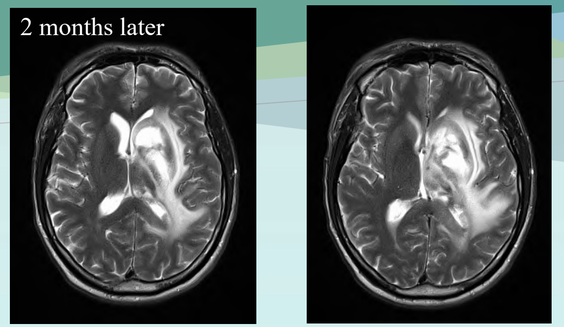


Image 2 and 3:
More extensive left cerebral hemisphere intra-axial T2 lesion involving the left corona radiata, left basal ganglia, left temporal lobe.

High-dose corticosteroids were commenced resulting in marginal clinical response associated with lessening of oedema on MRI but enlargement of the caudate lesion ***[Images 2 and 3]***

Furthermore, anti-fungal cover was started with Amphotericin-B. This combination resulted in considerable clinical and radiological improvement with near-complete resolution on repeat imaging. ***(Image 4)***

CD8 encephalitis is an emerging clinical entity which has demonstrated variable prognoses with high-dose steroids in the literature. One case series of fourteen patients showed five patients making a full recovery, four surviving with residual cognitive impairment and five dying **[3]**. Indeed, more data is required regarding its treatment and long-term outcomes. Given ongoing concerns regarding background undiagnosed lymphoma, serial imaging is required to ensure no development of new lesions, as steroid doses taper.

Conclusions

This case demonstrates diagnostic and treatment challenges that arise in the context of immunosuppression. CD8+ encephalitis is a severe CNS complication of HIV that if detected early can have a favorable prognosis with corticosteroid therapy.

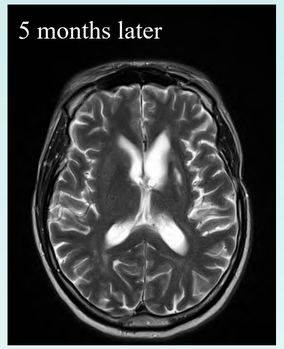
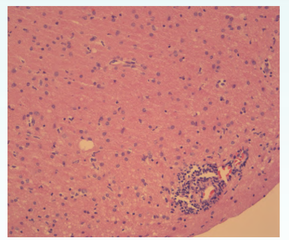
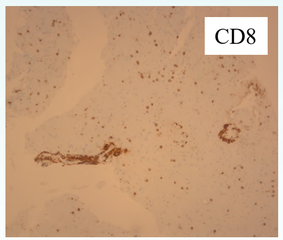


Image 4:
Significant decrease in the size of the left caudate nucleus/left periventricular mass

Images 5 And 6
Lymphocytic inflammation centered around vessels, microglial activation and astroglial reaction.
Sub-typing showing CD8 predominant population





References

[1] Zarkali A, Gorgoraptis N, Miller R, John L, Merve A, Thust S et al. CD8+ encephalitis: a severe but treatable HIV-related acute encephalopathy. Practical Neurology. 2016;17(1):42-46.

[2] Gray F, Lescure F, Adle-Biassette H, Polivka M, Gallien S, Pialoux G et al. Encephalitis with Infiltration by CD8+ Lymphocytes in HIV Patients Receiving Combination Antiretroviral Treatment. Brain Pathology. 2013;23(5):525-533.

[3] Lescure F, Moulignier A, Savatovsky J, Amiel C, Carcelain G, Molina J et al. CD8 Encephalitis in HIV-Infected Patients Receiving cART: A Treatable Entity. Clinical Infectious Diseases. 2013;57(1):101-108.