Neurological symptoms, high cerebrospinal fluid protein, lymphocytic pleocytosis and HIV: A case series

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Neurological presentations in patients living with HIV can be life-threatening. A wide variety of causes can be implicated and in many cases the origin is not identified. Using three cases of patients with neurological symptoms, a lymphocytic pleocytosis and high protein on cerebrospinal fluid (CSF) analysis and HIV we consider the range of underlying causes.

Case 1:
A 37year old healthcare worker presented with severe fatigue, progressing to confusion and aggression indicating acute personality change. She had no medical background. CSF showed a lymphocytic pleocytosis (29 WCC/cmm, 90% lymphocytes), raised protein (2280mg/l) and normal glucose. Lumbar puncture opening pressure was 40cm H^2O. A viral encephalitis was suspected, however CSF viral panel was negative. An early HIV infection was diagnosed (HIV architect +, Vidas p24 ag+/ab-, Innolia confirmatory test +). CSF HIV viral load was high (>30,000 copies/ml). The absence of an alternative infectious agent led to the consideration of encephalitis related to acute HIV infection. Antiretroviral therapy (ART) with good CNS penetration was initiated leading to rapid improvement and restoration of cognitive function.

Case 2:
A 68year old Ukrainian man presented with lower limb weakness, on a background of HIV, compliant on ART for 5months, and recent Positron Emission Tomography (PET) confirmed remission from diffuse large b-cell lymphoma (DLBCL). His CD4 count was 48(38.2%)cells/mm3 and his HIV viral load was not detected. CSF examination showed predominantly lymphocytic pleocytosis(810 WCC/mm3, 60% lymphocytes), raised protein(7959mg/l), low glucose(<0.1mmol/l). A diagnosis of Burkitt's Lymphoma was secured on CSF flow-cytometry with positive CD19/CD20 molecules and a high EBV viral load (24,760,676 copies/ml). The patient was palliated, as combined pathology rendered him unfit for intrathecal chemotherapy.

Case 3:
A 41year old Zimbabwean lady presented with severe headaches progressing to fluctuating GCS. CSF analysis showed a lymphocytic pleocytosis(355 WCC/cmm, 80% lymphocytes), raised protein(23,110mg/l) and normal glucose(4.3mmol/l). VZV DNA was detected in CSF and high dose Acyclovir was initiated for VZV encephalitis however the patient continued to clinically deteriorate. MRI brain reported severe abnormal leptomeningeal enhancement throughout both hemispheres and cerebellar oedema. HIV infection was diagnosed(HIV architect +, Innolia confirmatory test +). Further extensive investigations on multiple CSF samples and serum were negative, including flow cytometry and TB GeneXpert. Dexamethasone was initiated due to suspected CNS lymphoma. ART with high CNS penetration was initiated. Due to the unknown cause of this clinical and radiological picture TB medication were commenced. Despite broad-spectrum treatment the patient continued to deteriorate and fatal hydrocephalus developed.

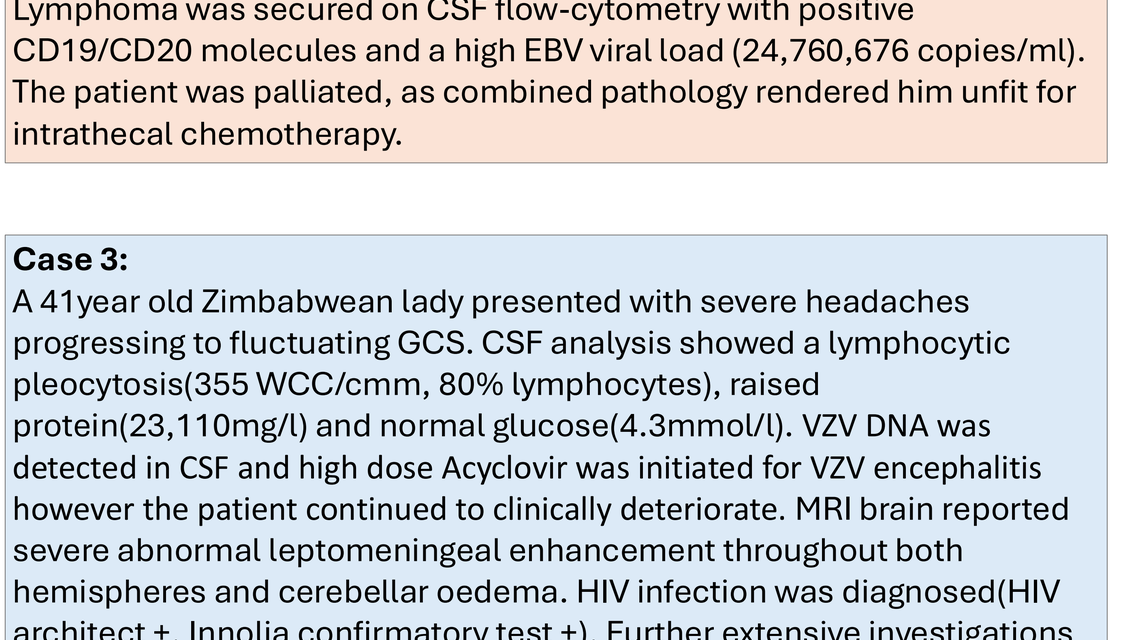

Fig 2: Diagnostic considerations in HIV patients with neurological symptoms and comparable CSF analysis: A summary of the case series

	Case 1	Case 2	Case 3
Clinical presentation	Acute personality change	Ascending paralysis	Severe headaches, Decreasing GCS
CD4 count		48 (38.2%) cells/mm3	34 cells/mm3
HIV viral load	571,732 copies/ml	Not detected	
P24 ag/ab	Antigen Positive/ Antibody Negative	-	-
CSF initial analysis	29 WCC/cmm 98% lymphocytes	810 WCC/cmm 60% lymphocytes	355 WCC/cmm 80% lymphocytes
	2,280mg/l protein	7,959mg/l protein	23,110mg/l protein
	3.2mmol/l glucose	<0.1mmol/l glucose	4.3mmol/l glucose
CSF infectious panel (EMV, CMV, HSV1/2, VZV, Enterovirus, JC virus, cryptococcal neoforms antigen, TB GeneXpert)	Negative	EBV >24 million copies/ml CMV <500 copies/ml	VZV DNA +
Serum infectious panel	Negative (Toxoplasma IgG and IgM, T.pallidum, Parvovirus B19 IgG, B.burgdorferi IgG, Malaria thick and thin film, Leptospira IgM, HBsAg, Anti-HCV, EBV, CMV)	EBV >34,000 copies/ml CMV >17,000 copies/ml TB GeneXpert: Negative	Negative (TB GeneXpert, HBsAg, Anti-HCV, CMV, EBV, cryptococcal neoforms antigen)
Autoimmune encephalitis/ vasculitis panel	Negative	Negative	Negative
Flow cytometry	Negative	CD19/CD20 molecules	Negative
MRI brain	No intracranial abnormality	Normal age-related changes	Extensive lepto-meningeal enhancement
Diagnosis	HIV encephalitis	Leptomeningeal Burkitt's Lymphoma	No definitive diagnosis - ?TB leptomeningeal disease

Fig 1: Investigations and results summary for Case 1-3.

Discussion:
HIV should be considered in any patient presenting with new neurological symptoms. This series of cases highlight a selection of the wide-reaching range of causes of acute neurological symptoms in HIV presenting with a comparable CSF analysis.