CASE REPORT

Extremely high HIV-1 viral load in a patient with undiagnosed clinical indicator disease for HIV infection

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SUMMARY

We report a case of a new diagnosis of HIV with an extremely high viral load presenting with HIV encephalopathy, in a 54-year-old woman who had been treated with 2 years of extended high-dose immunosuppressant therapy for a recalcitrant pruritic rash before diagnosis.

BACKGROUND

This case highlights that HIV should be considered as an important differential diagnosis of unexplained or recalcitrant rash, and that HIV status should be considered before starting long-term steroid and immunosuppressant use.

CASE PRESENTATION

A 54-year-old Zimbabwean woman presented to her general practitioner (GP), with a widespread pruritic macular erythematous rash across her arms, upper legs, trunk and back. The rash had gradually developed over the previous 3 days and no specific trigger could be identified. The patient had no other significant medical history, was not on any regularly prescribed medicine and had not taken any new over-the-counter or herbal medication. She was a non-smoker, drank no alcohol and had not travelled outside the UK for 14 years.

Her GP prescribed a 2-week course of prednisolone 20 mg once daily and referred her to a dermatology department. During the 2 weeks, there was mild improvement in the rash, but itching persisted.

Serology showed negative cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) and immunoglobulin E values, and normal creatine kinase.

A skin biopsy was performed 3 weeks after the prednisolone course had been completed without symptomatic improvement. Histology showed mild dermal oedema, with scattered eosinophils in the dermis and a superficial perivascular chronic inflammatory infiltrate. There was no evidence of granuloma annulare and no sarcoidosis.

Prednisolone was continued at a slightly increased dose of 25 mg once daily and, as the rash had not completely cleared, a repeat skin biopsy was performed after 6 months of steroid therapy. This showed an unremarkable epidermis, oedematous dermis, mild perivascular inflammation, and scattered mast cells and eosinophils. There were no features of fungal infection and periodic acid-Schiff

stain was negative. CD117 (mast cell growth factor receptor stain) showed scattered mast cells in keeping with urticarial rash of unknown origin. The patient remained on prednisolone for another 12 months. As symptoms were not improving, the patient's prednisolone was cross-weaned to ciclosporin over a period of 1 month. However, at this point, 18 months after her initial presentation to her GP, the patient was admitted to the hospital with lethargy and leg weakness resulting in poor mobility and falls. Her son had also noted that the patient had been developing memory and concentration difficulties. The patient's ciclosporin was discontinued and she was discharged with a diagnosis of ciclosporin toxicity.

Within 1 month she was re-admitted to the hospital after a fall. Examination revealed muscle wasting in the upper and lower limbs, and a symmetrical proximal weakness in the lower limbs. Her gait was wide based, cranial nerves were intact and there was mild cognitive impairment (Mini-Mental State Examination 27/30). White patchy areas were noted on the palate, which were removable with a spatula. There was no lymphadenopathy.

INVESTIGATIONS

MRI of the brain showed diffuse white matter changes and an atrophic cerebellum. Cerebrospinal fluid showed a raised protein (0.56 g/dL), but was otherwise normal. In view of the likely oral candidiasis, an HIV-1 antibody test was performed and was positive. CD4 absolute count was 2×10^6 cells/ μ L (1%), and HIV viral load 1 058 239 000 copies/ mm^3 (log 9.02). The virus was genotyped as Clade C wild type virus.

DIFFERENTIAL DIAGNOSIS

The brain MRI scan appearances were reported as non-specific but differential diagnoses included progressive multifocal leucoencephalopathy, HIV encephalopathy and encephalitis. The scans were reviewed by HIV specialists and a neuroradiologist. As the white matter changes were symmetrical, the diagnosis was HIV encephalopathy.

TREATMENT

The patient was started on antiretrovirals: truvada (tenofovir/emtricitabine) 1 tablet once daily, darunavir 800 mg once daily, ritonavir 100 mg once daily and raltegravir 400 mg two time a day.

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OUTCOME AND FOLLOW-UP

The patient had a good response to therapy. After 1 month, HIV viral load fell to 7420 copies/mm³ and CD4 count was 38×10⁶ cells/μL. At 6 months, HIV viral load was undetectable (<40 copies per mm³) and CD4 count 287×10⁶ cells/μL, and raltegravir was stopped. After a period of outpatient neurorehabilitation, the patient's memory and cognition significantly improved and currently, 1 year on from her diagnosis, she lives at home alone, independent with activities of daily living.

DISCUSSION

The 2008 National HIV Testing Guidelines endorsed by the National Institute for Health and Care Excellence (NICE) recommend that HIV testing should be offered to all patients presenting for healthcare where HIV (including primary HIV infection) is a differential diagnosis.^{1–3} A recent review of HIV testing noted that 22% of patients living with HIV are undiagnosed, and 50% of patients are diagnosed at a late stage⁴ (ie, with a CD4 count of <350×10⁶ cells/μL), and are therefore 10 times more likely to die in the first year after diagnosis than those with a CD4 count >350 cells.⁵

There is known to be a relationship between HIV viraemia and skin disease, with the odds of developing conditions such as pruritic papular eruption increasing fourfold with every log increase in plasma HIV RNA at antiretroviral therapy (ART) initiation.⁶

Viral loads of over 100 000 copies/mL at the start of ART are linked with a greater likelihood of disease progression.⁷ Use of high-dose steroids for extended periods is likely to increase HIV-1 viraemia, and one case report has suggested this may be due to inhibition of cytotoxic T-lymphocyte function.⁸

A phase II study of the role of immunoadjuvant prednisolone as therapy for HIV-associated tuberculosis found HIV RNA levels increased in the first month of prednisolone use across all levels of immune activation, compared with the placebo arm.⁹ One hypothesis is that prednisolone treatment increases viral replication via glucocorticoid response elements in the HIV genome,¹⁰ while it has also been suggested that prednisolone can have lytic effects on lymphocytes, releasing more replicating virus into the bloodstream.¹¹

This black African woman presented with a recalcitrant rash, which persisted despite treatment with various immunosuppressant drugs including steroids and ciclosporin over a period of almost 2 years. Several missed opportunities for HIV testing are noted. At the time of diagnosis, she had developed oral candidiasis and HIV encephalopathy, and CD4 count was 2×10⁶ cells/μL. An extremely high viral load of more than 1 billion copies/mm³ was found, and is, we believe, the highest ever HIV-1 viral load value reported. It was likely due to unopposed viral replication in the context of additional iatrogenic immunosuppression, which subsequently led to HIV encephalopathy.

In summary, this case demonstrates the importance of offering HIV testing to patients from high-risk groups presenting with clinical indicator diseases, and testing for HIV infection before the use of long-term immunosuppressive therapy.

We recommend that all primary care physicians and non-HIV specialists be aware of the BHIVA HIV testing guidelines and how they apply to their own patient cohort.

Learning points

- ▶ Skin disease, including recalcitrant dermatitis, can be an indicator of HIV infection and should prompt testing for HIV.
- ▶ All patients who are being considered for immunosuppressive therapy should be tested for HIV infection.
- ▶ Late diagnosis of HIV is associated with a 10-fold increase in mortality, and increased transmission and cost.
- ▶ The 2008 National Testing Guidelines aim to reduce the proportion of people with undiagnosed HIV infection by increasing testing by non-specialists and are a valuable resource for any healthcare professional.

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Contributors SF and SDS collected data, and drafted and revised the case report. RD revised the case report and was the lead clinician.

Competing interests None declared.

Patient consent Obtained.

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REFERENCES

- 1 UK National Guidelines for HIV Testing 2008. <http://www.bhiva.org/HIVTesting2008.aspx>
- 2 National Institute for Health and Care Excellence. *Increasing the uptake of HIV testing among black Africans in England. (Public Health Guidance PH33.)* 2011. <http://www.nice.org.uk/guidance/PH33>
- 3 National Institute for Health and Care Excellence. *Increasing the uptake of HIV testing among men who have sex with men. (Public Health Guidance PH34.)* 2011. <http://guidance.nice.org.uk/PH34>
- 4 Rayment M, Asboe D, Sullivan AK. HIV testing and management of newly diagnosed HIV. *BMJ* 2014;349:g4275.
- 5 May MT, Gompels M, Delpech V, et al., UK Collaborative HIV Cohort (UK CHIC) Study. Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. *AIDS* 2014;28:1193–202.
- 6 Chua SL, Amerson EH, Leslie KS, et al. Factors associated with pruritic papular eruption of human immunodeficiency virus infection in the antiretroviral therapy era. *Br J Dermatol* 2014;170(4):832–9.
- 7 Egger M, May M, Chêne G, et al. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet* 2002;360:119–29.
- 8 Harrer T, Bäuerle M, Bergmann S, et al. Inhibition of HIV-1-specific T-cells and increase of viral load during immunosuppressive treatment in an HIV-1 infected patient with Chlamydia trachomatis induced arthritis. *J Clin Virol* 2005;34:224–30.
- 9 Mayana-Kizza H, Jones-Lopez E, Okwera A, et al. Immunoadjuvant prednisolone therapy for HIV-associated tuberculosis: a phase 2 clinical trial in Uganda. *J Infect Dis* 2005;191(6):856–65.
- 10 Soudeyns H, Geleziunas R, Shyamala G, et al. Identification of a novel glucocorticoid response element within the genome of the human immunodeficiency virus type 1. *Virology* 1993;194:758–68.
- 11 Kirschner D. Dynamics of co-infection with M. tuberculosis and HIV-1. *Theor Popul Biol* 1999;55:94–109.

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