Acute varicella-zoster virus necrotizing meningoencephalomyelitis with sudden visual loss and paraparesis in an HIV-infected patient

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SUMMARY

We describe a case of acute varicella-zoster virus (VZV) hemorrhagic meningoencephalomyelitis in an HIV-infected patient. On admission the patient's CSF was mild haemorrhagic and xanthochromic after centrifugation and he had thoracic skin blisters. VZV DNA was isolated from both the thoracic blisters and CSF. Treatment consisted of aggressive antiviral, steroid and immunoglobulin therapy, which was able to stop disease progression. The patient survived but was left blind and paretic. In conclusion, a diagnosis of CNS infection caused by VZV, based upon CSF analysis and examination of the skin for typical blisters, requires aggressive empiric antiviral therapy in order to maximise patient survival.

KEY WORDS: VZV, Hemorrhagic meningoencephalomyelitis, HIV

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INTRODUCTION

VZV complications involving the CNS, such as necrotizing meningoencephalomyelitis, are estimated to occur in approximately 2% of patients with AIDS (Kleinschmidt-DeMasters *et al.*, 1998). The prognosis is very poor, with a median survival of only 16 days (McKelvie, 2002). Therefore aggressive empiric antiviral therapy should be commenced as soon as VZV CNS infection is suspected, based upon CNS analysis and the presence of skin blisters.

CASE PRESENTATION

A 55-year-old man was transferred to our hospital with a 7-day history of fever, headache and neck pain. On admission to the previous hospital, a CT-scan and MRI of the brain with gadolinium enhancement were both normal. Three days before admission to our hospital blindness suddenly occurred in the left eye, followed after two days by blindness in the right eye. The previous hospital had treated him with dexamethasone and ceftriaxone. On the day of transfer, an HIV-test result was positive.

On admission to our hospital the patient was blind in both eyes and had lumbar pain. On physical examination there was no neck stiffness but Lasègue sign was positive on both sides. There was no motor deficit. Abdominal reflexes were absent while tendon reflexes were normal. Finger-nose test revealed dysmetria on the left side. Sensory examination was normal.

Five skin blisters were noted on the right posterior area of his chest.

Lumbar puncture revealed mild haemorrhagic and xanthochromic CSF. The opening pressure was 20 cm H_2O, CSF protein concentration was elevated (1096 mg/dL; normal range <40 mg/dL), glucose level was normal (66 mg/dL). RBC count was 750 cells/µl and WBC count was 80 cells/µl

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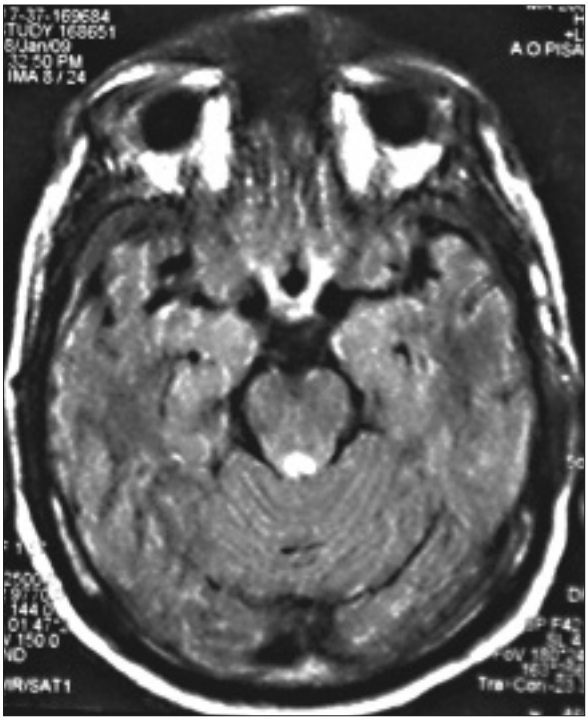

FIGURE 1 - *MRI of the patient's brain: T2 sequence demonstrated severe swelling of the optic nerves and chiasma.*

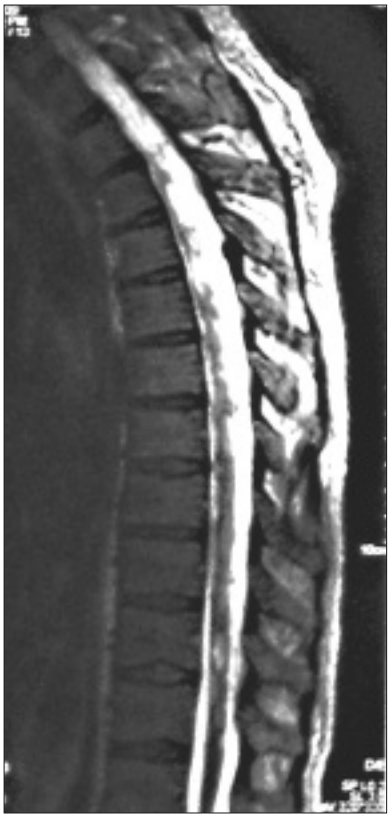

FIGURE 2 - *MRI of the patient's spinal cord: T2 sequence demonstrated severe cord swelling.*

(72 lymphocytes and 8 polymorphs). Blood $CD4^+$ T cell count was 3 cells/µl and HIV RNA level was 24,000 copies/ml. Treatment with 350 mg q12h IV ganciclovir, 400 mg qd IV fluconazole and 6 MU q6h IV benzylpenicillin was administered empirically.

Two days after admission, CMV antigenemia was positive (178 cells/200,000 cells), VZV DNA was detected by PCR in the CSF and skin blisters, while PCR for other herpes virus resulted negative. CSF HIV RNA levels were 1,330 copies/ml. The same day flaccid paresis occurred and MRI scan showed a diffuse meningeal enhancement, with bilateral optic neuritis and chiasm inflammation (Figure 1).

Additionally, MRI scan revealed cervical and thoracic myelitis with hyperintense lesions in T2 weighted images of the anterior, posterior and lateral white matter, with a "sugar-coating" pattern (Figure 2). Therefore, 90 mg/kg q12h IV foscarnet was associated to ganciclovir, along with high doses of steroids and IV immunoglobulin 30g for 3 and 5 days, respectively. Antiviral therapy was administered for 28 days. By day 15, CSF screened negative for VZV DNA. One week after admission, antiretroviral therapy was started with tenofovir, emtricitabine, ritonavir-boosted lopinavir and enfuvirtide; after 10 days of therapy, CMV antigenemia was negative. The patient survived but did not recover any lost visual or neurological function, and he was transferred to a rehabilitation unit.

DISCUSSION

While VZV complications involving the CNS are rare in patients with HIV/AIDS (Kleinschmidt-DeMasters *et al.*, 1998; Gray *et al.*, 1994; Sotrel 1998), the poor prognosis dictates that an aggressive antiviral treatment regimen is required, which is the approach that we utilised in our patient. VZV infections of the CNS have been reported in profoundly immunosupressed HIV-infected individuals (Kleinschmidt-DeMasters *et al.*, 1998; Gray *et al.*, 1994; Chretien *et al.*, 1993) with four variants recognised: multifocal encephalitis, ventriculitis, focal necrotizing myelitis, and vas-

culopathy leading to cerebral infarction (Gray *et al.*, 1994).

Compartmentalisation of VZV immunity in the CNS may explain the profound CNS changes that sometimes happen in the absence of systemic symptoms, because the immune response is more active in the CNS (Clark *et al.*, 2004). For this reason we also administered steroid and immunoglobulin therapy during antiretroviral therapy, because vasculitis may be associated (Chang *et al.*, 2009). We were able to avoid death in our patient, but permanent neurological defects were irreversible due to necrotizing lesions caused by VZV in the CNS. Necrotizing encephalomyelitis is a devastating complication of VZV in AIDS, and it is crucial to recognise this complication as early as possible. The presence of xanthocromic CSF and RBC in the CSF, suggestive of VZV infection, along with associated skin blisters (Chang *et al.*, 2009), requires immediate aggressive empiric antiviral therapy in order to treat this life-threatening condition. AIDS patients with a VZV CNS infection treated with a combination of ganciclovir and foscarnet or ganciclovir alone are reported to have a significantly better final visual acuity than those treated with either acyclovir or foscarnet (Moorthy *et al.*, 1997).

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