CASE REPORT

A slow progressor HIV-infected boy developing quadriplegia with evidence of Epstein-Barr virus associated smooth muscle tumour of the cervical spinal cord

Tanaporn Wilaisakditipakorn,¹ Pitchamol Vilaisaktipakorn,¹ Torsak Bunupuradah,² Thanyawee Puthanakit³

¹Department of Physiology, Chulalongkorn University, Bangkok, Thailand

²HIV-NAT, the Thai Red Cross AIDS Research Center, Bangkok, Thailand

³Department of Pediatrics, Chulalongkorn University, Bangkok, Thailand

Correspondence to

Dr Thanyawee Puthanakit, thanyawee.p@hivnat.org

Accepted 8 June 2015

SUMMARY

The authors report a case of slowly progressive HIV in an 11-year-old boy whose initial presenting AIDS-defining symptom was progressive quadriplegia with complete cord compression and pathological confirmation of Epstein-Barr virus associated smooth muscle tumour. Despite tumour removal, quadriplegia persisted as did ventilator dependence.

BACKGROUND

HIV-infected children have higher risk for malignancy than non-HIV infected children. It is estimated that this risk is 10 times higher (0.6 per 1000 versus 0.07 per 1000 person-years).¹ The most common malignancies in HIV-infected children are non-Hodgkin's lymphoma, followed by Kaposi's sarcoma and smooth muscle tumours.^{1 2} However, it is quite uncommon to have an HIV-related tumour as a first presenting symptom lead to diagnosis of AIDS.

CASE PRESENTATION

An 11-year-old Thai boy was referred from a provincial hospital to King Chulalongkorn Memorial Hospital (KCMH) in November 2013. His medical history was largely unremarkable, with no prior hospitalisations or known chronic medical problems. Four months prior to admission, his family reported development of low-grade fever, upper respiratory symptoms and weight loss, initially treated as bacterial pneumonia without improvement. Two years earlier, his mother had chronic cough and weight loss; she was tested for HIV and diagnosed as HIV positive. Her HIV antibody test was negative during pregnancy at gestational age of 12 and 24 weeks. The boy had been breastfed for 10 months. He therefore got tested for HIV antibody. The HIV antibody was positive and subsequent CD4 was 1%, 5 cells/mm³.

He had persistent lung infiltration; therefore he was diagnosed as possible pulmonary tuberculosis (TB) despite negative sputum acid-fast bacillus (AFB) smear and PCR for TB. He was empirically treated with isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E). He developed generalised rash, which led to discontinuation of ethambutol and start of ofloxacin (O) in its place. Two weeks later, the patient developed weakness and could not lift his arms. Owing to suspicion for

isoniazid toxicity as a potential culprit causing the weakness, the isoniazid dose was reduced. Yet, the patient's upper extremity weakness continued to progress, ultimately leading to quadriplegia. The HRZO regimen was then subsequently stopped. MRI was performed and revealed a heterogeneous, enhanced, intradural-extramedullary mass with extension into right C3/4 neural foramen as well as abnormal enhancement in the spinal cord above the lesion at the cervicomedullary junction, accompanied by leptomeningeal enhancement along the surface of cervical cord, conus medullaris and caudal equina nerve roots (figure 1). The patient's weakness continued to progress, involving the muscles crucial to breathing. He required endotracheal intubation and ventilator support. He was then referred to KCMH for further management.

Figure 1 MRI showing a smooth muscle tumour at cervical spine C3–4 levels: sagittal gadolinium-enhanced T1-weighted MRI with fat suppression of the cervical spine shows a well-defined, heterogeneous enhanced intradural-extramedullary mass (black arrows) and also abnormal enhancement in the spinal cord above the lesion (white arrow) at the cervicomedullary junction.

CrossMark

To cite:

Wilaisakditipakorn T, Vilaisaktipakorn P, Bunupuradah T, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210133

Figure 2 Microscopic pathology of Epstein-Barr virus (EBV)-associated smooth muscle tumour: Short spindle cells arranged in fascicular pattern with a few mitoses. EBV-encoded RNA (EBV RNA) in situ hybridisation (top right corner inset) shows expression of EBV RNA in tumour cells.

TREATMENT

At KCMH, near total tumour debulking was performed. Operative findings included a greyish-white rubbery, well-circumscribed, 2×5 cm intradural extramedullary tumour on the right anterolateral portion of the spinal canal with apparent compression on the spinal cord and tumour originating from the right dural wall. Pathological examination of the tumour showed mixed cellular and hypocellular necrotic areas, with tumour cells that were short, spindle cells mixed with round myoid cells arranged in a fascicular pattern. A mild degree of nuclear atypia and a few mitoses were noted. Immunohistochemical studies revealed strong smooth muscle actin expression but were negative for desmin and CD34. EBV-encoded RNA (EBER) in situ hybridisation demonstrated EBV RNA in almost all of the tumour cells (figure 2). The diagnosis of EBV-associated smooth muscle tumour (EBVSMT) was made.

Postoperatively, the boy remained quadriplegic and ventilator dependent. Prior to start of antiretroviral therapy (ART), his CD4⁺ was 1%, 3 cells/mm³. ART was immediately started with zidovudine, lamivudine and efavirenz. For his pulmonary problem, we reviewed chest X-ray film and repeated sputum PCR for tuberculosis, which turned out to be negative. Diagnosis of bronchiectasis was made and the antituberculosis drug was discontinued. Cotrimoxazole and azithromycin were started for mycobacterium avium complex and *Pneumocystis jiroveci* pneumonia prophylaxis.

OUTCOME AND FOLLOW-UP

Six weeks after starting ART, the boy's CD4 was 2%, 16 cells/mm³ and HIV-RNA was 191 copies/mL. His mother was trained to manage the boy's ventilator and to provide physical rehabilitation at home. At 48 weeks after treatment, his CD4 was 9%, 205 cells/mm³ and HIV RNA less than 20 copies/mL. His neurological examination revealed quadriplegia with motor power of hand grade I and he remained ventilator dependent.

DISCUSSION

We report a case of an 11-year-old boy who was diagnosed with HIV infection who presented with weakness of upper extremities and progressed to quadriplegia. MRI showed a heterogeneous enhanced intradural-extramedullary mass with extension into the right C3/4 neural foramen. Pathological study suggested spindle cell tumour with EBV-associated smooth muscle tumour.

Smooth muscle tumours rarely occur in healthy children, but are not uncommon in HIV-infected children.³ This tumour is

known to be associated with EBV, and is known as EBV-associated smooth muscle tumour (EBVSMT). EBVSMT is typically found in unusual organs (soft tissue, liver, lung, spleen, dura).³ In our patient, the tumour was found in the spinal cord, which is a rare presentation. Previously, this tumour was referred to as a leiomyoma, leiomyosarcoma, or smooth muscle tumour of uncertain malignant potential. Prevalence of leiomyosarcoma among HIV-infected children who had a tumour is only 3%.² The pathogenesis is presumed to be related to immune system impairment, a depletion of CD4⁺ T helper cells and loss of immune functions and complex interaction with other oncogenic viruses, such as EBV. EBVSMT usually presents late in the course of children with AIDS, which may be associated with a role of chronic immune suppression in tumour pathogenesis. The treatment of choice is surgical removal.⁴ Even though the tumour was removed, our patient did not improve. We postulate that this may be because of the delay in diagnosis and the fact that extension of the tumour into the spinal cord had already occurred, prior to surgery.

Adverse effect due to anti-TB drugs was considered as a potential aetiology for the boy's weakness. Isoniazid can cause peripheral neuropathy but weakness is not a common side effect of isoniazid. There is a prior case report of motor-dominant neuropathy related to isoniazid.⁵ However, the adverse effect is dose related and the symptoms should be reversible within the first few weeks after isoniazid discontinuation.

The route of HIV transmission of the patient was presumed to be mother-to-child, as the patient had never received blood transfusion and was not sexually active. Even though his mother's HIV tests were negative during pregnancy, the patient was breastfed for 10 months. We hypothesised that his mother acquired HIV infection during late pregnancy or the lactation period, which had high risk of transmission to the child. This scenario would make us unaware of the HIV exposure risk to the child. However, when the mother was diagnosed with HIV infection 2 years prior to the child's illness, the child should have been tested for HIV. This is a window of opportunity for earlier HIV diagnosis and to provide ART before development of severe immunosuppression and the advance of conditions such as cervical cord tumours.

In conclusion, we report a case of an 11-year-old boy with HIV infection who presented with weakness progressing to quadriplegia due to EBVSMT at the cervical spinal cord. This case illuminates a rarely presenting AIDS-defining illness leading to delay in diagnosis and poor treatment outcome. Furthermore, the mother-to-child HIV transmission in this case might have occurred when the mother had newly acquired infection during late pregnancy or during the lactating period.

Learning points

- ▶ All pregnant women should be HIV tested twice, at initial antenatal care and at the third trimester, to lower the possibility of under-diagnosis of HIV-infection.
- ▶ Once a woman is diagnosed with HIV infection, all of her children should get anti-HIV testing to minimise possible delayed diagnosis.
- ▶ Antiretroviral therapy initiation should not be delayed in severely immunosuppressed HIV-infected children.
- ▶ Epstein-Barr virus-associated smooth muscle tumours should be considered in HIV-infected children presenting with progressive weakness.

Acknowledgements The authors would like to thank Dr Suvaporn Anugulruengkit for caring for the patient and Dr Chitsanu Pancharoen for being our supervisor. The authors would like to thank Dr Sukalaya Lerdum and Dr Tauangtham Anekpuritanang for providing the radiological and histopathological material, respectively, presented in this article. The authors would also like to thank Dr Jeremy D Whyman for English editing of the manuscript.

Contributors TW, PV and TP wrote the manuscript. TP and TB reviewed and approved the final manuscript for submission.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Pancharoen C, Nuchprayoon I, Thisyakorn U, *et al.* Hospital-based epidemiologic survey of malignancies in children infected with human immunodeficiency virus in Thailand. *Pediatr Infect Dis J* 2005;24:923–4.
- 2 Biggar RJ, Frisch M, Goedert JJ. Risk of cancer in children with AIDS. AIDS-Cancer Match Registry Study Group. *JAMA* 2000;284:205–9.
- 3 Mueller BU. HIV-associated malignancies in children. *AIDS Patient Care STDS* 1999;13:527–33.
- 4 Chiappini E, Berti E, Ganesin K, *et al.* Pediatric human immunodeficiency virus infection and cancer in the highly active antiretroviral treatment (HAART) era. *Cancer Lett* 2014;347:38–45.
- 5 Zaoui A, Abdelghani A, Ben Salem H, *et al.* Early-onset severe isoniazid-induced motor-dominant neuropathy: a case report. *East Mediterr Health J* 2012;18:298–9.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow