

## CASE REPORT

# Opsoclonus–myoclonus–ataxia syndrome in an HIV-infected child

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## Abstract

Opsoclonus–myoclonus–ataxia (OMA) syndrome typically presents with chaotic eye movements and myoclonus with some patients exhibiting ataxia and behavioural disturbances. The pathogenesis may be inflammatory with an infectious or paraneoplastic trigger. We present a 13-year-old HIV-infected girl who was initially started on highly active antiretroviral therapy (HAART) in March 2013 with a CD4 count of 79 cells/cumm. Initially, the patient did not comply with treatment, resulting in a CD4+ count of 77 cells/mm<sup>3</sup> in November 2015 and prompting a new HAART scheme comprising lamivudine, tenofovir and ritonavir-boosted atazanavir. Shortly after starting this scheme, she developed OMA syndrome in January 2016. She was treated with intravenous immunoglobulin and methylprednisolone followed by oral steroids along with oral clonazepam and gradually recovered. We suggest immune reconstitution inflammatory syndrome as a possible aetiology of OMA in HIV-infected children.

## INTRODUCTION

Opsoclonus–myoclonus–ataxia (OMA) typically presents with chaotic eye movements and myoclonus with some patients exhibiting ataxia and behavioural disturbance [1]. The pathogenesis may be inflammatory with an infectious or paraneoplastic trigger. We present a 13-year-old girl with OMA who presented to us shortly after commencement of second line highly active antiretroviral therapy (HAART) and who recovered after immunosuppressive therapy.

## CASE REPORT

A 13-year-old girl presented to us in January 2016 with throbbing headache, nausea and jerky movements for 2 days. These jerks increased on standing and were associated with

uncontrolled jerky movements of the eyes. They used to subside on sleeping. She was found to be HIV infected in 2011 and was started on HAART with Zidovudine, Lamivudine and Nevirapine with Trimethoprim–Cotrimaxazole and Fluconazole prophylaxis in 2013 when her CD4 count was 79 cells/cumm. In November 2015, her CD4+ count dropped to 77 cells/mm<sup>3</sup> prompting a new HAART scheme comprising lamivudine, tenofovir and ritonavir-boosted atazanavir. Her HIV viral load was 28 387 copies/ml. In January 2016, her CD4 count improved to 429 cells/cumm and viral load decreased to 165 copies/ml.

On examination, weight was 27 kg (third centile), height was 144 cm (third centile). She was afebrile. Blood Pressure—110/74 mmHg. She was conscious, alert. She had marked opsoclonus in both eyes with jerky myoclonic ataxia as seen in Supplementary Video S1. She was unable to stand or walk without support. Deep tendon reflexes were brisk. Plantars were

†All authors were involved in patient management, preparation of manuscript and approving the final version.

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extensor. No neck stiffness was seen. Fundus examination was normal. On investigation, cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis (22 leucocytes/mm<sup>3</sup> with 100% lymphocytes), 67 mg/dl of proteins and 89 mg/dl of glucose. CSF Gram stain, Zeil Neilsen staining for tuberculosis and culture were negative. CSF immunoglobulins could not be done due to unaffordability. CSF Gene Xpert was negative. Thyroid function tests were normal. Serum TPO antibody titre was normal. Antinuclear antibody was weakly positive (+). Ultrasound examination of the abdomen and pelvis was normal. Urine for Vanyl Mandelic acid was normal. Mantoux test was negative and chest X-ray was normal.

Magnetic Resonance Imaging (MRI) Brain showed a symmetric, ill-defined hyperintensity on FLAIR and T2 weighted images in the cerebral matter bilaterally, periventricular white matter, corona radiata, centrum semiovale and bilateral internal capsules as seen in Fig. 1 with iso and hypointensity seen in T1 weighted images suggestive of demyelination as seen in Fig. 2. Subtle signal alteration was also seen in the middle cerebellar peduncles bilaterally.

Intravenous immunoglobulin (IVIg) at the dose of 2 g/kg was given slowly intravenously over 3 days. This was followed by three pulse doses of methylprednisolone each given intravenously at a dose of 30 mg/kg followed by oral prednisolone (1 mg/kg/day). Oral clonazepam was also started. Patient gradually improved (Supplementary Video S2). She is now on regular follow-up.

## DISCUSSION

OMA is characterized by continuous multidirectional saccadic eye movements accompanied by generalized myoclonus and, less frequently, cerebellar ataxia, postural tremor, encephalopathy and behavioural disturbances. It is also known as 'dancing eye and dancing feet syndrome' [2].

There are very few cases reported of OMA in HIV-infected patients [1, 3, 4] and only one case reported in children till now [3].

HIV-associated OMA may be the consequence of a dysregulated immune system in which a reduced CD4/CD8 ratio, in addition to a critical level of functional CD4+ cells for efficient CD8+ cytotoxicity, results in dysfunction of brainstem–cerebellar circuitry in susceptible individuals [1].

Opsoclonus–myoclonus symptoms may sometimes occur in patients with brainstem lesions together with palatal tremors, orofacial stereotypes and abnormal postural movements [5].

Kanjanasut et al. [4] reported two cases of HIV-related OMA syndrome. The first patient developed a sudden onset of OMA at the time of HIV seroconversion. The second patient experienced severe ataxia with a mild degree of myoclonus – opsoclonus, associated with an elevated CD4 count following the initiation of HAART, thus suggesting that OMA syndrome may be another rare manifestation of HIV infection at the time of seroconversion or during an immune restoration period. In our patient too, OMA was seen shortly after starting second line HAART and was associated with an elevated CD4 count and a low viral load.

Van Toorn et al. [3] postulated that immune reconstitution inflammatory syndrome was considered the most likely aetiology of OMA in an HIV-infected child because of the initial CD4 depletion and the onset of symptoms shortly after initiation of antiretroviral therapy. In our patient too, there was initial CD4 depletion after starting first line HAART, however shortly after starting second line HAART, symptoms of OMA were seen thus suggesting immune reconstitution inflammatory syndrome as a possible aetiology.

Infections (West Nile virus, Lyme disease), neoplasms (non-Hodgkin's lymphoma, renal adenocarcinoma), coeliac disease and allogeneic hematopoietic stem cell transplantation can cause opsoclonus. Newly identified autoantibodies include antineuroleukin, anti gliadin, antiendomysial and anti-CV2.

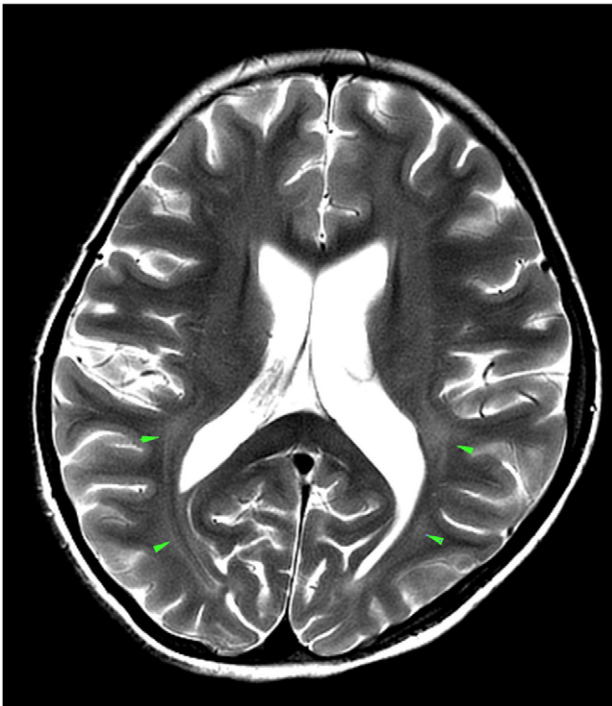


Figure 1: MRI Brain T2 weighted (Axial view) showing involvement of bilateral cerebral white matter, periventricular white matter, corona radiata, centrum semiovale and bilateral internal capsules.

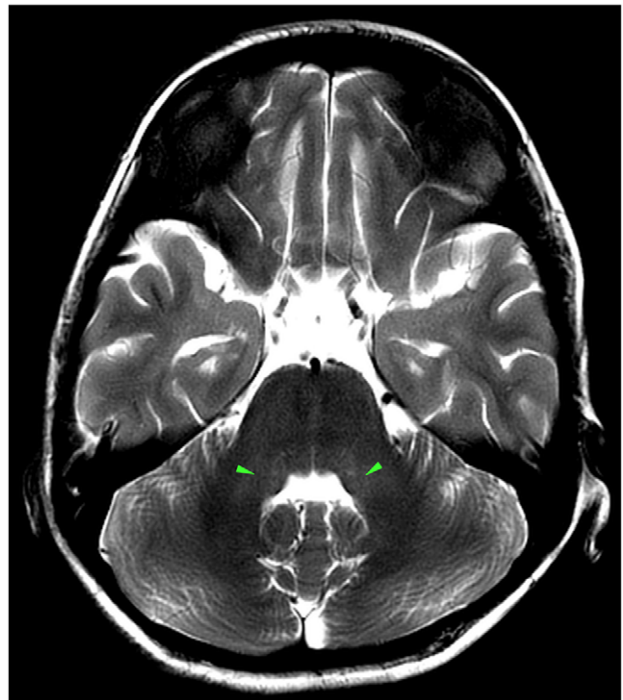


Figure 2: MRI Brain T2 weighted (axial view) showing demyelination in cerebral white matter, corona radiata, centrum semiovale and bilateral internal capsules; subtle signal alteration detected in the middle cerebellar peduncles bilaterally.

Evidence suggests that the autoantigens of opsoclonus reside in postsynaptic density, or on the cell surface of neurons or neuroblastoma cells (where they exert antiproliferative and proapoptotic effects). Most patients, however, are seronegative for autoantibodies. Cell-mediated immunity may also play a role, with B and T-cell recruitment in the CSF linked to neurological signs [6]. In our patient, we excluded other etiologies of opsoclonus such as neuroblastoma as well as lymphoma.

OMA may improve spontaneously when mild, or require immune therapy when symptoms are persistent [2]. Therapies used for OMA include IVIGs, prednisolone and anti-epileptic  $\gamma$ -aminobutyric acid agonist gabapentine. Rituximab, an anti-CD20 monoclonal antibody, seems efficacious as an adjunctive therapy [5–8]. Our patient responded to IVIG and steroids.

Thus, OMA in HIV-infected patients results due to an immune reconstitution syndrome and responds to immunosuppressive therapy.

### SUPPLEMENTARY MATERIAL

Supplementary material is available at Oxford Medical Care Reports online.

### ACKNOWLEDGEMENTS

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### CONFLICT OF INTEREST STATEMENT

None declared.

### ETHICAL APPROVAL

Taken from Hospital Ethics Committee.

### CONSENT

Patient's written consent was taken for publication.

### GUARANTOR

Dr Noella Pereira, Assistant Professor, Bai Jerbai Wadia Hospital for Children, Parel, Mumbai.

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