

Non paraneoplastic opsoclonus-myoclonus syndrome

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ABSTRACT

We analyzed the features of opsoclonus syndrome as a manifestation of post viral encephalopathy in 3 patients (one child and 2 adults). This is the first report of opsoclonus-myoclonus syndrome in the Arabian Peninsula. Symptoms appeared a few days after a viral-like illness in all patients. We excluded the possibility of paraneoplastic syndrome as investigations were carried out and follow-up did not reveal malignancy. One patient received a relatively long duration steroid treatment, another one received steroids in pulsed therapy, the third did not receive any specific treatment. The outcome was very good with improvement except in one who had severe sequelae.

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Opsoclonus myoclonus syndrome (OMS) is a rare but distinctive neurological disorder, which presents with abnormal involuntary arrhythmic, chaotic and multidirectional eye movements (opsoclonus). The opsoclonus is exacerbated by attempts at visual pursuit or re-fixation but often persists with eye closure and during sleep. Myoclonic manifestations or "tremulousness" represents the other feature of the syndrome. These usually involve all extremities, as well as axial muscles, and they are often associated with ataxia. Since the description of the opsoclonus in encephalitis as "eyes dancing" by Orzechowski,¹ other terms including "dancing eyes-dancing feet"² have been used to describe this disorder. Clinically, other abnormal eye movements may be distinguished from the opsoclonus. The ocular flutter consists of transient (less than a few seconds), rapid, small and only horizontal ocular oscillations. The ocular dysmetria is associated with cerebellar disorders resulting from overshooting followed by re-fixation and oscillations until the target is reached.³ Opsoclonus-myoclonus syndrome may complicate different malignancies in adults,⁴ however neuroblastomas is considered the most important

etiology in children.⁵ Post viral encephalopathic situations represent an other underlying cause of the syndrome that is known in children as infantile polymyoclonia.⁶ It has rarely been reported in other settings like bacterial meningitis, toxic and metabolic encephalopathies, hydrocephalus, brain stem tumors and thalamic hemorrhage.⁷⁻¹² We report 3 patients with OMS following viral-like illness in 2 adult males and presumably associated with adenoviral illness in one child. To the best of our knowledge, this is the first report of OMS in the Arabian Peninsula.

Case Report. Three cases of OMS were seen either by the Adult Neurology or Pediatric Neurology services of King Khalid University Hospital, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia (KSA) during the period from 1993 to 1998.

Patient One. A previously healthy 18-month-old Saudi girl presented in 1993 with a 5-day history of abnormal eye movements associated with unsteadiness and tremulousness of all extremities. She was fully

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vaccinated. On admission, she had congested throat and ears with vesicular skin rash involving the legs and forehead. Neurological examination showed rapid chaotic arrhythmic multidirectional eye movements (opsoclonus) associated with jerky movements that involved all extremities and increased with voluntary movements (myoclonus) and ataxia. Laboratory investigations showed normal complete blood counts (CBC), urea and electrolytes (U&E), and liver function tests (LFT). Erythrocyte sedimentation rate (ESR) was 6 mm/h. Homovanillic acid in the urine was normal. Cerebrospinal fluid (CSF) analysis showed normal proteins and glucose with 3/mm³ white blood cells (WBC) and no bacterial or viral growth on culture. Other cultures were negative from the throat and blood but adenovirus was grown in the stools and *Escherichia coli* in the urine. Neurotropic virus serologies (including cytomegalovirus (CMV), Epstein-Barr virus (EBV), coxsackie, rubella and varicella viruses) were negative. Chest x-ray and abdomen ultrasound examination were normal. Visual evoked potentials, brain auditory evoked potentials, as well as, computed tomography (CT) scan findings were normal. Video-electroencephalography did not reveal epileptic discharges. She was started on prednisolone 30 mg per day and urine infection was successfully treated with amoxicillin. Follow-up showed complete disappearance of the opsoclonus and myoclonus within 6 months but persistent ataxia. Prednisolone was reduced progressively to 10 mg daily during the first year and 5 mg daily during the following 2 years with progressive but very slow further improvement.

Patient 2. A Syrian 20-year-old male who has previously been healthy was admitted following a 7-day history of transient diplopia, recurrent vertigo and gait disturbance starting a few days after an upper respiratory tract infection. Examination showed rapid, multidirectional and irregular high amplitude eye movements (opsoclonus), ataxic gait, minor cerebellar dysarthria with scanning speech and dysmetria. Investigations revealed normal CBC, U&E, LFT and thyroid function tests. Erythrocyte sedimentation rate was 91mm/h. Analysis of CSF revealed 3 WBC/mm³, moderate elevation of proteins (0.7 g/l), normal glucose and negative gram stain and culture. There was no oligoclonal band detected. Serum antinuclear antibodies, rheumatoid factor, hepatitis B surface antigen (HBsAg) and anti human immunodeficiency virus antibodies were negative. Other neurotropic virus serologies were not carried out. Brain CT scan and magnetic resonance imaging (MRI) findings were normal. Visual evoked potentials and brain auditory evoked potentials did not reveal abnormalities but somatosensory evoked potentials showed normal responses for the upper limbs and absent cortical responses for the lower limbs. Chest X-ray and abdominal ultrasound examination findings were normal. Three days after admission, he developed jerky movements in all extremities with severe ataxia. There

was no objective improvement after high dose of steroid therapy (prednisolone 1g/day intravenous infusion for 5 days). Subsequent follow-up showed partial improvement of the abnormal ocular movements and of the myoclonus. However, 3 years later, severe ataxia still persisted.

Patient 3. A 38-year-old smoker presented with a 2-week history of upper respiratory tract infection and 7 day history of visual disorders with episodes of seeing flashes of light. Three days prior to his admission, he had episodes of vertigo, difficulty of fixation, dizziness and unsteadiness. He was diagnosed to have gastric ulceration one month before and was treated as such with ranitidine and antacids. Neurological examination showed abnormal multidirectional irregular eye movements of high amplitude (opsoclonus) and ataxic gait. Two to 3 days after admissions, he developed jerky movements of the extremities associated with mild dysmetria but no other abnormal signs. Psychological assessment revealed anxiety state that played initially a significant worsening factor. Investigations revealed normal CBC, ESR, and U&E. Liver function tests showed raised -glutamyl-transpeptidase of 93 U/l (normal = 11-50) and alanine aminotransferase of 64 u/l (normal = 13-40). Coagulation profile revealed prothrombin time of 43 (reference value 26-39 seconds) and international normalized ratio was one. Rheumatoid factor, antinuclear antibodies, anti DNA antibodies, HBsAg and anti hepatitis C virus were negative. Serologies for CMV, EBV, and coxsackie viruses were negative. Examination of CSF showed normal protein and glucose with no WBC. Culture of CSF was negative. Electroencephalography, visual, brain auditory and somatosensory evoked potentials revealed normal responses. Chest x-ray, electrocardiogram and brain CT scan and MRI findings were normal. He was given clonazepam 0.5 mg 3 times daily for 3 weeks and received the drug irregularly for the following 3 months. He showed slowly progressive improvement and had complete recovery within 6 months.

Discussion. Our cases represent the first reported series of opsoclonus myoclonus syndrome in KSA and included one child and 2 young adults. The opsoclonus appeared a few days after the onset of neurological symptoms in the second patient who initially had vertigo and ataxia; whereas it appeared earlier in the third. All patients had myoclonus. The clinical presentation and investigation results were consistent with non-paraneoplastic OMS. Malignancy, particularly neuroblastoma in the child, was excluded by proper investigations and follow-up for many years as well. Analysis of CSF showed normal results in patients one and 3, and revealed increased proteins in patient 2. Both situations, where the syndrome was associated with normal CSF or lymphocytic reaction, with moderate elevation of CSF proteins were reported.⁶ Viral cultures failed to show growth in our adult cases and revealed adenovirus in the stool culture of the child.

Autoimmune mechanism is generally accepted in the pathogenesis of this syndrome.⁶ In addition, the presence of increased number of reactive lymphocytes in the CSF of a patient with OMS complicating bacterial meningitis had suggested abnormal autoimmune response.⁷ The underlying mechanisms of the opsoclonus are not well known. Leigh and Zee¹³ suggested a dysfunction in one of 3 groups of neurons controlling the ocular motility in the reticular formation of the brain stem: normally, the pause cells are inhibiting the burst cells.¹³ An abnormal immunological response may be behind this disorder in the absence of toxic or metabolic causes since a flu-like illness usually precedes the onset. Such a mechanism was strongly supported by the discovery of antineuronal auto antibodies in the serum and CSF of patients with paraneoplastic OMS.¹⁴⁻¹⁷ Auto antibodies were also described in few cases of non-paraneoplastic OMS,^{15,18,19} however, they were not carried out in our patients. On the basis of the likely autoimmune mechanism in the etiology of OMS due to encephalitis or post-infectious sequelae, immunosuppressive treatment was successfully used including steroids.^{20,21} The first patient in our series had a long course of steroids with very good results. The second case did not respond at all to this treatment given in short and high dose course (pulsed therapy) as multiple sclerosis was initially suspected. The patient had significant neurological sequelae but no relapse 3 years after the onset. Spontaneous improvement has been reported by many authors.^{6,22,23} Accordingly; the third patient showed early signs of improvement without any specific treatment, particularly after prescribing clonazepam for anxiety and he improved completely without immunosuppressive treatment within 6 months. Recently, high dose intravenous immunoglobulin (IVIG) have been reported to be dramatically effective.^{24,25} None of our patients received that treatment since they were seen before the beneficial effect of IVIG was reported.

In conclusion, non-paraneoplastic opsoclonus myoclonus syndrome is distinct and, generally, a benign disorder, however important sequelae are possible. Immune suppressive drugs such as steroids or immune modulating therapy (IVIG) may be considered. Non-paraneoplastic opsoclonus myoclonus syndrome has a different prognosis from the paraneoplastic opsoclonus myoclonus syndrome although the underlying immunological mechanisms may be similar; and might warrant discussing them separately.

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