Opsoclonus myoclonus ataxia syndrome due to falciparum malaria in two Indian children

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Opsoclonus-myoclonus ataxia (OMA) syndrome is rare in children, mostly caused by neuroblastoma. Here, we present two very rare cases presenting with OMA due to falciparum malaria. Both of them responded to a high dose of falciparum malaria hormone and intravenous immunoglobulin without recurrence and complication.

Key words: Ataxia, child, malaria, myoclonus, opsonoclonus

Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder characterized by progressive opsoclonus (irregular, rapid, horizontal, and vertical eye movements), myoclonus, and cerebellar dysfunction. Evidence for an autoimmune mechanism includes the presence of serum autoantibodies to several neural antigens and improvement of symptoms with immunosuppressive therapy.[1] In English literature, no such pediatric case with opsoclonus-myoclonus ataxia (OMA) associated with malaria has been reported. One case has been reported in Spanish literature. We report the beneficial effects of high-dose adrenocorticotropic hormone (ACTH) and intravenous immunoglobulin (IVIG) in two children having falciparum malaria-induced OMA.
Case Report

Here, we are presenting two very rare cases we came across in a span of 1½ year. One of the patients was a 9-year-old boy born of nonconsanguineous marriage, presented with fever for 5 days along with the acute onset of dizziness followed by unsteady gait and jerkiness of both eyes and abnormal jerks of limbs. His past medical, immunization, family, and social history were unremarkable. On examination, he was conscious and alert. Cranial nerve examination was intact except for opsonoclus [Video 1]. The patient was irritable, but no cognitive or psychiatric abnormality was noted. Spontaneous myoclonus was noted throughout his body, exaggerated by active movement. His muscle power, tone, and reflexes were normal. He was unable to stand secondary to severe truncal ataxia. His sensory examination was intact. Blood examination revealed mild pallor with falciparum trophozoite; Plasmodium falciparum antigen (Plasmodium lactate dehydrogenase [pLDH]) was positive. Urinary catecholamine testing and cerebrospinal fluid (CSF) analysis including herpes simplex polymerase chain reaction and antibody for mycoplasma, antibody (IgM) viral capsid antigen of Epstein–Barr virus (EBV) were normal. Magnetic resonance imaging (MRI) of the brain with and without contrast was normal. Computed tomography (CT) scans of chest, pelvis, and abdomen (done immediately and 3 months later) did not reveal neuroblastoma. He was diagnosed as having OMA syndrome due to falciparum malaria. We started ACTH at a dose 75 IU/m²/day on the 4th day with continuation of artesunate, clindamycin, and other supportive measures. Fever subsided within 48 h. Neurologic symptom did not improve significantly over 2 weeks, so we doubled the dose.[8] The child responded within the next 10 days. To prevent relapse, monthly dose of 2 g/kg/day of IVIG was given. After 1 year, ACTH was stopped.

Another well-built boy of 6½ years presented with a similar history of fever which was diagnosed to have P. falciparum malaria (pLDH antigen positive) referred to us for ataxia. He was treated outside with artesunate and was afebrile. All general and neurological examination showed that eyes were normal except cerebellar signs—truncal ataxia, abnormal coordination tests, and mild hypotonia. MRI of the brain and CSF analysis were unremarkable. After 3 weeks, abnormal chaotic multidirectional rapid saccadic movement without intersaccadic interval suggesting opsonoclus developed. Ataxia became more severe and asymmetric myoclonus appeared. Higher mental function was normal except slight irritability. Repeat MRI of the brain, neuroblastoma screening with CT thorax and abdomen, and urine catecholamine analysis were unremarkable. We started high-dose ACTH (75 U/m²/dose twice daily) with our prior experience. He responded in 2 weeks. At present, he is also fine with a tapering dose of ACTH and a monthly dose of IVIG. Repeat neuroblastoma screen was normal.

Two children were followed up for 1½ year and 4 months, respectively. The first child is now without medication. During follow-up, no relapse occurred. Side effect was monitored closely for Cushingoid feature, hypertension, headache, obesity, and infection. No significant side effects were noted. They were supplemented with calcium and Vitamin D. Salt restriction was followed.

Discussion

Opsomyoclonus, myoclonic encephalopathy of Kinsbourne, or “dancing eyes-dancing feet” syndrome is a devastating and debilitating disease with an unfavorable outcome. The pathophysiology of OMA has been speculated to involve IgG and IgM autoantibodies directed against neural antigens in cerebellar Purkinje cells, cerebral cortical neurons, and axons. The autoantibodies in OMS are distinct and therefore suggest a causal relationship.[3] The immune mechanism may be a Type II or IV hypersensitivity. Up to 50% of children with OMA harbor neuroblastoma; rest are associated with flu vaccine, infection with Streptococcus EBV, Mycoplasma pneumoniae, St. Louis virus, varicella rarely malaria, hepatitis C, and human immunodeficiency virus.[5-7] Treatment for OMS from whatever the cause has not been uniformly successful. In children, this syndrome usually resolves with ACTH, or corticosteroid, but in most of the patients, symptoms recur after withdrawal. Most authors believe that in adults this syndrome needs no treatment as symptoms are self-limiting and resolve within 6–8 weeks.[9] There are other reports indicating that clonazepam, baclofen, valproate, and 5-hydroxytryptophan had provided much needed symptomatic relief to these patients. In children, as per the guideline of the National Organization for Rare Disorders, ACTH, IVIG, and rituximab are the best options.[9] Some authority shows beneficial effect of steroid in the form of pulse methyl prednisolone and oral prednisolone, but the National Organization for Rare Disorders did not demonstrate any benefit.[9] Gabapentin shows benefit in controlling eye movements in resistant opsonoclus.[10] In English literature, no such pediatric case with OMA associated with malaria has been reported. One case has been reported in Spanish literature. We have shown that high-dose ACTH and IVIG are safe and there was no relapse. Minimal side effects such as Cushingoid feature and systolic blood pressure just above 90th percentile were documented which responded to salt restriction and disappeared with stoppage of therapy in the first child.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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