East African Medical Journal Vol. 98 No. 8 August 2021
OPSOCLONUS MYOCLONUS SYNDROME IN A TWO-YEAR-OLD GIRL: A CASE REPORT
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OPSOCLONUS MYOCLONUS SYNDROME IN A TWO-YEAR-OLD GIRL: A CASE REPORT

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ABSTRACT

Opsoclonus Myoclonus Syndrome (OMS) is a rare disease that presents with disturbance in gait, muscle spasms, and irregular eye movements. and whose diagnosis and treatment can be challenging in a resource-constrained setting. This is a report of possibly the first documented childhood OMS in Kenya. The diagnosis is was challenging but successful treatment was achieved in a resource-constrained setting.

INTRODUCTION

Opsoclonus myoclonus syndrome, a rare nervous system disorder of uncertain aetiology and pathogenesis, has an estimated incidence rate of one in a million people per year. In children the peak age is 18 months with 50% of cases associated with neuroblastoma. The infectious or post-infectious cases have been associated with streptococcal infections, varicella, influenza, Epstein-Barr, hepatitis B, Human Immunodeficiency Virus, Coxsackie B among other infections. The diagnosis of OMS may be delayed or missed because of low index of suspicion or uncertainty in its clinical features. This paper presents one case identified in our hospital and possibly the first case to be described in Kenya.

THE CASE

A two-year-old female patient was brought to hospital with new onset unsteady gait that had developed over a period of two weeks. She was reported to be irritable and her sleep was characterized by short episodes interrupted by wakefulness and crying. Two days prior to presentation in hospital she had developed jerky movements of both upper and lower limbs, but they were not associated with loss of consciousness. A diagnosis of epilepsy was made in the out-patient clinic and the patient started on sodium valproate. She was reviewed after one month and noted to have deteriorated and could not stand, cried most of the time and her sleep episodes did not last more than half an hour. She was born in hospital and had no perinatal complications. Prior to the current illness, she had not had any

significant past medical illnesses and there was no family history of chronic illnesses.

On examination, her vital signs were normal. She was conscious but irritable and cried throughout the examination. She had myoclonic movements in both upper and lower limbs, and, had rapid vertical and horizontal nystagmus. The power in both upper and lower limbs was grade 3 and the deep tendon reflexes and tone were normal. A working diagnosis of opsoclonus myoclonus syndrome and differential diagnosis of acute cerebellar ataxia was made and she was admitted for investigations. The complete blood count and erythrocyte sedimentation rate were normal. Her renal function tests were normal. Brain and abdominal-thoracic MRI were normal. Cerebrospinal fluid had normal proteins and sugars and there was no micro-organism grown on culture. However, immunological studies for CSF antibodies were not done.

She was started on treatment for Opsoclonus Myoclonus Syndrome (OMS) with intravenous immunoglobulin at a dose of 2g/Kg total dose given in divided doses over five days and pulsed dexamethasone at 40mg/m^2/day for five days. After one week the irritability was less but she still had the opsoclonus and myoclonus. Rituximab at 200mg once a week for 4 weeks was added there was remarkable improvement. The irritability and opsoclonus resolved, she started talking, and walking with support. Given the incomplete resolution, a decision was made to give cyclophosphamidesix courses over a period of six weeks. Four months from the time of treatment initiation, both myoclonus and opsoclonus had resolved. The speech had improved to pre-treatment level and one year later there was no recurrence of symptoms.

DISCUSSION

The pathophysiology is thought to be autoimmune owing to the associated autoantibodies nervous system antigens and the good response to immunosuppressive therapy[1]. Central nervous system inflammation is supported by finding of increased B- lymphocytes in CSF and isolation of antibodies against intracellular and extracellular neuronal components of patients with OMS[2,3]. However, these markers are neither specific nor sensitive to be considered immunological bio-markers of OMS in children[3]. About 50% of the cases of OMS are paraneoplastic which in children is commonly associated with neuroblastoma. The remaining 50% of cases are idiopathic or may be associated toxic or metabolic brain disorders and infectious like Streptococcal infections, Mycoplasma pneumoniae infections, Varicella, Influenza, Epstein-Barr, hepatitis B, Human Immunodeficiency Virus, Coxsackie B viruses among other infections[4].

OMS occurs in children with a peak of 18 months and without gender predominance[5, 6]. It presents as an acute or sub-acute onset of behavioural changes including irritability and sleep disturbance[5,6]. Disturbance of gait presenting as clumsiness is often the first symptom to be noted[7]. Opsoclonus which is nystagmus in all planes and myoclonus presenting as jerky movements are key features that differentiates OMS from ataxia[6]. Language disturbance manifest as disturbance of expressive speech and may progress to mutism or aphasia[8]. This patient had a classic presentation however the diagnosis was delayed for four weeks consistent with experience of other centers and ascribed to rarity of the disorder and lack of specific diagnostic investigations [7].

Diagnosis is based on exclusion of other conditions that may present in a similar manner and by the response to treatment[4]. Lumbar puncture should be done to obtain CSF for analysis to exclude neurological infections and perform immunological assays. Urine collection for assay of HVA and VMA is recommended because of the association with neuroblastoma[9]. Radiological investigations are crucial for diagnosis of associated neuroblastoma, however normal imaging does not exclude presence of neuroblastoma. In the current case, although CSF studies were done, immunological investigations for neuro-inflammation were not done due to lack of facilities. Radiological investigations were done but no features of neuroblastoma were identified. Although neuroblastoma may be occult and difficult to identify even after all investigations[4.] The current patient has remained well two years after the diagnosis which supports a finding of no associated neuroblastoma.

The literature on treatment of OMS is scarce with largest recently published cross—sectional study based on a multi-center, multi-country registry recruiting 329 children[5] ascribed to the rarity of the disorder, which makes it impossible to do large scale clinical trials[9,10]. However, clinical features of both paraneoplastic and idiopathic OMS respond well to immunosuppressive therapy[5,9]. Neurological response to combined immunotherapy has been shown to be better and with less rates of relapse. Pranztelli and Elizabeth (2007) compared response to dexamethasone with or without intravenous immunoglobulin to dexamethasone, intravenous immunoglobulin rituximab combined immunotherapy (DEXIR-CI). Children on DEXIR-CI had better motor response as well as reduced neuro-inflammation[10]. The results were highly supportive of combined immunotherapy. Cyclophosphamide has also been used in both paraneoplastic and idiopathic cases of OMS, especially in the relapsing cases[5,10]. In one report it was shown that cyclophosphamide improved outcome in cases which had not responded to the initial immunosuppressive therapy. In the current case we used a regimen similar to DEXIR-CI but got partial response which progressed to complete response once we added cyclophosphamide.

There is no difference in outcome between OMS with or without associated neuroblastoma[10]. The disease may present with a monophasic phase where the patient heals with or without neurological sequalae[4]. Multiphasic disease presents with chronic/relapsing and has been reported to vary from 50 – 75% of cases[4]. Relapse is a challenge in treatment of multiphasic OMS because its timing is unpredictable[10]. Use of combined immunotherapy and diagnosis of idiopathic OMS has been associated with less rates of relapse[8]. A national registry of OMS is recommended to increase awareness, diagnosis and treatment.

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