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STEP-UP IMMUNOTHERAPY IN PEDIATRIC OPSOCLONUS–MYOCLONUS SYNDROME

Vasalli Sai Vinay*[1], S. K. Sharath Kumar[2], Nawaz Khan K. R.[3], Siddi Shoaib Akthar[4], Dr. Namratha Dumthi[5]

[1,2,3,4]Pharm D Intern, [5]Assistant Professor

[1,2,3,4,5]Department of Pharmacy Practice, TVM College of Pharmacy, BMCRC Ballari-583104 Karnataka, India.

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***Corresponding Author**

Vasalli Sai Vinay

Pharm D Intern Department of Pharmacy Practice, TVM College of Pharmacy, BMCRC Ballari-583104 Karnataka, India.

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ABSTRACT

Opsoclonus–myoclonus syndrome (OMS) is a rare, immune-mediated pediatric neurological disorder characterised by chaotic multidirectional eye movements, myoclonic jerks, ataxia, and behavioural disturbances. It is frequently associated with neuroblastoma and may lead to long-term neurodevelopmental complications if not diagnosed and treated promptly. We report the case of a 3-year-1-month-old male child diagnosed with OMS who presented for routine follow-up and ongoing immunomodulatory therapy. The patient initially exhibited classical neurological features, with normal neuroimaging and negative neuroblastoma screening, supporting an autoimmune aetiology. Management included high-dose intravenous methylprednisolone and rituximab, along with supportive nutritional therapy and close monitoring for adverse drug reactions. The treatment was well tolerated, and the child remained clinically stable without infusion-related complications. Laboratory investigations revealed microcytic anaemia, managed with iron supplementation. OMS requires early recognition, comprehensive evaluation for underlying malignancy, and aggressive immunotherapy to reduce relapse risk and improve neurological outcomes. Long-term multidisciplinary follow-up and caregiver education are essential due to the chronic and relapsing nature of the disorder and its potential impact on cognitive and motor development.

KEYWORDS: Opsoclonus–myoclonus syndrome, paediatric neurology, neuroblastoma, autoimmune encephalopathy, immunotherapy, developmental regression.

NTRODUCTION

Opsoclonus–myoclonus syndrome (OMS), also known as dancing eye syndrome, is a rare but severe paediatric neurological disorder. It predominantly affects infants and young children, most commonly presenting between 6 months and 3 years of age.[2] The estimated incidence is approximately 1 in 5 million children annually.[1] OMS is classically defined by a triad of opsoclonus, myoclonus, and ataxia, often accompanied by behavioural changes, sleep disturbances, irritability, and developmental regression.[2,3] These eye movements also persist during sleep. Myoclonus is the irregular and multifocal muscular jerks predominantly seen in trunk muscles, Where as the Ataxia is seen both in the trunk and as well as limbs, which presents as an inability to walk in an acute stage. In nearly 40–60% of paediatric cases, OMS is associated with an underlying neuroblastoma, highlighting its importance as a paraneoplastic neurological syndrome.[3,6] In the remaining cases, OMS may be post-infectious or idiopathic, with immune-mediated mechanisms playing a central role.[4] The rare presentation of OMS in a patient with severe acute malnutrition will throw light upon its multi-factorial causes, and the need for a multidisciplinary approach, both in terms of its investigations and management, is necessary.

ETIOPATHOGENESIS

Opsoclonus–myoclonus syndrome is widely regarded as an autoimmune disorder affecting the central nervous system. The pathogenesis involves an aberrant immune response directed against neuronal antigens, particularly cerebellar Purkinje cells and brainstem neurons.[1,4] In paraneoplastic OMS, tumour antigens expressed by neuroblastoma cells trigger immune responses that cross-react with neural tissue, resulting in neurological dysfunction.[4] Post-infectious OMS may follow viral or bacterial infections, suggesting immune activation secondary to infection.[3] Persistent immune activation can persist even after tumour removal, explaining the disorder's chronic and relapsing nature.[1]

PATHOGENESIS OF OPSOCLONUS–MYOCLONUS SYNDROME (OMS)

❖ TRIGGERING EVENTS

• Paraneoplastic: Neuroblastoma (children), small-cell lung/breast/ovarian tumours (adults)

• Post-infectious: Viral (EBV, Coxsackie, Influenza, HIV, etc.)

• Idiopathic immune dysregulation.

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❖ ABNORMAL IMMUNE ACTIVATION

• Activation of B lymphocytes → production of autoantibodies

• Activation of CD4+ and CD8+ T cells

• Cytokine release (IL-6, TNF-α, IFN-γ) causing neuroinflammation.

⬇

❖ AUTOIMMUNE TARGETING OF CNS NEURONS

• Antibodies against neuronal surface and intracellular antigens (Hu, Ri, Yo, neurofilament, cerebellar antigens)

• Molecular mimicry between tumour/infectious antigens and neuronal proteins

• Immune complexes cross the blood–brain barrier.

⬇

❖ **CEREBELLAR INVOLVEMENT**

• Purkinje cell dysfunction and loss

• Reduced GABAergic inhibitory output from cerebellar cortex

• Disinhibition of deep cerebellar nuclei (especially the fastigial nucleus).

⬇

❖ **BRAINSTEM & OCULAR MOTOR NETWORK DYSFUNCTION**

• Dysfunction of omnipause neurons in the pontine raphe nucleus

• Loss of inhibition of saccadic burst neurons

• Continuous, chaotic saccadic eye movements → Opsoclonus.

⬇

❖ **SPINAL AND CORTICAL MOTOR PATHWAY INVOLVEMENT**

• Disrupted cerebellar modulation of motor cortex

• Hyperexcitability of motor neurons

• Sudden involuntary muscle jerks → Myoclonus.

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❖ **NEUROBEHAVIORAL EFFECTS**

• Cerebellar–limbic pathway dysfunction

• Sleep disturbance, irritability, cognitive regression (children)

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❖ **CLINICAL SYNDROME (OMS)**

• Opsoclonus (rapid multidirectional eye movements)

• Myoclonus (brief shock-like jerks)

• Ataxia (gait and coordination impairment)
• Behavioural and sleep abnormalities.

CLINICAL FEATURES

The clinical presentation of OMS is distinctive but may evolve. Opsoclonus consists of rapid, involuntary, conjugate eye movements in multiple directions without intersaccadic pauses.[2] Myoclonus presents as sudden, brief muscle jerks involving the trunk, limbs, neck, or facial muscles.[3]

The diagnosis of opsoclonus–myoclonus syndrome is primarily clinical, supported by laboratory and imaging investigations. Magnetic resonance imaging (MRI) of the brain is usually normal, although mild cerebellar atrophy or nonspecific signal changes may be observed in chronic or untreated cases.

Comprehensive tumour screening is mandatory in all paediatric patients diagnosed with OMS. This includes imaging studies such as ultrasound, computed tomography (CT), or MRI of the chest, abdomen, and pelvis, as well as metaiodobenzylguanidine (MIBG) scintigraphy to detect neuroblastoma. Cerebrospinal fluid (CSF) analysis may reveal mild lymphocytic pleocytosis, elevated protein levels, or oligoclonal bands, supporting an inflammatory or autoimmune aetiology. Additional investigations may include autoimmune antibody panels and infectious screening to exclude alternative diagnoses.

Ataxia leads to gait instability, impaired coordination, and difficulty in sitting or standing in younger children.[2] Behavioural disturbances such as irritability, sleep disorders, emotional lability, and attention deficits are common.[5] Developmental regression, especially loss of previously acquired motor and speech milestones, is frequently observed.[5]

DIAGNOSTIC EVALUATION

The diagnosis of OMS is primarily clinical and supported by imaging and laboratory investigations. Magnetic resonance imaging (MRI) of the brain is usually normal, although mild cerebellar atrophy may be observed in chronic cases.[3]

Comprehensive tumour screening is mandatory and includes ultrasonography, CT or MRI of the chest, abdomen, and pelvis, along with metaiodobenzylguanidine (MIBG) scintigraphy to detect neuroblastoma.[6] Cerebrospinal fluid analysis may reveal mild lymphocytic pleocytosis or oligoclonal bands, supporting an autoimmune aetiology.[4]

STANDARD TREATMENT PROTOCOL FOR MANAGEMENT OF OPSOCLONUS–MYOCLONUS SYNDROME (OMS) IN PAEDIATRIC PATIENTS

Table No. 1: Stepwise Management of Opsoclonus–Myoclonus Syndrome in Children.

Step	Clinical Stage	Management Strategy
Step 1	Clinical suspicion of OMS	Detailed neurological examination; assessment of opsoclonus, myoclonus, ataxia, and behavioural changes
Step 2	Diagnostic evaluation	MRI brain (to rule out structural pathology); CSF analysis if indicated
Step 3	Malignancy screening	Mandatory evaluation for neuroblastoma using USG/CT/MRI abdomen and chest; MIBG scan.
Step 4	First-line immunotherapy	High-dose IV corticosteroids (methylprednisolone) ± ACTH ± IVIG
Step 5	Assessment of response	Clinical monitoring for reduction in opsoclonus, myoclonus, and ataxia
Step 6	Inadequate response/relapse	Second-line immunotherapy (rituximab, cyclophosphamide, or mycophenolate mofetil)
Step 7	Supportive management	Physiotherapy, speech therapy, behavioural therapy, and nutritional supplementation
Step 8	Long-term follow-up	Monitoring for relapse, neurodevelopmental outcome, and adverse drug reactions

MANAGEMENT STRATEGIES

There is no universally standardised treatment protocol for OMS; however, early aggressive immunotherapy remains the cornerstone of management.[1] First-line therapies include high-dose corticosteroids, adrenocorticotropic hormone (ACTH), and intravenous immunoglobulin (IVIG).[7]

Opsoclonus–myoclonus syndrome is an immune-mediated neurological disorder that requires early and aggressive immunotherapy to prevent long-term neurological sequelae. Once OMS is clinically suspected, prompt neurological evaluation and neuroimaging are recommended to exclude alternative diagnoses. Although MRI brain findings are often normal, imaging is essential as part of the diagnostic workup.

A crucial component of OMS management is mandatory screening for underlying neuroblastoma, as OMS is a well-recognised paraneoplastic neurological syndrome in paediatric patients. Even in the absence of malignancy, immunotherapy should not be delayed. First-line treatment includes high-dose intravenous corticosteroids such as methylprednisolone, ACTH, and intravenous immunoglobulin. These agents suppress immune-mediated inflammation and often result in clinical improvement. However, a significant proportion of patients experience partial response or relapse.

In refractory or relapsing cases, escalation to second-line immunotherapy is recommended. Rituximab, a monoclonal antibody against CD20-positive B lymphocytes, has shown efficacy in reducing relapse rates and steroid dependence. Other agents such as cyclophosphamide and mycophenolate mofetil may be used in selected cases.

Supportive therapy, including physiotherapy, speech therapy, and behavioural interventions, plays a vital role in improving functional and neurodevelopmental outcomes. Due to the chronic and relapsing nature of OMS, long-term follow-up is essential to monitor disease activity, developmental progress, and adverse effects related to prolonged immunosuppressive therapy.

In refractory or relapsing cases, second-line immunosuppressive agents such as rituximab, cyclophosphamide, or mycophenolate mofetil may be used.[7] Surgical removal of an underlying neuroblastoma is essential but does not eliminate the need for immunotherapy.[6] Long-term rehabilitation therapies are vital for functional recovery.

Management of OMS requires

- Monitoring for corticosteroid-related adverse effects (hypertension, hyperglycemia, infections)
- Observation for infusion-related reactions with rituximab
- Dose adjustment and tapering strategies
- Documentation and reporting of adverse drug reactions (pharmacovigilance)

PROGNOSIS AND FOLLOW-UP

Although mortality is low, long-term neurological morbidity is common in children with OMS. Persistent motor deficits, cognitive impairment, speech delay, and behavioural abnormalities are frequently reported.[5,8] Relapses may occur during infections or periods of immune stress.[8]

Early diagnosis and prompt immunotherapy significantly improve outcomes.[1] Long-term multidisciplinary follow-up is essential to monitor neurodevelopmental progress and disease recurrence.[8]

CASE REPORT

Patient Information

A 3-year 1 month-old male child, a known case of opsoclonus–myoclonus syndrome, presented to the paediatric department for routine follow-up. The patient was diagnosed with OMS at the age of 2years 11 months and has been on regular treatment since diagnosis. Past Medical History The child had been previously diagnosed with opsoclonus–myoclonus syndrome at the age of 2 years 11-months following complaints of abnormal eye movements, myoclonic jerks, and gait instability. Whereas MRI of the brain was normal, and neuroblastoma screening was negative. The patient was treated with IVIG and corticosteroids, following which partial clinical improvement was observed based on clinical features and neurological evaluation. The patient has been on regular follow-up and immunomodulatory treatment as per standard management protocol.

Presenting Complaints (Follow-Up Visit)

The child presented for planned methylprednisolone infusion as part of ongoing treatment. There were no new complaints, such as fever, seizures, worsening abnormal movements, or developmental regression, reported by the parents.

Clinical Examination on Follow-Up

On examination, the child was conscious, alert, and cooperative for age. Vital signs were stable at presentation. Systemic examination, including cardiovascular, respiratory, abdominal, and neurological systems, was within normal limits. No acute distress or focal neurological deficits were observed.

INVESTIGATIONS

COMPLETE BLOOD COUNT	RESULT	REFERENCE RANGE
Haemoglobin	9.6	13-14 gm%
Total WBC count	11200	4000-11000 cells/cumm
Neutrophils	55	40-70%
Lymphocytes	40	20-40%
Eosinophils	02	3-6%
Monocytes	03	2-10%
Basophils	0	0-1
RBC count	5.06	5.5-6.5 millon/cumm
Platelet count	2.90	1.5-4.5 lakh/cumm
MPV	8.4	7-11Fl
PCV	33.0	45-55%
MCV	62.4	80-100Fl
MCH	18.9	27-34pg

MCHC	29.0	31-36%
RDW-CV	16.0	11.5-14.5%
PDW-CV	15.5	10-18%
Serum Electrolytes		
Sodium	141	136-145 mEq/L
Potassium	4.3	3.4-5.0 mEq/L
Chloride	101	96-106 mEq/L
Renal profile		
Blood urea	20	15-45 mg/dl
Serum creatinine	0.7	0.2-1.0mg/dl

Treatment and Management

Treatment, Monitoring, and Adverse Drug Reaction Assessment

The child was managed with intravenous immunomodulatory therapy as part of the ongoing treatment protocol for opsoclonus–myoclonus syndrome. Inj. Methylprednisolone 300 mg IV once daily was administered for a duration of 6 days. In addition, inj. Rituximab 250 mg IV, diluted in 250 ml of normal saline, was administered as a slow intravenous infusion over several hours under strict medical supervision.

During the administration of rituximab, the child was placed under continuous monitoring. Vital parameters, including blood pressure, heart rate, respiratory rate, and oxygen saturation, were monitored at regular intervals before, during, and after the infusion. Blood pressure monitoring was given particular importance due to the potential risk of infusion-related hypotension associated with rituximab therapy.

The patient was closely observed for infusion-related reactions and adverse drug reactions, such as hypersensitivity reactions, fever, chills, rash, respiratory distress, hypotension, and gastrointestinal disturbances. No infusion-related reactions or hemodynamic instability were observed during the treatment period.

Supportive therapy included syrup multivitamin 5 ml orally twice daily for 7 days and syrup calcium 5 ml orally once daily for 7 days to support nutritional status and minimise corticosteroid-related adverse effects. Throughout the treatment course, the child remained clinically stable and hemodynamically normal.

The pharmacotherapy was well tolerated, with no evidence of corticosteroid-related adverse effects such as hypertension, hyperglycemia, or infections, and no rituximab-related adverse drug reactions noted. Adverse drug reaction monitoring was performed as part of routine

pharmacovigilance. Following completion of therapy, the child was planned for discharge with advice for regular follow-up.

Discharge medication

SL.NO.	NAME OF MEDICATION	DOSE AND ROUTE	FREQUENCY
1.	Syp. mutivitamin	5ml -PO	1-0-1
2.	Syp. iron	5ml-PO	1-0-0
3.	Syp.calcium	5ml-PO	1-0-1

The child was discharged in a clinically stable and hemodynamically normal condition after completion of the planned immunomodulatory therapy. The discharge medications were prescribed as supportive therapy to aid nutritional supplementation and to prevent potential deficiencies associated with prolonged illness and corticosteroid use.

Syrup multivitamin was prescribed to support overall nutritional status and immune function. Syrup iron was advised to prevent iron deficiency and support haematological health, while syrup calcium was included to maintain bone health and minimise corticosteroid-associated bone loss.

Parents were counselled regarding proper dosage, administration, and adherence to the prescribed medications. They were also educated about possible minor adverse effects and advised to report immediately if any unusual symptoms such as vomiting, rash, reduced appetite, or behavioural changes occur.

The child was advised to have regular follow-up in the paediatric and neurology outpatient department to monitor neurological status, treatment response, and developmental progress. Caregivers were instructed to seek immediate medical attention if the child develops fever, seizures, worsening abnormal eye movements, increased myoclonic jerks, or any signs suggestive of relapse.

Long-term follow-up was emphasised due to the relapsing nature of opsoclonus–myoclonus syndrome and the need for ongoing monitoring of therapeutic efficacy and adverse drug reactions.

FOLLOW-UP PLAN

The child was advised to undergo regular follow-up to monitor neurological status, treatment response, and early detection of relapse.

- First follow-up: After 7 days in the paediatric outpatient department
- Subsequent follow-up: After 1 month in paediatric neurology OPD
- Long-term follow-up: Every 3 months or earlier if symptoms recur

During follow-up visits, the child will be assessed for

- Recurrence or worsening of opsoclonus or myoclonus
- Developmental milestones and behavioural changes
- Need for continuation or modification of immunotherapy
- Monitoring for delayed adverse drug reactions.

CAREGIVER COUNSELING AT DISCHARGE

Caregivers were counselled regarding

- Strict adherence to prescribed discharge medications
- Importance of scheduled follow-up visits
- Early recognition of warning signs such as abnormal eye movements, increased jerky movements, seizures, fever, or behavioural regression
- Immediate hospital visit in case of any acute deterioration

DISCUSSION

Opsoclonus–myoclonus syndrome (OMS) is an uncommon pediatric neuroimmunological disorder that typically manifests in early childhood and is characterised by chaotic eye movements, myoclonic jerks, ataxia, and varying degrees of behavioural and developmental impairment. The condition is widely considered immune-mediated and may occur as a paraneoplastic phenomenon, post-infectious sequela, or idiopathic autoimmune disorder. Due to its relapsing nature and potential for long-term neurodevelopmental complications, early recognition and sustained immunotherapy are essential for optimal outcomes.

In the present case, a 3-year-1-month-old male child with a previously established diagnosis of OMS was evaluated during a scheduled follow-up visit. The child initially presented at 2 years 11 months of age with classical neurological features suggestive of OMS. Diagnostic evaluation at the time of diagnosis revealed normal brain imaging and a negative neuroblastoma workup. This observation is consistent with existing literature, which indicates that neuroimaging findings may be normal in OMS and that a substantial proportion of cases occur without an identifiable underlying malignancy, supporting an autoimmune aetiology. The child had earlier received first-line immunotherapy in the form of intravenous immunoglobulin and corticosteroids, resulting in partial clinical improvement. However,

incomplete response and the risk of relapse are well recognised in OMS, often necessitating prolonged treatment or escalation to additional immunosuppressive agents. During the current follow-up, the child was clinically stable, with no evidence of symptom exacerbation or developmental regression, and was admitted for planned immunomodulatory therapy. High-dose intravenous methylprednisolone was administered to suppress ongoing immune-mediated neuronal inflammation. Corticosteroid pulse therapy remains a key component in the management of OMS due to its rapid anti-inflammatory and immunosuppressive effects. In addition, rituximab was introduced as part of the treatment strategy. Rituximab, a monoclonal antibody targeting CD20-positive B cells, has shown increasing utility in pediatric OMS, particularly in cases with suboptimal response to conventional therapy or those requiring long-term disease control. Its use in this child reflects a proactive approach aimed at reducing relapse frequency and improving neurological prognosis.

Laboratory investigations revealed anemia characterized by reduced haemoglobin levels, low mean corpuscular volume, and elevated red cell distribution width, suggestive of microcytic hypochromic anaemia, likely secondary to iron deficiency. A mild elevation in total leukocyte count was noted, which may be attributable to corticosteroid therapy or physiological stress. Renal function tests and serum electrolytes were within normal limits, indicating preserved organ function during immunotherapy. These findings emphasise the importance of routine haematological and biochemical monitoring in children receiving long-term immunosuppressive treatment.

The immunotherapy regimen was well tolerated, and no infusion-related or drug-related adverse effects were observed. Continuous monitoring during rituximab infusion, particularly of hemodynamic parameters, was crucial in preventing and promptly identifying potential complications. The absence of adverse reactions in this case highlights the safety of rituximab when administered with appropriate precautions and monitoring protocols. Supportive treatment at discharge included multivitamins, iron, and calcium supplementation. Iron therapy was indicated to correct the identified anaemia, while calcium supplementation was prescribed to counteract potential corticosteroid-induced effects on bone health. Such supportive measures play a vital role in maintaining nutritional status and minimising treatment-related complications in pediatric patients with chronic neurological conditions. Given the chronic and relapsing course of OMS, long-term follow-up remains a critical aspect of management. Regular clinical assessments focusing on neurological status,

developmental milestones, and behavioural changes are essential for early identification of relapse and timely adjustment of therapy. Caregiver education regarding warning signs and adherence to follow-up schedules further contributes to improved disease monitoring and overall outcomes.

CONCLUSION

Opsoclonus–myoclonus syndrome is a rare, immune-mediated pediatric neurological disorder requiring early diagnosis and sustained immunomodulatory therapy. In this case, the child showed good clinical stability and tolerance to high-dose methylprednisolone and rituximab, with no observed adverse drug reactions. Timely escalation of immunotherapy, along with appropriate supportive care and close long-term follow-up, is essential to reduce relapse risk and improve neurological and developmental outcomes in children with OMS.

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