

Opsoclonus-myoclonus Syndrome with Neuroblastoma in Children and their Anaesthetic Management

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ABSTRACT

Opsoclonus-myoclonus syndrome (OMS) or the dancing eye syndrome, is a rare inflammatory neurological disorder often with paraneoplastic aetiology. It has an incidence of 1 in 1000,000 population worldwide. Opsoclonus-myoclonus syndrome is associated with 2-3% of patients having neuroblastoma. The authors present 5 cases of OMS in children who had neuroblastoma and underwent surgical resection. The median age was 26 (14-36) months. Male: female ratio was 1:1.5. All the patients had moderate to severe symptoms. Duration of symptoms at presentation varied from 3 days to one and half years. The possibility of OMS should be considered in all children presenting with probable neurological symptoms. Pharmacological therapy combined with surgery results in a good outcome. Balanced anaesthesia with the most commonly used drugs can be safely administered in the patients with opsoclonus-myoclonus syndrome.

Key Words: *Opsoclonus, Myoclonus, Neuroblastoma, Child, Anaesthesia.*

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Opsoclonus-myoclonus syndrome (OMS), also known as dancing eye syndrome, opsoclonus-myoclonus-ataxia syndrome, and Kinsbourne syndrome, is a rare inflammatory neurological disorder often with paraneoplastic aetiology and an incidence of 1 in 1000,000 population worldwide.¹ The authors present an experience of anaesthetic management of tumour excision under general anaesthesia (GA) for five children who had OMS associated with neuroblastic tumours over seven years. To the best of authors' knowledge, this is the first case series discussing anaesthetic management in patients with OMS. For anaesthesia, surgery, and data publication, written informed parental consent was sought.

Case-1 was an 18-month-old 11-Kg girl child who presented with an inability to walk and involuntary movements for the last seven days. There was a history of (h/o) immunisation two days before the onset of symptoms. Opsoclonus, slurring of speech, and irritability were also associated. She was diagnosed with a case of OMS. Her routine investigations, CECT (contrast-enhanced computed tomography) chest/abdomen, MRI (Magnetic resonance imaging) brain and EEG (Electroencephalography), and 24-hour VMA (Vanillyl mandelic acid) were normal.

The child was treated with ACTH (Adrenocorticotrophic hormone) and IVIG (Intravenous immunoglobins). Six months later, she had a relapse co-relating with the tapering of ACTH. At this point, the USG (ultrasonography) and CECT abdomen revealed a retroperitoneal mass. Exploratory laparotomy was done under General Anaesthesia (GA) with endotracheal intubation. The patient was premedicated with oral midazolam 0.5 mg/Kg and induced with IV fentanyl 1.5 mcg/Kg, IV thiopentone 5 mg/Kg, O₂, N₂O, sevoflurane, and rocuronium. Caudal block with 0.25% bupivacaine with 1 mcg/Kg fentanyl was given. Oxygen, N₂O, sevoflurane, and rocuronium were used for maintenance.

Case-2 was a 14-month, 9 Kg boy who presented with fever and loose stools for three days. Symptoms included tremors and abnormal movements of limbs and regression of milestones for one month. Opsoclonus was minimal and intermittent. There was a history of rashes two months back. The initial diagnosis was diarrhoea with infantile seizures and a diagnosis of OMS was made later by a paediatric neurologist. The tumour was detected on MIBG (Meta-iodobenzylguanidine) scintigraphy scan and the CECT abdomen, whereas USG was normal. Exploratory laparotomy was done under GA with endotracheal intubation. The child was premedicated with an oral midazolam 0.5 mg/Kg and induced with IV fentanyl 2 mcg/Kg, IV propofol 2 mg/Kg, O₂, air, sevoflurane, and rocuronium. The caudal catheter was placed and analgesia was maintained with 0.2% ropivacaine and fentanyl. Oxygen, N₂O, sevoflurane, and rocuronium were used for maintenance.

Case-3 was a 3-year 10 Kg girl. She presented with a three days history of inability to stand and bear weight, inability to sit

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without support, weakness in the upper limb, and jerky movements of the head. Intermittent opsoclonus, irritability, and excessive crying were present. There was a history of fall from bed 15 days back. She also had a few episodes of vomiting. The initial diagnosis was cerebellar ataxia which was later changed to OMS. Ultrasound-guided FNAC and CECT abdomen revealed tumour suggestive of neuroblastoma. Exploratory laparotomy was done under GA with endotracheal intubation. The child was premedicated with an oral midazolam 0.5 mg/Kg and induced with IV fentanyl 2 mcg/Kg, IV propofol 2 mg/Kg, O₂, air, sevoflurane, and rocuronium. Oxygen, N₂O, sevoflurane, and rocuronium were used for maintenance.

Case 4 was a 3-year 13-Kg boy who presented with a one-and-half-year history of frequent falls while walking and jerky movements of the whole body. The child's condition gradually worsened and he could not walk without support. Abnormal eye movements, irritability, and seizures were present. Seizures were controlled on syrup levetiracetam and valproate. Left adrenal mass was detected in the MRI abdomen while the MRI brain was normal. Exploratory laparotomy was done under GA with endotracheal intubation. The child was premedicated with oral midazolam 0.5 mg/Kg and induced with IV fentanyl 2 mcg/Kg, IV propofol 2 mg/Kg, O₂, air, sevoflurane, and cisatracurium. The epidural catheter was placed and analgesia was maintained with 0.125% bupivacaine and fentanyl. Oxygen, N₂O, sevoflurane, and cisatracurium were used for maintenance.

Case-5 was a 27-month-old 12-Kg girl. She presented with a difficulty in walking, on and off slurring of speech, tremors, and abnormal eye movements from the past year. Right paravertebral lesion at the D3-4 level was detected in MIBG, while in chest X-ray and CECT chest and abdomen could not detect the tumour. Thoracotomy was done under GA with endotracheal intubation. The child was premedicated with an oral midazolam 0.5 mg/Kg and induced with IV fentanyl 2 mcg/Kg, IV propofol 2 mg/Kg, O₂, air, sevoflurane, and rocuronium. Analgesia was supplemented with 0.25% bupivacaine and morphine via the epidural catheter. Oxygen, N₂O, sevoflurane, and rocuronium were used for maintenance.

After surgery, neuromuscular block was reversed with IV neostigmine and IV glycopyrrolate. The trachea was extubated and the children were shifted to the post-anaesthesia care unit. All drugs administered in epidural space were preservative-free. No regional block was given in case 3; case-1 received a single-shot caudal block and epidural analgesia was continued until 48 hours postoperatively in the rest of the cases. Nonsteroidal drug (NSAID) used for postoperative analgesia was diclofenac sodium in cases 1 and 4 and IV paracetamol in remaining three cases. Anaesthesia as well as analgesia were chosen as per the discretion of the concerned anaesthesiologist. Antiepileptics and other drugs were continued in the perioperative period.

All the patients were started on ACTH and IVIG after being diag-

nosed with OMS. The perioperative period was uneventful with minimal opsoclonus or myoclonic jerk. On histopathological examination, all the tumours were neuroblastic (neuroblastoma, ganglioneuroblastoma, or ganglioneuroma). The locations of tumour was retroperitoneal in case-1, abdominal paravertebral in case-2, abdominal extra-adrenal in case-3, adrenal in case-4, and thoracic paravertebral in case-5, respectively.

Children were followed up with a pediatric neurologist, and ACTH, IVIG, and antiepileptic drugs were continued after surgery. Two children had relapsed after surgery. Within a year, case 2 had a relapse and was managed with pulse cyclophosphamide and rituximab. After six months of continued treatment, the fourth child also had a relapse and was given rituximab. All the children showed improvement in neurological symptoms and are managing well.

The diagnosis of OMS is clinical. It is characterised by associated ocular, motor, sleep, behavioural and language disturbances, often with marked irritability. The usual age of onset is 1-6 years.¹

The median age of patients was 26 months (14-36 months), male: female ratio (1:1.5), locations, and neuroblastic character of the tumour are similar to other studies.² Patients had moderate to severe symptoms varying from 3 days to one and half years at presentation as reported earlier.² As found in case 4, seizures have not been reported earlier except in one adult patient but that was a case of co-existing cerebral malaria.

Long undiagnosed peripheral course, antecedent immunisation, rashes, and other atypical presenting symptoms have also been reported earlier.² The condition is often misdiagnosed due to several factors, including the disease's rarity, atypical presentation, the appearance of ataxia before other symptoms, and intermittent and fleeting opsoclonus. Early diagnosis of OMS is essential for specific treatment and intensive tumour search to improve the neurological outcome. Awareness of entity and meticulous history-taking is the most critical tool for diagnosis.

Anaesthetic problems include major surgery, paediatric age group, and associated drug therapies (corticosteroids, ACTH, IVIG, and chemotherapy). None of the studied patients had issues like increase in weight, blood pressure or sugar, electrolyte disturbance, or renal dysfunction despite being on ACTH and IVIG therapy. The location and nature of neuroblastoma are paramount.

General anaesthesia with propofol, O₂, N₂O, Sevoflurane, fentanyl, remifentanyl, morphine rocuronium, pancuronium, atracurium, neostigmine, glycopyrrolate diclofenac, paracetamol, ketoprofen, dipyron, and ketorolac in these patients have been used safely in children with OMS.³⁻⁶ Cisatracurium thiopentone and propofol were used in these cases; thiopentone may be preferred as it suppresses myoclonus. Thiopentone abolished the worsening of opsoclonus and myoclonus

following I/M ketamine in an infant with OMS.⁵ Atropine has been used for the reversal of neuromuscular block however, the use of atropine in diagnostic radiology was associated with transient worsening of symptoms. In the present series, caudal block, caudal catheter, and the lumbar epidural were used with no apparent adverse effects. Among regional analgesia literature reports only one case in which caudal block was used.⁶ Multimodal analgesia is advised for better pain management and managing irritability found in these children. Regional anaesthesia should be planned only after assessing the tumour's location and ruling out any invasion of the neuraxial plane.

Studies have reported poor outcomes with partial response, post-surgical complications, high relapse rate, and even worsening symptoms in OMS associated with neuroblastoma.² Here two children (cases 2 and 4) had relapsed after surgery, both presented late and required more aggressive pharmacological treatment. Case 1 and 3 presented early and did not have a relapse after tumour resection along with medical management.

All the patients had overall good outcomes with combined surgery and pharmacotherapy. Relapses could be managed with pharmacotherapy.

The possibility of OMS should be considered in all children presenting with probable neurological symptoms. Pharmacological therapy combined with surgery results in a good outcome. Balanced anaesthesia with the most commonly used drugs can be safely administered in the patients with opsoclonus-myoclonus syndrome.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS' CONTRIBUTION:

AG: Conception of the work and drafting.

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MP: Drafting and editing.

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