International Journal of Medical Anesthesiology

E-ISSN: 2664-3774
P-ISSN: 2664-3766
www.anesthesiologypaper.com
IJMA 2023; 6(2): 09-13
Received: 15-02-2022
Accepted: 22-03-2022

Dr. Mustafa Mohammed Salih
Department of Pediatric Anaesthesia, Children Welfare Teaching Hospital, Medical City, Baghdad, Iraq

Corresponding Author:
Dr.Mustafa Mohammed Salih
Department of Paediatric Anaesthesia, Children Welfare Teaching Hospital, Medical City, Baghdad, Iraq

General Anaesthesia for a baby with Metachromatic Leukodystrophy

Dr. Mustafa Mohammed Salih

DOI: https://doi.org/10.33545/26643766.2023.v6.i2a.388

Abstract
Mitochromatic Leukodystrophy is a progressive degenerative disorder of white matter. Patients with this disease frequently require anaesthesia for various diagnostic and surgical procedures. These patients pose a lot of anaesthetic problems like seizures, spasticity, risk of aspiration, and copious secretions, in addition to other organs dysfunctions. Our case report is about provision of general anaethesia for a female child for laparoscopic cholecystectomy and gastrostomy tube placement.

Keywords: Metachromatic Leukodystrophy (MLD), gallbladder, neurodegenrative disease

Introduction
Metachromatic Leukodystrophy (MLD) is a genetic disorder that affects nerves, muscles, other organs, and behavior. It belongs to lysosomal shingolipid storage group, and listed in the family of leukodystrophies [1]. It is progressive and neurodegenrative disease mainly affecting central nervous system's and peripheral nervous system's myelin sheath [2].
MLD is caused by deficiency of the enzyme arylsulfatase A or saposin B. [3] This deficiency leads to accumulation of sulfatide which damage myelin in the central and peripheral nervous systems leading to loss of motor and cognitive skills [4]. So it is typical white matter disease. White matter damage causes progressive deterioration of motor skills. Sulfatide accumulates in other organs like kidnies and gallbladder.

Various types of MLD according to age are classified as

1) **Late Infantile MLD:** (50-60%) most common form. Is seen around 2 years of age. Gradual loss of speech and walking (gait disturbance), muscle tone first decrease then increase to point of rigidity. Patient usually not survives beyond 5 years.
2) **Juvenile MLD:** (20-30%) seen in age between 3 and 16 years. Frequent falls, convulsions, loss of muscle control, difficulties in speaking and swallowing, later ends in decerebrate posture, behavioral problems and mental deterioration, poor school performance, and dementia. Patient dies 10-20 years of onset of the disease.
3) **Adult MLD:** (15-20%) seen over 16 years of age. Difficult walking and speaking, diminished vision, loss of hearing, abnormal behavior, psychiatric symptoms like delusions or hallucinations, and progressive dementia [5, 6].

MLD is reported to occur in 1in 40,000-160,000 individuals worldwide [7]. It is inherited as autosomal recessive trait with gene located on chromosome 22q13-13qter [8].
MLD patients often require general anaesthesia for diagnostic and therapeutic interventions e.g. magnetic resonant imaging, gastrostomy tube placement, central catheter placement and removal, tendon release surgery, abcess drainage, gastero-eosophageal hernia repair, endoscopy, tracheostomy and change tracheostomy [9].
This group of patients presents a lot of anaesthetic concerns during perioperative period like convulsions, risk of aspiration, airway complications, copious oral and tracheobronchial secretions, impaired swallowing, chronic immobility, dystonia, and spasticity [10]. So care must be given to avoid pressure necrosis and iatrogenic fractures during positioning and transfer.
Other anaesthetic concern is that most of these patients can be on anticonvulsant therapy, steroids, or other chronic medications which need continuation during perioperative period.

In addition, attention must be directed to investigate liver function and coagulation searching for any deterioration because of anticonvulsants or adrenal insufficiency because of steroids [11].

Temperature management is a well-known concern in these patients and require careful consideration.

Case Report

Our case is 33 months old girl with weight of 12 kg. Presented for laperoscopic cholecystectomy and feeding gastrostomy tube placement in Children Welfare Hospital in Baghdad on November 22nd of 2022. Her disease started 3 months ago as progressive muscle weakness started in both lower limbs ascending to include the abdomen then upper limbs associated with spasticity which led to contractures in both upper and lower limbs, later involved the pharynx leading to difficulties in swallowing.

The patient was on oral Baclofen 4 mg. twice daily. It was not interrupted till the time of operation. No history of convulsions or anticonvulsant therapy.

Preoperative laboratory investigations were done including complete blood picture, blood glucose, serum electrolytes, renal and hepatic function tests, coagulation study (figure 1). All results were within normal apart from increase in AST level which is explained as a result of Baclofen.

Chest x-ray shows lateral deviation of vertebral column due to spasticity (figure 2). ECHO study was normal.

Problems expected with induction of anaesthesia were immobility, spasticity, copious oral secretions, risk of aspiration, and difficult intubation.

At induction of anaesthesia vital signs were: Heart rate (HR) = 110 BPM, Respiratory rate (RR) = 22, Blood pressure (BP) = 110/50 mmHg. Skin temperature = 36.6 ºC, Oxygen saturation (SpO2) = 97% (on room air) the patient was anxious and crying.

Monitors were connected which included: Pulse oximetry, ECG, NIBP, and Temp. (Nasal probe).

19/11/2022

Test Form

Tests	Result	Unit	Normal Range
B-Glucose (R)	98	mg/dl	Up to 160
B - Urea	23	mg/dl	15 - 45
S - Creatinine	0.5	mg/dl	0.5 - 1.3 male * 0.5 - 1.1 Fem
S - Sodium (Na)	139	mmol/L	135 - 153
S-Chloride	109	mmol/l	98 - 108
S- Calcium (Ca^{+2})	9.2	mg/dl	8.1-10.5(Ad) * 10 - 12 (chil) * 8 - 13 (NB)
S – Total Bilirubin	0.5	mg/dl	Up to 1.0
S – Alkali. Phosph	30	IU/L	21 – 92 (Ad) * 71 – 142 (Chil.)
S – Alt (SGPT)	11	IU/L	Up to 15
S – AST (SGOT)	42	IU/L	Up to 20

Viral Screening Test

Test	Result
HCV	Negative (- ve)
HIV	Negative (- ve)
HBs Ag	Negative (- ve)

Hematology Report

Test	Result	Unit	Normal Range(Age & Sex related)
Haemoglobin	113	gm/L	120 - 160
PCV	35	%	37 - 50
MCV	86	FL	76 - 96
MCH	28.6	Pg	27.0 - 32.0
RDW	13.5	%	11.5 - 14.5
MCHC	322	gm/L	320 - 360
RBC	3.9	m/µL	3.80 - 6.50
WBC	11.7	x 10^9/L	4.0 - 11.0
Differential			
Neutrophils	36	%	40 - 75
Lymphocytes	58	%	20 - 45
Monocytes	05	%	0 - 10
Eosinophils	01	%	0 - 6
Basophils	00	%	0 - 1
Other Cells	----		
ESR 1st. hr.		mm/hr.	
Platelets count	380	x 10^9/L	150 - 400
Retic	----	%	

Blood Group A **RH (D)** **Positive (+ ve)**

Fig 1: Laboratory investigations

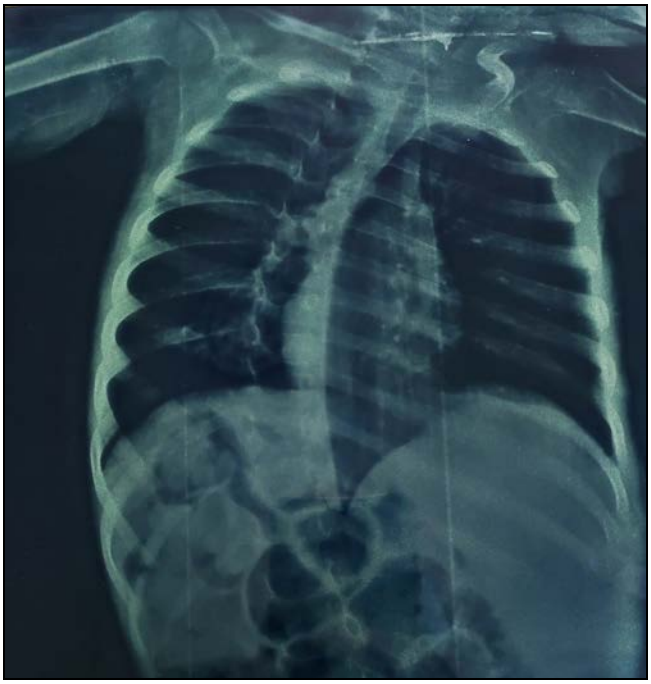

Fig 2: Chest x-ray

The patient premedicated with Glycopyrrolate 100 *u*g. i.e. and Esomeperaozole 10 mg. i.e. followed by preoxygenation with 100% O2 for 2 minutes then Midazolam 0.5 mg i.e., oral suctioning, Propanol 20 mg., Remifentanyl 10 *u*g, and Rocuronium 15 mg, cricoid pressure (Rapid sequence induction (RSI), then Laryngoscopy using usual curved blade, and intubation with 4.5 mm ID cuffed Endotracheal tube (ETT). We noticed decrease in the spasticity after propofol which rendered intubation easy. A Nasogastric (NG) tube size 12 FG was inserted easily.

Ventilation was with pressure controlled mode (PCV) using inspiratory pressure (IP) of 11 cm H2O, RR = 18, Positive end expiratory pressure (PEEP) = 4 cm H2O.

After induction vital signs were: HR=130 BPM, BP = 120/80, EtCO2 =33 mmHg.

Maintenance was with Sevoflurane 2% in O2 50%, with Remifentanyl infusion at a rate of 2 *u*g/min. now HR=104, BP = 90/50, Temp. = 36.1 ºC.

Laparoscopic cholecystectomy started with insufflation pressure of 10 cmH2O, flow of 2 L/min., EtCO2 increased to 40 mmHg. So RR increased to 22/min. The operation lasted 80 minutes (65 minute laparoscopy and 15 minutes gastrostomy tube placement).

2 increment doses of Rocuronium (2 mg) were given at minutes 30 and 50. 220 ml of Ringer's solution was given. And Paracetamol 150 mg given. Temperature control was with forced air warming device (Bair-Hugger) set at 38 C which increased to 43 C to manage the drop of patient's temperature to 36.1 ºC.

At the end of surgery, Remifentanyl infusion stopped, after 5 minutes, with the effort of spontaneous breathing, Sugamadex 25 mg was given to reverse muscle relaxant. The patient responded with adequate spontaneous breathing (VT = 140 ml, RR=24/min), she opened her eyes, and cough. Extubation done.

The patient developed mild spasticity and shivering, she was managed by active warming and Midazolam 0.5 mg. after 15 minutes she was calm, waking with simple tactile stimulation, breathing comfortably, her SpO2 was 97% with room air, then started crying searching for her parents. So transferred to PICU.

In the PICU, the patient was conscious, crying, spontaneously breathing with oxygen nasal cannula, looked in pain, Morphine 1 mg IV, and Baclofen 4 mg given through gastrostomy tube. At night spasticity retuned to as preoperative state, the night dose of Baclofen 4 mg given through gastrostomy tube.

Postoperative day; spasticity continued as same, vital signs were stable. The patient discharged to the ward.

Discussion

MLD is a white matter disease. It is a disorder of myelin sheath that affects central and peripheral nervous systems. In the late infantile type, as in our case, peripheral neuropathy can be the initial symptom, before central progression [1].

Continuation of the usual treatment of anticonvulsants, steroid, or muscle relaxant (Baclofen) is very important, as sudden withdrawal may lead to convulsions, adrenal insufficiency, and increased spasticity.

Baclofen acts on GABA-B receptors in the dorsal horn of the spinal cord. So it is centrally acting muscle relaxant that is effective in relieving muscle spasm. Sudden withdrawal leads seizure.[1]Interferences are possible between baclofen and curare and general anaesthetics. They may be responsible for neuromuscular block augmentation, heart rhythm disorders, arterial hypotension or increased sedation but weaning is much more [12]. However, it is documented that Baclofen can cause hepatic injury and elevated liver enzymes [13].

As the disease progresses it leads to dysphagia and drooling of secretions that needs placement of gastrostomy which facilitates feeding. Risk of aspiration is present because of that. So rapid sequence induction (RSI) is the choice.

Premedication started with Glycopyrrolate to decrease copious secretions with minimal effect on heart rate, proton-pump inhibitor (Esomeprazole) is given to decrease gastric acidity. Midazolam is given to decrease muscle tone and increase convulsion threshold.

Both inhalation and intravenous induction are safe. However, intravenous induction is preferred because of rapid onset which meets the requirement of RSI, in addition to the availability of IV. Line. Propofol, Thiopentone, [10] Sevoflurane, Isoflurane, opiates, and local anaesthtics all have been used without complication [1]. Ketamine should be avoided due to its ability to lower seizure threshold [14].

We avoided Succinylcholine due to the theoretical risk of hyperkalemic cardiac arrest because of exrtra-junctional receptors proliferation. However, there are no reported cases of its use in MDL [1]. Another cause to avoid Succinylcholine is its fasciculation which may cause iatrogenic bone fracture.

So, RSI reverted to the modified version; using Rocuronium 1mg/kg with cricoid pressure. Non depolarizing neuromuscular blockers (Atracurium, Rocuronium, and vecuronium) have been noted to be safe in these patients.[1] Intraoperative doses of IV. Anaesthetics and muscle relaxants need to be increased due to increased hepatic enzymes function seen in patients on chronic anticonvulsant therapy [15].

Maintenance continue with Sevoflurane and Remifentanyl infusion as both are documented to be safe for these children [16], in addition to their properties in being short acting agents which do not prolong to postoperative period.

Special care is given to temperature control to avoid shivering and increase oxygen demand. Measures such as raising operating room temperature, warning of IV. Fluid, using closed circuit, and using of forced air warmer device which is an effective method to avoid hypothermia [17].

Care is also given to posture and transport to avoid pressure necrosis and iatrogenic fractures which result from malnutrition and spasticity [15].

Reversal of neuromuscular blockade done with Sugamadex (2 mg/kg) which is effective reversal of Rocuronium, although Neostigmine is also appropriate and documented for antagonism of neuromuscular blockers for these patients [1].

Potential complications from sedation are: hypoxia, vomiting, bradycardia, arrhythmia, and convulsion. Documented complications post-extubations are: hypothermia, aspiration pneumonia, and bronchospasm [16].

Postoperative critical care is required for frequent suctioning, chest physiotherapy, and positioning. It is important to consider pain management, temperature control, continuous monitoring, and most important, continuation of preoperative medications (anticonvulsants, steroids, etc.) to avoid withdrawal symptoms of these drugs. The patient was not on chronic steroid therapy, so we did not find an indication to add steroid to the management as it is not wise to add side effects of steroid in face of uncertain benefit. The patient was not on chronic steroid therapy, so we did not find an indication to add steroid to the management as it is not wise to add side effects of steroid in face of uncertain benefit.

Regional anaesthesia has been relatively contraindicated in patients with neurological disorder, in addition abnormal posture and difficult communication with the baby. But Hernandez-Palazon *et al*. used epidural anaesthesia in patient of metachromatic leukodystrophy for pain management [1].

Conclusion

MLD frequently requires general anaesthesia for surgical procedures aimed to correct the sequalae of the disease. It presents a lot of anaesthetic problems during perioperative period and carries risks of many anaesthetic complications. However, management of these patients needs special attention and a thorough knowledge about these issues that will result in better outcome. Identification of these issues in the preoperative assessment of the patient and careful selection of anaesthetic technique will allow provision of safe anaesthetic care.

Nevertheless, reports suggest that complications rate may be substantially lower than suspected, and benefits of the necessary procedures significantly outweigh the risks [18]. So we can say confidently, that in experienced hands general anaesthesia is well tolerated in most of these children.

Conflict of Interest

Not available

Financial Support

Not available

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How to Cite This Article
Salih MM. General Anaesthesia for a baby with Metachromatic Leukodystrophy. International Journal of Medical Anesthesiology. 2023;6(2):09-13.