Perioperative Management of a Patient with Congenital Myasthenia Gravis for Elective Caesarean Section

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ABSTRACT

Congenital disorders of neuromuscular transmission are commonly referred to as congenital myasthenia gravis because of their clinical similarity to the immune-mediated disease. Differentiation between the immune-mediated and congenital forms of the disease is important, because therapy established for the former may not be appropriate for patients with the latter presentation. The course of this rare neuromuscular disorder during pregnancy and its influence on anaesthesia remain largely unknown. We report on the case of a 32-year-old parturient suffering from congenital myasthenia gravis scheduled for elective caesarean section. The perioperative management of this patient who underwent the operation under spinal anaesthesia was reviewed. The effects of anaesthetic agents and techniques on the course of congenital myasthenic patients may need further review in the light of latest findings in the electrophysiology, genetic and therapeutic studies of this syndrome.

Keywords: Anaesthesia, pregnancy, myasthenia gravis, congenital, caesarean section, subarachnoid

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INTRODUCTION

Congenital myasthenia or congenital myasthenic syndrome (CMS)[1-3] represents a group of rare genetic disorders, which arise from presynaptic, synaptic or postsynaptic defects. The syndrome typically presents at birth or during the first 2 years of life with weakness of the extra-ocular muscles; generalised weakness is usually mild and non-progressive[4]. Siblings are often affected in these disorders, suggesting autosomal recessive inheritance[4,5]. A positive edrophonium chloride test is consistent with diseases of neuromuscular transmission, seen in both the congenital and immune mediated diseases. However, antibodies to the acetylcholine receptors (AchR) are absent in congenital myasthenia[6,7].

Distinction between patients with congenital myasthenia and those with auto-immune myasthenia gravis is important for appropriate medical therapy. Some cases of congenital myasthenia are resistant to acetylcholinesterase inhibitor therapy[8]. Conventional medical therapies for immune-mediated myasthenia like immune suppressants and plasmapheresis are inappropriate in congenital myasthenia.

The influence of pregnancy on the clinical course of this sub-group of myasthenia gravis is largely unknown. The anaesthetic implication in the light of current reports elucidating the different pathophysiologic etiologies and clinical manifestations of congenital myasthenia gravis is the possibility that congenital myasthenic patients may behave differently from the immune-mediated myasthenics, in response to anaesthetic drugs and techniques. A review of the anaesthetic management of these patients, some who are receiving novel therapy like the use of quinidine[9,10] may be appropriate.

CASE REPORT

A 32-year-old Indian lady was diagnosed to have myasthenia gravis since the age of three years. Edrophonium (Tensilon) test and electromyography conducted confirmed the diagnosis. The absence of acetylcholine receptor antibody in her serum and a family history of a brother with the same disease clinched the diagnosis of congenital myasthenia gravis. Clinically, she has bilateral ptosis and complete external opthalmoplegia. The disease has pursued a fluctuating course, with exacerbations that necessitated multiple hospital admissions. She had experienced episodes of dysphagia and proximal weakness in which she had difficulty standing up from the squatting position. There was no prior history of respiratory embarrassment requiring mechanical ventilatory assistance.

Her condition responded to anti-cholinesterase treatment and she needed increasing daily dosages over the years. At the time of her pregnancy, her pyridostigmine dosage was 120 mg orally every 6 hours which was maintained throughout the three trimesters of gestation. A decision for an elective caesarean section at full term was made in consultation with the patient and her family. There was great concern that she would

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not be able to achieve a normal vaginal delivery because of the possibility of fetopelvic disproportion, as she only weighed 45 kg with a height of 1.53 metres. Furthermore, the neurologist was concerned that her medical condition would be complicated by fatigue if her labour was prolonged or difficult. These potential risks to maternal and fetal well-being swayed the decision towards an electively-timed caesarean section.

Pre-operative visit revealed obvious bilateral ptosis with opthalmoplegia but there was no symptom of dyspnoea or dysphagia. Premedication consisted of her usual dose of pyridostigmine and ranitidine 150 mg in the morning of the operation. Sodium citrate (0.3 M) 30 ml was served half an hour before surgery.

The surgery was performed under spinal anaesthesia. Intravenous preloading with 1 litre of lactated Ringer's (balanced salt) solution was established prior to anaesthesia. Using a 25-gauge Quincke needle, bupivacaine (0.5 %) 1.5 ml with fentanyl 15 micrograms was injected at the level of 3rd-4th lumbar interspace. Sensory blockade ascending till the fifth thoracic dermatomal level was achieved within 4 minutes. Close verbal communication with the patient was maintained intra-operatively. She did not experience any difficulty in breathing or swallowing. The patient remained haemodynamically stable, with a total of 2 litres of crystalloids administered intravenously. The caesarean section was uneventful with minimal blood loss and the total operative time was 40 minutes. The patient was closely monitored in the post anaesthetic care unit for 2 hours, during which recovery of the lower limb motor power was noted. The patient requested for analgesia 280 minutes after the commencement of subarachnoid anaesthesia. Post-operative analgesia included 2 doses of intramuscular pethidine 75 mg of 8-hour interval and subsequently oral doses of mefenamic acid 500 mg 8-hourly for 3 days.

Post-operatively, the patient was monitored in the high dependency unit for 48 hours. In addition to continuous pulse oximetry monitoring, assessment of speech, respiration (including 6-hourly vital capacity measurements which ranges between 0.65 to 0.8 litres) and swallowing was done every four hours. Her regular dose of oral pyridostigmine medication was resumed 6 hours after surgery. Clinically, she did not display any sign or symptoms of exacerbation during the postoperative period in hospital. Her newborn was observed in the special care unit for 2 days and remained asymptomatic. Both the patient and baby were discharged on the 5th post-operative day.

DISCUSSION

The true frequency of congenital myasthenia may be under-estimated, as they can be confused with immune-mediated myasthenia. In pregnancy, the course of myasthenia gravis has been reported to be highly variable and unpredictable in the antepartum period. Outcome in a previous pregnancy is not predictive of what the future course might take in a subsequent pregnancy. When exacerbations occur, they often surface in the first trimester or in the post-partum period. A potential hazard of anti-cholinesterase drugs is the stimulation of the uterine cholinergic receptors leading to an increase in uterine tone and contractions. This may suggest a higher risk of spontaneous abortion or premature labour in myasthenic parturients receiving anticholinesterase therapy. Myasthenia gravis has not been shown to affect the course of labour and is not, in itself, an indication for caesarean section. However, it would be undesirable for labour to be prolonged and exhausting[11]. The use of outlet forceps would help shorten the second stage of labour.

There is little in the literature with regard to the optimum technique of anaesthesia for caesarean section in patients with congenital myasthenia. The main problem revolves around the anaesthetist's ability to anticipate and manage three variables: The muscle weakness produced by the patient's disease, the perioperative anticholinesterase medication and the surgeon's requirement for muscle relaxation. Both regional and general anaesthesia have been used for caesarean delivery in myasthenic patients. If it is electively determined that the patient requires caesarean delivery, regional anaesthesia is recommended[12]. This overcomes the problem of titration of neuromuscular blocking agents as well as the risk of anticholinesterase overdose which may itself cause excessive muscle weakness. Careful attention should be given to respiratory muscle and bulbar weakness which may be present before or after surgery. This will predispose the patient to aspiration, chest infection or respiratory failure. General anaesthesia with endotracheal intubation is more appropriate if bulbar weakness or respiratory inadequacy is present as it ensures protection of the airway and adequate ventilation[12,13] although postoperative ventilation may be necessary.

Some authors recommend the use of spinal anaesthesia over the epidural technique which requires larger doses of local anaesthetic drugs. There is concern that high blood levels of local anaesthetic drugs may interfere with neuromuscular transmission[14-17]. Studies have however suggested that effects of systemic blood levels of local anaesthetic drugs on neuromuscular transmission only become significant at levels which cause death in experimental animals[17]. There is no evidence of increased sensitivity of the neuromuscular junction to local anaesthetic drugs in myasthenics. However, it is known that local anaesthetic drugs given

in anti-arrhythmic doses can enhance neuromuscular blockade from both depolarizing and nondepolarizing muscle relaxants[14,17]. There have been reports of epidural anaesthesia being used safely for caesarean section and vaginal delivery in myasthenic patients[11,18,19].

Subarachnoid bupivacaine 7.5 mg with l5ug fentanyl was found to be adequate in our local Asian population for caesarean section, with no excessive blockade or problems of respiratory depression[20]. Addition of subarachnoid fentanyl prolonged the effective analgesia and reduced the need for analgesia in the immediate post-operative period. This subarachnoid dose of bupivacaine and fentanyl used in this patient was found to be reliable. There was satisfactory anaesthesia and adequate surgical relaxation with no untoward complications. The regression of the block was also in accordance to that observed in the local population[20]. The use of a combined spinal-epidural technique would have the added advantage of supplementing the anaesthesia in the event of inadequate block and for post-operative analgesia.

The post partum period may be hazardous as reports have shown that as much as 30% of pregnant myasthenic patients have exacerbated symptoms within three weeks of delivery[11]. The anticholinesterase requirements may vary and repeated evaluation of ventilation (including measurements of vital capacity), swallowing and speech is recommended. It is suggested that the myasthenic patient be monitored for at least 10 days in the hospital to allow for adjustments in anticholinesterase therapy if needed[13]. The patient's usual anticholinesterases may have to be given intravenously until oral medications can be taken. Equivalent doses of intravenous pyridostigmine 4 mg can be used to replace oral doses of 120 mg and intravenous neostigmine 1 mg replacing oral doses of 30 mg[21].

The return of bowel function in women after caesarean section is often rapid post-operatively as there is minimal bowel manipulation, the surgery is of short duration and there is low rate of peritonitis[22]. Early resumption of normal diet following caesarean section has not been shown to interfere with the return of normal bowel function[23]. Regional anaesthesia ensures minimal interference with gut function with decreased incidence of nausea and vomiting, thus allowing early resumption of oral anticholinesterase therapy.

The infants of mothers suffering from congenital myasthenia may display symptoms at birth and follow the course of this chronic illness, similar to that observed in adults[14]. It is thus prudent to monitor the newborn closely with monitoring and resuscitative facilities in case symptoms appear.

In conclusion, the continual exploration in the diagnosis and the therapeutic approaches of congenital myasthenia would undoubtedly change the management strategies of pregnant patients and those requiring anaesthesia. A minimum interference technique based on subarachnoid block has been successful in this case. The management of the myasthenic parturient and her perioperative care ultimately depends on a multi-disciplinary team consisting of obstetrician, neurologist, anaesthetist, neonatologist and trained nursing staff to ensure an optimum outcome.

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