

## Emergency Caesarean section in a patient with known sickle-cell disease and myasthenia gravis

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### Abstract

A 33-year-old patient with known sickle-cell disease (SS) booked for antenatal care at the Lagos University Teaching Hospital at six weeks gestational age. She had been diagnosed with myasthenia gravis three years prior to presentation and placed on oral anticholinesterase and steroid therapy, but her compliance was poor. She had had an operative delivery six years previously, under a general anaesthesia relaxant technique. It had been complicated by delayed emergence and residual muscle weakness, necessitating postoperative ICU admission for mechanical ventilation.

In the index pregnancy, she had an emergency Caesarean section with bilateral tubal ligation under a combined spinal-epidural technique. A level of sensory block of T6 was achieved with 2.8 mL of 0.5% hyperbaric bupivacaine administered intrathecally. Towards the end of surgery, analgesia was supplemented through the epidural catheter with injection of 25 µg fentanyl in 6 mL of 0.25% plain bupivacaine. Supplemental oxygen was administered via a Hudson mask at 4 L/min. A live male baby with Apgar scores of 9 and 10 at one and five minutes, respectively, was delivered. The intraoperative period was uneventful.

Postoperatively, she was managed in the high care unit. Postoperative analgesia was achieved via the epidural catheter with 6 mL of 0.125% bupivacaine and 2 µg/mL fentanyl four hourly for 48 hours. Subsequent recovery was uneventful. She was discharged to the postnatal ward on the fourth day post-surgery, and home with her baby 10 days later.

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### Introduction

The management of the parturient with multiple intercurrent medical illnesses presenting for surgery poses an enormous challenge to the anaesthetist. Pregnancy by itself is associated with physiological changes, which place the patient at risk of developing complications during surgery and anaesthesia.<sup>1</sup> This risk of increased morbidity and mortality is further increased by the presence of concurrent diseases.<sup>2</sup> Sickle-cell disease (SS) is an inherited, autosomal recessive disorder, characterised by defective haemoglobin (Hb). It affects primarily people of African heritage.<sup>3</sup> Myasthenia gravis is an autoimmune disorder resulting from the production

of antibodies against the acetylcholine receptor, and is characterised by progressive skeletal muscle weakness upon sustained effort.<sup>4</sup> The perioperative management of a parturient with known Hb SS and myasthenia gravis for operative delivery is reported. The considerations with regard to the anaesthetic implications of these diseases, their coexistence, and a suitable choice of anaesthetic technique are discussed.

### Case report

A 33-year-old parturient presented for an elective Caesarean delivery and bilateral tubal ligation at the Lagos University Teaching Hospital (LUTH).

She was being managed by the haematology unit for SS. She was also being managed by the neurology unit for myasthenia gravis, which had been diagnosed nine years previously. Her medications were oral neostigmine and prednisolone.

She had registered for antenatal care at six weeks gestation and attendance was regular. The index pregnancy was her second and her first child was alive. Her first delivery had been by emergency Caesarean section under general anaesthesia on account of cephalopelvic disproportion. She required admission to the ICU for postoperative mechanical ventilation, on account of residual muscle weakness.

This latest pregnancy had been largely uneventful except for periods of anaemia, for which she was admitted at 36 weeks gestation. Her packed cell volume (PCV) was 18% and her Hb was 6 g/dL. Urea and electrolytes were normal. She was admitted for bed rest. Blood was taken for investigations, as well as for grouping and cross-matching. On ultrasound examination the following were seen: a singleton foetus with good cardiac activity and limb movement, and an estimated weight of 2.35 kg; a cephalic presentation in a longitudinal position; and a posterior placenta. On the fourth day after admission, she was transfused with two units of packed red blood cells. On the following day she went into spontaneous labour and was booked for an emergency Caesarean section.

An anaesthetic preoperative assessment of the patient was carried out. She claimed to have been compliant with her medication for myasthenia gravis until five months earlier. Physical examination revealed a young woman, not in respiratory distress, mildly jaundiced and well hydrated. She was mildly pale, and there was bilateral pitting pedal oedema up to the lower third of the legs. There was mild weakness of the extraocular muscles, as evidenced by the presence of strabismus, and power was 4/5 in both upper limbs, with predominantly proximal muscle weakness.

The remainder of her physical examination was normal. Her PCV was 24%. The patient was counselled for a regional anaesthetic technique (combined spinal-epidural anaesthesia) and informed consent was obtained. She was premedicated with 10 mg of metoclopramide and 50 mg ranitidine IV, as well as oral neostigmine 15 mg and prednisolone 10 mg. Two units of genotype AA whole blood were grouped, cross-matched and screened for surgery.

Intraoperative monitoring comprised an ECG, NIBP and pulse oximetry. Baseline values were a pulse rate of 82 beats/minute and blood pressure of 115/70 mmHg. Intravenous access was established peripherally with an 18G cannula and she was preloaded with 1 000 mL of normal saline.

A lumbar epidural was sited in the L3/4 interspace using an aseptic technique, with the patient in the sitting position. A test dose of 2 mL of 2% plain lidocaine was given to exclude intrathecal injection. The stylet was then reintroduced and the Tuohy needle left in the intervertebral space. The L4/5 interspace was then identified, and a 26G Quincke needle was introduced in the midline. Dural puncture was confirmed by backflow of clear cerebrospinal fluid. Spinal anaesthesia was initiated using 2.8 mL of 0.5% heavy bupivacaine. The epidural catheter was then threaded into the epidural space and secured. The patient was placed in the supine position with a 15° left lateral tilt and supplemental oxygen was given via a Hudson mask with a reservoir bag at 4 L/min. A T6 level of anaesthesia was confirmed using pin-prick sensation.

Haemodynamics and oxygen saturation were stable intraoperatively and a live male baby was delivered. Apgar scores at one and five minutes were 9 and 10, respectively. Oxytocin 5 IU was given IV, and another 30 IU added to the IV infusion. Due to the unavailability of misoprostol in the hospital and the need to avoid the use of ergometrine in this patient because of its vasoconstrictive effect, an additional bolus dose of oxytocin 5 IU was administered when the surgeons noted unsatisfactory uterine contraction. Estimated total blood loss was 800 mL, and two units of whole blood and 2 L of crystalloids were infused.

Towards the end of surgery, she complained of mild pain at the operation site and analgesia was supplemented through the epidural catheter with 6 mL of 0.25% bupivacaine with 25 µg of fentanyl.

Postoperatively, she was transferred to the high care unit for monitoring. Postoperative analgesia was achieved with 6 mL of 0.125% bupivacaine with 2 µg/mL fentanyl injected epidurally four hourly. She received physiotherapy postoperatively, as well as 100 mg IV hydrocortisone and an additional unit of packed cells. She restarted her medications on the second postoperative day and the epidural catheter was removed. The remaining stay in the high care unit was uneventful, and she was discharged to the postnatal ward on the fourth postoperative day and subsequently

discharged home with her baby on the 10th day post-surgery.

## Discussion

Improvements in the medical care of patients with SS have increased the numbers surviving into adulthood, thus increasing the numbers seen in pregnancy.<sup>5</sup> Pregnancy aggravates the medical complications of the disease and the disease itself complicates pregnancy. An increased tendency to pre-eclampsia, preterm labour and low birth weight babies has been reported in pregnant women with SS, resulting in high levels of maternal and perinatal mortality.<sup>6</sup> A multidisciplinary approach to peripartum management is suggested.

Anaesthetic principles include adequate peri-operative hydration, oxygenation and meticulous postoperative management, including respiratory therapy.<sup>3</sup> Blood transfusion therapy remains a mainstay in the management of the SS patient and preparation for surgery is a recognised indication for transfusion.<sup>7</sup> Other indications include increasing hypoxaemia, acute chest syndrome, multiple gestation, pre-eclampsia, septicaemia, splenic sequestration and progressive anaemia. A preoperative haemoglobin level of 10–11g/dL is considered optimum to avoid excessive blood viscosity, which predisposes to the sickling process.<sup>8</sup>

Myasthenia gravis is an autoimmune disorder resulting from the production of antibodies against the acetylcholine receptor. This leads to a reduction in the number of functional receptors at the neuromuscular junction.<sup>4</sup> It is an uncommon disease, with an overall prevalence rate of 13–15 per 100 000. Epidemiological data on myasthenia gravis for Nigeria and West Africa are currently unavailable; however, Bateman et al reported an annual patient myasthenia gravis seropositivity rate of 2.6 per million in South Africa.<sup>9</sup> In Nigeria, Ojini et al reported a total of 27 cases over a five-year period at the LUTH,<sup>4</sup> while Bakari and Onyemelukwe reported a total of 10 patients seen over a 10-year period at the Ahmadu Bello Teaching Hospital in Zaria.<sup>10</sup> Myasthenia gravis has a peak in the third to fifth decade and a second peak in the seventh decade. In the 20–40 year age group, it tends to affect females more than males, in a ratio of 2:1. However, in the over-40-years age group, the female:male ratio is 1:4.

The disease is characterised by skeletal muscle weakness upon sustained effort, and it commonly affects the ocular, bulbar and limb muscles.<sup>4</sup>

Immune suppression with steroids or azathioprine, boosting neuromuscular transmission with cholinesterase inhibitors, and removing antibodies by plasmapheresis and thymectomy, are the four main treatment regimens.<sup>11</sup> The main concerns of the anaesthetist relate to perioperative respiratory and bulbar muscle strength, as well as the effects of treatment for the disorder.<sup>12</sup>

The course of myasthenia gravis is highly variable and unpredictable during pregnancy, as well as after delivery. Patients may have disease exacerbation, crisis or even remission. They are also at risk of developing respiratory failure, adverse drug reactions, or even death.<sup>13</sup> Mitchell and Bebbington reviewed the performance of myasthenia gravis patients during pregnancy in a Canadian centre<sup>14</sup> and found that 45% experienced antepartum exacerbations ranging from muscle weakness to respiratory failure. Similarly, Plauche reported that exacerbation occurred in approximately 41% of patients during pregnancy and 29.8% of patients postpartum.<sup>15</sup> Four per cent of patients died because of worsening of the disease or complications of therapy.

The coexistence of these two disorders in the same patient has several implications. Bone marrow suppression has been reported in pregnant patients with myasthenia gravis.<sup>16</sup> Igarashi et al<sup>17</sup> suggested that this could be due to a colony-forming unit suppressive factor produced by the autoimmune mechanism. This may have contributed to the repeated periods of severe anaemia observed in this patient. Although this patient was not on the immunosuppressant azathioprine, its long-term use is reported to result in megaloblastic anaemia.<sup>18</sup> In addition, both disorders predispose the patient to muscle weakness and hypoventilation with resultant hypoxia, which may precipitate the sickling process.

Surgery is a stressful process and therefore spontaneous vaginal delivery is recommended.<sup>19</sup> Caesarean delivery was indicated in this patient who had had a previous Caesarean section for cephalopelvic disproportion.

The anaesthetic management of the myasthenic patient must be individualised to the severity of the disease and the type of surgery. These patients tend to have an abnormal response to muscle relaxants, increased sensitivity to sedatives and a restricted respiratory capacity.<sup>4</sup> Sensitivity to nondepolarising agents has been described in patients with minimal disease (ocular symptoms only), those in apparent remission and those with subclinical undiagnosed disease.<sup>20,21</sup>

Preoperative assessment of patients with myasthenia gravis must evaluate the risk of postoperative respiratory compromise and the need for postoperative ventilation. Careful assessment of preoperative pulmonary function will aid in the prediction of postoperative respiratory problems.<sup>22</sup> There is controversy concerning continued administration of anticholinesterase therapy perioperatively. On the one hand, use of anticholinesterases may potentiate vagal responses, inhibit metabolism of ester local anaesthetics and suxamethonium, and increase requirements for nondepolarising neuromuscular blockers. On the other hand, because exacerbations very often occur in the immediate postpartum period, it would seem beneficial to continue anticholinesterase therapy perioperatively.<sup>22,23</sup> Sedative premedication should be avoided in these patients. This patient received her anticholinesterase and steroid therapy preoperatively, and resumed it as soon as oral intake was re-established.

Several researchers have evaluated the safety of various techniques of anaesthesia for the parturient with myasthenia gravis presenting for surgery, and have concluded that regional anaesthesia is the technique of choice for Caesarean delivery.<sup>24-26</sup> This negates the issues of titration of neuromuscular blocking agents and the risk of anticholinesterase overdose, which itself may cause excessive muscle weakness. Epidural anaesthesia reduced the requirement for systemic medication, even in the postoperative period. The use of general anaesthesia and endotracheal intubation is recommended for Caesarean delivery in patients with respiratory insufficiency, because it ensures protection of the airway and adequate ventilation. The administration of epidural anaesthesia with fentanyl and bupivacaine has been shown to result in better postoperative pulmonary function.<sup>26</sup>

Babies of women with myasthenia gravis are at risk of developing a transient form of the disease, which persists for approximately three weeks.<sup>17</sup> Rates of neonatal myasthenia gravis are as high as 10–20%, and it is attributed to transplacental transfer of antibodies. Affected babies present with respiratory distress and inadequate suck reflex.

Postpartum monitoring of the myasthenic patient is important. Reports have shown that as many as 30% of pregnant myasthenic patients have exacerbated symptoms within three weeks of delivery.<sup>15,19</sup> Weakness after surgery presents a special problem in myasthenic patients, and those with the severe form of the disease may

require a period of postoperative ventilation. Anticholinesterase therapy is restarted at a reduced dose in the immediate postoperative period and gradually increased as necessary as the patient becomes ambulant. Anticholinesterase requirements may vary, and repeated evaluation of ventilation (e.g. measurements of vital capacity), swallowing and speech is recommended. The use of regional anaesthesia in our patient ensured minimal interference with bowel function, and a decreased incidence of nausea and vomiting thus allowing for early resumption of her oral anticholinesterase therapy by the second postoperative day.

## Conclusion

Achieving optimal management of the parturient with intercurrent medical diseases demands adequate preoperative evaluation and optimisation of the patient as well as planning an anaesthetic technique that takes into account the pathophysiology of these disease conditions. The choice of a combined spinal-epidural anaesthetic in this study was associated with minimal physiological interference and was successfully used to prevent perioperative complications in this patient.

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