19. de Groot AN, van Dongen PW, Vree TB, Hekster YA, van Roosmalen J. Ergot alkaloids. Current status and review of clinical pharmacology and therapeutic use compared with other oxytocics in obstetrics and gynaecology. *Drugs* 1998;**56**:523–35.
20. Breton C, Haenggeli C, Barberis C, Heitz F, Bader CR, Bernheim L et al. Presence of functional oxytocin receptors in cultured human myoblasts. *J Clin Endocrinol Metab* 2002;**87**:1415–8.
21. Lee ES, Uhm KO, Lee YM, Kwon J, Park SH, Soo KH. Oxytocin stimulates glucose uptake in skeletal muscle cells through the calcium-CaMKK-AMPK pathway. *Regul Pept* 2008;**151**:71–4.
22. Haeseler G, Stormer M, Mohammadi B et al. The anesthetic propofol modulates gating in paramyotonia congenital mutant muscle sodium channels. *Muscle Nerve* 2001;**24**:736–43.

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Maternal myasthenia gravis complicated by fetal arthrogryposis multiplex congenita

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ABSTRACT
We report the management of a 24-year-old primigravid woman who was diagnosed with myasthenia gravis at 20 weeks of gestation. Maternal symptoms improved with therapeutic plasma exchange, steroids, immunoglobulin therapy and pyridostigmine. Despite this, the fetus had arthrogryposis multiplex congenita due to trans-placental transfer of anti-acetylcholine receptor antibodies. The baby was delivered by elective caesarean section at 34 weeks of gestation but died in the immediate postpartum period. The mother underwent thymectomy within five weeks of delivery. The implications of myasthenia gravis for both the mother and baby are discussed.

Keywords: Pregnancy; Myasthenia gravis; Arthrogryposis multiplex congenita; Plasmapheresis; Caesarean section; Combined spinal-epidural

Introduction

Myasthenia gravis is an autoimmune disease characterised by anti-acetylcholine receptor (anti-AChR) antibodies causing impaired neuromuscular transmission and muscle weakness. It is twice as common in women and during pregnancy one-third of patients experience an exacerbation.[1–5] Anti-AChR antibodies can cross the placenta resulting in 10–15% of infants developing neonatal myasthenia gravis.[3] The effect on the newborn is usually transient,[3] however, irreversible damage to the fetus may result in arthrogryposis multiplex congenita (AMC). AMC presents with decreased fetal movements, polyhydramnios and multiple joint contactures.[6] Experience of managing fetal myasthenia gravis is limited.[7] We present the case of maternal myasthenia gravis resulting in fetal AMC.

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Case report

A 24-year-old nulliparous woman was referred to a combined obstetric and cardiac clinic at nine weeks of gestation because of a history of valvuloplasty for congenital pulmonary stenosis. She had a normal exercise tolerance throughout her life. An echocardiogram showed mild pulmonary stenosis (gradient 25 mmHg). A referral was made to our hospital at 20 weeks due to the maternal history and increased fetal nuchal translucency (3.6 mm) with a (46XX) karyotype. On scanning, multiple abnormalities were seen: an absent stomach bubble, abnormal fetal profile, hypoplastic nasal bone, clenched fists, hyperextended toes and reduced limb flexion, suggesting a neuromuscular disorder. Maternal blood was positive for anti-AChR antibodies with a level of >20 nmol/L (normal range <0.45 nmol/L). A neurologist had recently seen the mother for an intermittent, 4-year history of blurred and double vision, but a diagnosis of myasthenia gravis had not been considered.

Plasmapheresis reduced maternal anti-AChR antibody levels with improvement in maternal strength. Due to persistent fetal ultrasound scan anomalies, the option of

termination was offered but declined by the patient. Pregnancy continued with fortnightly plasmapheresis sessions. At 25 weeks the patient was symptom free with normal pulmonary function tests (vital capacity 4.4 L, forced expiratory volume in 1 s 3.6 L, peak expiratory flow rate 510 mL/s, total lung capacity 6 L). A caesarean section was planned if fetal head hyperextension persisted at the time of delivery. Vital capacity monitoring was continued until delivery and remained stable (3.85–4.15 L).

At 27 weeks the patient was admitted due to increasing weakness. Interval improvement was noted with plasmapheresis and oral prednisolone 10 mg/day increasing to 100 mg on alternate days, plus oral pyridostigmine 30 mg three times a day and intravenous IgG (1 g/kg) by infusion at 0.5 ml/kg/h increasing to a maximum of 4 mL/kg/h after 1 h. At 31 weeks the patient developed significant polyhydramnios that required repeated amniodrainage of up to 3 L. Two doses of betamethasone resulted in hyperglycaemia requiring insulin therapy.

A multidisciplinary conference resulted in a plan for elective caesarean section under combined spinal-epidural (CSE) anaesthesia at 34 weeks. With the patient sitting, under aseptic conditions, the skin was infiltrated with 1% lidocaine at L3-4. The epidural space was located at 8 cm with a 16-gauge Tuohy needle. Using a needle-through-needle technique a 26-gauge atraumatic spinal needle was passed through the Tuohy needle and 2.0 mL 0.5% hyperbaric bupivacaine with 300 μg diamorphine injected intrathecally. A catheter was then inserted into the epidural space. The patient was then placed supine with left lateral tilt. Monitoring included electrocardiogram (ECG), non-invasive blood pressure and pulse oximetry. Pressure points were protected and sequential calf compression devices put in place. Blood pressure was maintained with increments of 0.1 mg phenylephrine; intravenous hydrocortisone 100 mg given before surgery. A bilateral block to T4 to cold was achieved. A live 2754 g female baby was delivered, with dysmorphia, an extended fixed neck, and arthrogryposis (contractures) in all limbs. Apgar scores were 2 and 0 at 1 and 5 min, respectively with poor tone and no respiratory effort. Venous cord pH was 7.37. The baby was intubated but noted to be difficult to ventilate and oxygen saturations remained low. A heart rate to 90 beats/min deteriorated necessitating chest compressions, two doses of adrenaline 0.3 mL 1:10 000 fluids and 8.4% sodium bicarbonate 2 mL/kg were given via an umbilical vein catheter. Resuscitation was discontinued after 31 min. Post-mortem examination confirmed fetal akinesia deformation sequence (Pena-Shokeir phenotype) with no internal structural malformations. There were no significant histopathological abnormalities of brain or spinal cord, but the skeletal muscle showed amyoplasia (fat and connective tissue infiltration).

The mother's postoperative recovery was uneventful and she was discharged after two days with arrangements for follow-up. A postnatal computerised tomography (CT) scan showed a nodular mass in superior thymus and thymectomy was performed 5 weeks postpartum. Histology showed hyperplasia of the thymus. The patient is currently asymptomatic, remaining on pyridostigmine and a reducing dose of steroids.

Discussion

Myasthenia gravis is an autoimmune disease with an incidence of about 1:30 000,[8] and onset usually in early adulthood. Exacerbations have been witnessed during pregnancy and the postparturm period.[9,10] Circulating IgG autoantibodies block acetylcholine binding, accelerate ACh receptor degradation, and lyse the postsynaptic neuromuscular membrane.[11] Autoantibodies to muscle specific kinase (MUSK) can inhibit formation of the neuromuscular junction with symptoms of myasthenia gravis.[12]

Myasthenia gravis was suspected in our patient following fetal ultrasound scanning. The finding of anti-ACh receptor antibodies in the blood has a sensitivity of 80–96%[13,14] for a diagnosis of myasthenia gravis; however, other tests include imaging such as chest X-ray, CT and magnetic resonance imaging scanning to identify thymomas or alternative diagnoses such as a lung tumour causing Lambert–Eaton syndrome. Imaging tests during pregnancy may, however, not be feasible. Thymomas are rare neoplasms of the thymic epithelial cells normally responsible for directing T lymphocyte maturation.[15] Abnormally conditioned T lymphocytes are released into peripheral circulation and are likely responsible for 10–15% of myasthenia gravis cases.[16,17] Thymectomy results in complete clinical remission in about 46% of patients at five years.[18]

Medical treatment of myasthenia gravis is aimed at enhancing neuromuscular transmission with anticholinesterases and suppressing or removing antibodies: Pyridostigmine an acetylcholinesterase inhibitor, immunosuppression with prednisolone, plasmapheresis to remove anti-AChR antibodies and intravenous immunoglobulin which binds circulating antibodies are common therapies.[19]

Arthrogryposis multiplex congenital is characterised by multiple muscle contractures developing in utero due to a lack of fetal movement. It has an incidence of 6.2 per 100 000 *live* births.[20] Although a genetic basis exists for some cases, trans-placental transfer of maternal anti-AChR antibodies may also block the fetal neuromuscular junction;[21] however, AMC remains rare. The condition may be mild and compatible with life or severe and resulting in miscarriage, stillbirth or neonatal death. In our case the baby had fetal akinesia deformation sequence (Pena-Shokeir phenotype) and amyoplasia; a lack of growth and muscular devel-