Normal vaginal delivery in a patient with autosomal recessive limb-girdle muscular dystrophy

Carin Black MBBS and **Joanne Said** FRANZCOG CMFM

The Royal Women's Hospital, Parkville, Victoria, Australia

Summary: The limb-girdle muscular dystrophies (LGMDs) are a group of genetically determined disorders of skeletal muscle, predominantly affecting the pelvic and shoulder-girdle musculature. The clinical course is variable but steadily progressive. Type 2A LGMD is the most frequent form, accounting for approximately 30% of identified cases. There are few reports of patients with Type 2A LGMD undergoing pregnancy and delivery. This case outlines a successful vaginal delivery in a woman with this condition.

Keywords: high-risk pregnancy, maternal–fetal medicine, neurology, perinatal medicine

CASE REPORT

The patient, a 24-year-old primigravida, presented for antenatal care at The Royal Women's Hospital, Melbourne at 26 weeks gestation. Her neurological diagnosis was established at the age of 17 years on the basis of a muscle biopsy, which showed diagnostic features of myopathy. Further immunohistochemical studies using Western immunoblotting were arranged and proved consistent with Type 2A limb-girdle muscular dystrophy (LGMD). Her parents were consanguineous and her sister, aged 15 years, was experiencing similar symptoms at that time but had not undergone formal investigation.

At the time of diagnosis the patient underwent calf tendon releases, with no subsequent neurological review. Prior to pregnancy she was unable to walk without assistance and relied on family members to support her while she walked. This included assistance to rise from the seated or lying position. She was unable to run or climb stairs. Her routine booking blood tests were essentially normal except for an elevated glucose tolerance test, consistent with gestational diabetes, which responded to dietary measures. Her body mass index at booking was 26 kg/m².

She underwent neurological review at 32 weeks gestation. Examination revealed shoulder-girdle weakness with inability to lift her arms above her head, symmetrical lower limb weakness, calf hypertrophy and wasted quadriceps and hamstring muscles, with power 2/5 in the limb girdles. Echocardiogram, electrocardiograph and pulmonary function tests were performed and were essentially normal. A caesarean section for delivery was initially recommended by the neurology team on the basis of her poor motor function and concerns that this may preclude a vaginal delivery. However, in conjunction

with the patient's wishes, a vaginal delivery was proposed, with assistance in the second stage of labour if required.

Serial ultrasounds in the third trimester showed appropriate fetal growth. Her antenatal course was complicated by a fall at 34 weeks gestation resulting in a right medial malleolar fracture. This necessitated the use of a wheelchair for mobility, and subcutaneous heparin was commenced for deep venous thrombosis prophylaxis.

At 39 weeks gestation, induction of labour was recommended due to unstable blood sugars and numerous social and logistical issues, including difficulty for carers to arrange transport to the hospital for appointments. Artificial rupture of membranes was performed and an oxytocin infusion was commenced. A fentanyl-bupivacaine epidural was inserted for analgesia at the patient's request. Following a four-hour first stage full dilatation was confirmed. Pushing commenced and a normal vaginal delivery of a live female with Apgars 8 and 9 was achieved 75 minutes later. She sustained a small second degree perineal tear which was repaired.

She was discharged home two days postpartum with strong family supports and appropriate neurological follow-up. Unfortunately, she has not attended her obstetric follow-up appointment and has not been contactable via phone.

DISCUSSION

There are 10 known autosomal recessive LGMDs, labelled A–J.¹ Chromosomal loci, gene sequences and protein products have been identified for each type.² Type 2A LGMD is the most prevalent,^{1,3} caused by mutations in the gene coding for calpain 3.^{1,4,5} The function of calpain 3, which binds to connectin in the muscle fibre, is unknown,^{5–7} as is the mechanism by which deficiency causes muscular dystrophy.

Type 2A LGMD is characterized by symmetrical and selective proximal atrophy with no facial muscle disturbance and normal intelligence.¹ The clinical diagnosis is suggested by elevation in serum creatinine kinase and myopathic features on electromyography; however, the diagnosis is best confirmed

Correspondence to: Dr Joanne Said, 7th floor Research Precinct, The Royal Women's Hospital, 20 Flemington Road, Parkville, Victoria 3052, Australia
Email: jsaid@unimelb.edu.au

by either muscle biopsy or genetic testing.^{5,6} Muscle biopsy can confirm features consistent with muscular dystrophy, and immunohistochemical testing can be used to further specify the diagnosis, using antibodies directed against LGMD-related proteins.^{3,6} In this context, it is possible to identify calpain 3 deficiency in muscle via Western blot analysis. Genetic testing may be required to further clarify a mutation of calpain 3.^{3,6}

Autosomal recessive LGMDs typically manifest in the first or second decade of life,¹ with steady progression of symptoms, and the majority of patients lose independent ambulation within 10 years of disease onset.⁸ Patients affected tend to be of reproductive age, presenting potential challenges for pregnancy and delivery. Women may be at a point of borderline function at conception, with considerable problems arising from pregnancy-related changes in weight and activity.⁷ In this case, though her mobility deteriorated during pregnancy and mobility aids were recommended, only after sustaining an ankle fracture did the patient accept the use of a wheelchair to mobilize.

Women with LGMD may undergo significant progression of symptoms during pregnancy. Pronounced pelvic-girdle and trunk muscle weakness may occur, which may increase the need for obstetric intervention.^{2,9} Severe cases of LGMD can be associated with respiratory compromise further exacerbated by the physiological demands of pregnancy. Respiratory compromise secondary to severe diaphragmatic involvement may cause hypoventilation.¹⁰ Cardiomyopathies are not typical of LGMD but conduction abnormalities may occur, and pulmonary hypertension from restrictive lung disease may cause right heart failure.¹¹ Caesarean section is generally recommended for delivery in the presence of abnormal blood gases, vital capacity below 1–1.5 L, pulmonary hypertension or right heart failure, weak diaphragm or abdominal muscles, or pelvic abnormalities.¹²

Regional anaesthesia is preferable to general anaesthesia in patients with muscular dystrophy, as anaesthetic agents such as suxamethonium and volatile gases may cause life-threatening complications such as rhabdomyolysis and malignant hyperthermia.¹¹ Regional anaesthesia also avoids intubation and ventilation, which in patients with poor lung function preoperatively, can result in significant postoperative pulmonary complications including atelectasis and chest infection.¹¹

Preconceptual planning is important, in order to identify patients at risk of respiratory complications. Pregnancy is contraindicated if vital capacity is less than 1 L, if pulmonary hypertension is present, or if arterial $paCO_2$ is raised.⁸ Genetic counselling may be advisable, particularly if the maternal disorder has a significant heritable component. In this case,

prenatal genetic diagnosis was declined by the couple, and considering the autosomal recessive inheritance of Type 2A LGMD and the fact that the couple were not genetically related, the risk of the fetus having LGMD was very low.

There are limited cases in the literature reporting pregnancy and delivery in patients with LGMD,^{8,12,13} with these cases possibly reflecting the milder end of the disease spectrum in women who are more likely to bear children. There is no consensus regarding recommended mode of delivery in these women. It is important to individualize their obstetric management given the heterogeneity of the disease and to realize that vaginal delivery is not always contraindicated, particularly given that trial of labour may be safer than exposure to the potential risks of a caesarean delivery. Although assisted vaginal delivery seems more common in this cohort of patients due to inefficient maternal expulsive efforts, this case supports the suitability of normal vaginal delivery, in the absence of contraindications.

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