Myophosphorylase deficiency (McArdle disease) in a patient with normal pregnancy and normal pregnancy outcome

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Summary: McArdle disease is a rare, mostly autosomal recessive disorder of deficient myophosphorylation of glycogen in skeletal muscles. Recent knowledge regarding this condition means that women of childbearing age with McArdle disease can expect to labour normally without ill effect. We report a case of a 30-year-old woman in her first pregnancy who had an episode of exercise-induced myoglobinuria with a significant rise in serum creatine kinase (CK) levels in early pregnancy who then laboured normally but did require a caesarean section for a malposition of the fetal head.

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

INTRODUCTION

We report a woman who presented in her first pregnancy with a known diagnosis of myophosphorylase deficiency (McArdle disease). She had an initially complicated pregnancy with an episode of myoglobinuria and very significant creatine kinase (CK). She laboured but required a lower segment caesarean section for failure to progress in second stage of labour. A recent publication describing 14 women reported no specific problems.¹ We wish to add the experience from our case reported here to information regarding current management of this condition.

CASE REPORT

A 30-year-old woman in her first pregnancy was referred to the Maternal Fetal Medicine Unit at Royal North Shore Hospital Sydney Australia at 10 weeks gestation, estimated from menstrual dates and first trimester screening ultrasound. She gave a history of poor exercise tolerance as a school child during sport activities, specifically swimming, and the development of myositis at the age of 23 years, thought initially to be due to an intercurrent viral infection. Her symptomatology did not settle and subsequent investigations in 2003 included a muscle biopsy which showed increased glycogen and absent phosphorylase enzyme and a positive forearm occlusion test confirming the diagnosis of McArdle disease. At seven weeks gestation following an episode of swimming 25 m she developed severe muscle pain and myoglobinuria and a CK of 23,500 IU/L (her usual non-pregnant CK level was in the range 1000–2000 IU/L [normal range 40–300 IU/L]). At that time her creatinine remained normal (50 µmol/L) even though her liver function tests were abnormal (lactate

dehydrogenase 627 U/L, aspartate aminotransferase 356 U/L and alanine aminotransferase 103 U/L) consistent with muscle damage rather than renal damage. At that point (2008) a literature review showed that there had been little obstetric input into the literature regarding McArdle disease and pregnancy for several decades. Once reviewed, it was decided that she would be closely supervised throughout the pregnancy and that labour and vaginal delivery would be the aim. She was to receive intravenous glucose during labour, regional anaesthesia for pain relief and assistance with delivery once second stage of labour was reached. She was reviewed by the clinical genetics team and an echocardiogram was performed and was normal. She was seen regularly with consultations with the nephrologists and the anaesthetic team. Her CK levels were regularly assessed and ranged from 342 IU/L at 11 weeks up to 753 IU/L at 31 weeks and back to 109 IU/L at 38 weeks. Her urine, which was regularly screened, was consistently negative for myoglobin.

At 39 weeks after spontaneous rupture of the membranes she was admitted to delivery suite. Labour was augmented 10 hours later and she was fully dilated 6.5 hours after establishing labour. Analgesia was maintained via an epidural block and intravenous 4% dextrose N/5 saline was infused throughout the labour. An uncomplicated lower uterine segment caesarean section was performed after lack of progress in the second stage of labour due to persistent occipito posterior presentation. Adequate anaesthesia was obtained with the epidural block and a live male infant weighing 3900 g with Apgar scores of 9 + 9 and arterial pH of 7.32 and venous pH of 7.37. The baby was breast fed by two hours of age and there were no postnatal problems for mother or baby. The CK level rose to 1376 the day after delivery but the urine was clear of myoglobin. Her postoperative course was uncomplicated and she was discharged with her baby on day 6 (within the Diagnosis Related Group for caesarean section and intercurrent medical condition of 7.0 days). In mid-2010 she returned for care in

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her second pregnancy and had an elective repeat caesarean section without incident in early 2011.

DISCUSSION

McArdle disease (glycogen storage disease type V) first described in 1951 is a rare, predominantly autosomal recessive inherited disorder of deficient myophosphorylation of glycogen in skeletal muscles² with marked heterogeneity in severity.¹ The reported incidence in Norway is 1:650,000³ but more recently rates of 1:100,000 in Texas are quoted.¹ The disorder results from mutations of the single gene that encodes for the muscle glycogen phosphorylase at 11q13.⁴ The subsequent deficiency of substrate for the muscle cells during exercise can result in rhabdomyolysis, myoglobinuria and acute renal failure with a significant number of patients having a raised serum CK even at rest.³ The disorder is often noted to be associated with exercise intolerance in childhood with the development of muscle pain and stiffness. The first report of pregnancy and labour in a woman with McArdle disease was in 1973 and the authors of that paper were able to discuss the options of management with Dr McArdle.⁵ Their patient progressed to a Keilland's forceps delivery. A further report in 1984 described a woman who underwent caesarean section with general anaesthesia in labour at 33 weeks for hypertension and suspected intrauterine growth failure.⁶ In both these papers the authors recommended intravenous glucose peripartum as the administration of glucose and fructose had been noted to relieve muscle symptoms. This has been supported in other publications.^{1,7,8}

More recent literature supports the concept of there being few adverse effects during pregnancy and subsequent labour thus suggesting that labour and vaginal delivery are not precluded.¹ Perez *et al.* and Maté-Muñoz *et al.* report that adults with McArdle disease can re-condition their fitness with pre-exercise sucrose administration⁹ and that training is possible under controlled conditions.¹⁰ Bollig *et al.*³ had also reported that patients with McArdle disease can have significant complications associated with surgery and anaesthesia such as hypoglycaemia, rhabdomyolysis, myoglobinuria, acute kidney injury and malignant hyperthermia. The literature favours regional anaesthesia with concerns being raised regarding muscle relaxation during general anaesthesia.³

Our patient developed myoglobinuria following swimming in early pregnancy which settled. Labour occurred and as expected the myometrium not being skeletal muscle performed without problems and she reached full dilatation but developed a persistent occipito posterior presentation and was not

deliverable vaginally. Her caesarean section under epidural anaesthesia was routine and uncomplicated.

In summary, McArdle disease is a rare inherited glycogen storage disorder. With close surveillance during pregnancy these women can be allowed to labour with intravenous glucose administration, with the aim of achieving vaginal delivery. Should caesarean section be required then regional anaesthesia is preferable and safe.

DECLARATIONS

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