Case Report

Myotonic Dystrophy and Pregnancy

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Abstract

Myotonic dystrophy is the most common neuromuscular disease in adults with a prevalence of 2.4-5.5 per 100,000. Here we describe two cases of DM and discuss their obstetric complications. Our first case concerns a 39 year old multipara whose pregnancies were complicated by recurrent abdominal pain, polyhydramnios and post partum haemorrhage which was attributed to DM. In our second case we discuss the management of a 27 year old woman with di-chorionic, di-amniotic twins. Chorionic Villous Sampling at 11 weeks revealed one of the fetuses, a male; to be afflicted by DM. Selective termination of the affected twin was performed. Unfortunately, she developed severe oligohydramnios and chronic liquor leak. This resulted in the intra-uterine death of the second twin 5 days later. Our cases highlight the importance of prenatal diagnosis and prompt genetic counselling. A multidisciplinary team approach is required in the management of such high risk cases.

Introduction

DM is a progressive systemic disease. It is characterised by myotonia, myopathy of voluntary and involuntary muscles, frontal alopecia, lens opacities, intellectual deterioration, cardiac conduction defects, alveolar hypoventilation and various endocrinopathies. Symptoms vary greatly, ranging from just cataracts presenting at a later age to involvement of multiple organ systems resulting in extreme muscle weakness and breathing difficulties after birth.[1-3] It has a worldwide distribution, involving most ethnic groups with an autosomal dominant inheritance pattern. Men with this disorder generally have gonadal atrophy and infertility; however affected women can become pregnant. When they do become pregnant, their myopathy may worsen; resulting in serious obstetrical complications.[2]

Case 1:

The first case concerns a 39 year old multiparous woman with significant family history of DM. She was not particularly bright at school and missed classes frequently due to recurrent illnesses. Her first pregnancy ended in spontaneous miscarriage, at 15 weeks of gestation. In her second pregnancy, she presented with abdominal pain and underwent an appendicectomy at 19 weeks. The pregnancy progressed to spontaneous labour at 40 weeks, resulting in a healthy boy weighing 3,110 grams. Her delivery was complicated with atonic post-partum haemorrhage (PPH) of 1500ml, which was managed successfully by Syntocinon. Her third pregnancy was complicated by several episodes of abdominal pain. Ultrasonography (USG) revealed a large baby and mild polyhydramnios. Labour was induced at 41 weeks and a baby boy weighing 4500 grams was delivered. The neonate was floppy and had pyrexi. He subsequently recovered. She again had significant PPH of 1800mls requiring blood transfusions.

Her present pregnancy was complicated by marked polyhydramnios. She had multiple admissions with abdominal pain and recurrent urinary tract infections (UTI). Emergency C-Section was performed at 38 weeks due to breech presentation; giving birth to a male baby weighing 3,620 grams. At birth, the neonate was floppy requiring oxygen. He was initially fed via a nasogastric tube but later changed to intravenous feeding as he developed aspiration pneumonia. Chromosomal polymerase chain reaction (PCR) confirmed DM. Even 4 months later, he remained floppy with poor head control, facial palsy, bilateral iris and retinal colobomata, bilateral talipes requiring orthopaedic intervention and physiotherapy.

Case 2:

The second case concerns a 27 years old woman with significant familial history of DM. As her father suffered from DM, she along with her siblings underwent extensive investigations including electomyographic (EMG) studies in 1983. All of her investigations were normal. However, her eldest brother showed some signs of DM later in life.

In 1998, when she first became pregnant, she requested predictive testing for DM and was found to have an expansion in the DM gene. Pre-natal diagnosis suggested the foetus to be affected with expansion of the DM gene greater than hers. She underwent medical termination, at 16 weeks. This was complicated by retained placenta requiring evacuation of retained products of conception (ERPC).

In 2002, she again became pregnant. Chorionic villous sampling (CVS) confirmed the foetus of not being affected. Spontaneous labour occurred at 38 weeks and a healthy baby boy weighing 3,610 grams was delivered.

In her present pregnancy she conceived di-chorionic, di-amniotic twins. CVS at 11 weeks, revealed one male foetus,

to be affected by DM. A week later, she underwent selective termination. During the next three weeks, the surviving pregnancy developed severe oligohydramnios. Chronic liquor leak was diagnosed. Termination was advised in view of a 95% risk of pulmonary immaturity; however she elected to continue her pregnancy. USG at 25 weeks demonstrated retarded foetal growth with severe oligohydramnios. 5 days later the foetus died in-utero. Medical termination was performed. The foetus was delivered and the placenta removed piecemeal under anaesthesia.

Discussion

Phenotypically, DM can be divided in 4 main groups. The 'Mild type' is characterised by cataract and mild weakness affecting elderly patients. 'Adult type' starts after puberty and progresses slowly with cardio-vascular, gastro-intestinal and respiratory manifestations. 'Childhood type' occurs from 1-10 years of age and is characterised by hypotonia, learning difficulties and limited motor skills. 'Congenital DM' is the severest form with symptoms of generalised muscular hypoplasia and mental retardation. About 75% of these babies die within the first year.[3-6]

The DM gene is located on the long arm of chromosome 19 band 13q. It codes a protein kinase found in skeletal muscle, where it possibly plays a regulatory role. This gene contains an unstable tri-nucleotide repetition Cytosine-Thymine-Guanine (CTG). In normal subjects the number of repeats ranges from 5 to 38, however in the classical form of DM that is DM1, the CTG pattern is repeated as many as 2000 times, disrupting the normal function of the protein. Consequently, leads to DNA instability correlating with increasing severity and early onset of the disease.[7]

CTG repeat size can change when passed from one generation to the next, for reasons unknown. Moreover, this instability is biased, as the repeats almost always enlargers when inherited. This phenomenon is called 'genetic anticipation'. Anticipation is more pronounced in the maternal transmission of the gene.[7]

Mildly affected women can be symptom free but are at 50% risk of transmitting the condition to their offspring and may give birth to an infant that is severely affected.[8] Contralaterly if the father has transmitted the mutation, the affected offspring has a form of the disease, which often presents late and is of comparable severity to that of the father.[9]

Prenatal testing can be performed to determine whether the foetus has inherited DM. Diagnosis is possible by either chorionic villous biopsy or amniocentesis with a DNA analysis measuring the CTG repeat count. This testing may be done if complications develop during pregnancies that are suspicious for congenital DM, or if a parent has tested positive. A positive test with a large repeat expansion indicates that the foetus is likely to have a severe congenital form of DM. Termination of pregnancy at this stage is a difficult decision and parents should be offered careful counselling.[7]

Pregnancy is associated with an exacerbation in this myopathy.[2] Major antepartum complications include polyhydramnios, preterm labour, UTI and placenta praevia.[10] Polyhydramnios can result from decreased swallowing of liquor and is an indication of severe muscular dysfunction of the foetus as seen in our case 1. Polyhydramnios of unknown aetiology may thus be the first sign of DM. It predisposes to preterm labour, uterine inertia and PPH. Perinatal mortality is 15-16% compared with 1.9% in the normal population and mainly attributed to congenitally affected foetuses in conjunction with pregnancy complications.[5,6]

First stage of labour is usually prolonged although a rapid first stage has been described. The second stage is often complicated by poor voluntary effort secondary to muscular dysfunction requiring assisted delivery by vacuum or forceps.[4,6] Third stage of labour is frequently complicated by PPH due to inadequate uterine contraction or placental adhesion, as seen in case 1 or retained placenta as in case 2. Cases involving placenta accreta and increta have also been described.[6,10]

Patients with DM are particularly sensitive to anaesthetics. Intra and post-operative complications are relatively frequent. Administration of depolarising relaxants can result in severe myotonic spasms. Marked respiratory depression may occur as a response to barbiturates. Therefore, patients in labour should not receive heavy sedation, and local and regional anaesthetics are preferable to general anaesthesia.[6] Reduction in maximum expiratory pressure and retained secretions may occur during the peri-operative period which can result in aspiration, atelectasis and broncho-pneumonia.

Conclusion

Pregnancy with DM is a rare entity. If the mother is known to be affected, prenatal diagnosis and prompt genetic counselling should be offered. The option of termination should be discussed. If by choice pregnancy is continued, successful management would require a multidisciplinary team approach involving obstetricians, physicians, anaesthetists, paediatricians and geneticists.

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