Case report

Fluctuating clinical myotonia and weakness from Thomsen’s disease occurring only during pregnancies

David Lacomis *, Jorge T. Gonzales, Michael J. Giuliani

Room F878, Department of Neurology, University of Pittsburgh, 200 Lothrop St., Pittsburgh, PA 15213, USA

Received 11 December 1998; received in revised form 12 February 1999; accepted 12 February 1999

Abstract

Advances in molecular genetics are allowing better phenotype to genotype correlation of the non-dystrophic myotonic disorders. We report a 32-year-old woman, who first noted myotonia that was associated with weakness during her first pregnancy. The work-up disclosed that she had Thomsen’s disease which is not known to be associated with weakness. In addition, her myotonia was of the fluctuating type and occurred (symptomatically) only during two pregnancies. We discuss the evaluation of myotonia in the pregnant woman which led to the diagnosis of Thomsen’s disease and we conclude that in exceptional cases, fluctuating myotonia and weakness occurs in autosomal dominant chloride channel myotonia (Thomsen’s disease). © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Myotonia; Pregnancy; Myotonia congenita; Peripheral nervous system diseases

1. Introduction

With advances in molecular genetics, the non-dystrophic and dystrophic myotonias have become better characterized and the non-dystrophic types are known to consist of disorders with mutations affecting sarcolemmal chloride and sodium channels. Exceptions to some previously held beliefs regarding clinical features of the non-dystrophic myotonias are being uncovered and will likely increase as these genetic studies allow genotype to phenotype correlation. In this paper, we provide additional exceptions to two of these ‘beliefs’ [1–7].

First, it is known that ‘potassium-aggravated’ myotonias, such as the sodium channel disorder myotonia fluctuans [8], are associated with fluctuating myotonia; however, significantly fluctuating chloride channel myotonia was only recently reported by Wagner et al. [9]. We now report another patient with fluctuating chloride channel myotonia (Thomsen’s disease type). A second belief is that among chloride channel myotonias, only the Becker’s autosomal recessive variant is known to cause weakness. Our patient also had weakness which occurred only during pregnancy. Although it is known that myotonia may worsen in pregnancy, it is interesting that the fluctuations of myotonia and weakness manifested only during pregnancies.

We discuss these unusual phenotypic features and review the approach to the evaluation of the pregnant woman with myotonia, since the type of myotonic disorder has implications on pregnancy, labor, delivery and fetal outcome.

2. Case report

A 32-year-old woman first noted stiffness in the left hand and difficulty releasing her grip during the third month of her first pregnancy. Subsequently, she noted intermittent leg stiffness and persistent weakness when climbing stairs. Prior to pregnancy, she denied these or other neurological symptoms. However, a brother and
a paternal female cousin had diagnoses of ‘myotonic syndromes’ associated with stiffness but without weakness. These family members felt the stiffness was a nuisance, but they were not incapacitated. The patient’s neurologic examination revealed mild but definite proximal weakness (graded Medical Research Council 4 out of 5) in the upper and lower extremities. There was no percussion myotonia.

The creatine kinase was normal and a slit lamp examination revealed no cataracts. Nerve conduction was normal and cold immersion and exercise tests [10] were unremarkable. Genetic testing for myotonic dystrophy [11] was negative. An electromyogram revealed myotonia in all muscles examined, but motor unit potentials were normal.

Shortly after the uncomplicated delivery of a normal baby, the patient noted significant improvement in muscle strength and stiffness. A year later, her neurologic examination was normal and a repeat needle electrode examination demonstrated widespread myotonia; but, as compared to her previous EMG, the myotonia was not present in all muscles examined. The patient went through a second pregnancy with full recurrence of the same symptoms which again resolved following delivery.

Since additional family members were available for genetic testing (courtesy of G. Feero and E. Hoffman), linkage analysis for chloride and sodium channel mutations was performed. At that time, other affected relatives were identified (Fig. 1). The disorder was not linked to the sodium channel gene [12] and linkage analysis for the chloride channel gene [4] was uninformative. Polymerase chain reaction single strand conformer polymorphism analysis followed by sequencing of the chloride channel gene [5] revealed a previously described Thomsen’s disease mutation, a G-A transition at position 689, which results in a substitution of a glutamic acid for a glycine residue [3].

3. Discussion

3.1. Evaluation of myotonia in the pregnant woman

Our patient presented during pregnancy with symptoms suggestive of myotonia. We performed an electromyogram to confirm the presence of myotonia. The exact sensitivity of EMG in detecting electrical myotonia in the myotonic syndromes is uncertain, but it is likely to be very high, especially in adults [10]. Following the EMG, we undertook an evaluation to determine the cause of myotonia. It is known that both dystrophic and non-dystrophic myotonias may worsen with pregnancy [13–16] and rarely present during pregnancy [9,14,16,17]. In addition, agents used to treat premature labor, especially ritodrine and fenoterol can worsen myotonia [24,25].

In pregnancy, there is some urgency to elicit the cause of myotonia, since myotonic dystrophy can adversely affect pregnancy, labor and delivery and result in a significantly affected offspring [14–16,18,19]. In comparison, the non-dystrophic myotonias are usually benign. An exception is a report of a patient who probably developed myotonia involving the respiratory muscles at 39-weeks of gestation, manifesting as breathlessness during inspiration which resolved after delivery [13].

Our first step, therefore, was to exclude myotonic dystrophy even though the patient did not have typical features, such as distal or facial weakness with atrophy. In addition, there were no cardiac arrhythmias and cataracts, seen in 60–80% of young adult patients with myotonic dystrophy, were also absent [19]. Nevertheless, we used genetic testing in an algorithmic approach to definitively exclude the diagnosis (Fig. 2).

In consideration of other forms of dystrophic myotonia, the presence of proximal weakness and autosomal dominant inheritance raised the possibility of proximal...
myotonic myopathy (PROMM). However, the patient did not have other features of PROMM such as cataracts (present in 50–100%) and muscle pain (present in 40%) [20–22]. Myotonia (from PROMM) manifesting during pregnancy has been reported in two patients, but myotonia itself is not usually prominent in PROMM [22]. There is only one rare case reported of neonatal onset of probable PROMM with hypotonia [23] and there are no reports of problems with labor or delivery.

After excluding these disorders, the work-up was less urgent and our attention later concentrated upon the non-dystrophic myotonic disorders. Of these disorders, only the autosomal recessive Becker’s variant of myotonia congenita is associated with weakness. However, the inheritance pattern in our family was autosomal dominant. Genetic studies for congenital myotonia, which are less readily available than DNA testing for myotonic dystrophy, disclosed that our patient harbored a known chloride channel mutation consistent with Thomsen’s disease. It is important to note that in the autosomal dominant chloride channelopathy kindred presented by Wagner et al., one of the family members also first noticed myotonia during pregnancy and another recalled episodes of stiffness during pregnancies [9]. However, our patient was different because of weakness which is not known to be associated with Thomsen’s disease. In addition, prior to the report by Wagner et al., it was not known that chloride channel myotonias can fluctuate to the degree that was noted in our patient. Such variability in phenotypes is likely to become more commonly observed as genetic testing for non-dystrophic myotonias is easier to obtain.

Finally, the reason for the pregnancy related exacerbations of myotonia and sometimes weakness, is unknown. It is thought that myotonia might increase because of increased progesterone which might affect intracellular and increase extracellular potassium. Conceivably, there could also be, as yet, undefined alterations in chloride channel conductance, sodium channel openings, or second messenger systems. The sophisticated microelectrode studies that would be required to examine such hypotheses have not been performed.

Acknowledgements

The authors appreciate the genetic studies performed by G. Feero and E. Hoffman.

References


