Original articles

Congenital myotonic dystrophy: respiratory function at birth determines survival

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SUMMARY The clinical features of 14 neonates with congenital myotonic dystrophy were retrospectively reviewed. These babies represent all the new cases of congenital myotonic dystrophy seen in this department since 1982. Twelve babies were referred because of either difficulties in diagnosis or difficulties in the management of their respiratory problems. Of the 14 babies, 13 had birth asphyxia, 11 were premature, and four had intrauterine growth retardation. Ten babies required artificial ventilation from birth. Abnormalities on chest radiography included thin ribs ($n=9$) and raised right hemidiaphragms ($n=5$). Recurrent episodes of collapse and consolidation of the lungs secondary to poor swallowing occurred in all ventilated babies. All babies ventilated for longer than four weeks died of respiratory complications before the age of 15 months. One baby was successfully extubated after diaphragmatic plication, but he died a few months later. Duration of ventilation was the best guide to prognosis.

Congenital myotonic dystrophy is one of the commonest muscle disorders that presents in the neonatal period. The incidence is at least one in every 3500 live births.^{1,2} Mildly affected babies are hypotonic, have problems sucking and swallowing,³ usually have facial diplegia, and may have limb contractures. More severely affected babies are asphyxiated at birth and require intermittent positive pressure ventilation for poor respiratory effort. Difficulty in swallowing leads to recurrent aspiration.

Myotonic dystrophy is a dominantly inherited disease, but in babies with congenital myotonic dystrophy the mother is invariably the affected parent.⁴ Characteristically she has mild symptoms and is not diagnosed until after the birth of an affected baby.⁵ She may give a history of recurrent miscarriage, stillbirth, or previous neonatal death and the current pregnancy may be complicated by polyhydramnios and poor fetal movements.⁶ The polyhydramnios is secondary to poor fetal swallowing.⁷ The diagnosis is confirmed by clinical and electromyographic examination of the mother for evidence of myotonia. There is no evidence of myotonia in the neonate and histological examination of a muscle biopsy specimen is unhelpful.⁸ The fact that babies with congenital myotonic dystrophy are born almost exclusively to affected mothers has led

to the hypothesis that an abnormal uterine environment acts on fetuses who have inherited the dominant gene.⁹

Mortality in congenital myotonic dystrophy is usually caused by respiratory complications within the first year of life.² Only recently has the true incidence of severe respiratory complications in these infants become apparent because of the more widespread use of neonatal intensive care. In previous years death was frequently attributed to birth asphyxia or pulmonary hypoplasia without any underlying diagnosis. The ventilatory management of babies with congenital myotonic dystrophy is a serious problem that has not received much attention in published reports. We have noted a poor prognosis associated with long term ventilation and thought it would be helpful to review our cumulative experience during the past six years.

Patients

Since 1982, 14 babies with congenital myotonic dystrophy, born to 12 mothers, have been referred to this unit. Eight babies were transferred after birth for treatment of their neuromuscular condition; two were transferred in utero because problems were anticipated after the diagnosis had been made in the

Table 1 Clinical details of 14 babies with congenital myotonic dystrophy

Case No	Gestation (weeks)	Hydramnios	Poor fetal movements	Mode of delivery	Apgar score		Intubated	No of days ventilated	Result of chest radiograph	Result of ultrasound scan of head	Outcome
					One minute	Five minutes					
1	34	Yes	Yes	Emergency Lower segment caesarean section	2	6	Yes	11	Thin ribs	Ventricular dilatation	Died (11 days)
2	35	Yes	Yes	Normal vaginal delivery	2	4	Yes	112	Raised hemidiaphragm	Subarachnoid haemorrhage on computed tomography	Died (9 months)
3	32	No	?	Normal vaginal delivery	7	9	No	0	Not known	Ventricular dilatation	Alive (5.5 years)
4	34	Yes	?	Elective Lower segment caesarean section			?	16	Not known	Ventricular dilatation	Alive (5.5 years)
5	40	Yes	Yes	Normal vaginal delivery	1	7	Yes	0	Thin ribs and raised hemidiaphragm		Alive (5 years)
6	37	No	Yes	Emergency Lower segment caesarean section	1	2	Yes	0	Thin ribs	Ventricular dilatation	Alive (3.5 years)
7	34	Yes	?	Emergency Lower segment caesarean section	4	5	Yes	31	Thin ribs	Ventricular dilatation	Died (14 months)
8	38	No	Yes	Elective Lower segment caesarean section	0	3	Yes	1	Thin ribs	Ventricular dilatation	Alive (2.5 years)
9	36	Yes	Yes	Elective Lower segment caesarean section	6	7	Yes	49	Thin ribs	Ventricular dilatation	Died (14 months)
10	35	Yes	?	Normal vaginal delivery	4	5	Yes	12	Thin ribs and raised hemidiaphragm	Ventricular dilatation	Alive (2 years)
11	34	Yes	?	Normal vaginal delivery	1	5	Yes	1	Thin ribs and raised hemidiaphragm	Ventricular dilatation	Alive (22 months)
12	36	Yes	?	Normal vaginal delivery	3	5	Yes	7	Thin ribs and raised hemidiaphragm	Ventricular dilatation	Alive (7 months)
13	36	Yes	Yes	Forceps	3	7	Yes	0	Thin ribs and raised hemidiaphragm	Ventricular dilatation and subarachnoid haemorrhage on computed tomography	Alive (4 months)
14	35	Yes	Yes	Forceps	0	1	Yes	31	Thin ribs and raised hemidiaphragm	Ventricular dilatation	Died (31 days)

mother, two were seen in the outpatient department, and two were born in the unit to a mother living in this area. Three mothers had been diagnosed after the birth of a previously affected baby, and only two mothers had been diagnosed before any pregnancy. In all babies the diagnosis was confirmed by examination of the mother.

Clinical details of all 14 babies are shown in the table and a full history of one baby is documented (case 14). Fig 1 shows the typical facial features of one of these babies.

Results

All 14 babies were extremely hypotonic. Eleven were born prematurely, eight had abnormal presentations, and four had birth weights below the third centile. Thirteen babies showed signs of severe birth asphyxia with Apgar scores of 5 or less at five minutes. Ten babies had thin ribs on chest radio-

graphy, and elevated hemidiaphragms were noted in six. Ten babies required continuous ventilation after delivery; in eight of these aminophylline was used in an attempt to extubate successfully. In one baby (case 2) plication of the elevated hemidiaphragm led to successful extubation, but he died five months later from severe pneumonia. All four babies who were ventilated for over a month died. Of the babies who survived for 15 months or more the longest time that any had required ventilation was 16 days.

Twelve babies had ventricular dilatation on ultrasound scans. This was mild and non-progressive in all but one case, which was complicated by intraventricular haemorrhage. Two babies had subarachnoid haemorrhage shown on computed tomography.

Case report

Case 14. This male infant was born in our hospital at 35 weeks' gestation by forceps delivery. His 27 year old mother had been diagnosed as having myotonic dystrophy after the death of a previously affected baby. The present pregnancy was complicated by extreme polyhydramnios and poor fetal movements. Serial ultrasound scans had shown no fetal breathing. The baby was severely asphyxiated with an Apgar score of 0 at one minute. Assisted ventilation was hampered by copious thick secretions and his Apgar score was still only 1 at 10 minutes, and 4 at 20 minutes. Examination showed obvious hypotonia, immobile facies with a triangular shaped mouth, and mild contractures of the hips. Chest radiograph showed thin ribs and a raised right diaphragm (fig 2). Ultrasound examination of the head showed mild bilateral ventricular dilatation. Despite evidence of severe asphyxia the baby had no seizure activity on a continuous electroencephalogram.

The baby made minimal independent respiratory efforts and could not be weaned off the ventilator. Continued positive airway pressure was also unsuccessful. His ventilation was hampered by thick salivary secretions and recurrent episodes of pulmonary collapse and consolidation. These were treated with intensive physiotherapy and antibiotics when indicated. Screening of his diaphragm with the baby making independent respiratory effort showed little useful movement, but no paradox of either hemidiaphragm. He was given aminophylline in an attempt to wean him off the ventilator. His respiratory effort was monitored from chest electrodes and although there was an increase in the rate and amplitude of his respiratory excursions these did not lead to much improvement in ventilation. By the age of 5 weeks there was no increase in his already limited voluntary movement, and no improvement

Fig 1 Characteristic triangular shaped mouth and bilateral facial diplegia (case 8).

Fig 2 Chest radiograph showing the raised right hemidiaphragm, thin ribs, and collapse and consolidation of the right upper lobe (case 14).

to suggest that he might become independent of the ventilator. After review of the previous babies that we had treated with congenital myotonic dystrophy who had been ventilated for longer than one month the prognosis was thought to be hopeless, and after discussion with his parents it was decided to discontinue the artificial ventilation. This was done under sedation and he died soon after without distress.

Discussion

Babies with congenital myotonic dystrophy who have uncomplicated neonatal courses should survive although their intellectual development is usually poor.³ Their hypotonia improves and all children will eventually walk. Clinical myotonia does not appear until late in childhood although electromyographic myotonia may develop after the first year.² Congenital myotonic dystrophy is therefore a biphasic disease and at present there is little understanding of the aetiology of the initial hypotonia with its associated problems.

The 14 children in this group are not typical of babies with congenital myotonic dystrophy as they were obviously selected for referral because of severe hypotonia and respiratory distress. Eleven of the babies were born before 37 weeks' gestation compared with only six in Harper's retrospective

study of 60 babies.² The under representation of premature babies in Harper's study is likely to be the result of lack of intensive care facilities in the past and babies died shortly after birth before a diagnosis was made. Several authors have reported a poor prognosis associated with prematurity,^{10 11} and this fact may partially explain the difference in the outcome of the babies reported by Harper compared with our own. In our babies, however, there was no association between outcome and gestational age, and the baby who was most premature (at 32 weeks' gestation—case 3) did not require intubation at birth and now attends a normal school. The most important factor determining the severity of congenital myotonic dystrophy may be maternal as it seems that individual mothers produce babies with a similar degree of muscle disease. Cases 3 and 13 are siblings and have both done well. In case 14 the previous baby had fatal respiratory problems despite intensive care, and in the study of Silver *et al*¹⁰ three siblings all died shortly after birth.

The respiratory complications of congenital myotonic dystrophy start in utero with poor fetal breathing that results in pulmonary hypoplasia.^{12 13} Reduced fetal breathing in fetuses with muscle disease is usually attributed to muscle weakness alone. In babies with congenital myotonic dystrophy there may also be poor respiratory drive caused by an abnormal brain. We have previously reported the high incidence of ventricular dilatation present at birth.¹⁴ The effects of pulmonary hypoplasia are compounded by poor respiratory effort at birth, which seem to be caused by acute perinatal asphyxia, muscle weakness, and possibly a central neurological problem.

Assessment of asphyxia in babies with neuromuscular problems is difficult. A low Apgar score because of poor tone and poor respiratory effort does not always imply asphyxia. Heart rate alone may serve as a better guide to the extent of asphyxia and to the success of subsequent resuscitation. Although muscle biopsy specimens taken for diagnostic purposes are usually unremarkable on histological examination, poorly developed muscle has been found at necropsy, particularly in the diaphragm and the pharynx.^{10 15 16} This finding has led to the theory that there may be an arrest in fetal muscle maturation, although the cause remains unknown.¹⁶ The final factor contributing to poor respiratory effort at birth is central respiratory drive depression. In babies with abnormal muscle, and abnormal brain as indicated by ventricular dilatation, the reaction to maternal anaesthesia may be adverse. A baby with comparatively mild weakness may therefore be in poor condition at birth despite being

delivered by elective caesarean section (for example, case 8—who subsequently required only one day of ventilation).

The presence of hypoplastic ribs on chest radiograph suggests poor fetal breathing.^{17 18} Although Fried *et al*¹⁸ found that respiratory problems were more likely in babies with thin ribs on radiography, in this study this finding was not always linked to a poor prognosis. It is difficult to assess degree of hypoplasia on radiography, and therefore difficult to draw conclusions about the amount of fetal breathing that has taken place. With improved antenatal ultrasound, serial screening of fetal breathing may become a more reliable guide to prognosis, where the diagnosis has already been made in the mother.¹⁹

There may also be evidence of diaphragmatic hypoplasia as shown by a raised hemidiaphragm. This has been confirmed at necropsy in babies suffering from congenital myotonic dystrophy.¹⁰ Of interest was the fact that despite clinical evidence of bilateral diaphragmatic disease in case 14, the right hemidiaphragm was much higher on the radiograph than the left. The preponderance for right sided raising has been previously noted.²⁰ Silver *et al*¹⁰ found evidence of necrosis of the diaphragm as well as hypoplasia and postulated overstretching by intra-abdominal pressure with moulding by the right lobe of the liver to account for this sign. If one side of the diaphragm is more severely affected it may interfere with respiration by moving paradoxically. One of the babies (case 2) was successfully extubated after the plication of his right sided hypoplastic diaphragm, but he died six months later.

The therapeutic role of aminophylline in babies with congenital myotonic dystrophy is unclear. In five of our babies it may have been helpful in weaning them off the ventilator, but the effect of administration on breathing pattern was only monitored in one baby (case 14). In this baby we noted increased respiratory excursions but these were insufficient to permit extubation. Aminophylline may work by stimulating central respiratory drive or by directly increasing the strength of muscle contractions.^{21 22} Further research on the use of aminophylline in ventilatory failure in congenital myotonic dystrophy would be valuable.

This present study has been useful in highlighting the poor prognosis in babies who are continuously dependent on assisted ventilation. All four babies ventilated for over one month subsequently died even if they were eventually weaned off the ventilator. We therefore considered it reasonable in our last case to withdraw ventilation as he had made no progress during one month, and he had no paradoxical movement of the right hemidiaphragm that would have been correctable by surgery. This was

acceptable to the parents who had witnessed our many attempts to wean the baby off the ventilator. We believe our experiences may help others who have to manage this difficult problem.

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