

Pregnancy, Labour and Delivery in Myotonic Dystrophy

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Abstract

Thirty-two women older than 25 years, affected by Myotonic Dystrophy (MD or Steinert disease), were evaluated retrospectively about the course of their pregnancies, delivery and health of their son at birth.

Among 40 pregnancies we have observed 13 abortions, 6 threatened abortion, 9 preterm deliveries, 2 cases of preeclampsia and 2 of hepato-cholestasis; at delivery 9 times a dynamic dystocia occurred. Caesarean section was made 11 times; in 4 cases severe anaesthetic problems occurred.

Fetuses weight at term was in average 3250 g. Twelve of 27 fetuses developed disease precociously; one of these died within the first 24 hours. Affected sons had a number of CTG triplet repetition clearly higher than those observed in their mothers (mean 1654 ± 454 versus 665 ± 212). During pregnancy, eight of these developed a polyhydramnios that represents the most frequent cause of preterm delivery.

The entity of mother's expansion doesn't seem to influence the course of pregnancy or complication type and entity.

Key words: myotonic dystrophy, pregnancy, delivery, labour, CTG expansion.

Basic Appl. Myol. 7 (5):351-355, 1997

Reproductive function in Myotonic Dystrophy (MD) is frequently affected in male subjects [6, 7], while in female appears on the whole normally efficient [2]. We recently reported some cases that show serious complications during pregnancies such as placental pathologies [3] and polyhydramnios [13, 5].

Clinical studies on case series are few and rather dated [14]; the most recent data [8] show a high incidence of complications, especially abortion, neonatal death, polyhydramnios, retained placenta and placenta praevia.

A high risk of maternal mortality was reported, in particular in women in which the pathology was unknown, when undergoing to caesarean section for serious anaesthetic problems.

Genetic investigation has been only recently available; by this technique it is possible to make a certain diagnosis of maternal or fetal MD and also it allows to evaluate its gravity.

Material and Methods

32 women older than 25 years (range 27-62 years) affected by MD were evaluated. Diagnosis was made by DNA analysis. DNA was extracted from peripheral blood

according to standard procedures. The (CTG)n expansion was detected by Southern blotting.

Each patient was carefully asked for number and course of pregnancy, on delivery date and on baby health. Furthermore abortion and pregnancy case sheets were examined. Voluntary pregnancy terminations were excluded.

For statistical analysis the Student-*t* test and χ^2 for unpaired data were used.

Results

The (CTG)n expansion (Exp) in our patients ranged from 268 to 1550 (mean 778 ± 355 , median 750). In 6 patients it was greater than 1000, 4 of them were married.

24 out of 32 patients were married: among married women the mean expansion resulted 735 ± 362 , unmarried women showed a mean expansion of 966 ± 385 . No significant difference between the two groups was found.

19 out of 24 married patients had been pregnant. Among the other 5, 2 were affected by unexplained sterility (Exp 920, 1180), 1 was married with an azoospermic man and 2 decided to avoid pregnancy for the genetic risk of MD transmission.

Pregnancy, labour and delivery in MD

Pregnancies occurred between 1960 and 1996. Mean age of our patients at delivery was 27 ± 3 years. During pregnancy maternal symptomatology of MD were present in 11 cases.

Abnormal blastocyst implantation

In one case a tubaric abortion occurred and a salpingectomy was made.

Pregnancy length

We observed (Tab 1):

- 13 spontaneous abortions (11 in the 1st trimester and 2 in the 2nd) (Fig 1). 5 patients had threatened abortion in the 1st trimester and subsequently delivered 2 at term and 3 pre-term.
- 9 preterm deliveries (fig 2). Three patients had threatened abortion previously. Eight babies were affected by MD. Preterm delivery resulted more frequent in affected fetuses than in healthy fetuses ($\chi^2 4.219$, $p < 0.04$) such as polyhydramnios ($\chi^2 10.580$, $p < 0.001$).
- 17 at term deliveries: previously in three case occurred a threatened abortion and in a case a preterm threatened delivery.
- 1 post-term delivery at the 43rd week.

Medical disorders of pregnancy

Uncomplicate pregnancies ended in spontaneous at term delivery were 6 (15%).

During pregnancy, labour or post-partum period complications occurred in 17 patients (Fig. 3).

In 10 patients a polyhydramnios was found: this was followed by a preterm labour in 6 cases (between 32nd and 37th gestational week). Between affected fetuses 9 out of 12 (75%) developed a polyhydramnios; this is a percentage significantly higher than that observed in healthy subjects ($1/15 = 6.6\%$). Complications were not more frequent when disease were already developed.

Delivery way

Vaginal deliveries were 16 (59%), Caesarean section were 11 (41%).

In 4 cases the vaginal delivery was guided, three times vacuum extractor was necessary and two times a caesarean section was made, all for dynamic dystocia.

Caesarean section indications were reported in the table II.

Table I. Pregnancy length.

Abortions	Pre-term deliveries	At term deliveries	Post-term deliveries
11 in the 1 st trimester			
2 in the 2 nd trimester	9	17	1

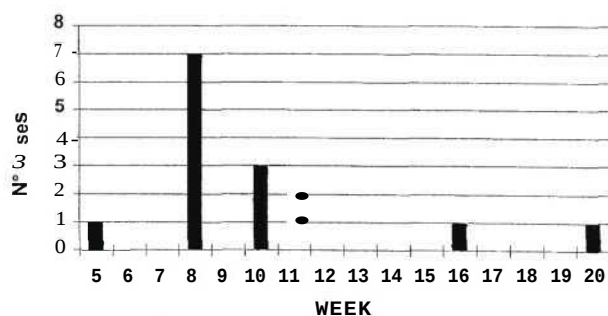


Figure 1. Abortion number in relation to gestational age.

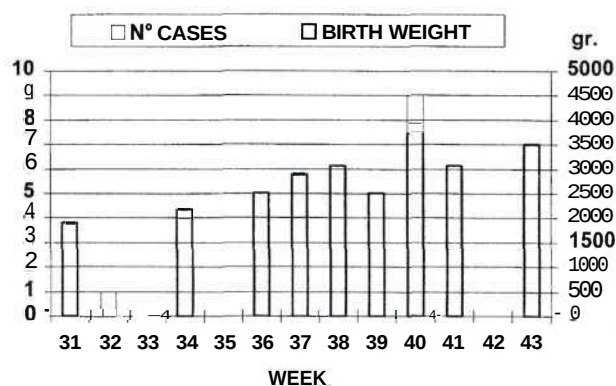


Figure 2. Gestational week at delivery and the birth weight are shown. The affected fetus delivered at 32nd gestational week, died in the first 24 hours: his birth weight and his expansion are unknown.

Abnormalities of the 3rd stage of labour

In a patient placental delivery was incomplete (and a curettage was made); in all other cases it was spontaneous and apparently complete.

Anaesthesia in obstetrics operations

General anaesthesia was made in 10 cases, spinal anaesthesia in one case.

The newborn

Birth weight in newborns at term was 3205 ± 519 g.; in three apparently physiological pregnancies, the newborns at term showed a light growth retardation (weights 2520, 2500, 2750 g), one of these babies resulted affected by MD.

A premature baby, delivered at 32nd week, showed the stigmas of congenital MD and he died in the 1st 24 hours.

In our case series 12 out of 27 fetuses were affected by congenital MD; their Exp was 1654 ± 454 in average, always higher than their mother (Tab. HI). No correlation was found between mother and son expansion.

Discussion

Certainly our study is limited by the fact that collection data was based on retrospective analysis of case sheets which resulted frequently incomplete. Their compilation, in fact, was not aimed to study the relationships between MD and pregnancy, but on actual clinical problems of the single clinical MD patient. Surprisingly in most patients the diagnosis was made subsequently at pregnancy.

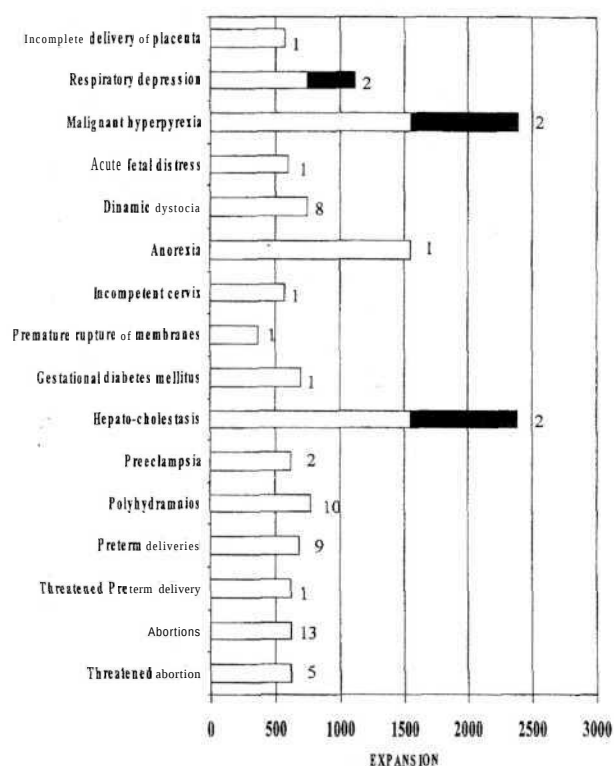


Figure 3. All complications occurred in our case series during pregnancy, labour and post-partum period and the median of the expansion for a number of cases equal or more than 3, the single expansion for one or two cases are reported. The number of cases is indicated near the band.

We haven't sufficient data to evaluate the muscular symptomatology during pregnancy; we don't know how much labour lasted and we haven't informations about the modality of uterine contractions. It is also possible that complications are underestimated and particularly some lethal complications may be escaped, even if the family investigation excludes this possibility. However it isn't easy to collect a personal case series on the pregnancy course of women affected by a rare disease, especially if symptomatology appears in the adult age and if it can be ignored for a long time.

Furthermore we tried to make a careful research combining a detailed history and clinical sheets examination. The determination of CTG expansion both in mothers and in the majority of sons allowed us, for the first time, to evaluate a case series with a certain diagnosis and to study

Table III. Behavior of affected fetuses pregnancies.

	Mother Exp	Week at delivery	polyhydramnios	Fetus Exp
1	624	36	absent	-
2	600	36	absent	1677
3	570	38	absent	1700
4	743	36	present	1576
5	814	37	present	1300
6	365	31	absent	750
7	400	36	present	1370
8	400	32	present	-
9	1036	34	present	1909
10	833	36	present	2154
11	895	39	present	2300
12	700	38	present	950

In table III was reported data on Exp of mothers than delivered affected fetuses, Exp of their fetuses, gestational week at delivery and presence of polyhydramnios.

the influence on pregnancy and delivery of various degree of mother and fetal disease.

In 1985, in his retrospectively case series (102 pregnancies), Harper [4] found a high percentage of abortion, neonatal deaths, altered placental delivery, placenta praevia and Caesarean sections.

Our data, for a large part, are in agreement, but show also some important differences. We found a single case of neonatal death compared to 12% of Harper's study, probably for the general improvement of delivery and neonatal assistance during recent years. In our case series deliveries occurred especially after 1975, while in Harper's series before.

We believe that the more frequent use of Caesarean section (41% against 11% in Harper's series) and of oxytocin can explain the lower incidence of incomplete delivery of membrane. We did not find any patient suffering from placenta praevia while it occurred in 6% in Harper case series; we believe that this difference is casual.

We found a high incidence of preterm deliveries (33%) that Harper describes more rarely. This difference may depend on criteria that we used to define this aspect (delivery at 37th gestational week or before) and/or on the possibility to have precise data by case sheet examination.

Table II. Caesarean section indications.

PROM	dinamic dystocia	pre-eclampsia	poly-hydramnios	breech presentation	post-term pregnancy	"myotonic dystrophy"
1	2	2	3	1	1	1

Only 6 of 40 pregnancies had had an uncomplicated course and resulted in a spontaneous at term delivery; furthermore pregnancy in MD shows frequently problems caused by various conditions.

A first pathogenetic factor may be the uterine smooth musculature that physiologically is capable of contractions obviously important in the course of pregnancy and still more active during labour and delivery. MD involves not only striated muscle but also heart and smooth muscle and therefore we believe that also uterine contractions may be altered.

Shore and MacLachlan [12] studied elettromyographically non pregnant uterus and they found incoordinate contractions. Sciarra and Steirr [11] documented manometrically abnormal uterine contractions during labour with a delayed relaxation phase. This alteration is analogous to what happens in striated muscle: the so called "myotonic phenomenon", characteristic sign of disease, consists on inability to obtain relaxation after contraction. Naturally a correct alternation of contraction and relaxation is necessary to obtain either a pregnancy and a labour physiological course.

We believe that the altered uterine contraction activity may be the cause of the threatened abortions (5 cases = 19%), preterm deliveries and dynamic dystocia (9 cases = 33%), which in some cases made Caesarean section and oxytocin or vacuum extractor use necessary.

A second factor could be represented by the possible fetal disease. MD is a dominant disease, homozygote forms are unknown and therefore we can expect a 50% of vertical transmission. The triplet instability, perhaps during the post-zygotic phase, determines a greater genetic defect in the children of an affected mother ("anticipation") who inherits a more serious illness. Anticipation was found also in our case series. Whereas it is possible that the first symptoms of disease can appear already during the fetal life and can condition the pregnancy course.

Certainly the fetal disease is the most important cause of polyhydramnios that we found frequently in MD (10 cases = 37%) compared to the general population (1%) and nine times involved affected fetuses.

Polyhydramnios generally depend on an altered swallowing, likewise in anencephalic fetus, or on heart or renal failure. In MD an abnormal swallowing has been documented and it is due to striated and oesophageal muscle involvement.

In more than half of polyhydramnios a preterm delivery occurred, probably induced by an uterine hyperextension. Therefore fetus disease is the most frequent reason of preterm delivery.

Polyhydramnios required sometimes Caesarean section for respiratory problems induced by a diaphragm elevation.

Finally fetal illness was the reason of the only neonatal death that we found.

Our data confirm a high incidence of abortions 32% (13/40) versus 15-20% observed in general population, frequently in the first trimester.

We want to underline that 4 out of 10 cases submitted to Caesarean section with general anaesthesia suffered from serious complications: 2 cases of malignant hyperpyrexia followed by heart failure and 2 cases of marked respiratory depression which required mechanical ventilation.

These represent serious and known complications [10-9] induced not by pregnancy but by anaesthetic drugs administered during surgery. All these 4 patients already showed muscular symptomatology, but their disease was still ignored and the diagnosis was made only after surgery.

We therefore conclude that in at risk cases it is necessary to avoid administration of depolarizing muscle relaxants and anticholinesterase agents and it seems advisable to make a spinal or peridural anaesthesia [1].

We failed to demonstrate a relationships between the entity of the expansion and pregnancy and delivery complications even if the patient with higher expansion, showed hepato-cholestasis and, after caesarean section, malignant hyperpyrexia followed by cardio-circulatory arrest.

In conclusion pregnancy in MD women is possible even if frequently it shows complications such as abortions, preterm deliveries and dynamic dystocia.

A large part of these depend from fetus illness, that actually may be diagnosed by amniocentesis. These complications don't make inadvisable pregnancy. Furthermore it must be carefully followed, monitoring uterine activity, fetal movements and amniotic fluid volume.

Anaesthesiological problems must be taken in a great attention since anaesthesia can provoke potentially lethal risks. It's to avoid some drugs and also the Caesarean section indication must be carefully weighed.

Diagnosis may be problematic because muscular symptomatology can begin at different age, in the less serious forms after pregnancy, and therefore may be unknown.

It's also important that when a subject affected by Steinert disease is recognized in a family, all relatives (especially younger) are examined and it is useful to make a genetic study in order to carefully follow pregnancies and to offer to the couple a genetic counsel.

Acknowledgements

This paper was supported by Telethon grant n° 640.

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