DUCHENNE'S MUSCULAR DYSTROPHY: SOCIORELIGIOUS BELIEF DELAYS DIAGNOSIS AND GENETIC COUNSELLING

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SYNOPSIS

Two maternally related stepbrothers with Duchenne's Muscular Dystrophy (DMD) are described. The elder brother was diagnosed only at the age of 10; the younger brother aged 5, was diagnosed on a routine screening of all the proband's siblings. Maternal family studies revealed that the disease was transmitted in an X-linked recessive manner, and that it had also affected a large proportion of the males in the previous generation all of whom died before the age of 18. None had been previously diagnosed.

A witchdoctor's curse apparently cast on all mal offsprings three generations earlier had been long believed by the family to be responsible for the deaths. No child had therefore been seen by a doctor prior to the inevitably delayed diagnosis of the condition in the proband.

The genetics and social conditions affecting the extended family are discussed and the difficulties of early case detection and genetic counselling in the rural context are highlighted.

INTRODUCTION

DMD is an X-linked recessive disorder affecting only males and transmitted by females. It is perhaps the commonest form of chronic neuromuscular disorder of childhood with an incidence of between 1 in 3000-5000 live births (1). The condition may be characterised by delayed walking in a child, and is often followed by symptoms of proximal muscle weakness around 5 years of age with a progressive loss of ambulation thereafter. Impaired intelligence is now also a well recognised feature of the disease. Death is usually due to respiratory or cardiac complications often before the age of twenty.

Because of its relatively late onset of symptoms, it is not unusual to have more than one affected child in the same family. Between 13-18% of children with DMD are born into families in whom there is already an affected child who has not been diagnosed (2, 3).

This paper describes an unusual family in which at least 7 out of 10 males were affected over two generations and where diagnosis had been inevitably delayed by a family belief in a wtichdoctor's curse laid on the proband's maternal greatgrandfather three generations previously.

CASE REPORTS

Case 1

A 10 year old Malay boy was brought to hospital by his grandparents for entry assessment into a handicap centre because he could no longer be cared for in his rural home. He was found to be of below average intelligence with marked wasting of his pelvic, shoulder girdle and proximal limb muscles. He could not stand or walk. Pseudohypertrophy of the calf muscles was marked. There was a history of delayed walking in early childhood. The serum creatine kinase (CK) was markedly elevated at 10,860 iu/L (Normal 24-170 iu/L) and muscle biopsy was consistent with a diagnosis of DMD. ECG showed evidence of left ventricular strain. Electromyographic studies were not done.

Case 2

Case 2, the 5 year old maternal stepbrother of the proband was 'discovered' on clinical and CK screening of all siblings. He started walking only at the age of 3 and at the time of diagnosis he was having difficulty in rising from the chair. He walked with a marked waddling gait and employed Gower's manoeuvre (climbing hands on legs) in rising from a lying to a standing position. The proximal muscles of the lower limbs were wasted as were those of the pelvic and shoulder girdles. He was also of below average intelligence. The serum CK was 4480 iu/L and muscle biopsy showed changes compatible with DMD. ECG was within normal limits.

THE FAMILY HISTORY

The above cases had a common mother. The maternal family tree (Figure 1) was constructed from independent interviews with the proband's maternal grandfather and grandmother who had no prior knowledge of the disease or its mode of inheritance.

The grandmother was confirmed to be an asymptomatic carrier on the basis of a raised serum CK — 446 iu/L. The proband's mother must also be a carrier although her CK was normal. Normal CK in a carrier is not unusual; around 35% of all carriers do not have an elevated serum CK level (4). All other living members of the family who were investigated were clinically normal and had normal serum CPKs, except the proband's stepsister (Fig. 1 — IVb) who although clinically normal and asymptomatic had a raised serum CK (249 iu/L).

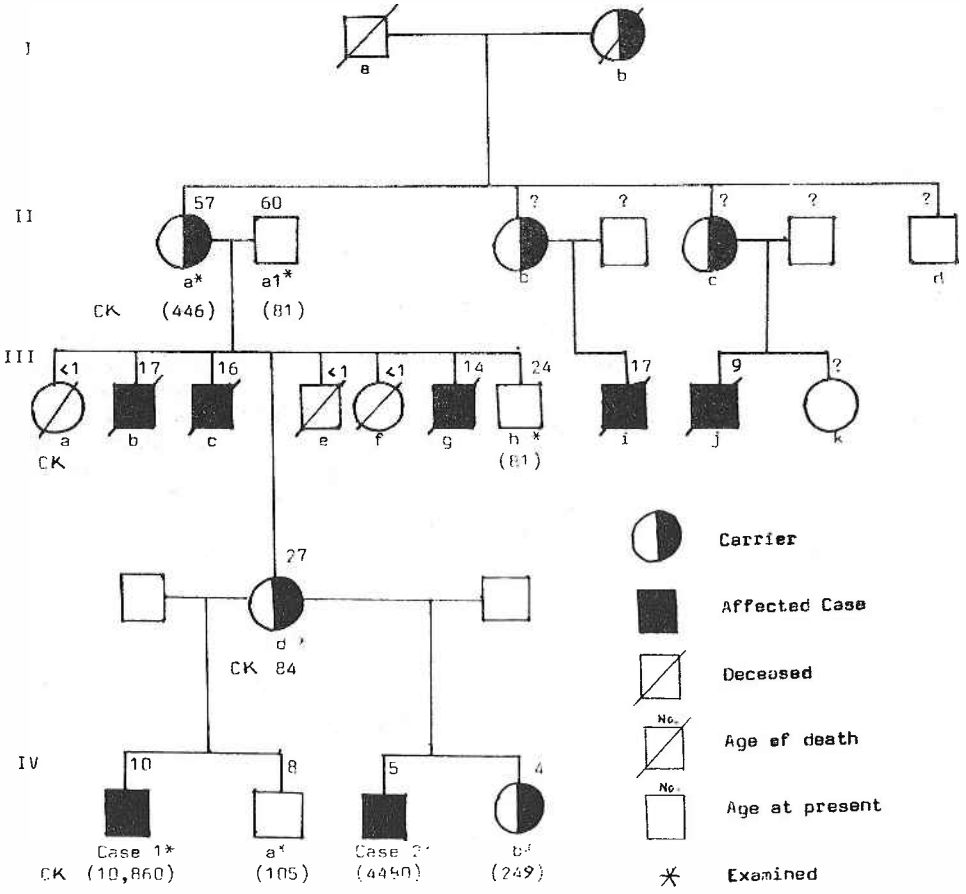

FIGURE 1 THE FAMILY TREE

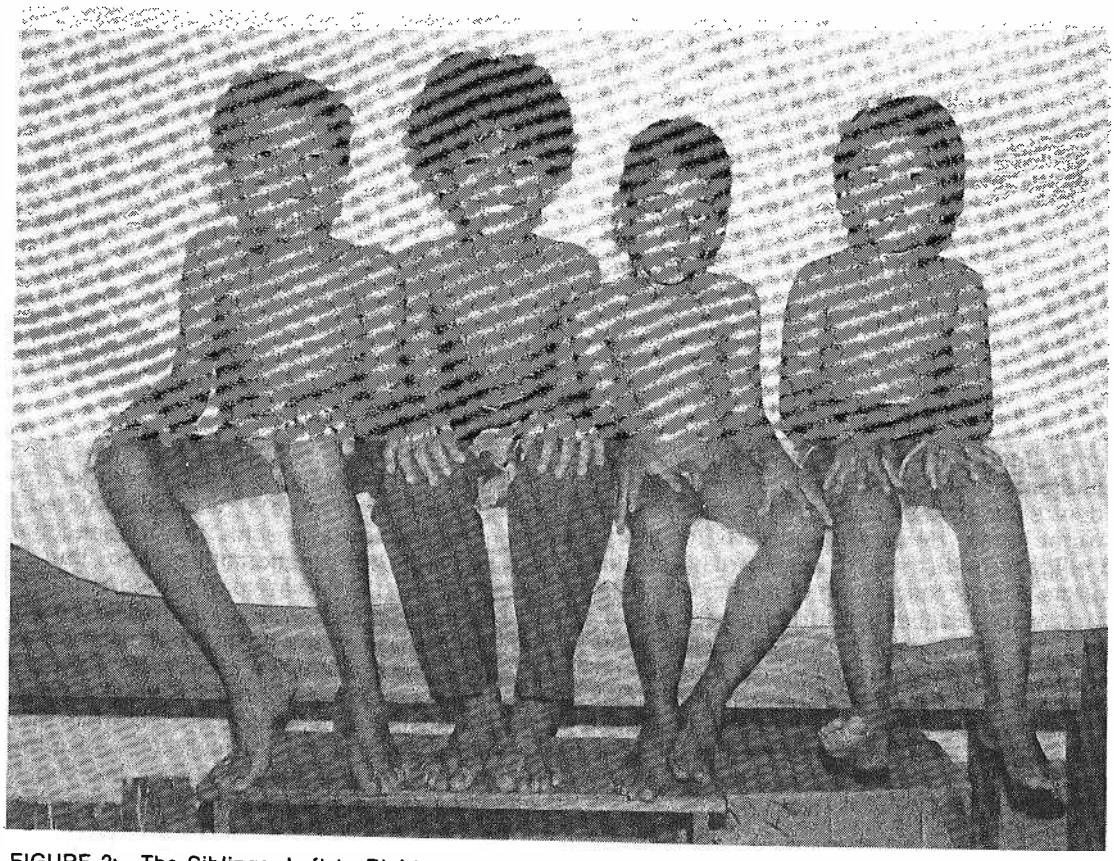

FIGURE 2: The Siblings: Left to Right — Case 1 (Proband); his brother IVa (Normal), his stepbrother Case 2, and his stepsister IVb (Carrier)

The diagnosis of DMD in any deceased offspring was based on affirmation from the grandparents of at least four out of the following six easily observable criteria in the deceased's history.

i) Delay in walking during early childhood.
ii) Waddling gait as a child.
iii) Difficulty during childhood in rising from chairs, squatting positions, etc.
iv) The repeated use of Gower's manoeuvre in rising from a recumbent position at some point in the child's history.
v) Wasting of pelvic and shoulder girdle and proximal limb muscles.
vi) Eventual inability to walk by the age of 12.

The grandparents were unable to give the precise cause of early death in nearly all cases as none of the affected offsprings had been seen by a doctor.

DISCUSSION

1.Genetic and Social Consideration

In this extended kindred study the defective X-linked gene was transmitted by the proband's great maternal grandmother (Ib) who must be a carrier, to all her daughters who became carriers (IIa, b, c — Fig. 1) Genetic counselling would not have been possible at this stage as the carriers would have been clinically undetectable. The only male offsprings in this generation was normal (IId).

The defective gene however manifested itself in the following generation (III); at least 5 out of a total of 7 males born to the three daughters were affected and died before the age of 18. The fact that diagnosis was not made in this generation despite the large number of affected children is the outstanding and most tragic feature of this extended family history.

The proband's grandparents related that because of a severe misdemeanour by the proband's greatgrandfather (Ia) over half a century ago, a curse had been out on the latter by the village witchdoctor ("bomoh") to the effect that subsequent male offsprings in the family would be "weak" and would die early. This curse was secretly believed and feared by the proband's grandparents (IIa, a_1) and when their male offsprings (generation III) became physically afflicted, no attempt was made to take them to the doctor or a rural hospital; they were in fact kept at home and sheltered from society. While poor health screening facilities have been reported as being responsible for delay in diagnosis of DMD in a rural family (5), we believe this is the first reported case of delay in the diagnosis of DMD due to a socio-religious taboo.

All the offsprings of generation III were born within a span of some 8 years. The proband's grandparents recall that a walking abnormality was only first noticed at the age of 5 in the second child (IIIb) — the first child (IIIa) having died in infancy. By this time most of the other offsprings would have been born and genetic counselling of the grandparents would have been too late. The social tendency for rural inhabitants to have large families in a short space of time may therefore severely limit the benefit of genetic counselling.

A similar case of 6 out of 7 affected male children

with DMD has been reported in a rural African family by Moose and also emphasises this problem (5).

The only surviving female from generation III was the proband's mother who was a carrier (IIId). Because the proband was mentally and physically retarded, this was a source of domestic stress and contributed to the breakup of the mother's first marriage. The proband was sent to live with the grandparents and the mother remarried. The tragedy repeated itself in the birth of a second affected male child (Case 2). This second marriage also ended in a separation. That early genetic counselling might have prevented this tragedy is obvious, yet because of the circumstances of the case, diagnosis was delayed and counselling was too late to be of benefit to the mother.

In female carriers, the risk of giving birth to an affected child is 1 in 4. This risk applies to each pregnancy and is not meant to be the risk distributed throughout the total number of children. Both the proband's mother and grandmother were unfortunate in this respect. Despite the odds, the mother produced two affected males and the grandmother 3 affected males. This is of course meant to reflect the randomness of genetic assortment in meiosis and not the potency of any witchdoctor's curse although understandably it may be hard to convince rural folks that this is so.

The final caveat in this study is that although the proband's step-sister (IV b) may at present be clinically normal, her raised serum CK suggests that she is a carrier. Close follow-up and repeat measurement of her CK levels will be necessary. Genetic counselling will need to be given in the future if the myth of the witchdoctor's curse is to be broken.

ii) Prevention

Theoretically, neonatal screening of new born males using Antonik's method of serum CK analysis on a drop of blood might have been useful in early diagnosis in generation III and therefore prevent the birth of the affected males later. But this method was not available at that time. Even if it was, interpretation of an elevated CK for example, in the first affected newborn in the absence of a history of an affected male at that stage would have been fraught with uncertainties because false positives are common. It might however have been usefully employed in the early diagnosis of the proband (generation IV) if the family history was available at his birth. The proband's mother would then have been diagnosed as a carrier much earlier and could have received genetic counselling. The pros and cons of a neonatal screening programe for DMD in developed countries is still a matter for debate (6, 7, 8), but in rural situations where home delivery is largely still the norm, it would be a difficult programme to initiate. There is however little doubt that the earlier the diagnosis is made, the more helpful and relevant the genetic counselling that can be given.

It can be seen that the strong belief in a socio-religious taboo had prevented any medical diagnoses in generation III. Had this not been so, an earlier diagnosis could have been made and genetic counselling could have been given to the proband's mother. The subsequent pregnancies and tragedy in the proband's generation might then have been avoided. This is in theory at least. In practice it is difficult to be sure. Rural traditions are powerful factors and often the socio-economic importance attached to the production of offsprings may over-ride any parental concern that the children may turn out abnormal. Genetic advice may therefore be given but there is no guarantee that the parents will heed it (6); indeed in a rural situation it is often likely that they will not. This problem presents a strong case for persistence and patience in genetic counselling.

CONCLUSION

This paper highlights the tragedy that DMD can bring to an extended family and the need for prevention by early diagnosis, carrier detection and genetic counselling. Traditional socio-religious belief about the disorder may delay all these measures.

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