Myotonic Dystrophy and Polycystic Disease of the Kidneys

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In families with myotonic dystrophy various abnormalities have been described both in affected patients as well as in apparently unaffected members of these families (Bell, 1947; Caughey and Barclay, 1954; Klein, 1958; Caughey and Myrianthopoulos, 1963; Pruzanski, 1965). The present report concerns a family with myotonic dystrophy in which three affected sibs also had polycystic disease of the kidneys (Fig.). This association has apparently not been described previously.

The Family Studied

The proband is III.9 (N.L.), aged 44, the eldest of five children. At the age of 31, on both clinical and radiological grounds, she was found to have bilateral polycystic kidneys. Three years later, evidence of myotonic dystrophy was discovered. The muscle disease has progressed, but at the age of 44 she is still able to work as a clerk. Her blood pressure is 180/110 mm. Hg, but there is no albuminuria and renal function is good. She is unmarried.

III.10 (E.L.), aged 42, refused to be seen. Her relatives say that she is quite healthy.

III.11 (W.L.) is aged 41. At the age of 26, symptoms of myotonic dystrophy developed and have since progressed, but she is still able to work as a clerk. She is unmarried. Her renal function is good and her kidneys are not palpable. However, an intravenous pyelogram revealed bilateral polycystic kidneys. Her blood pressure is 150/90 mm. Hg.

III.12 (F.L.), aged 38, is a schoolmaster. Symptoms of myotonic dystrophy developed at the age of 31, and he is now severely afflicted. He has some frontal balding and rather small testes. Clinically and radiologically there is no evidence of polycystic kidneys and his blood pressure is 140/80 mm. Hg. His wife has been pregnant on 12 occasions with 6 miscarriages and six living children IV.11-16. The eldest child IV.11 is 12 and has some slight myotonia in her left hand. The remaining children are less than 10 years old and at present appear to be normal on clinical examination.

III.13 (J.L.), aged 36, has moderately severe myotonic dystrophy and bilateral polycystic kidneys both clinically and radiologically, with a blood pressure of 170/120 mm. Hg and a blood urea of 45 mg./100 ml. He is balding, and has small, soft testes. His wife has never been pregnant.

C.L. is the father of this family of five. He is now aged 70 and is fit and well. His blood pressure is 180/80 mm. Hg. There are no signs or symptoms of any neuromuscular disorder and no evidence of cataracts. His right kidney is just palpable but normal. His urine is normal. He refused an intravenous pyelogram. His own family consists of his parents and 8 sibs, most of whom are now dead or could not be traced, but none appears to have had any kidney or muscle disorder.

The mother of the family and wife of C.L. is II.5 (A.L.). She died at the age of 57 in 1951, 5 days after being admitted to hospital as an emergency. On admission she was uraemic with a normal blood pressure. Her blood urea was 700 mg./100 ml. but fell to 400 mg./100 ml. following intravenous fluids. Her kidneys were not palpably enlarged on clinical examination. Unfortunately a necropsy was not performed. No mention was made by her medical attendants at the time of her final illness of any apparent neuromuscular abnormality. Thus it appears that though she obviously carried the gene for myotonic dystrophy she did not have any clinical manifestations of this disease. She died of uraemia possibly as a result of polycystic disease of the kidneys.

II.3 (C.B.), a sister of II.5 (A.L.), died at the age of 73 from heart disease. There was no evidence that she had ever suffered from muscle weakness or kidney disease. In the last years of her life her vision deteriorated and her family believed she had cataracts. She had four sons III.5-8, one of whom (III.7) died in infancy after a scald. The eldest son (III.5), now aged 54, had a coronary thrombosis in 1957. His blood pressure at present is 180/115 mm. Hg. There is no suggestion of muscle disease and an intravenous pyelogram was normal. He has one daughter aged 28 who is healthy.

III.6 (J.B.), aged 52, developed symptoms of myotonic dystrophy at the age of 47 and is now greatly incapacitated and has had to give up his clerical job. He has not desired or had sexual intercourse for some

FIG. Pedigree chart.

years. He has three daughters, twins aged 16 and one aged 13. His blood pressure is 115/80 mm. Hg and there is no radiological or clinical evidence of polycystic kidneys.

The youngest son III.8 (H.B.), aged 46, is perfectly healthy and had a normal intravenous pyelogram. He has four children aged 1 to 9 years who all appear to be healthy.

II.2 (aged 85), II.4 (aged 73), and III.3 (aged 40) have been examined and no evidence of any neuromuscular abnormality or of polycystic disease of the kidneys was found. II.1 died at age 50 with bronchopneumonia but does not appear to have had myotonic dystrophy.

III.1 and III.2 died in infancy and III.4 at the age of 38 from carcinoma of the bronchus.

Both I.1 and I.2 died many years ago, I.1 at the age of 44 and I.2 at the age of 48. I.1 died from an 'abscess on the liver' and I.2 from pneumonia. No further details are known.

Discussion

Myotonic dystrophy is characterized by wasting and weakness of the distal musculature, myotonia, cataracts, mental dullness, and in the males frontal baldness and testicular atrophy. It is inherited as an autosomal dominant trait (Bell, 1947; Maas and Paterson, 1950; de Jong, 1957; Lynas, 1957; Klein 1958, 1961; Caughey and Myrianthopoulos, 1963).

There have been numerous reports of various abnormalities in both affected and unaffected individuals in families with myotonic dystrophy (Bell, 1947; Caughey and Barclay, 1954; Klein, 1958; Caughey and Myrianthopoulos, 1963; Pruzanski, 1965). Such abnormalities have included hare-lip

and cleft palate, congenital heart disease, neurofibromatosis, spastic paraplegia, amyotrophic lateral sclerosis, mental retardation, deaf mutism, epilepsy, certain limb deformities, including syndactyly and talipes, and eye defects such as microphthalmos, colobomata, and optic atrophy. It has been suggested that women with the fully developed disease are especially liable to have children with one of these defects (Bell, 1947; Caughey and Barclay, 1954).

Though it appears to be generally accepted that a significant proportion of patients with myotonic dystrophy are mentally retarded (Walton and Natrass, 1954; Barwick, Osselson, and Walton, 1965), it seems possible that some of the other reported associations may have been fortuitous. It is difficult to believe that all these abnormalities represent manifestations of the same pleiotropic gene. Henke and Seeger (1927) appear to have been the only investigators to compare the incidence of congenital abnormalities in families with myotonic dystrophy with the incidence in control families and they found no significant difference. Despite frequent reports of congenital abnormalities in families with myotonic dystrophy, the simultaneous occurrence of this condition and a specific, apparently *unrelated* abnormality (thus excluding mental retardation and various endocrine dysfunctions (Caughey and Myrianthopoulos, 1963)) in *more than one* member of a particular family has been described in only a few instances. Fleischer (1918) described two members of a family who both had congenital deformities of the hands and feet as

well as myotonic dystrophy; Klein (1958) described myotonic dystrophy and bilateral cleinocamptodactyly in cousins; and Bell (1947) cites a family in which microcephaly and possibly myotonic dystrophy were present in sibs, and another family in which a father and son both had myotonic dystrophy and a congenital anomaly of the eyelids. In the family studied by Heathfield and Miller (1965) a man with myotonic dystrophy and spastic paraplegia had two sons with spastic paraplegia but so far no evidence of myotonic dystrophy. In all other reports of congenital abnormalities in families with myotonic dystrophy either the reported abnormality was found in only one person in the family (affected or apparently unaffected) or in two persons in a family but only one of them had myotonic dystrophy.

With regard to the association of polycystic disease of the kidneys and myotonic dystrophy, Dalgaard (1957) in his monograph on polycystic disease of the kidneys referred to the occasional association with 'muskulo-skeletal abnormalities' but no details were given. However, that type of polycystic disease of the kidneys which presents in adult life is usually inherited as an autosomal dominant trait (Osathanondh and Potter, 1964), and it is possible that in this family the two diseases were inherited independently since careful examination of subjects with myotonic dystrophy and their unaffected sibs in another branch of the family revealed that none of them has polycystic disease of the kidneys. The apparent association of the two conditions may, therefore, be fortuitous. However, at present it is not possible to resolve the question as to whether an observed association with myotonic dystrophy is fortuitous or not until more is known of the underlying biochemical abnormality and pathogenesis of this disease.

Summary

A family with myotonic dystrophy is described in which three affected sibs also had polycystic disease

of the kidneys. Apparently this association has not been described previously.

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