Myotonic dystrophy, syringomyelia, and 2/13 translocation in the same family

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SUMMARY The present report describes a sibship with 2 individuals affected by myotonic dystrophy and a third with syringomyelia. The mother was affected by myotonic dystrophy. A balanced 2/13 translocation was detected in the individual with syringomyelia, in one affected by myotonic dystrophy and in their clinically normal father. The association between the phenotypic anomalies and the chromosome alteration is coincidental.

Myotonic dystrophy (MD) is an inherited disorder which depends on an autosomal dominant gene, the expressivity of which varies both in the age of onset and in the severity of symptoms (Klein, 1958). It starts in adolescence or early adult life with myotonia. The fully developed disorder is characterized by muscular atrophy and weakness, cataract, mental defect, frontal baldness, hyperostosis cranii, and certain endocrine disorders, such as gonadal atrophy. Sensitivity is not usually altered, but some reports refer to a decreased sensitivity of the extremities (Rossolino, 1902; Maas and Peterson, 1950; Weingarten and Gerstenbrand, 1958). The only cases of typical syringomyelia associated with myotonic dystrophy were reported by Weingarten and Gerstenbrand (1958) in a family with 4 individuals affected by both disorders.

Cytogenetic findings in individuals affected by myotonic dystrophy are not consistent. Fitzgerald (1962) reported that 5 out of 7 patients were mosaic, with normal cells and cells with an additional small acrocentric chromosome. Mutton and Gross (1965) found chromosome alterations in 5 of 12 patients: a female with a deletion of the short arm of a G, another with a deletion of the short arm of a D, and a presumptive mosaic 46,XX/45,X; the remaining 2 males showed a high frequency of chromatid and isochromatid gaps and breaks. No significant chromosomal anomalies were detected in the series of 8 patients described by Jackson (1965),

in 2 patients reported by Cecchini *et al* (1970), or in 10 patients studied by one of us (Levisky, in preparation).

Case reports

Case III.43. The proband (D.S. 170551) (III.43, Fig. 1) was affected by myotonic dystrophy. When he was 8, flexion and extension of hands became impaired. The facies was typical: mouth always open, flapping ears, incipient baldness. The electromyogram was typical of myotonia. At slit-lamp examination, corneal and anterior segment alterations were not seen; discrete anterior and posterior subcapsular polychromatic opacities of the lens in both eyes were present. The patient was mentally deficient, with an IQ inferior to that of a 5 year-old child (Infantile Raven Test). Genitalia were normal. Serum CK activity was normal.

Case III.42. The proband's brother (E.S. 070544) (III.42, Fig. 1) was affected by syringomyelia. When he was 7, he developed slight difficulty in flexing his left fifth finger, mainly in cold weather. Weakness, slight wasting, and a decrease of sensitivity in his left hand were observed when he was 14. At present the patient complains of decreased sensitivity and wasting in his left foot. When he was 22, he was unable to flex, extend, adduct, abduct, and oppose his fingers; there was diminished muscular strength in the left hand and in the left forearm, decrease of tactile sensitivity in the superior limbs, trunk, neck, inferior third of the face, and in the internal side of the distal third of the lower right limb. Electromyogram showed degeneration of all nerve fibres of the muscles in the left hand that were examined; degeneration of some nerve fibres of the superficial flexor of the

Fig. 1. Pedigree of the propoitus.

left hand fingers; involvement of various nerve fibres of the right hand muscles; discrete peripheral involvement of other muscles of the upper left limb, and distal involvement of the upper right limb. Myelography revealed enlargement of the spinal canal at the lower cervical region. X-ray film showed cervical hyperlordosis and platibasia; open posterior arch of the atlas; dorsal kyphoscoliosis with rotation of the dorsal vertebrae. The electroencephalogram was normal. In 1971 he was submitted to a craniotomy of the posterior fossa and laminectomy C₁ and C₂. Syringomyelia, arachnoiditis process of the posterior fossa, and discrete Arnold-Chiari malformation were found.

Case III.47. The propoitus' sister (S.S. 070459, III.47, Fig. 1) was affected by myotonic dystrophy. At the time of birth (after seven months of pregnancy) she was hypotonic. There was a deficit of neuropsychomotor development: she sat at the age of 1½ years and walked when she was 2. Difficulty in flexing and extending the hands was noticed when she first tried to hold objects. The facies was characteristic, with open mouth and flapping ears. The electromyogram was typical of myotonia. Slit-lamp examination did not show anything abnormal. Genitalia were normal. Serum CK activity was normal. She had severe mental deficiency.

Case II.8. The propoitus' mother (M.S. 130326, II.8, Fig. 1), was affected by myotonic dystrophy. Besides the 3 affected children she had 2 stillbirths and 1 abortion. The first symptoms started with difficulty in opening and closing her hands at 36 years of age. The electromyogram was typical of myotonia. At slit-lamp examination no corneal or anterior segment alterations were observed; discrete anterior and posterior subcapsular polychromatic opacities of the lens were present. Electroencephalogram was normal. CK level was normal. X-ray of the cranium showed diffuse osteoporosis. She had severe mental retardation.

Cytogenetic investigations

Chromosome analysis was performed on peripheral blood leucocytes, and the procedure of Caspersson *et al* (1971) was used to obtain Q-band patterns.

Individuals II.7, III.42, and III.43 showed a karyotype with 46 chromosomes, in which a D group chromosome had an increased long arm and a No. 2 was replaced by an almost metacentric chromosome, about the size of the chromosomes in the C group. The fluorescence pattern on the proximal two-thirds of the long arm of the long acrocentric corresponded to that on the long arm of a chromosome 13, and the distal one-third of its long arm showed a pattern similar to that on the distal third of the long arm of a No. 2. The banding pattern of the other abnormal chromosome was similar to that on the short arm and proximal two-thirds of the long arm of a No. 2 (Fig. 2).

The abnormal chromosomes were interpreted as resulting from a translocation between the long arms of a No. 2 and a No. 13. The breakpoints were probably localized on band 4 of region 1, on the long arm of No. 2, and on band 4 of region 3, on the long arm of No. 13. The chromosome constitution of these individuals may be written: 46,XY,t(2;13)(2pter→2q24::13q34→13qter; 13pter→13q34::2q24→2qter).

Twelve other relatives of the propoitus, including his sister affected by myotonic dystrophy, had a normal karyotype (Fig. 1).

Discussion

The translocation here described occurs in clinically normal individuals, one with syringomyelia and a third affected by myotonic dystrophy. Two individuals affected by the dystrophy have a normal karyotype. It is, therefore, concluded that the chromosome rearrangement is balanced and its association with the phenotypic anomalies is coincidental. Apparently balanced translocations involving chromosome No. 2 and a D group chromosome have been reported (Lisco and Lisco, 1967; Wurster *et al*, 1969; Davidson *et al*, 1970). In the reports of Reisman and Kasahara (1968) and Genest *et al* (1971) congenital anomalies were associated with the chromosome rearrangements in a way which suggests that the latter were unbalanced. Ricci *et al* (1968) described a malformed child with partial monosomy D and partial trisomy 2, whose

FIG. 2. Q bands: the translocated chromosomes der(2) and der(13), and their normal homologues, in the brother of the probandus (III.42).

mother was a balanced carrier of a 2/D translocation.

The relation between syringomyelia and myotonic dystrophy is not clear. In the family here reported the only individual with syringomyelia did not present myotonic dystrophy. Apparently the three individuals with myotonic dystrophy did not have syringomyelia, but the precision of the sensitivity test was not satisfactory because of their mental deficiency. Weingarten and Gerstenbrand (1958) observed the occurrence of both disorders in each of 4 sibs and suggested a varied expression for the myotonic dystrophy gene, without, however, discarding the possibilities of casual association or a new hereditary disorder.

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