D/D Translocations in Males Examined for Military Service

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Summary. Three males with Robertsonian translocations were found in a sample of 1115 males examined for military service. One was a 14/15 translocation, and two were 13/14 translocations. One was spontaneous and two familial. The segregation rate of the translocations did not deviate significantly from unity in the sibships where the mother was the carrier, whereas all five children had the translocation in the two sibships where the father was the carrier. There were no abortions and no aneuploid chromosome abnormalities in the progeny of carriers with D/D translocation. There were no indications of any association between the D/D translocations and physical or mental development.

The ascertainment bias in most cases of previously published D/D translocations makes it difficult to calculate risk of non-disjunction and abortion in D/D carriers.

We have studied three males with D/D translocation found among Danish males examined for military service.

Material and Methods

Examination for military service is compulsory in Denmark. All males are registered for this examination, and all but severely handicapped persons are required to be examined at a mean age of 19.

The present study comprises a representative sample of all males registered to be examined for the first time for military service during spring 1969 and autumn 1970 in one (no. 4) of the seven areas which make up the distribution of Denmark as far as examination of males for military service is concerned. Area no. 4 with a population of 781,753 in 1965 comprises the mid-eastern part of Jutland centred around the second largest city of Denmark (Århus). The population in this area can be considered representative of the Danish population outside Copenhagen.

The sample comprised 3840 males. Chromosome examination was made on all males with a stature of 181 cm and over, males with testes of 12 ml or less as measured with Prader's orchidometer (Prader, 1966) as well as all those males who were not required to be examined for military service because of their severe physical or mental disability.

Chromosome examination was made on 48 hour leucocyte cultures, and analysis was made on orcein- as well as fluorescence-stained preparations.

Results

We found two males with karyotype 45,XY,-13,-14,+t(13q14q) among the 1013 males with a stature of 181 cm or more and one with karyotype 45,XY,-14,-15,+t(14q15q) among the 49 males with testes 12 ml or smaller and 181 cm or less in height.

The prevalence of D/D translocation among the 1115 males selected for chromosome examination was 2.69/1000, and the prevalence among the total population sample was 0.78/1000.

In a study at the Cytogenetic Laboratory, Risskov, of consecutive liveborn children in a Danish maternity hospital during a two-year period we found a frequency of D/D translocations of 1.39%, the frequency of D/D translocations in 31801 liveborn children from six different studies was 0.72/1000 (95% confidence limits $0.44 = 1.10/1000$) (Sergovich *et al*, 1969; Stewart *et al*, 1969; Walzer, Breau, and Gerald, 1969; Gerald and Walzer, 1970; Lubs and Ruddle, 1970a and b; Ratcliffe *et al*, 1970; Hamerton *et al*, 1972; Friedrich and Nielsen, 1973).

The parents of propositus no. 4060 had a normal chromosome constitution as seen in Fig. 1a.

As seen in Fig. 1b propositus no. 5043 inherited the translocation from his mother who is both

FIG. 1. Family pedigrees.

physically and mentally healthy. His two elder sibs have normal karyotypes. Two of his mother's four sibs (II.7 and II.11) have the 13/14 translocation. His two maternal uncles have three and two children, respectively, all five carry the 13/14 translocation and all are healthy. A maternal half cousin (III.4) has the karyotype 47,XXY.

The 13/14 translocation was found in eight of the 14 relatives of this propositus with a verified risk of

having this translocation (57.1%). None of the 13 relatives have any physical or mental disorders, and there are no indications of any remarkable differences in physical or mental development between those who carry the translocation and those who do not. There is no remarkable difference between the size of sibships in families with or without the 13/14 translocation.

Fig. 1c shows the pedigree of propositus no. 2800,

who inherited the 14/15 translocation from his mother, who is word blind and had difficulties at school, but is otherwise healthy.

The elder brother (III.1) has a normal karyotype. He is healthy but had difficulties at school mainly due to word blindness. The elder sister (III.3) who has the 14/15 translocation had no difficulties at school. The younger sister (III.5) with normal chromosomes had difficulties at school due to word blindness like her oldest brother, whereas the youngest sister (III.6) with the 14/15 translocation had no difficulties at school and no word blindness. The children of sister no. III.3, one of whom has the 14/15 translocation, are both healthy; they have not yet started school.

The dizygotic twin sister (II.3) of the maternal grandmother (II.2) is healthy and has the karyotype 46,XX. One of her sisters (II.4), who is a Jehovah's witness, did not want to have a blood sample

taken; she is healthy. A brother (II.7) of the maternal grandmother, who is word blind, has a normal karyotype. The youngest brother of the maternal grandmother (II.6), who is healthy, refused to have a blood sample taken. Three of the six relatives at risk of having the translocation in generations III and IV had the 14/15 translocation.

Karyotypes of the probands and some of their relatives are shown in Figs. 2, 3, and 4.

Case Reports

Propositus No. 4060 is a 20-year-old single business school student with karyotype 45,XY,-13,-14,+t(13q14q); his parents and only brother had normal karyotypes.

The father and mother were both 31 years old when the proband was born; the mother suffered from tuberculosis and rachitis during childhood. She has

FIG. 2. Quinacrine-stained D chromosome from proband no. 5043 and some of his relatives with $t(13q14q)$.

FIG. 3. Quinacrine-stained D chromosomes from proband no. 2800 and some of his relatives with $t(14q15q)$.

FIG. 4. Quinacrine-stained chromosomes from propositus no. 4060 with karyotype 45,XY,-13,-14,+t(13q14q).

received different types of drug therapy for nervousness and hemicrania, and she was operated for breast cancer at the age of 37. When she was pregnant with the propositus, she felt miserable and unable to go through the pregnancy and was given some pills which were supposed to produce abortion. The younger brother is healthy, but has difficulties at school.

The propositus has been operated several times for harelip and cleft palate. He had difficulties at school and was to a great extent a 'problem boy'. He has been involved in petty criminal activities on several occasions, and he often stole money at home which he used to buy friends and influence.

He left school at the age of 17, but later got a fairly good degree at a business school.

He easily becomes nervous if exposed to any form of stress, and he had a nervous breakdown during a recent examination. He has, however, gradually become more quiet and well balanced. He has never had sexual difficulties.

At psychiatric examination at the age of 20 he appears quiet and well balanced but he is somewhat nervous

when discussing emotionally loaded subjects. He appears mentally mature for his age, there are no psychopathological symptoms, and he is of normal intelligence.

Physical examination shows a 186-cm male with scars after operation for harelip. Physical examination shows otherwise normal features.

Propositus No. 5043, a 20-year-old single cook's apprentice with karyotype 45,XY,-13,-14,+t(13q14q).

The father was 35 and the mother 28 years old when he was born; both are healthy. The propositus did not like going to school, and he had great difficulties in arithmetic. He has worked as a messenger boy, an unskilled labourer, and a cook's apprentice.

He bites his nails and suffers from anxiety. He was hot-tempered as a boy, but during recent years has become quieter. He describes himself as shy and has difficulties in making contact with others. He has always suffered from enuresis and he was not conscripted for military service on account of this.

Psychiatric examination at the age of 20 showed him to be quiet, immature, and somewhat passive. He

appears to be in the lower part of the normal intelligence range.

Physical examination shows a 185-cm tall man who weighs 60 kg. Sole-pubic length is 92 cm and arm span 186 cm. The musculature is scantily developed. There are no neurological abnormalities. The beard growth is scanty (he has not shaved yet). Hair growth on body, legs and arms is normal, and the fat distribution is normal. Testes, penis, and scrotum are of normal size.

Propositus No. 2800, a 21-year-old single locksmith with karyotype 45,XY,-14,-15+t(14q15q).

The father was 28 and the mother 24 years old when the propositus was born, they are both healthy.

He had difficulties at school and never liked going to school. He was one of the worst trouble-makers in his class and was expelled from school.

He has finished his apprenticeship as a locksmith with great difficulty. He often quarrelled with his superiors and was once or twice dismissed from his job as an apprentice, but was reinstated due to his father's efforts at conciliation.

He has had a considerable alcohol consumption, especially when he was an apprentice.

At examination at the age of 21 he is talkative, somewhat restless, and immature. He appears to be in the lower part of the normal range as far as intelligence is concerned.

Physical examination is not possible as the propositus does not want to cooperate. He does not appear to have any hypogonadal signs. He is comparatively short, 165 cm, of slender build but seems to have a normally developed musculature. His beard growth seems to be normal, there is no gynaecomastia. At the examination for military service his testes were found to be below 12 ml, measured with Prader's orchidometer.

Discussion

The finding of males with D/D translocation among 1115 males examined gave a prevalence of 2.69/1000 or 0.78/1000 when calculated on the total population sample of 3840. The finding of a prevalence greater than 2/1000 among males with stature of 181 cm or more and testis size below the normal range might indicate that males with D/D translocation were either taller than expected or had an increased risk of having a testis size below the normal range. There have been no reports concerning stature in males with D/D translocations, but there have been some reports of infertility in such cases (Walker and Harris, 1962; Kjessler, 1964; Yunis *et al*, 1964; Wilson, 1971).

There is, however, no indication of infertility or decreased fertility in any of the family members with D/D translocation in our study, compared with those with normal chromosome constitutions as seen in the pedigrees.

The 14/15 translocation found in propositus no. 2800 is rare. Cohen (1971) made a survey of 64 people with D/D translocation and found that 77% were 13/14 translocations, 9% 13/15 translocations, 5% 14/15 translocations, 8% 13/13 translocations, and 1% 15/15 translocations.

One of the three propoiti had a spontaneous D/D translocation. Cohen (1971) found that 77% of 64 D/D translocations were familial.

We found that all five children of the two males carrying the translocation had inherited the translocation, whereas only three of eight relatives at risk in the sibships where the mother carried the translocation and three of seven where the parent carrier was unknown had the translocation. This correlates with the findings by Hamerton (1970) of a ratio of 1.7:1.0 of D/D translocation to normal chromosome constitution in sibships where the father was the carrier, and 1:1 in sibships where the mother was the carrier. Hamerton (1970) concluded that these findings indicate that sperms carrying the translocation chromosome have some selective advantage over sperms with normal chromosomes.

We found no abortions or any indications of children who might have had an aneuploid chromosome constitution. The results of analysis of a large number of families with D/D translocations have been controversial. Jacobs *et al* (1970) studied 14 families with D/D translocations, no individual with trisomy D or G was found in these families. Dutrillaux and Lejeune (1970) analysed 67 families and found a risk up to 5% for women carrying a D/D translocation of having a child with D or G trisomy, whereas Hamerton (1970), who analysed 42 families, found no significant increase in the risk of G or D trisomy in the progeny of carriers of a D/D translocation. These authors, however, concluded that analysis of randomly ascertained propoiti were necessary in order to make reliable calculations concerning the risk of non-disjunction in the progeny of persons with D/D translocations.

All three propoiti had difficulties at school; in two of them this was due specially to behaviour disorder. No. 2800 with a 14/15 translocation was expelled from school due to behaviour problems. No. 4060 committed petty larceny while at school. He has managed considerably better after leaving school and this also seems to be so for propositus no. 2800, even though he has had difficulties in finishing his apprenticeship as a locksmith due to his impulsiveness and quick temper. Both propoiti nos. 4060 and 2800 are immature and unrealistic concerning their future plans.

No. 5043 describes himself as being hot-tempered and impulsive as a child, but he has now become quieter. He suffers, however, from anxiety and has difficulties in making contact with others. He had enuresis till the age of 18 and had had a large alcohol consumption between the ages of 18 and 19.

All three cases have thus had behaviour problems and problems in social adjustment. They appear mentally immature for their age, but there are no indications from the family studies that such behaviour and maturity problems were more common among near relatives with the D/D translocation than among those with a normal chromosome constitution; the similarity in the personality development of the three propositi is very likely to be fortuitous and in no way connected with the translocation and loss of satellite and short-arm material in a D chromosome.

From yet unpublished studies of families with Dp – at our laboratory there have been no indications of any personality disorder connected with loss of satellites or short arms of a D chromosome.

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