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Twins and Klinefelter's Syndrome

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Introduction

A frequency of 5.4% twin births in 18 sibships with patients with Klinefelter's syndrome was reported by Nielsen (1966). The material has been extended to 20 patients with sex chromosomes XXY and 5 patients with sex chromosomes XY/XXY comprising altogether 161 births, 8 of which are twin births and 1 a triplet birth, giving a frequency of multiple births of 5.59% which is 3.4 times the expected frequency of 1.62% ($\chi^2 = 13.58$, $P < 0.001$).

The Present Study

The present study is a family investigation of one of the 20 patients with sex chromosomes XXY, a 28-year-old single unskilled labourer who is a triplet himself.

Fig. 1 shows the pedigree of the propositus, who is the affected triplet in sibship h. The zygosity of the triplets, of whom this patient is the only one alive, is doubtful, since his two triplet-brothers were stillborn, and the birth report contains no information of placenta or zygosity. Both stillborn triplet-brothers were normally

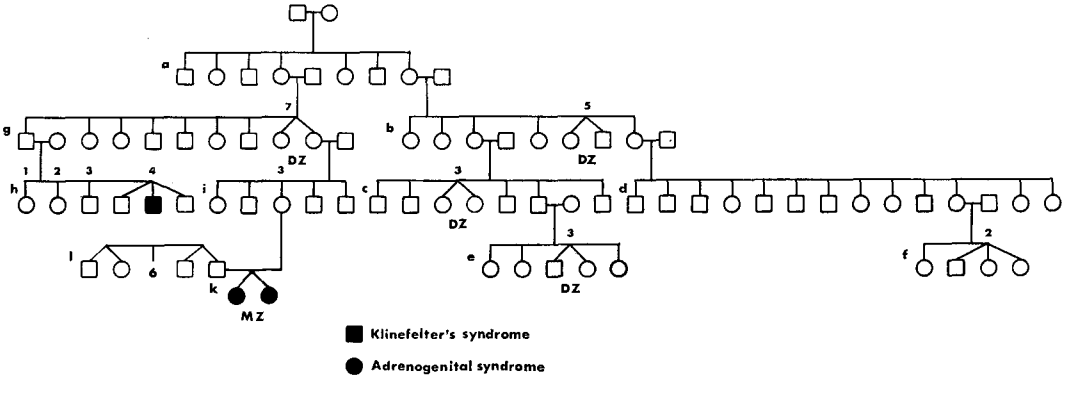

Fig. 1

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developed. In the family of the proband there were 5 twin births and 2 triplet births in three generations.

In sibship d. there are three boys with diabetes mellitus; in sibship g. there is a mentally retarded girl. The two girls in the triplets f. 2, died shortly after birth, they were normally developed. The zygosity of the two girls is not known. The MZ twins in sibship k. had adrenogenital syndrome, one of them died at the age of 4. The twin brother of the father of the twins in sibship k. died at the age of 3 months.

Of the 19 children from the 9 multiple births found in the 25 sibships of patients with sex chromosomes XXY and XY/XXY, 10 died before the age of 3 (53% mortality).

Discussion

Twin mortality in the general population is approximately two to three times greater than the mortality for single births, but a mortality of multiple births up to the age of 3 years of 53%, which is 11 times the mortality of 4.8% among single births in the Klinefelter sibships, indicates that some of the twins and triplets born in the Klinefelter sibships might have had chromosome abnormalities contributing to the high frequency of twin mortality.

The finding of a high frequency of twin-births in sibships of patients with Klinefelter's syndrome correlates with the twin frequency in sibships of patients with Turner's syndrome as found by Nance and Uchida (1964) who studied the sibships of 34 patients with Turner's syndrome and found 7 twins out of the total number of 128 births giving a frequency of 6.3%. Boyer et al (1961) studied the sibships of 63 patients with Turner's syndrome and 236 births and found a twin frequency of 2.1%, and Lindsten (1963) found a twin frequency of 2.5% in 57 sibships with Turner's syndrome and 160 births. The pooled twin-birth frequency in the three studies is 3.2%. No previous systematic studies of twins in the sibships of Klinefelter's syndrome have been made, but Stewart and Barber (1963) found a twin frequency of 2.7% among 180 near relatives of 9 patients with chromatin-positive Klinefelter's syndrome compared with the frequency of 1.0% twins among 275 relatives of 15 patients with chromatin-negative Klinefelter's syndrome.

The comparatively high frequency of multiple births in the Klinefelter sibships found in the present study might to a certain extent be correlated with the higher maternal age for patients with Klinefelter's syndrome of 34.6 ± 9.1 for the 20 patients with 47, XXY and 32.6 ± 6.0 for the 5 patients with 46, 47, XY/XXY, compared with 29.3 ± 6.1 in the general population as the DZ twin-birth frequency increases with maternal age as shown by Dahlberg (1926). The twin-birth frequency in Denmark from 1921 to 1925 varied from 0.60% in the age group 15-19 to 2.27% in the age group 35-39, and 0.79% in the age group 45+.

The different maternal age groups and the total number of twins in the present study are, however, too small to make any statistical age correlation possible.

A frequency of multiple births of 5.59% compared with an expected frequency of 1.62% is, however, most probably not only due to a higher maternal age.

If the comparatively high frequency of twins in the sibships with Klinefelter's syndrome as well as Turner's syndrome is confirmed by further studies, this will indicate a relation between the cause of sex chomosome non-disjunction and multiple births or between the predisposition to non-disjunction and multiple births.

Summary

A multiple birth frequency of 5.59% has been found in 25 Klinefelter sibships, which is statistically significantly higher than expected ($P < 0.001$).

A family investigation of a patient with Klinefelter's syndrome, who is a triplet himself, revealed 5 twin births and 2 triplet births in three generations.

The mortality of the 19 children from the 9 multiple births born in the 25 Klinefelter sibships was 53% up to the age of 3. Such a high mortality indicates that some of the twins and triplet births might have suffered from chromosome disorders contributing to the high mortality.

If the comparatively high frequency of twins in the sibships with Klinefelter's syndrome as well as Turner's syndrome is confirmed by further studies, this will indicate a relation between the cause of sex chromosome non-disjunction and multiple births or between the predisposition to non-disjunction and multiple births.

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RIASSUNTO

In 25 fratrie di Klinefelter è stata riscontrata una frequenza di nascite multiple (5.59% significativamente superiore a quella attesa ($P < 0.001$). L'indagine familiare di un trigemino affetto da Klinefelter, ha rivelato 5 nascite gemellari e due nascite trigemellari in tre generazioni. La mortalità dei 19 membri delle 9 nascite multiple nelle 25 fratrie di Klinefelter è risultata del 53% fino all'età di tre anni; una mortalità così elevata indica che alcuni dei gemelli avrebbero potuto essere affetti da alterazioni cromosomiche. Se ulteriori studi di fratrie con sindrome di Klinefelter e Turner continueranno ad indicare un'elevata frequenza di gemelli nelle stesse fratrie e famiglie, come risulta dal presente studio, ciò potrà indicare un'analogia fra il meccanismo della non-disgiunzione dei cromosomi sessuali e quello dello zigotismo gemellare, perlomeno a livello disposizionale.

RÉSUMÉ

Une fréquence de naissances multiples de 5.59%, significativement plus élevée de celle théorique ($P < 0.001$), a été trouvée chez 25 souches de Klinefelter. L'étude de la famille d'un patient de Klinefelter, triplet lui-même, a démontré 5 naissances gémellaires et 2 naissances de triplets sur trois générations. La mortalité des 19 membres des 9 naissances multiples dans les 25 souches de Klinefelter est de 53% jusqu'à trois ans. Une mortalité si élevée indique que quelques uns des jumeaux auraient pu être atteints d'altérations chromosomiques. Si de prochaines études sur des souches de Klinefelter ou Turner indiqueront encore une fréquence élevée de naissances multiples dans les mêmes souches, l'on pourra avancer l'hypothèse d'une analogie, tout au moins dispositionnelle, entre non-disjunction des chromosomes sexuels et phénomène gémellaire.

ZUSAMMENFASSUNG

Bei 25 Klinefelter Sippen wurde festgestellt, dass die Frequenz der Mehrlingsgeburten (5.59%) wesentlich höher war als die Erwartung ($P < 0.001$). Die Sippenuntersuchung eines Drillings mit Klinefelter Syndrom ergab in drei Generationen 5 Zwillings— und 2 Drillingsgeburten. Die Sterblichkeit der 19 Paarlinge aus 9 Mehrlingsgeburten in den 25 Klinefelter Sippen betrug bis zum Alter von drei Jahren 53%. Eine so hohe Sterblichkeit beweist, dass einige der Zwillinge vielleicht an Chromosomenalterationen litten. Falls weitere Sippenuntersuchungen beim Klinefelter bzw. Turner Syndrom noch — wie in vorliegender Arbeit — ein häufigeres Zwillingsvorkommen in denselben Sippen und Familien anzeigen, so kann das für eine Wirkungsanalogie zwischen der Non-Disjunction der Geschlechtschromosome und der Zwillingseiigkeit (zumindest in der Prädisposition) sprechen.

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