An XXYY Male Presenting with Aggression
A Case Report

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SUMMARY

An abnormally tall 21-year-old Caucasoid male was referred for psychiatric assessment for pathological aggression and mental subnormality. He showed many of the phenotypic features of Klinefelter's syndrome. Cytogenetic studies revealed a 48,XXYY karyotype. The significance of the association of this karyotype with aggressive behaviour is discussed.


The 47,XXY chromosomal pattern, which characterizes the clinical syndrome first described by Klinefelter et al., was later delineated by Jacobs and Strong. Since then patients have been described with several numerical variants of this pattern. One of these variants, first described by Muldal and Ockey as the 'double male', possesses the 48,XXYY chromosome constitution and hence has a Klinefelter syndrome with an additional Y chromosome. Over 60 such patients have now been described; 53 of these were reviewed by Borgaonkar et al. These authors concluded that such patients showed certain features which distinguish them both from men with XXY patterns and from those with XYY patterns. A few subsequent cases have been reported, but the condition remains sufficiently uncommon to warrant documentation of a further case, in which this chromosome constitution is associated with mental subnormality and serious behavioural problems.

CASE REPORT

A 21-year-old Caucasoid male was referred to the Psychiatric Unit of Johannesburg General Hospital by his parents. He was the eldest of their 3 children, all males; the remaining 2 were aged 17 and 15 years. At the time of his birth his father was 23 and his mother 22 years old. The pregnancy was perfectly normal, and there was no history of infections, drugs or irradiation. He was delivered at term, but caesarean section was necessary due to cephalopelvic disproportion. His birth weight was 2.4 kg.

The patient was regarded as mentally normal until he was 3 years old, and until he was 14 years his height was about average for his age. At the age of 3 he suffered from an acute respiratory condition which necessitated tracheotomy; the anoxia preceding this was thought to have caused brain damage, and he did not start school until he was 7 years old. He was unable to cope with ordinary schooling, and from the age of 11 attended special schools. He left school at the age of 17, having passed Std VI (normally the 8th year of schooling). There was no history of seizures at any time.

For a year after leaving school he worked on the railways, and was then inducted into the army. After 6 weeks in the army he suffered a 'nervous breakdown' and was discharged as unfit. He returned to his former employment, but resigned after 3 months following an argument with a fellow-worker. For the past 2 years he has neither worked nor sought employment.

His parents complained of his aggressive and argumentative behaviour. He has always been jealous of his younger brothers, with whom he quarrels constantly. At school he was bellicose and lacked friends. Two years ago an argument ended in violence, and a charge of assault was laid against him but was later withdrawn.

He has on occasion shown violence towards his family's domestic servant, and his latest hospital admission was precipitated by his attempting to shoot a neighbour's servant with a (fortunately unloaded) gun. He drinks excessively when he gets the chance and has run away from home on many occasions, sometimes ending up in distant cities. His conduct is generally asocial and he locks himself into his room for long periods. His family can no longer cope with him, and want him to be committed to a psychiatric institution.

Both parents and his 2 younger brother are of average intelligence and well-adjusted socially. There is no family history of mental illness or subnormality except in the maternal grandfather, who was a heavy drinker. In the father's family all members are above the 50th percentile for their sex in height, and 1 paternal uncle is reputed to be 200 cm tall.

Clinical Examination

The patient was quiet and co-operative throughout the examination, but was obviously intellectually subnormal. He spoke of feelings of aggression towards his younger brother. On questioning he expressed heterosexual preferences and boasted of having 4 girlfriends simultaneously.

He was a tall, thin individual with android body contour, although there was slight rounding of the hips (Fig. 1). There was no evidence of acne or of gynaecomastia. Axillary hair was sparse, pubic hair was gynaecoid in distribution and facial hair was absent. His weight was 56 kg, his total height 194 cm and his crown-pubis
height 90.5 cm, the upper/lower body ratio being 0.874. His arm span was 191 cm. The penis was of normal adult size with a terminal urethral opening. Both testes had descended into a normal rugose scrotum, but were very small in size, the left having a diameter of 1.5 cm and the right 2 cm. Both were soft in consistency.

![Fig. 1. The proband, illustrating the tall asthenic physique with slight gynaecoid rounding of the pelvis and normally developed penis.](image)

Simian creases were absent from the hands, and the fingers had a somewhat spatulate appearance (cf. Borgaonkar). Both fifth fingers were short, with clinodactyly and camptodactyly. His feet were disproportionately short for his height, and all the toes were widely spaced and had dysplastic nails. No skeletal anomalies or clinical signs suggesting neurological abnormality were noted.

### Special Investigations

An electro-encephalogram disclosed occasional episodic 6-waves in both temporal areas, more marked on the right, but there was no evidence of a focal lesion or of paroxysmal activity. X-ray examination of the skull was normal. A seminal fluid ejaculate of 0.6 ml was totally azoospermic. His serum hormone levels were: FSH 7.0 ng/ml (normal 0.6 - 2.7); LH 11.6 ng/ml (normal 1.3 - 2.9); testosterone 245 ng/ml (normal 250 - 1000); and midday cortisol 10.5 μg/100 ml (normal 4 - 16). His and his parents' red cells were all Xg (a+).

His total IQ, assessed on the SA Wechsler Adult Scale, was 52, with a verbal component of 42 and a performance component of 67. Since the patient was unco-operative, the total IQ was thought to be higher than 52. He refused to perform a DAP projective test. A report on his behaviour in the ward stated that he lacked constructive motivation and made little attempt to relate to those around him. He exhibited a low tolerance to frustration.

The dermatoglyphic patterns were in the ranges previously described for normal men. The finger patterns consisted of 3 whorls and 2 ulnar loops on the right hand and 2 whorls and 3 ulnar loops on the left. The total finger ridge count was 140 and the total a-b ridge count 77. The palmar triradius was normally placed and there were open patterns in the palmar hypothenar and thenar areas.

### Cytogenetic Studies

Buccal epithelial nuclei were 33% X chromatin-positive; the normal female range in this laboratory is 20 - 48% with the Klinger thionin stain. Quinacrine fluorescence revealed two Y bodies in 78% of nuclei, duplex Y bodies in 5%, single Y bodies in 14% and only 3% without a Y body at all (cf. Robinson). Chromosome studies were carried out on peripheral blood metaphases with a modified trypsin-Giemsa technique, quinacrine mustard fluorescence and C-banding. Fifty cells examined had a modal number of 48 chromosomes, karyotype 48,XXYY. There was no evidence of mosaicism. Trypsin-Giemsa banding (Fig. 2) confirmed the presence of 2 X chromosomes, and quinacrine fluorescence (Fig. 3) and C-banding established the presence of 2 Y chromosomes. Both parents showed normal karyotypes, with no evidence of mosaicism in 50 cells.

### DISCUSSION

In 1965 Jacobs et al. found that about 2% of the men in a maximum security hospital had the chromosomal constitution 47,XYY. Subsequent studies on prison populations supported the suggested association of an extra Y chromosome with male criminality. Casey et al. surveyed a population of 942 men in a maximum security hospital and discovered that 7 of the 21 found to be X chromatin-positive had the karyotype 48,XXYY, but of 4015 mentally subnormal men studied by Jacobs et al. only 1 was found to have this chromosomal constitution. It therefore appeared unlikely that diminished intelligence per se was an adequate explanation for the criminal tendencies of such men.

Surveys of newborn males have disclosed an incidence of XYY pattern of only approximately 1/1000, while that of XXYY pattern is much lower. Only 2 such neonates have been recorded, and recent surveys of more than 30 000 infants have disclosed none at all.

The hypothesis that the relative frequency of men with an extra Y chromosome in criminal institutions represents a causative relationship between this chromosomal con-
stitution and aggressive behaviour has been tested by Price and Whatmore, who have shown that, in fact, the crimes they commit are more often against property than against the person. Using the criterion of unusual height, known to be a character associated with possession of an extra Y chromosome, Witkin et al. surveyed 4,558 Copenhagen men representing the top 15.9% of the height distribution of those born during 1944, 1945, 1946, and 1947, and karyotyped 4,139. Twelve men had an XYY pattern and 16 an XXY pattern, and a search in the penal registers disclosed that 5 of those with an XYY constitution and 3 with an XXY pattern had been convicted of one or more criminal offences. Comparison of the frequency of crimes of violence, however, showed no significant difference between men with XYY, XXY and normal XY karyotypes, while all the convicted men were mentally below average. The authors consequently concluded that the criminality of men with extra sex chromosomes was, after all, related rather to lowered intelligence than to any abnormally aggressive tendencies or to excessive height. (Psychodynamically, tallness is a factor in aggressive behaviour.) There were no men with an XXYY pattern in this series. Of the 53 men with an XXYY pattern reviewed by Borgaonkar et al., 66% were referred for investigation because of intellectual impairment and behavioural problems; most of the latter involved aggression.
The physical stigmata of the syndrome associated with this 'double male' chromosomal complement include abnormally great stature. These men tend to be even taller than those with an XYY pattern, probably because the two types of aneuploidy combined in them each produce some increment in height; 80% over the age of 16 but only 31% under 16 years of age attained a height above the 90th percentile. It would appear, therefore, that excessive stature would only provide a useful criterion for diagnosis of the condition in about one-third of affected prepubertal boys. The patient reported here in fact only grew excessively tall after puberty, and considering the history of tallness in his father's family, autosomal factors may have played some part in this. Borgaonkar et al. state that a reduced ratio of the upper to the lower body segment, as found in our patient, is also characteristic.

Primary and secondary sexual characteristics do not differ significantly from the classic Klinefelter's syndrome. Some degree of testicular atrophy is always present. Penile size, gynaecomastia, hair distribution, body contour and skeletal anomalies are variable, according to Borgaonkar et al.; there is nothing characteristic about the variations found in our patient. The hormone levels of XXY males are not usually significantly different from those of XYY men; aspermatogenesis, as evidenced by elevated FSH levels without a rise in the LH values, and without Leydig cell aplasia, is usual. In our patient the LH and FSH levels were raised, and there was decreased testosterone production, indicating spermatogonial and Leydig cell dysfunction.

Non-specific electro-encephalographic changes indicative of immaturity, such as those observed in our patient, have been found in nearly 20% of cases. The great majority of reported patients have shown some degree of intellectual subnormality, whereas the level of intelligence of XXY and XYY males is much more variable. Price et al. found that mental subnormality was diagnosed no more frequently in criminals with an XYY pattern than in the total criminal population studied.

Variations in sex chromosome number have been found to influence the autosomally inherited dermatoglyphic traits. Hunter and Borgaonkar et al. have suggested that the dermatoglyphic patterns in individuals with XXY and other sex chromosome aneuploidies are sufficiently distinct from one another and from those of normal XY controls to be of diagnostic significance. A study of dermatoglyphic patterns in men with an XXY pattern, however, demonstrated the same features as in those with XYY patterns. It would consequently appear to be difficult to differentiate between the two conditions on dermatoglyphic patterns alone. In XYY males the patterns were found to be too variable to be of practical diagnostic help. The dermatoglyphic patterns in our patient were not found to differ in any significant way from those of normal XY males.

Although there remain some doubts about whether the possession of an extra Y chromosome in itself predisposes to aggressive behaviour, the evidence that the association with it of an extra X chromosome is almost invariably accompanied by mental subnormality coupled with irrational aggression, is convincing and is supported by the case reported here. These traits, combined with abnormal tallness, small testes and a decreased upper/lower body segment ratio, should be suggestive of the possibility of this variant of the Klinefelter syndrome, and require chromosomal investigation for its confirmation or exclusion.

ADDENDUM

Since submission of this case report, we have investigated a further XXY male who is 194 cm tall and has testicular atrophy. He was originally referred for psychiatric assessment of uncontrolled emotional behaviour, social maladjustment and subnormal intelligence.

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REFERENCES