Sex-Chromatin and Sex-Chromosome Abnormalities in Male Hypogonadal Mental Patients

By JOHANNES NIELSEN and MARGIT FISCHER

The present study is part of a sex-chromatin survey in a mental hospital. It has been made as a preliminary step in finding the prevalence and incidence of sex-chromosome abnormalities among patients with mental illness; and it also has the purpose of studying the psychopathological and genetic aspects of sex-chromosome abnormalities. The study comprises all clinically hypogonadal patients referred by the psychiatrists at this hospital to the cytogenic laboratory during a period of approximately 1 month. In a survey of this kind we can expect to find patients with certain abnormalities of the sex chromosomes.

METHOD

Bilateral buccal scrapings were taken from each of the patients and stained by the Feulgen method. One hundred nuclei were analysed from each pair of scrapings. Drumstick analysis was done on the seven patients whose chromosomes were also investigated. Chromosome analysis was carried out partly on peripheral-blood cultures in seven patients, and partly on skin cultures in two of the seven patients.

RESULTS

Tables IA and IB show the 59 patients referred as cases with hypogonadal symptoms and signs. All cases are distributed according to sex, age, marital state, diagnoses, hypogonadal signs, and sex-chromatin pattern; in nine cases the results of chromosome analysis are given.

Three cases were found to have Klinefelter's Syndrome (Klinefelter et al., 1942). All three had typical symptoms of this disorder (Table IA). They were chromatin positive with 20, 24 and 31 per cent. cells with one chromatin body; one patient had 10 per cent. cells with two chromatin bodies. Drumsticks were found in five, three and three neutrophil leucocytes out of 500 in the three cases respectively (Table IA). Autosomes were apparently normal in the three cases of Klinefelter's Syndrome, as in the six other cases whose chromosomes were analysed. In the two cases with one chromatin body, sex-chromosome constitution was found to be XXY and the total number of chromosomes was 47; as expected in the case with two chromatin bodies, the number of chromosomes was 48 with an XXXY sex-chromosome constitution.

The four chromatin negative male patients who had chromosome analysis had apparently normal sex-chromosomes as well as autosomes. There is a great difference in clinical appearance of the three cases with Klinefelter’s Syndrome and the other cases picked out as cases with hypogonadal symptoms, the main difference being the size and consistency of testes. Only one of the chromatin negative cases (No. 14,012) had testes smaller than normal, but with normal consistency (Table IA). This might be a case of what is called false Klinefelter’s Syndrome or chromatin negative Klinefelter’s Syndrome, but no testis biopsy was made.

The five women referred as patients with hypogonadal signs were chromatin positive. Two patients who had chromosome analysis had 466 chromosomes, sex-chromosomes XX, and normal autosomes. None of them had amenorrhoea or signs of Turner’s Syndrome; virilism was more pronounced than hypogonadal signs.

CASE HISTORIES

Case No. 32,840

A 60-year-old single male with the diagnosis of psychogenic paranoid psychosis and the sex-chromosome constitution of XXXY, 48 chromosomes, and normal autosomes. Klinefelter’s syndrome.
The father who was a coach builder, was 30 years old when the patient was born, and he died of pernicious anaemia at the age of 60. There are no indications that he suffered from any mental illness. The mother was 26 years old when the patient was born. She died at the age of 86, 3 months prior to the admission of the patient to the Aarhus State Hospital. She never suffered from any mental illness or serious somatic disorders.

The patient is the elder of two siblings. The sister, who was 3 years younger than her brother, died of lymphosarcoma coli at the age of 16. She did not suffer from any mental illness, but otherwise very little is known about her. There are no known cases of mental deficiency, endocrinological or other hereditary disorders in the rest of the family.

The patient got through his 7 years of compulsory school attendance in a two-classed village school. He was dull, but learned to read and write fairly well. Conditions at home were stable and harmonious and the patient managed fairly well as long as his mother could take care of him. He left home at the age of 15 and worked on a farm during a 6-month period. He then left, giving the reason that he did not get enough to eat. He never left home again, but managed to help a little at home. At the age of 30 he was given a disability pension on account of backache and mental subnormality, as he was unable to take care of himself.

When the mother was placed in a nursing home, and more so after her death 3 months before his admission to hospital, he developed a complex of persecutory delusions, such as that brown carriage grease was coming through the television, and that neighbours interfered with his thoughts, talked threateningly to him, and attacked him through the television.

At the time of admission he was clearly oriented but completely convinced about the reality of his paranoid delusions. There was adequate emotional and intellectual contact, but he was somewhat apathetic and only reacted emotionally when the psychiatrists expressed any doubt of the reality of his paranoid delusions. Intelligence was judged as being somewhat below normal level.

Since admission he has been happy, friendly, easy to contact, well oriented but constantly convinced about the reality of his paranoid delusions. He has never been hallucinated. He is childish in his behaviour, happily and busily occupied by stringing beans. He enjoys playing simple games. He was offered discharge to a recreation home, but preferred to stay at the State Hospital, from where he was later transferred to a psychiatric nursing home under the State Hospital.

He never shaved and he never had any sexual intercourse. His physical appearance is that of a woman with a fat feminine truncus with mamma development. He has no beard, scanty auxiliary hair growth, feminine pubic hair distribution, scanty hair growth on the extremities and a soft white feminine skin. Testes are the size of cherry-stones and soft without the usual testicular sensibility and consistency.

Neurological examination and electroencephalogram are normal. X-ray of spine shows thoracic kyphosis and lumbar scoliosis with halisteresis of all bodies.

Hormone investigation shows a urinary excretion of follicle stimulating hormone of 120 m.u. per 24 hours (normal range for that age 13—130 m.u., mean 43 m.u. per 24 hours). 17-ketosteroid excretion is 6·10 mg. per 24 hours (normal range for that age 7—17 mg. per 24 hours), androgenic fraction is 0·65 mg. (normal range 1·3—4·0 mg.).

Psychological testing with WAIS, Inculcation test, Colour-form, Rorschach, and Association test showed verbal I.Q. of 73, performance I.Q. of 74, and a total I.Q. of 72. The patient's work with the tests is characterized by lack of energy and a tendency to give up, which makes the results of the tests more doubtful. Intellectual function is in accordance with a placing in the borderline area to oligophrenia, but it is remarkable that tests which measure ability previously learned are performed according to an intelligence in the subnormality area. Poor performances are seen in tests needing energy and concentration. The poor co-operation makes it difficult to seek out the so-called organic traits such as memorizing, reconstruction, and direction difficulties. The Rorschach test shows an immature personality on a childish level of development. A massive dependency need is seen. Vague and more doubtful features in the Rorschach and Association tests give suspicion of failing sexual identification.

Conclusion. A 60-year-old single man with Klinefelter's syndrome who always functioned according to an intellectual placing in the borderline between subnormality and oligophrenia, but managed quite well until puberty and was able to stay out of a psychiatric institution until shortly after his mother, who had taken care of him previously, died. At the time of his mother's illness and death he developed a paranoid psychosis with no hallucinations, no autism and no disorder of thinking. This psychosis is thought to be a psychogenic paranoid psychosis in a person with intelligence in the borderline line between subnormality and oligophrenia, and with an immature, childish, dependent, self-referring, and primitive personality.

Case No. 35342

A 33-year-old single male with the diagnosis of psychogenic paranoid psychosis and the sex-chromosome constitution of XXY, 47 chromosomes and normal autosomes. Klinefelter's syndrome.

The father, who was a merchant, was 41 years old when the patient was born. She died at the age of 64, 5 years prior to the admission of the patient to the Aarhus State Hospital. The father never suffered from any mental illness or serious somatic illness. The mother was 56 years old when the patient was born. She died at the age of 64, 5 years prior to the admission of the patient. She never had any mental disorders or serious somatic illness.

The patient is number 5 of 7 siblings, 4 brothers and 1 sister, who are all healthy mentally and physically and all of whom have been doing well socially. A maternal uncle committed suicide in relation to his wife being unhappy, but otherwise there is no mental illness, mental deficiency or other somatic disorder in the family.

The patient developed normally as a boy and did fairly
siblings were harmonious and stable. After leaving school he worked as a farmhand until the age of 30 when he bought a farm with some of the 170,000 kr. he inherited when his father died.

There has been only a short period of sexual relation at the age of 30–31 with a housekeeper, whom the patient, however, was not able to satisfy sexually. There have been no sexual relations since the age of 31, and never any homosexual relations.

The paranoid symptoms for which the patient was admitted have developed gradually during the 3 years he has owned the farm which he has had some trouble managing. During those 3 years he has become more and more suspicious concerning the neighbours, eventually to the extent that he was convinced that they had stolen part of his crop, poisoned his dog and also tried to poison him by putting opium in his food and tobacco. He heard the voices of the neighbours and on two occasions saw his deceased father staring at him from the wall.

On admission the patient was conscious and well orientated. Adequate intellectual and emotional contact was established with him. He was paranoid and rather secretive, pretending to know much more than he was telling. He was childishly immature, appearing as having an intelligence slightly below normal level. He was not hallucinated, depressed or manic.

He has a rather small skull, slender long extremities with poorly-developed musculature and genu valgus. Truncus is rather fat, with small mammae. The pubic hair distribution is feminine and there is scanty hair growth on the chest. Testes are very small, slightly harder than normal, with decreased testicular sensibility. Neurological examination and electroencephalogram are normal.

Hormone investigation shows a urinary excretion of 190 m.u. per 24 hours (normal range 6–75 m.u., mean 30 m.u. per 24 hours). 17-ketosteroid urinary excretion is 25.40 mg. per 24 hours (normal range 10–25 mg. per 24 hours). Androstosterone fraction is 7.50 mg. per 24 hours (normal range 2.0–7.0 mg. per 24 hours). Oestrogen excretion is around 50 m.u. (normal range 20–80 m.u.).

During his stay in the hospital the patient was treated with chlorpromazine and insulin-corn. His paranoid ideas disappeared during the treatment with insulin-corn and he has not been hospitalized during the year that has passed since his first hospitalization. He was seen a couple of times in the out-patients' clinic during the first months after his discharge and he presented no psychotic signs, especially no paranoid traits. No psychological tests were made during the hospitalization as no psychologist was available at that time.

Concluding. A 33-year-old single man with Klinefelter's Syndrome who developed normally until puberty and managed fairly well later, but not as well as any of his siblings by whom he is considered below normal intelligence and without sufficient ability, energy and initiative to run his farm which he only got because of the inheritance from his father of a rather big sum of money.

During the first 3 years of running his farm the patient found out that he did not manage it nearly as well as the neighbours, his crop was smaller and his profit less than theirs. He also realized that he was not able to satisfy a woman sexually. During this period of stress he gradually developed a paranoid psychosis, believing that a plot was made by the neighbours whom he accused of stealing his crop and trying to poison his animals and himself. The patient never presented any signs of autism or disorder of thinking and only mild occasional hallucinations were described before he was admitted, but never observed during admission. The psychosis is thought to be of psychogenic origin brought on by the above mentioned stress in a person with I.Q. in the lower part of the normal range, an immature, sensitive personality with little initiative typical of patients with Klinefelter's Syndrome.

Case No. 20,616

A 41-year-old single man with the diagnosis of alcoholism and character disorder and the sex-chromosome constitution of XXY, 47 chromosomes and normal autosomes. Klinefelter's syndrome.

The father, who is a butcher, was 27 years old when the patient was born, he has had no mental illness and no serious somatic disorders. The mother was 23 years old when the patient was born. She has never suffered from any mental illness or from any serious somatic disorders. The patient is a dizygotic twin, and he has a 2-year-old sister who suffers from cryptogenic epilepsy. His twin brother who is married and has two children is healthy mentally and physically with no hypogonadal symptoms or signs. There are no cases of mental deficiency, mental illness, or other disorder in the family except for the sister suffering from cryptogenic epilepsy.

The patient did fairly well at school and up till the age of 15 when he left school. He had a good harmonious home and the parents still support him and take great interest in his doings. From around the age of 15 he became increasingly dependent on other people, sensitive, weak, ambivalent, and easily influenced by mates with a bad reputation. Under this influence he started having a periodically large alcohol consumption. He was an apprentice in a shipyard for 18 months, a farmhand for 6 months, and then trained as a mechanic. He later changed to the field of metal grinding. He often left his jobs untimely and had great difficulty in settling down. He was arrested for drunkenness a few times. After drinking spells, he often was rather depressed and miserable and was helped economically and morally by his parents.

He was admitted to the Aarhus State Hospital, at the age of 29 years, after a drinking spell, in relation to a depression and a suicidal attempt 3 months previously, caused by his twin brother's departure for a job at sea. On the day of admission he had again threatened to commit suicide, and the parents dared not keep him at home. He stayed in the hospital for 2 weeks and during the next 13 years he was admitted to the State Hospital...
<table>
<thead>
<tr>
<th>Case Number</th>
<th>Age (years)</th>
<th>Marital State</th>
<th>Diagnoses</th>
<th>Hypogonadal Symptoms and Signs</th>
<th>Percentage of Chromatin-positive Cells in Buccal Smears</th>
<th>Drumsticks per 500 Neutrophil Leucocytes</th>
<th>Chromosomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.207</td>
<td>62</td>
<td>Married</td>
<td>Schizophrenia</td>
<td>Feminine fat distribution. Mammary development. (Treated with peroxyn because of masturbation and exhibitionism)</td>
<td>0</td>
<td>—</td>
<td>—</td>
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<tr>
<td>14.310</td>
<td>59</td>
<td>Single</td>
<td>Hysterical neuritis, Intellectual subnormality</td>
<td>Small hands. Poorly-developed muscles. Soft white skin with scanty hair on extremities</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>18.309</td>
<td>40</td>
<td>Single</td>
<td>Schizophrenia</td>
<td>Adipous with tendency to feminine fat distribution</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>19.087</td>
<td>40</td>
<td>Single</td>
<td>Schizophrenia</td>
<td>No hypogonadal signs but 18-year-old treated with physostigmin and psychoendosilism.</td>
<td>0</td>
<td>1</td>
<td>43 44 45 46 47 48 49 —   1 20 — 49 — XY</td>
</tr>
<tr>
<td>19.381</td>
<td>33</td>
<td>Single</td>
<td>Schizophrenia, Feemblemindedness</td>
<td>Tendecy to feminine fat distribution. Soft white skin with scanty hair growth on extremities</td>
<td>0</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>20.616</td>
<td>41</td>
<td>Single</td>
<td>Alcoholism, Character disorder</td>
<td>Impotence since the age of 34. Very small soft testes of prepubertal size. Slender extremities with poorly-developed muscles. Mammary development.</td>
<td>31</td>
<td>5</td>
<td>43 44 45 46 47 48 49 — 2 1 30 1 — XXY</td>
</tr>
<tr>
<td>21.188</td>
<td>36</td>
<td>Single</td>
<td>Schizophrenia</td>
<td>Tendency to feminine fat distribution.</td>
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<td>—</td>
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<tr>
<td>27.765</td>
<td>31</td>
<td>Single</td>
<td>Psychogenic paranoid psychosis,</td>
<td>Rather small testes. Feminine fat distribution</td>
<td>4</td>
<td>1</td>
<td>43 44 45 46 47 48 49 — 5 17 3 — XY</td>
</tr>
<tr>
<td>32.664</td>
<td>41</td>
<td>Single</td>
<td>Schizophreniform psychosis, Transvestitum</td>
<td>None</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>32.840</td>
<td>60</td>
<td>Single</td>
<td>Psychogenic paranoid psychosis, Intellectual subnormality</td>
<td>Never sexual intercourse. No beard growth. Scanty auxiliary and pubic hair. Feminine pubic hair distribution. Mammary development. Feminine fat distribution. Slender extremities with poorly-developed muscles</td>
<td>*24 (10% Bz)</td>
<td>3</td>
<td>43 44 45 46 47 48 49 — 1 3 4 1 XXXXY</td>
</tr>
</tbody>
</table>

*The data includes various clinical observations related to the diagnoses and symptoms, along with notes on chromosome patterns and the presence of certain conditions. The table provides a detailed view of the distribution of male patients in terms of case numbers, ages, marital statuses, diagnoses, and associated symptoms, along with the percentage of chromatin-positive cells and other relevant data points.
them with 20 cases of hypogonadotropic eunuchoidism, anorchia, castration or cryptorchism and with 20 cases of sexual abnormality with no organic basis, mainly neurotics with alteration in libido or with homosexuality. All patients with Klinefelter’s Syndrome showed apathy, hypokinesia, and timidity. They were usually idle, tired easily and slept much; they had few vital interests; they were usually shy, restrained, had few friends and were pusillanious. In their tastes and diversions they resembled overgrown children. The Rorschach test disclosed a raised index of stereotopy, lack of original answers and no answers M and C. The Raven test indicated poor capacity for observation, comparing and reasoning by analogy. The Wechsler test showed a slight predominance of performance I.Q. over verbal I.Q. The average full-scale I.Q. was 81 compared with 101 in the 20 cases of hypogonadotropic eunuchoidism, anorchia, castration and cryptorchism, and 112 in the 20 cases of psychoneuroses and homosexuality. Roskamp (1959) described a case of Klinefelter’s Syndrome who grew up in a mother-deprived and very stressful environment. At the age of 22 he is described as a primitive, sexually-immature, weak-willed, aggression-repressed personality with strong sado-masochistic tendencies.

Dengler (1960) has described a 21-year-old patient with Klinefelter’s Syndrome who developed normally till the age of 17, at which time he withdrew from friends and lost initiative. He considered himself different from others, and had difficulties in talking with others, especially with girls. He became changeable of mood with reactive depressions and suicidal thoughts and he began drinking because of this. He was treated with Testosterone, F.S.H., and psychotherapy with doubtful results.

Aresin (1960) investigated a case of Klinefelter’s Syndrome in a man of 35 years who had his first erection and emission around the age of 26. At about this age he also became restless and periodically depressed with suicidal thoughts. He was admitted to psychiatric institutions and diagnosed variously as suffering from schizophrenia, psychopathy, and neurosis. At the age of 35, when the diagnosis of Klinefelter’s Syndrome was made, he was depressed, hypochondriacal and sensitive. He tired easily and lacked persistence.

Thomsen (1962) found five patients with Klinefelter’s Syndrome in a mental hospital, three of them had a diagnosis of psychopathy, one of hysterical neurosis and feeblemindedness, and one suffered from epilepsy. The patients were all described as psychoinfantile, unstable, with lack of initiative. They had a tendency to reactive depressions. I.Q. was normal in one, in the borderline between normal and intellectual subnormality in three, and one was feebleminded.

Warburg (1962) investigated a case of Klinefelter’s Syndrome, who was described as a dependent, easily influenced, quiet conscientious man who had suffered from a reactive depression at the age of 35. He had difficulties in living up to his masculine role sexually as well as characterologically. He was further described as suffering from a mild intellectual reduction.

**Discussion**

Among 14 male patients with hypogonadal symptoms and signs found during a 1-month period by the clinicians in a mental hospital, out of approximately 450 patients, three cases were found to have abnormal sex-chromosome pattern. All three patients suffer from Klinefelter’s Syndrome. None of their parents or grandparents suffered from any mental disorder. The father of patient No. 32,840 suffered from pernicious anaemia and this patient’s only sister died of lymphosarcoma. A sister to patient No. 20,666 suffers from epilepsy which is probably cryptogenic, but his twin brother is healthy. The mother of patient No. 34,342 had diabetes mellitus and his maternal uncle committed suicide.

The age of the mothers of these three patients at the time they were born was 26, 23, and 36 respectively, and the age of the fathers was 30, 25, and 41 years. None of them were last in a long row of siblings; one of the patients was first of two, one was second of three, and one was fifth of seven siblings.

All three cases of Klinefelter’s Syndrome developed normally till around the age of puberty. There are no indications that any of...
them grew up in a specially stressful environment, and in none of the cases is there any clear family disposition to psychosis or mental deficiency.

As far as somatic constitution is concerned, they have small atrophic testicles, decreased libido, and decreased ability to have sexual intercourse. They have scanty beard growth, feminine pubic hair distribution, slender extremities, and poorly-developed musculature.

In Klinefelter's Syndrome there is an abnormal sex-hormone balance with increased urinary excretion of follicle stimulating hormone and often decreased excretion of androgenic hormone.

The sex-chromosome abnormality in Klinefelter's Syndrome with the supernumerary X-chromosome, together with the sex-hormone abnormality, the infertility, the decreased libido and potency, and the affective reaction to their sexual indifference and incompetence, are factors which all probably help to shape the personality of these patients. This is characterized by immaturity, psychoinfantilism, lack of initiative, lack of spontaneousness, and lack of endurance, and originality, together with a vague awareness of being different from other men. These personality factors, together with a borderline intelligence or decreased ability to use a normal intelligence, make such persons especially susceptible to stress even of a very minor degree.

On account of the above-mentioned facts as supported by our cases, it is hypothesized that such persons are apt to develop reactive depressions or psychogenic paranoid psychoses as our three cases did. It might also be suspected that such patients would easily develop hysterical conversion reactions which has also been found by Nielsen (1965) in patients with Klinefelter's Syndrome admitted to a neurological ward because of hysterical symptoms and signs. It might further be expected that such immature, unstable, easily influenced persons would have a tendency to mild forms of delinquency (Nielsen, 1964), a hypothesis which is supported by the findings of Forssman and Hummer (1963) and Henriksen (1964), who found that 2 per cent. of delinquents had Klinefelter's Syndrome.

As happened in two of our cases, it might be expected that many patients with Klinefelter's Syndrome apply for and get disability pensions in their thirties because of poor social adjustment, backache on account of osteoporosis, lack of initiative, and asthenic symptoms (Nielsen and Olsen, 1965).

The frequency of Klinefelter's Syndrome in the normal population is 1.96 per 1,000, as found by Maclean et al. (1964) by studying 10,000 newborn boys. The frequency of Klinefelter's Syndrome in institutions for mental deficiency is between nine and ten per 1,000, as found by Barr et al. (1960), and Maclean et al. (1962), and the frequency of Klinefelter's Syndrome is found to be 11 per 1,000 in all male patients in a mental hospital and 20 per 1,000 in all male patients without schizophrenia (Nielsen, 1964).

**Summary**

A sex-chromatin and chromosome study of patients with hypogonadal symptoms and signs was made. Three of the 14 men were found to be cases of chromatin positive Klinefelter's Syndrome, two with 47 chromosomes and sex chromosomes XXY, one with 48 chromosomes and sex-chromosomes XXXY.

Case histories of the three patients with Klinefelter's Syndrome are presented, and the psychopathology of these cases discussed. The similarities in the three cases are immaturity, lack of initiative, lack of spontaneity, and lack of endurance, and originality, together with a vague awareness of being different from other men. These personality factors, together with a borderline intelligence or decreased ability to use a normal intelligence, make such persons especially susceptible to stress even of a very minor degree.

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