hands were unusual-looking with triphalangeal thumbs bilaterally and mild clinodactyly of the fifth finger bilaterally (fig 2). The thumbs were not opposable. The hallux was short with probable short metatarsal. No other skeletal abnormalities were noted. The skin showed many areas of depigmentation in linear patterns as well as whorls. Neurological examination showed mental retardation, but no specific defects.

LABORATORY STUDIES
Metabolic screening including routine urine analysis and urine screens for homocystine, ketones, and mucopolysaccharides were normal. A haematological evaluation, including white blood cell count, was normal with a haematocrit of 39 and a haemoglobin of 12-8. Chromosome analysis showed a normal 46,XX karyotype using multiple banding techniques. There was a large marker on the short arm of chromosome 22.

DERMATOGLYPHS
The dermatoglyphs of the proband were studied. The digital patterns showed 6 arches and 4 loops. (R: A,A,A,Lu,Lu; L: Lr, Lu, A,A,A,) with a total finger ridge count of 72. The axial t distance was raised (R, 33%; L, 28%) suggesting a t' to t" placement of the triradius. Several palmar triradii were absent, and two interdigital triradii were present. Both palms showed some dissociation, open thenar patterns, and Au hypothenar patterns. Palmar mainline formulas were: R: Oid0.5°.1.11; L: Oid0.5°.0.0.11.

Discussion
This patient shows skin findings that are compatible with the diagnosis of hypomelanosis of Ito. In addition, she has the unusual finding of triphalangeal thumbs. This hand abnormality has been described in other syndromes, such as the Holt-Oram syndrome, Fanconi's anaemia, and as an isolated defect. However, this patient's skin pigmentation, mental retardation, hypertelorism, and the abnormal thumbs are most likely the result of a single pathological process rather than the simultaneous occurrence of two or more unrelated syndromes or congenital defects. This may represent a variant of the syndrome of hypomelanosis of Ito or possibly a new syndrome involving triphalangeal thumbs.

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References

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A case of Klinefelter’s syndrome with 47,Xi(Xq)Y karyotype*

SUMMARY A patient with Klinefelter’s syndrome is described, in whom a 47,Xi(Xq)Y karyotype was established by trypsin-Giemsa and by BrdU acridine banding studies.

Several cytogenetic variants of Klinefelter’s syndrome have been described besides the most common 47,XXY condition. Most of them are represented by

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Case reports

other numerical aberrations involving the X or Y chromosome or both. In this report we describe a case of Klinefelter's syndrome where the additional chromosome was an isochromosome for the long arm of X.

Case report

The 33-year-old proband was admitted to the endocrine ward of our hospital for bilateral gynaecomastia. The family history showed no consanguinity and no genetic abnormalities. Both parents were in good health when the patient was born; the father was aged 35 and the mother 33. One sister aged 36 is normal. The father died at 62. At 13 the proband had acute glomerulonephritis and at that time his development was thought to be normal. Delayed puberty was first treated at the age of 20, but without success, using human chorionic gonadotrophin (HCG) and human menopausal gonadotrophin (HMG). Testosterone was then administered in order to enhance sexual maturity.

On examination the patient was in good physical condition, was alert and intelligent, and had been happily married for 5 years. He reported satisfactory sexual activity even without testosterone therapy. His height was 168 cm, span 168 cm, weight 63 kg.

Bilateral gynaecomastia was present and his testes were small (1 x 0.8 x 0.8 cm) and firm. His penis and pubic hair were stage T4. The prostate was small. Azoospermia was confirmed in repeated examinations of his ejaculate. Routine laboratory tests, electrocardiogram, and chest and skull x-rays were within normal limits.

ENDOCRINOLOGICAL STUDIES

Plasma testosterone was low in basal condition (1.1 ng/ml) and rose to 3.3 ng/ml after stimulation with HCG (5000 IU/day x 3 days im), and FSH and LH levels were raised.

Exogenous LH-RH and TRH stimulation tests were also done (table).

CYTOGENETIC STUDIES

A Barr body present in 20% of the cells in a buccal smear was larger than that of normal females (fig 1a). In peripheral blood lymphocytes all metaphases showed 47 chromosomes, represented by 44 autosomes and three sex chromosomes. One X and the Y chromosome had normal structure; the second X appeared as a large metacentric, and was interpreted as an isochromosome for the long arm, i(Xq), on the basis of the symmetrical banding pattern obtained both with the G banding and the BrdU banding techniques (fig 1b, c). Only a single centromeric constriction could be seen. In all metaphases from the BrdU-treated cultures the late replicating X corresponded to the i(Xq).

TABLE  Plasma gonadotrophin response to exogenous luteotrophic hormone releasing hormone (LH-RH 100 μg iv) and plasma prolactin response to thyrotrophic hormone releasing hormone (TRH 200 μg iv)

<table>
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<tr>
<th>Time (min)</th>
<th>-10</th>
<th>0</th>
<th>+10</th>
<th>+20</th>
<th>+30</th>
<th>+40</th>
<th>+60</th>
<th>+90</th>
<th>+120</th>
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<tbody>
<tr>
<td>FSH (mlU/ml)</td>
<td>60.4</td>
<td>75.4</td>
<td>74.2</td>
<td>101.4</td>
<td>106.6</td>
<td>109.0</td>
<td>128.7</td>
<td>117.7</td>
<td>118.0</td>
</tr>
<tr>
<td>LH (mlU/ml)</td>
<td>22.3</td>
<td>25.4</td>
<td>50.2</td>
<td>69.7</td>
<td>77.5</td>
<td>75.3</td>
<td>72.8</td>
<td>67.5</td>
<td>68.1</td>
</tr>
<tr>
<td>PRL (ng/ml)</td>
<td>3.9</td>
<td>4.3</td>
<td>54.3</td>
<td>160.3</td>
<td>166.6</td>
<td>160.6</td>
<td>180.7</td>
<td>98.2</td>
<td>98.0</td>
</tr>
</tbody>
</table>

FIG (a) Large sex-chromatin on buccal smear. (b) G banding of X, i(Xq), and Y chromosomes. (c) BrdU-acridine orange banding of X, i(Xq), and Y chromosomes.
DERMATOGLYPHIC ANALYSIS

Fingertip pattern analysis showed a high number of arches, and small loops were present only on three fingers of both hands: R \(_4\)L\(_4\)(4); L \(_3\)L\(_4\)(7); L \(_3\)L\(_5\)
(3). The total ridge count was 14. The \(a\)-\(b\) ridge count was 91 (right hand, 44; left, 47). The \(a\)-\(d\) angle on the left hand was 38\(\cdot\)5\(^\circ\), with a \(t\) axial triradius; however the measurement of the distal deviation\(^8\) gave a value of 21\%, which corresponds to a \(t\)’ position. On the right hand the axial triradius was ulnar extralimital, in association with an arch radial hypothenar pattern. Parents and relatives were not examined.

Discussion

On the basis of clinical and endocrinological findings, the proband can be classified as a case of Klinefelter’s syndrome. The main symptoms, azoospermia and hypergonadotropic hypogonadism, are present, together with bilateral gynaecomastia.

The peculiar feature of this case is the chromosomal constitution. On the basis of G and BrdU banding patterns the extra chromosome was identified as an isochromosome for the long arm of the X, karyotype 47,Xi(Xq)Y. Further support was given by the large size of the sex chromatin, which indicated that this chromosome formed the Barr body and was, by extrapolation, selectively inactivated, in agreement with the general rule for structurally abnormal Xs.\(^4\)

A similar state has been reported only in one other case,\(^5\) while in others the i(Xq) was associated with mosaicism.\(^6\) The rarity of i(Xq) in males contrasts with its relative frequency in females, where it accounts for about 20\% of gonadal dysgenesis cases,\(^7\) though generally with mosaicism.\(^8\)

The obvious explanation is that at least one complete X is required for development, and therefore the i(Xq) is seen in males only when associated with numerical aberrations of the X. Therefore, the origin of a karyotype 47,Xi(Xq)Y depends on the occurrence of two different mutational events: a non-disjunction resulting in the numerical abnormality and a centromeric misdivision responsible for i(Xq). Since no mosaicism was detected in our patient, the two events probably occurred jointly or separately during gametogenesis in either parent. It might also be speculated that the two events are somehow causally related, if it is assumed that the previous formation of i(Xq) favours non-disjunction, or that failure of X chromosomes to pair (in the mother) could favour misorientation of one of the univalent Xs and thus lead to transverse division at the centromere, that is to misdivision.\(^9\)-\(^11\) Xg blood group evidence\(^12\) and correlation with the advanced age of the father,\(^13\)\(^14\) on the other hand, suggest paternal origin of most cases of i(Xq), especially those with a 45,X line. It could be postulated that paternal gametes bearing an i(Xq) are favoured in comparison to maternal i(Xq), which in 50\% of cases would result in non-viable i(Xq)Y zygotes. However, in our case, we were not able to establish the parental origin of the two events, because of the lack of informative markers.

As for the dermatoglyphic patterns, the extra double dose of Xq may be responsible for the low TFRC. We conclude that Xq trisomy (with two doses inactivated) with a single dose of active Xq is enough to induce a similar clinical syndrome as the presence of an entire additional X chromosome.

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References


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Announcements

Perspectives in Biology and Medicine announces the Dwight J Ingle Memorial Award for authors under 35: a $500 award for the best essay (in English) submitted in competition between 1 March and 31 December 1980. For details, see the autumn 1979 issue or write to the Editorial Office, Perspectives in Biology and Medicine, Culver Hall 403, 1025 E 57th Street, Chicago, Illinois 60637, USA.

The 6th International Congress of Human Genetics will be held in Jerusalem, Israel on 13-18 September 1981.

Application forms are available from the Congress Secretariat, PO Box 983, Jerusalem, Israel.
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