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resembling those of SLO syndrome, especially when atypical clinical or developmental signs are present. Although limitations in our diagnostic abilities exist, when patient’s presentations do not conform to established descriptions of clinical syndromes, an exhaustive search for other aetiologies must be made.

The authors wish to thank Ms Regina Kobli for expert assistance in the preparation of this manuscript.

References


Incontinentia pigmenti in a boy with Klinefelter’s syndrome

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SUMMARY A boy with the cutaneous lesions of incontinentia pigmenti is described. Chromosomal analysis revealed the 47,XXY karyotype of Klinefelter’s syndrome. Since incontinentia pigmenti trait is usually lethal in males, the possibility of the second X chromosome protecting against fetal death is discussed.

It has been suggested that the pattern of inheritance of incontinentia pigmenti (IP) best fits that of an X linked dominant trait which is lethal in males.1 2 Nonetheless, male cases have been recorded and constitute 2 to 3% of all reported cases.1 2 All but two of these male cases occurred as sporadic new mutations. We describe a patient with incontinentia pigmenti and Klinefelter’s syndrome, a combination which has only been previously reported once.3

Case report

A boy aged one year presented to the Dermatology Clinic with a history of linear, whorled, macular, streaky pigmentation predominantly over the right side of the trunk but also extending on to one leg (figure). This was noticed in the first month of life but was not present at birth. No preceding inflammatory, vesicular, or warty skin eruption was observed by the parents or any of the baby’s medical attendants.

At birth he was light for dates (2050 g at 41 weeks’ gestation). Neonatal blood films showed no evidence of eosinophilia. At his 18 month assessment his weight and head circumference were below the 3rd centile. He was noted to have small epicanthic folds, low set ears, elfin facies, and his skull was wider posteriorly than anteriorly, but psychomotor development was normal. As his testes were small and soft, Klinefelter’s syndrome was suspected and chromosome analysis revealed a karyotype of 47,XXY. He was assessed again at the age of two when he had developed conical, hypoplastic canine teeth. However, his hair was normal and his eyes were normal apart from a transient strabismus.

His father was aged 29 at the birth of the child and his mother 26. They were both Caucasian and were not related. His mother had had one previous pregnancy which spontaneously aborted after 12 weeks’ gestation. Both parents were examined fully and neither had any sign of pigmentary disturbance, its residual changes, or other features of incontinentia pigmenti. The mother’s teeth were normal and both parents had normal karyotypes. Xg(a) blood groups were carried out by Dr Tippett on the proband and his parents. All were Xg(a–).
Discussion

This patient has skin changes typical of the pigmen-
tary phase of IP. The pigmentary phase is the most
constant sign of the syndrome and is not necessarily
preceded by vesiculation or verrucous changes,
which were absent in 10-7% and 23.8% of cases,
respectively, in a collected series. Apart from his
resolving strabismus and the dental defect, he has no
other stigmata associated with IP at present.

Statistical analysis of 74 sibships supports the
theory that IP has an X linked dominant inheritance
which is lethal in males. However, male patients
occur sporadically (2 to 3%) and most are believed
to represent new mutations, since only two reports
of affected males born to affected mothers have
been found. How these males escape the post-
ulated lethal effects of the abnormal gene is un-
known, but those that survive are no more severely
affected than their female counterparts. The possi-
ability of this being due to a half chromatid mutation
has been debated, but another possible explana-
tion has been the suggestion that affected males may
have Klinefelter's syndrome or XX/XXY
mosaicism. Few of the reported male patients have
had their testes examined, which provided the clue
here, and few have had their karyotypes checked.
There is only one previous report of XXY Kline-
felter's syndrome in incontinentia pigmeni. There
are reports of normal XY karyotypes, but in these
patients Klinefelter mosaicism cannot be excluded.

It is tempting to speculate that the presence of an
additional X chromosome protected the patient
from the lethal effects of the IP gene as it is thought
to in females. This would apply whether the patient
represented a new mutation or inherited the IP gene
on the X chromosome from his mother.

To be protective the additional X chromosome
with a presumed normal allele would require to be
derived by non-disjunction in the first meiotic
division of either spermatogenesis or oogenesis.
Alternatively, the new mutation could have occurred
in one chromatid at the second meiotic division
of oogenesis followed by non-disjunction. Unfortu-
nately, Xg(a) blood grouping did not provide infor-
ation as to the source of the additional X
chromosome.

Hodgson et al recently reported two girls with
IP and both showed balanced de novo X;autosome
translocations involving band Xp11. They therefore
suggested that this band might be the site of the IP
gene locus. They also noted that the normal
X chromosome was inactivated and discussed
explanations as to why the IP gene had not proved
lethal.

Wieacker et al showed that fibroblasts grown from
normal and pigmented areas of skin contained the
same X chromosome. They suggested that this
supported the hypothesis that the transition from
inflammation to hypertrophy could reflect normal
cells replacing the defective ones expressing the
mutant allele by means of somatic selection against
the defective cells. This theory would apply to the
two X chromosomes of Klinefelter's syndrome.

Chromosome analysis of other males with the
syndrome, with exclusion of mosaicism, may clarify
the inheritance of the disorder. The new recom-
binant DNA methods should, when sufficient
probes are available, allow proof of the mode of
inheritance.

We should like to thank Dr P Tippett of the MRC
Blood Group Unit, The Galton Laboratory,
London, for the Xg(a) blood groups.
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References


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doi: 10.1136/jmg.24.7.439

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