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.

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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 Tippet on the proband and his parents. All were Xg(a-).

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URE Pigmentation on trunk of proband.

Discussion

This patient has skin changes typical of the pigmentary 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.² 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.² 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.^{4,5} How these males escape the postulated lethal effects of the abnormal gene is unknown, but those that survive are no more severely affected than their female counterparts.² The possibility of this being due to a half chromatid mutation has been debated,^{1,4,6} but another possible explanation has been the suggestion that affected males may have Klinefelter's syndrome or XX/XXY mosaicism.⁶ 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 Klinefelter's syndrome in incontinentia pigmenti.³ There are reports of normal XY karyotypes, but in these patients Klinefelter mosaicism cannot be excluded.^{1,6}

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. Unfortunately, Xg(a) blood grouping did not provide information as to the source of the additional X chromosome.

Hodgson *et al*⁷ 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*⁸ 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 recombinant DNA methods should, when sufficient probes are available, allow proof of the mode of inheritance.

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