

Klinefelter's syndrome and maternal XX/XXX mosaicism

Sir,

We wish to document a rare case of a 46,XXY male, whose mother was shown to have a karyotype of 46,XX/47,XXX. Very few cases have been reported in the literature. The first two were found in Germany by Rosenkranz (1965), and were the only children with chromosomal abnormality in the 28 offspring of nine trisomy X females (Carr, 1969). To the authors' knowledge, the only other two cases of Klinefelter's syndrome with a trisomy mother were reported by Baikie, Dartnell, and Lickiss (1972) and Geisler, Svejcar, and Degenhardt (1972). Theoretically, half of the children of fertile 47,XXX females should be either 47,XXY males or 47,XXX females. This genetic expectation is not borne out in surveying the available literature on children of 47,XXX females (Bartalos and Baramki, 1967; Court Brown, 1969; Reisman and Matheny, 1969) or on mothers of 47,XXY males (Nielsen, 1969; Nielsen *et al*, 1969). Most of the speculation concerning this rarely observed condition attempts to explain why the 50% expected rate is not met (Bartalos and Baramki, 1967; Reisman and Matheny, 1969). It has been suggested that an XX ovum is lethal, which seems unlikely. The more likely explanation would seem to involve a preferential segregation in which the secondary oocyte containing XX becomes a polar body during the disjunction process in meiosis I. In the present case, the aetiology of the extra X chromosome is unclear. The extra X chromosome in the male proband (XXY) could have come from an XX bearing egg produced by disjunctive separation of the three Xs or by non-disjunction of two of the synapsized Xs during meiosis or from a XY bearing sperm produced by non-disjunction of the sex chromosomes in spermatogenic meiosis. The propositus is a 25-year-old-single white male, a sociopath with drug abuse, whose biological father is deceased. His 26-year-old full sister and 18-year-old stepbrother are normal. There is no outstanding history of illness in the family, other than the mother's 46,XX/47,XXX mosaicism. The available data do not allow the determination of the aetiology of Klinefelter's syndrome in this patient; we merely wish to put this case on record with the few other reported cases in the literature.

Yours, etc,

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Hirschsprung's disease and congenital deafness

Sir,

The author has encountered a case of short segment Hirschsprung's disease and profound bilateral sensory neural deafness in a male infant. This brings the number of cases reported in the literature to eight. Skinner and Irvine (1973) discussed the possible relationship between an ototoxic drug such as streptomycin and concluded that in only one case was there convincing evidence that streptomycin might have played a part in the aetiology (case 4). However, in case 2, the patient received a short course of streptomycin at 5 months and subsequently was noted to be deaf between 1 and 2 years of age. My patient also had a short course of an ototoxic drug, namely kanamycin, which was given in a dosage completely appropriate for his age (15 mg/kg) with a total dosage lasting for four days, during which time there was no evidence of any renal impairment. This drug was given in the newborn period for suspected septicaemia and raises the possibility that patients with Hirschsprung's disease may be unusually susceptible to ototoxic drugs, even when these are given in appropriate dosages.

Skinner and Irvine (1973) conclude that the association of Hirschsprung's disease and congenital deafness would be expected to occur purely by chance in about one in every five million births. An attempt was made to assess the frequency of the association by surveying the caseload of Hirschsprung's disease known to the British Columbia Registry for Handicapped Children over the years 1964-72, inclusive. The Registry has multiple sources of ascertainment (Lowry *et al*, 1971) and it is recognized that the time of ascertainment of deafness will be considerably delayed as compared to the ascertainment of Hirschsprung's disease. Hence the cohorts who are born in the last two years of the study period in question may very well contain cases of deafness; however, those cases born in 1971 or earlier would be expected to have been ascertained if deafness was present. It is of interest to record that the incidence (1 in 4700 livebirths) in British Columbia is almost exactly equal to that in Cincinnati and Denmark (Passarge, 1967). From a total caseload of 66, there are two cases of Hirschsprung's disease associated with Down's syndrome, one with trisomy 16, one with X/XX/XXX mosaicism, and another with the Smith-Lemli-Opitz syndrome (Lowry, Miller, and MacLean, 1968). The case of Hirschsprung's disease and deafness is not included in our incidence figures, since this particular child was born in

Ontario and the family moved to British Columbia while he was still an infant, thus we are unable to calculate from our data whether the association of the two diseases is more frequent than one per five million livebirths.

Yours, etc,

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