

Case Reports

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A Case of 48,XXXX Female with Normal Intelligence

Mental retardation has frequently been noted in patients with extra sex chromosomes. The following case report details a girl with 48,XXXX sex chromosome constitution and normal intellectual potential.

Case Report

The patient was first seen at age 3 years 9 months because of slow development of speech. She was the second child of a 25-year-old mother who had a normal pregnancy, labour, and delivery. Birth weight was 2892 g. The father was 28 years of age. There are two female sibs, aged 6 and 2 years, and both are in good health. No miscarriages are reported.

Physical examination revealed an attractive child who was 88 cm tall and weighed 13.7 kg, both of which were within the lower 20th centile for her age and sex. She had epicanthal folds, incurved 5th fingers, widely-spaced nipples, and bilateral external tibial torsion. Her speech was unclear but she related warmly and appropriately to the examiner.

Because of the speech difficulty language, speech, and hearing were evaluated. On audiometric screening, hearing was judged normal in both ears. The patient was found to have a severe articulation problem with a delay in both receptive and expressive language.

Psychological testing was performed the same day as

the physical examination. Despite her indistinct speech, she scored a mental age of 3 years 9 months (IQ 100) on the Stanford-Binet Intelligence Scale, Form L-M. Followup testing at age 5 years showed the patient to be functioning within the normal range using the Wechsler Intelligence Scale for Children: verbal IQ=106, performance IQ=94, full scale IQ=101; mental age=5 years 1 month.

Laboratory studies included normal skull films, PBI, urinalysis, CBC, and Guthrie test. A 24-hour urine screen for amino acids was normal and the turbidity test for mucopolysaccharides was negative.

Cytogenetic Studies. Leucocyte culture of peripheral blood was performed by standard methods. Fifty cells were counted and the chromosome complement was 48 with no evidence of mosaicism, and the extra chromosomes were in the C group (Fig. 1). Buccal smear on two occasions showed the presence of up to 3 Barr Bodies (Fig. 2) compatible with tetra X chromosome constitution. The detailed buccal smear studies are summarized in Table I.

Skin biopsy was requested but not granted. Chromosome analysis of peripheral leucocyte culture from each parent showed normal chromosome complement.

The dermatoglyphic pattern of the patient was analysed and is shown in Table II. The unusual features include low ridge count, radial loop on the right 4th finger, and the 'X' formulation of line C on the left palm.

Discussion

A recent summary of the age, IQ, and clinical features of 10 cases of 48,XXXX females has been presented (Telfer *et al*, 1970). In addition other

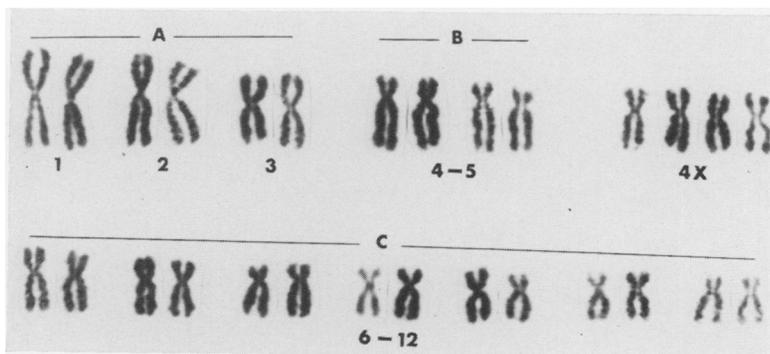


FIG. 1. Partial karyotype of the probanda showing 48,XXXX chromosome complement.

cases are described in the literature (Hanicka *et al*, 1969; Sokolowski, Knaus, and Kleczkowska, 1969; Berkeley and Faed, 1970; Duncan, Nicholl, and Downes, 1970; Park, Tyson, and Jones, 1970). It can be observed that all these tetra X females were mentally retarded; however, this may represent a biased sampling done primarily among mentally

retarded populations. Our patient probably represents an exception to the previously reported definitive correlation between 48,XXXX females and mental retardation. The normal IQ of this case could, however, be explained on the basis of an undetected chromosomal mosaicism. The IQ of 100 as measured by the Stanford-Binet Intelligence Scale is exactly average or normal for the patient's age. She has been enrolled in a preschool language programme where her teachers report normal academic skills for her age, and this has been objectively substantiated by the normal scoring on the Wechsler Intelligence Scale for Children.

It has been stated that the tetra X females have a false air of Down's syndrome (de Grouchy *et al*, 1968; Lejeune and Abonyi, 1968), but the general appearance of the present case did not suggest this except for the epicanthal folds. Tallness has also been observed in several of the previous reports (Anderton *et al*, 1968; Lejeune and Abonyi, 1968; Park *et al*, 1970); our own patient is in the lower 20th centile for height for her age and sex. These findings tend to indicate that there is no clear-cut clinical picture associated with tetra X females.

Low dermal ridge counts have been reported in association with X chromosome hyperploidy (Telfer *et al*, 1970). The low ridge count of this patient is consistent with this observation. The finding of radial loops on the 4th finger of the right hand and the 'X' formulation of line C on the left palm of the current case represents two further unusual dermatoglyphic features.

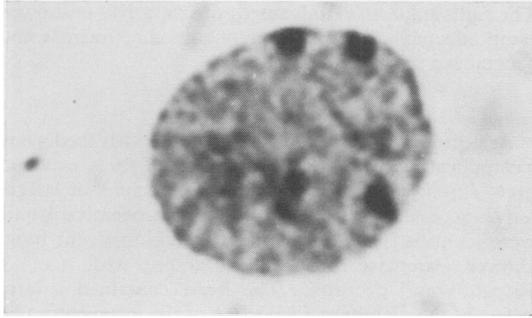


Fig. 2. Buccal smear of the proposita showing 3 Barr bodies.

TABLE I

THE FREQUENCY OF ORAL MUCOSA CELLS WITH 1, 2, AND 3 BARR BODIES FROM A 48,XXXX GIRL

	No. of Barr Bodies				Total
	0	1	2	3	
No of cells	254	70	130	72	526
Percentage	48.3	13.3	24.7	13.7	100

TABLE II

DERMATOGLYPHS OF THE HANDS OF THE PATIENT

Digits													
	Left					L	Total	R	Right				
	5	4	3	2	1				1	2	3	4	5
Patterns	A	U	U	U	U				U	U	U	R	U
Ridge counts	0	0-4	0-12	0-6	0-6	28	60	32	11-0	1-0	12-0	0-7	1-0

Palms

	D	C	B	A	Axial Triradius		HT	T-1 ₁	1 ₂	1 ₃	1 ₄
					Height	ATD Angle					
Left	11(10)	X	7(6)	1	27%	63°	A ^u /A ^c	O	O	O	O
Right	7	5*	5*	3	22%	59°	A ^u /A ^c	O	O	O	L

Sum of ATD angle 122°. Simian crease: none. Partial simian crease: none.

Summary

Mental retardation has been shown to be the prime feature of the 48,XXXX condition from the literature. A first case of this chromosome disorder with normal intelligence is presented.

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A Case of Double Aneuploidy, 47,XXY,14-t(13q14q)+, also Probably Homozygous for the Cystic Fibrosis Gene

Case History

The propositus was born weighing 3405 g after an uneventful 42-week pregnancy; at birth his mother was

aged 26 and his father 27. Multiple congenital abnormalities were evident—a central scalp defect, microphthalmia, cleft soft palate, and prominent heels suggested the trisomy 13 syndrome (Patau *et al*, 1960). In addition, there was widening of cranial vault sutures, a unilateral accessory auricle, cardiomegaly, a small penis, and partially-descended testes, ulnar deviation at the wrists, low-set thumbs, and normal palmar creases, whilst the finer dermatoglyphs were not distinguished. The right ankle was subluxated; the right hallux showed camptodactyly. He died from pneumonia, uraemia, and generalized sepsis at 8 days.

Necropsy

At necropsy there was severe bilateral otitis media and a complicating basal meningitis; swabs of these exudates grew *Pseudomonas aeruginosa*. Focal lesions of coagulative necrosis with colonies of Gram-negative bacilli were identified in adrenals, liver, and kidney; the lungs showed extensive bronchopneumonia, with foci of vasculitis and necrosis. The heart contained a large defect of the membranous portion of the interventricular septum, and there was moderate preductal coarctation. There was excessive notching of the spleen and several splenunculi were present. The kidneys were of normal size, but on the cut surface small pale nodules diffusely scattered through the parenchyma obliterated much of the corticomedullary differentiation. These nodules were made up of microcystic areas and tangles of tubules and were not clearly differentiated. The testis appeared normal on gross and microscopic examination with conventional staining procedures.

The pancreas appeared firmer than normal; histological examination showed a general increase in interstitial fibrous tissue, scantily infiltrated with mononuclear cells, and an atrophy of acinar tissue. Inspissated secretions were seen in each acinus, with attenuation of the epithelial cells. Islet tissue was unaffected. Many larger ducts contained inspissated secretions, with small areas of microcyst formation. A reassessment of sections of the trachea and gut showed, in both, a widening of the mouths of the mucous glands, with the acinar elements distended by inspissated secretions. A pathological diagnosis of mucoviscidosis was made.

Cytology and Tests for Cystic Fibrosis

Chromosome analysis in PHA-stimulated lymphocytes showed a modal count of 47; there was a missing D, an extra 3, and an extra C. Quinacrine fluorescence (Bobrow and Pearson, 1971; Caspersson, Lomakka, and Zech, 1971) showed the sex-chromosome constitution to be XXY, and the autosomal constitution 14-t(13q14q)+. Further examination of the translocation chromosome showed an area of intense fluorescence adjacent to, but on the 14q side of the centromere; such bright fluorescence is characteristic of the proximal part of the 13 short arm, suggesting that within the translocation chromosome the whole of the 13 was represented, excepting the most distal parts of the short arm (Fig. 1).

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