Turner's Syndrome

By

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Endocrine disorders are well-known to be capable of inhibiting growth. Growth is promoted by the somatotropic hormone, the thyroid hormone and the androgens. A decrease in the synthesis of any of these hormones leads to a retardation of growth.

Not all disturbances of growth are due to endocrine factors. In primordial dwarfism the production of somatotropic hormone is normal but the organism is not sufficiently sensitive to it; these babies are usually born with subnormal weight. Pituitary dwarfs, on the other hand, are born with normal weight. Maternal hormones promote intrauterine development, and any reduction of their effect may retard growth.

In some cases of primordial dwarfism there are no changes whatever except the retardation of growth, while in other cases the retardation may be accompanied by different developmental anomalies. To the latter category belong infants suffering from progeria, further gonadal aplasia or dysplasia. Cases of this kind have been termed sexogenic dwarfism by Rössle and Wallart [8].

Although gonadal dysplasia is a frequent condition, its diagnosis is often difficult. With the advancement of diagnostics, however, more and more asymptomatic cases are recognized as gonadal dysgenesis which were earlier diagnosed as pituitary dwarfism. Some slight developmental anomalies described and correctly interpreted prior to the general use of chromosomal examinations are a great help in differential diagnosis.

A characteristic example is Turner's syndrome. This condition displays a number of characteristic features, such as a height below 145 cm, a narrow bulging chest, underdeveloped lower jaw, gothic palate, short neck with pterygium. Osteoporosis and retarded ossification have likewise been described. The mammillae are undeveloped, and there are hairs on the neck and the back. The skin shows naevi and telangiectases. Other frequently observed symptoms are coarctation of the aorta, renal malformations, colour blindness, ptosis, strabism, mental deficiency and hardness of hearing. Lymphogenic oedema, especially in the distal part of the extremities, may be present at birth. With these common symptoms all kinds of developmental anomalies may be associated.

TABLE I

Case No.	Age years	Height cm	Osseous development	Chest	Malformations	Pubic hair	Internal sex characteristics	Sex chromatin	Chromosomes	Laboratory tests		
										17-ketosteroids	Oxysteroids	Gonadotr. hormone
1	14	130	Suggestive of 16—17 years	Shield shaped	Pigmented spots on face. Rudimentary 4th toe of left foot	sparse	Resistance pointing to uterus	Barr neg.	XO 45	6.1 mg/ 24 hrs		normal
2	16	136	Suggestive of 14 years	Normal	Pigmented spots on face and legs. Rudimentary 4th toe on left foot	none	At laparoscopy no structures suggestive of genital organs in lesser pelvis	Barr neg.	45	4.0 mg/ 24 hrs		5.2 mg/ 24 hrs
3	11	121	Suggestive of 8—9 years	Shield shaped	Short neck. Protruding scar on face. Gothic palate. Striae. Strabism	none	At laparoscopy no uterus palpable, its site occupied by connective tissue. Rudimentary ovary and tubes	Barr neg.	Mosaicism XO/XX	2.8 mg/ 24 hrs	1.2 mg/ 24 hrs	20—30 U.
4	14	121	3 years' retardation. Irregular metacarpal bones. Loose structures	—	Cubitus valgus. Pterygium colli. Mongolism	none	At laparoscopy a 6 cm thick structure instead of uterus; cord corresponding to uterine tube. No ovary	Barr neg.		2.7 mg/ 24 hrs	1.5 mg/ 24 hrs	50 U

We have observed four cases of Turner's syndrome. Their most characteristic features are listed in Table I.

Symptoms may be so conspicuous as to reveal Turner's syndrome at first inspection, as happened in our cases Nos. 3 and 4, where the patients had a pterygium colli. Although retarded growth, short neck and ossification disorders were present in cases Nos. 1 and 2 also, these symptoms were less manifest. In case 2 no uterus or ovary was found at laparoscopy while the radiograph revealed just slight changes in the bones. In case No. 1 ossification was accelerated, while retardations of 2 to 3 years were observed in the rest. Gonadotrophin excretion was increased in one case, and there was adiposity with atrophic striae in another. The fourth toe of the left foot was rudimentary in cases Nos. 3 and 4. It was precisely this anomaly which pointed to Turner's syndrome in case 3. The buccal mucosa was Barr-negative in all cases.

Chromosomal examinations were made in three patients, and the Denver system was used for the evaluation of the chromosomes. Figs. 1 and 2 illustrate the chromosomal pattern in case No. 1.

In cases Nos. 1 and 2 the chromosomes were studied in leucocytes cultured from peripheral blood, by the method of MOORHEAD et al. [6] as modified by SCHULER [9]. Sex chromatin was examined in smears prepared from the buccal mucosa. A total of 32 cells was analyzed in case No. 1; 30 cells each contained 45 chromosomes, and 2 cells, 44 chromosomes. The number of examined cells totalled 14 in case No. 2; 13 cells contained 45, and 1 cell 44 chromosomes.

In case 3 the chromosomes were examined in cells taken from the fascia lata. The number of observed mitoses was 15; 45 chromosomes were found in 11, 46 chromosomes in 4 cases. The configuration was 44A XO in the cells with 45 chromosomes, and 44A XX in those with 46 chromosomes. The chromosomal picture revealed, thus, an XO/XX mosaic pattern with the predominance of XO.

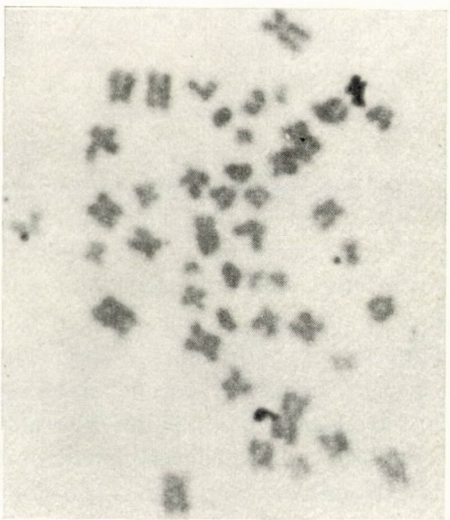

FIG. 1. Chromosomal pattern in a cell cultured from peripheral blood. Number of chromosomes, 45. Orcein stain, ×2800

DISCUSSION

Of our four cases, only patient No.1, a girl of 14 years, had some pubic hair. The growth of pubic hair in females is governed by the androgens of the adrenal, and LIPSETT [5] has

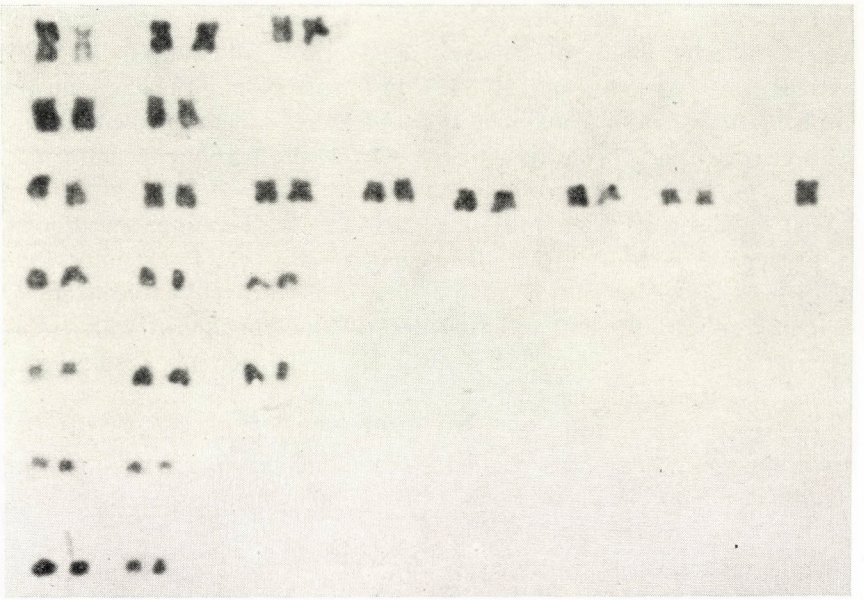

FIG. 2. Chromosomes grouped according to the Denver system. A sex chromosome is missing, the existing one being X

shown that their synthesis is reduced in Turner's syndrome. The centres of ossification were better developed in the patient with pubic hair, a phenomenon that may also have been due to increased androgenic effect. The growth of the patient was nevertheless stunted. Renal dysfunction has also been observed in Turner's syndrome and adrenal oestrogens may provoke menstruation-like haemorrhages [2].

In case No. 3 obesity and striae on the outer aspect of the thigh were present. They were ascribed to pituitary hyperfunction, a condition frequently met with in cases of childhood gigantism. In this instance, however, growth was retarded in spite of the supposed pituitary hyperfunction. WILLEMSE [11] described a case of Turner's syndrome with acromegaly due to an eosinophile pituitary adenoma. Although the epiphyseal lines were not closed, there was no growth; this was explained by supposing that the bone was insensitive to growth hormone. This case is a further proof of growth being primordially disturbed in gonadal dysgenesis.

Colour blindness is frequent among patients with Turner's syndrome [7]. FORD et al. [4] observed that one of the sex chromosomes is missing in such patients. The existing X chromosome is, according to these authors, of maternal origin, since the fathers of such patients are mostly not colour blind, and hereditary colour blindness linked to the X chromosome is recessive in females so that it remains latent in the heterozygous mother. Meiotic nondisjunction presumably

causes the sperm fertilizing the ovum to lose its sex chromosome.

The sex-chromosome pattern is variable in Turner's syndrome; apart from XX, XO and XY, various forms of mosaicism have been described. Chromosomal examination is of aetiological importance. Analysis of the sex chromatins does not always shed light on the genetic origin of the disease. Patients with the mosaic pattern XX/XO may be Barr-positive. It is imperative to make further examinations in such cases; Barr positivity makes the chromosomal examination by no means superfluous.

XO is the most usual and typical configuration in gonadal dysgenesis. Frequently nothing but connective tissue displaying neither ovarian nor testicular characteristics is found at the site of the ovary. In other cases the gonads may assume transitional forms with predominant male or female features.

The indifferent primitive gonad consists of cortex and medulla; the ovary develops from the former, the testis from the latter. Accordingly, gonadal dysplasia appears in two forms.

(i) Rudimentary medullary elements of the primitive gonad (Leydig cells, testicular tubules) only are found in cases of medullary hypoplasia, the cortex is represented by connective tissue. The sexual character of the genital organs is sometimes uncertain or feminine in such cases, but the secondary sex characters show virilization. The cells contain no sex chromatin. The chromosomal pattern is usually XO or XY, but some cases show a mosaic pattern and cells with XY sex chromosomes are predominant. Cases of male pseudohermaphroditism have also been described, when the patients had both uterus and Fallopian tube, although the gonads were actually testicles in spite of the gonadal dysgenesis.

(ii) Rudimentary cortical elements of the primitive gonad (primordial follicles) with no medullary elements can be found in cases of cortical hypoplasia. The genital organs are unmistakably feminine and infantile, and the secondary sex characters may be slightly feminine. The sex chromatin pattern may be negative or positive, the sex chromosome configuration either XO or XX. Cells with the latter configuration are predominant in cases of mosaicism. Sometimes growth may be normal and secondary female sex characteristics appear at puberty; even feeble menstruations may occur. Yet, such patients remain sterile owing to incomplete ovarial differentiation.

If the sexual gland is essentially ovarian, the sex chromosome configuration may be XX, and the patient is, of course, Barr positive. Dysgenesis in such cases is presumably due to some injury suffered by the indifferent gonad at a very early period, or, else, cells with XX chromosomes predominate in the mosaicism, as has been noted above.

FERRIER et al. [3] are of the opinion that mosaicism — in contrast to pure XO cases — may at least to some extent prevent the development of concomitant abnormities. Developmental disorders were nevertheless character-

istic of our patient with XO/XX mosaicism (No. 3). Such cases need not, however, contradict FERRIER's contention, since cells with XO chromosomes were probably in majority. In any case, our present observations seem to suggest that, without mosaicism, even a typical XO pattern does not necessarily entail a great number of developmental anomalies and the full severity of the syndrome. Our case No. 2, for instance, was comparatively poor in symptoms, despite an XO chromosomal pattern. Abnormalities (pterygium, lymphoedema, etc.) were, on the other hand, most numerous in our case No. 3, the one with XX/XO mosaicism. The number and gravity of abnormalities seem therefore to vary from individual to individual, irrespectively of the ratio between the XX and XO types of cell.

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SUMMARY

Turner's syndrome has been discussed in connection with four cases. The chromosomal pattern was examined in three of them. The cells contained 45 chromosomes in two cases, where only one sex chromosome was present. The third case revealed an XO/XX mosaicism and it was in this patient that the symptoms of Turner's syndrome were most pronounced.

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