Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 15 (3–4), pp 295 – 299 (1974)

45,X/46,XY/47,XYY mosaicism in a phenotypic female with gonadoblastoma

By

MAGDA OSZTOVICS, GY. IVÁDY, P. RUZICSKA, ERICA M. BÜHLER and L. KIRÁLY

Pál Heim Children's Hospital, Budapest; National Institute of Public Health, Budapest; Department of Genetics, University Paediatric Clinic, Basel, Switzerland

Received June 11, 1974

A case of a phenotypic female patient with 45,X/46,XY/47,XYY mosaicism found in lymphocytes as well as in cell cultures prepared from a gonadoblastoma removed by adnexectomy is reported. The two investigated tissues displayed a different distribution of the three cell lines.

CLINICAL FINDINGS

The patient was born when her mother and father were 41 and 46 years old, respectively. This was the first pregnancy of the mother during her marriage of 2 years. The parents are healthy and cytogenetically normal. The father is a dizygotic twin. The next child, a healthy and cytogenetically normal girl was born 2 years after the birth of the proband. Gestation time was normal, birth weight was 3200 g, height 42 cm. Until the age of 5 years the parents were not concerned about her short stature. In the subsequent years a hypertrophy of the clitoris was observed; it was attributed to the androgenic treatment prescribed by the family physician in order to enhance the child's growth.

At the age of 18 years, the patient was referred to us for chromosome investigation because of primary amenorrhoea and absence of normal puberty. At that time, her height was 156 cm. Her breasts were undeveloped, she had no axillary hairs and her pubic hair showed a masculine pattern. She had hirsutism on the face and limbs, and a well-developed musculature. Together with a prominent larynx and chin, these features gave her a masculine appearance.

Clinical examination revealed some minor malformations such as cubitus valgus, deep hair line, pigmented naevi and shortness of the IV. metacarpal bones on hands and feet. The genitalia including the vaginal meatuses were normal but for an enlarged clitoris (Figure 1).

Exploratory laparotomy revealed a small uterus located in the right pelvic cavity and Fallopian tubes. On the right side neither a gonad nor a fibrous streak was seen, while on the left side, a testicle-like gonad of the size of a bean was found. This was removed and identified

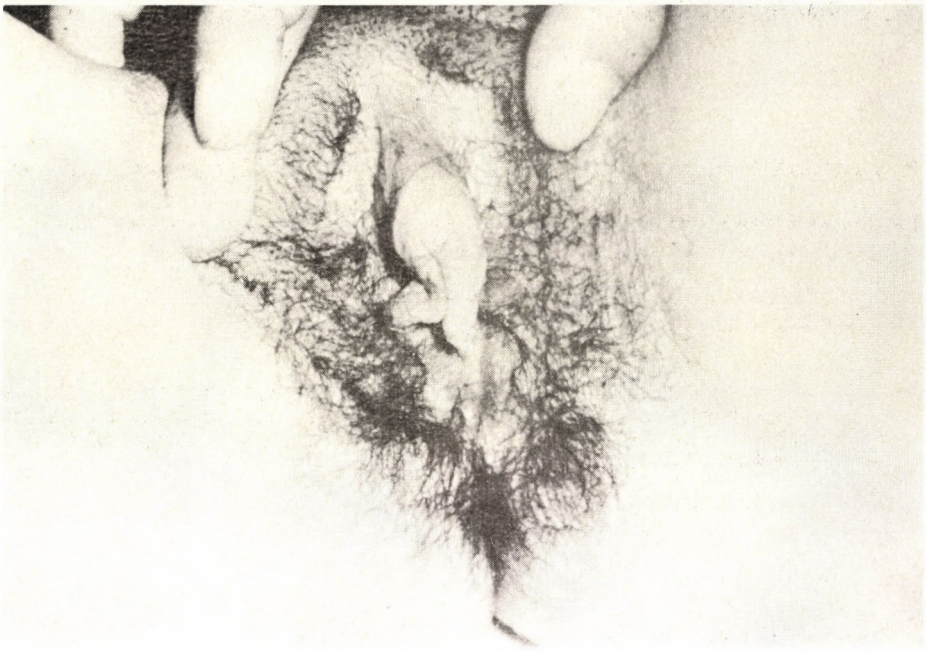

FIG. 1. External genitalia of the proband with 45,X/46,XY/47,XYY mosaicism

as a gonadoblastoma. It measured 12 mm in diameter, it was firm in consistency with a smooth external surface. Microscopic examination showed (a) remnants of the cortical part and dysgenetic seminiferous tubules; (b) interstitial Leydig cells in large groups without malignant appearance; (c) Sertoli cells in folliculoid arrangement separated by connective tissue strands; (d) cells possessing large round nuclei with clear cytoplasm; (e) calcified concretions which were sudanophilic and Schiff positive (Figure 2).

In view of her age, oestrogen therapy was prescribed. It must be added that she is a promising sprinter, whose degrees at school have been excellent and uninfluenced by her inhibited personality due to the abnormal sexual development.

CYTOGENETIC FINDINGS

There were neither Barr bodies in the buccal smear, nor drumsticks in the blood smear. Y bodies were detected in the blood: 10% of the cells contained single and 23% double fluorescent bodies.

Chromosome investigations revealed a triple mosaicism, 45,X/46, XY/47, XYY, in the lymphocytes as well as in the cells cultivated from the gonadoblastoma. The distribution of the three cell lines in the two tissues is shown in Table I. Fluorescent metaphasis with YY is presented in Figure 3.

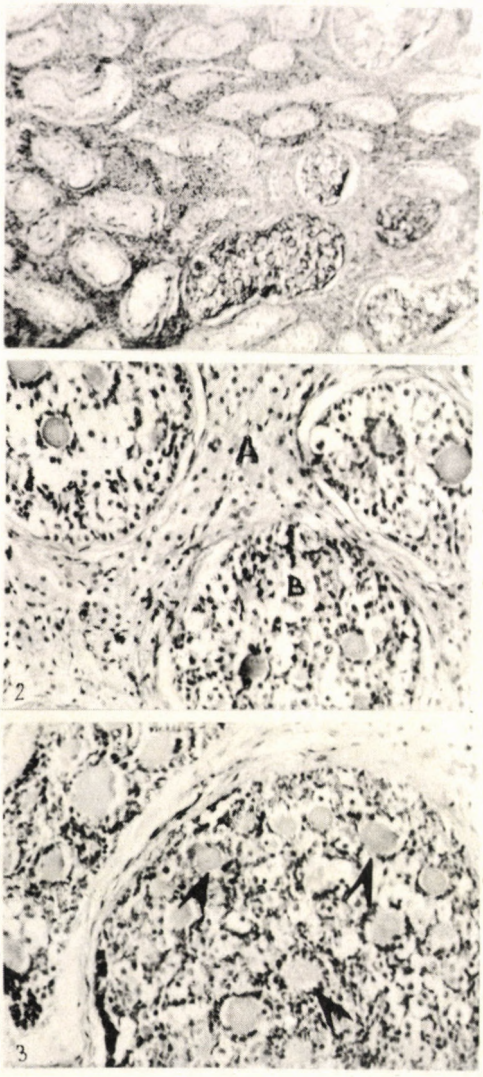

FIG. 2. Sections of the gonadoblastoma showing dysgenetic seminiferous tubules (1), Leydig cells and Sertoli cells (2), and calcified concretions (3)

DERMATOGLYPHIC EXAMINATION

Dermatoglyphic studies showed a total ridge count of the fingers higher than the mean of the normal female population, but it could not be assessed as pathologic since it was in the range of the expected values inherited from the parents. TRC of the proband was 169; those of the father and mother were 175 and 139, respectively.

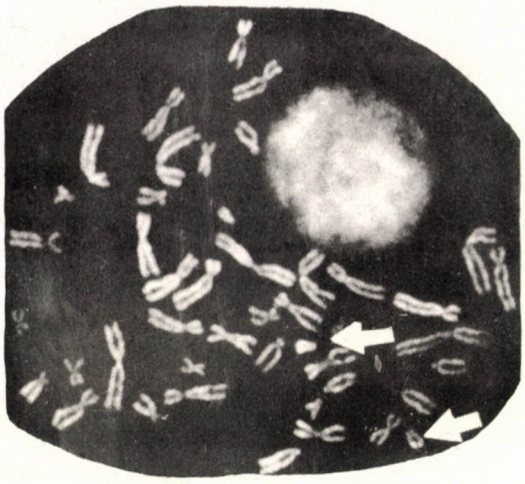

FIG. 3. Fluorescent metaphasis with YY in the cell culture of the blood

DISCUSSION

Double mosaicism with XYY cell line in the blood has been reported in two cases only [6, 10], while in one patient X/XYYY was found [2]. Triple mosaicism with XYY cell line in the lymphocytes is also a rare finding [7, 9, 3, 5, 8]. Quadruple mosaicism, Y/XY/XXY/XYY, was reported in one case only [4]. A variety of phenotypes has been observed in these subjects. Five showed a masculine appearance and four a Turner phenotype. In one patient short stature, primary amenorrhoea but normally developed secondary sex characteristics were found. Mosaicism with XYY cell line associated with gonadoblastoma was observed in four patients including the present case. No relation between the external appearance and the presence of this tumour could be established.

TABLE I

Tissue	No. of cells examined	No. of cells with the karyotype		
		45.X	46.XY	47,XYY
Blood	144	89	3	52
Gonadoblastoma	64	25	36	3

TABLE II

Authors	Cell lines in tissues			
	blood	skin, fascia	gonad	
Jacobs et al. [6]	X>XYY	X>XYY		
Cooper et al. [1]	XYY	X>XYY		
Hsu et al. [5]	XY>X–XYY	XY>X–XYY	X>XY–XYY	(streak)
Roubin et al. [8]	X>XY>XYY	X>XY	X>XY	(dysgenetic gonad)
Ferrier et al. [3]	XYY>XY>X	X>XYY	X>XYY	(gonadoblastoma)
Present case	X>XYY>XY		XY>XYY>X	(gonadoblastoma)

In some patients, chromosome examinations were made not only in the lymphocytes but also in other tissues (Table II).

In the majority of cases, a different distribution of cell lines has been found in the investigated tissues. Triple mosaicism in the gonadoblastoma was observed only in the present case and once in the fibrous streak. It is questionable whether an adequate number of cells can be analyzed representing the real distribution of the different cell lines in a tissue. Nevertheless, in the present case the difference between the proportion of XY and XYY cells in the lymphocytes and gonadoblastoma was remarkable. This means that after the somatic non-disjunction the original XY line was more preserved in the gonad than in the blood.

REFERENCES

1. COOPER, H. L., KUPPERMAN, H. S., RENDON, O. R., HIRSCHHORN, K.: Sex chromosome mosaicism of type XYY/XO. New Engl. J. Med. **266**, 699 (1962).
2. COX, D., BERRY, C. L.: A patient with 45,X/48,XYYY mosaicism. J. med. Genet. **4**, 132 (1967).
3. FERRIER, O. E., FERRIER, S. A., SCHÄRER, K. O., GENTON, N., HEDINGER, C., KLEIN, D.: Disturbed gonadal differentiation in a child with XO/XY/XYY mosaicism: relationship with gonadoblastoma. Helv. paediat. Acta **22**, 479 (1967).
4. FINLEY, W. H., FINLEY, S. C., COCORIS, J. G., PITTMAN, C. S.: Four stemline mosaicism (XO/XY/XXY/XYY) in an infant with ambiguous external genitalia. J. clin. Endocr. **28**, 239 (1968).

5. Hsu, L. Y., Hirschhorn, K., Goldstein, A., Moloshok, R. E.: The role of Y chromosome in females with mosaicism. Abstract 38. Pediat. Res. **2**, 297 (1968).
6. Jacobs, P. A., Harnden, D. G., Buckton, K. E., Court Brown, W. M., King, M. J., McBride, J. A., MacGregor, T. N., MacLean, N.: Cytogenetic studies in primary amenorrhoea. Lancet **1**, 1183 (1961).
7. Milcu et al. cit. Ferrier et al.
8. Roubin, M., Grouchy, J. de, Josso, N., Menibus, C. H. de: Mosaique 45,X/46,XY/47,XYY chez un sujet atteint d'un syndrome de Turner. Ann. Génét. **16**, 123 (1973).
9. Schoen cit. Ferrier et al.
10. Sune, M. V., Centeno, J. V., Salzano, F. M.: Gonadoblastoma in a phenotypic female with 45,X/47,XYY mosaicism. J. med. Genet. **7**, 410 (1970).

Dr. M. Osztovics
Gyáli út 4
H–1097 Budapest, Hungary