Gonadoblastoma in a Phenotypic Female with 45,X/47,XYY Mosaicism

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Gonadoblastoma is a rare ovarian dysgenetic tumour with clinical, hormonal, and histological characteristics which led Scully in 1953 to recognize it as being a distinct entity among germ cell neoplasms. It corresponds to the so-called gonocytoma III in Teter's classification of gonadal malignancies. The tumour is composed of germ cells, Sertoli-granulosa cells and interstitial Leydig cells. Calcified concretions in the parenchyma are a conspicuous feature (Teter, 1963). Gonadoblastoma usually occurs in patients with a female phenotype showing primary amenorrhoea, signs of masculinization and a negative sex chromatin pattern (Philip and Teter, 1964). Where chromosomal studies have been done, several cases have been reported as 46,XY (Brøgger and Strand, 1964; Frasier, Bashore, and Mosier, 1964; Cohen and Shaw, 1965; Ferrier *et al.*, 1967; Teter and Boczkowski, 1967; Freeman and Miller, 1969; H. B. Taylor, 1969, personal communication to Freeman and Miller, 1969). Other karyotypes found are 45,X/46,XY mosaics (Teter, 1960; Siebenmann, 1961; Philip and Teter, 1964; Borghi *et al.*, 1965; Strumpf, 1965; Teter and Boczkowski, 1967); 45,X/46,XX fragment (McDonough *et al.*, 1967; R. M. Richart and O. J. Miller, 1969, personal communication to Freeman and Miller, 1969); 45,X/46,XYq - (Desjeux *et al.*, 1969); and 47,XYY/46,XY/45,X (K. Hirschhorn, 1969, personal communication to Freeman and Miller, 1969; Hsu *et al.*, 1968). The purpose of this note is to report such a case in association with gonadal dysgenesis in a chromatin negative, phenotypical female with 45,X/47,XYY mosaicism.

Case Report

The patient, referred to us by Dr. G. Vissoky, was a 21-year-old normal-looking white female of short stature (142 cm.), primary amenorrhoea, and slight hirsutism in the face and limbs. She had normally developed secondary sex characteristics with normal breasts and the usual distribution of axillary and pubic

hair. Pelvic examination revealed that the labia majora were hypotrophic and the nymphae of prepubertal type. Exploratory laparotomy gave evidence of a small, normally shaped and sited uterus. A normal Fallopian tube and a hard ovary with an intact capsule measuring 3 cm. diameter constituted the left adnexa. On the right was a Fallopian tube with a thick mesosalpinx. The peritoneal cavity was free. An adnexectomy was carried out, and the microscopical examination, performed by Dr. M. Graudenz, showed that the left ovary was composed of (a) alveoli and cords of big, round cells with vacuolated cytoplasm isolated by connective tissue; the general aspect of these areas resembled a dysgerminoma; (b) cells with small and oval nuclei (Sertoli-granulosa cells) and dense cytoplasm: these cells surrounded the germ cells or enclosed small pseudofolliculate cavities resembling the structures of Call-Exner bodies; they showed calcified concretions forming irregular and sometimes large masses; (c) fibrous stromas with nests of Leydig-like cells. Reinke's crystalloids were not found. Subsequent laparotomy with total hysterectomy and right adnexectomy revealed a hypoplastic uterus and left normal Fallopian tube, absence of the right ovary and a mesosalpinx with tubular embryonic structures of the Wolffian type. *Laboratory findings:* gonadotropins, 3.6 mouse units/24 hr.; 17-KS: 4.7 mg./24 hr.; phenolsteroids; 210 µg./24 hr.; corticoids; 1.3 mg./24 hr.

Cytogenetic Studies

As shown in the Table, the sex chromatin in buccal smear preparations was negative, as well as the drumsticks in neutrophils. Chromosome counts (peripheral leucocytes microculture) revealed two modal numbers: 45 and 47. Karyotypic analysis of four cells with 45 chromosomes and six with 47 revealed a mosaicism of the 45,X/47,XYY type (Fig. 1 and 2). Karyotypes of metaphases having 46 chromosomes showed a random loss of chromosomes.

Discussion and Summary

The great variety of karyotypes that have been reported in individuals with gonadoblastoma suggests that this rare tumour may be due to several different kinds of sexual abnormalities. The external appearance of such persons is also variable,

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FIG. 1. 45,X karyotype.

FIG. 2. 47,XYX karyotype.

ranging from that of a normal female to that of a somewhat eunuchoidal male with obvious genital maldevelopment. Our patient was of short stature, which is an uncommon finding. On the other hand, 45,X/47,XYX mosaicism has been rarely

TABLE
CYTOGENETIC FINDINGS

Chromosome Counts				
< 45	45	46	47	Total
1	18	3	28	50

Drumsticks in 1000 neutrophils: Zero
Sex chromatin in buccal smear: (a) Left: 1/100
(b) Right: 1/100

described and in all cases in association with a phenotype of gonadal dysgenesis without gonadoblastoma (Jacobs *et al.*, 1961; Cooper *et al.*, 1962). The case presented here seems, therefore, to be unique, though the 45,X/46,XY/47,XXY mosaics with gonadoblastoma reported by Hsu *et al.* (1968) and K. Hirschhorn (1969, personal communication to Freeman and Miller, 1969) may presumably have had a similar origin (somatic Y non-disjunction), with the preservation of the original XY cell line.

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