TECHNICAL REPORT
32-70
業 績 報 告 書

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# AN XY HUMAN FEMALE WITH OVARIES

## 卵 巣 を 有 す る X Y 女 性

TETSUJI KADOTANI, M.D. 角谷哲司
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ABCC

ATOMIC BOMB CASUALTY COMMISSION

国立予防衛生研究所—原爆傷害調査委員会

JAPANESE NATIONAL INSTITUTE OF HEALTH OF THE MINISTRY OF HEALTH AND WELFARE

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HIROSHIMA AND NAGASAKI, JAPAN

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## CONTENTS
## 目　次

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# AN XY HUMAN FEMALE WITH OVARIES

## 卵巣を有するXY女性

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## SUMMARY

A female patient hospitalized with primary amenorrhea was studied cytogenetically. She was diagnosed clinically and pathologically as afollicular ovarian dysgenesis, with the presence of a vagina, a uterus, bilateral fallopian tubes, and the absence of testes as well as of the somatic signs of Turner's syndrome.

Chromosome studies were carried out on cultured leukocytes and fibroblasts derived from several different organs. An apparently normal male chromosome constitution of 46, XY, was found and the DNA replicating pattern and the fluorescent staining property observed in cultured leukocytes of this patient were consistent with that of normal male cells. The possible mechanisms for the occurrence of the XY sex-constitution in a phenotypical female are discussed.

## INTRODUCTION

Female patients with a sex-chromosome constitution indistinguishable from a normal male have occasionally been seen. In general, XY females have been diagnosed by exploratory laparotomy and have been found to have gonadal agenesis, with and without other abnormalities, or male pseudohermaphroditism.[1-8] The present report describes a phenotypic female with afollicular ovarian dysgenesis and an XY sex-chromosome constitution.

## 要 約

原発性無月経で入院した一人の女性患者について細胞遺伝学的調査を行なった．患者は臨床的および病理学的に無卵胞性卵巣形成不全と診断された．膣，子宮，両側の卵管を認めるが，精巣はなく，ターナー症候群の徴候もない．

染色体調査は培養リンパ球およびいくつかの器官の培養線維芽細胞で行なった．患者は46，XYで正常な男性の染色体構成を示し，培養リンパ球におけるDNA合成様式および蛍光染色法による染色性も正常男性細胞と一致した．表現型のうえでは女性であるこの患者におけるXYの性染色体構成の出現の機構について考察した．

## 緒 言

正常な男性と全く区別できない性染色体構成を示す女性が時々発見されている．一般にXY女性は，試験開腹術によって診断され，性腺無形成およびそれにその他の異常が伴っていることや男子仮性半陰陽を呈することがある．[1-8] 本報告書では，表現型は女性であるが，無卵胞性卵巣形成不全およびXYの性染色体構成を示した1例について述べる．

## CASE PRESENTATION

The patient is the eighth daughter of 10 live-born children, of whom one male and four female sibs died during their neonatal periods (Figure 1). She is phenotypically a female (Figure 2) and was hospitalized for evaluation of primary amenorrhea at the age of 31 years. She was born to a normal, healthy 43-year-old father and 40-year-old mother who was also healthy, and had no history of taking drugs during her pregnancy. The patient had a history of measles and pneumonia in childhood, a head contusion at 7 years of age, gonorrhea at 13 years, and epilepsy which developed at age 30. She married at 23 years of age, but has had no history of pregnancy. The patient's height was 163.8 cm (64.5 in), weight 52.0 kg (115.6 lb) and arm span 176 cm (69.3 in). She had slightly masculine appearance together with small breast development and relatively scanty axillary and pubic hair. She showed no webbing of the neck or cubitus valgus, and had a normally developed vulva and clitoris (Figure 3). The remainder of the examination was normal. No gonads were palpable in her labia majora or in her inguinal region. The vagina admitted two fingers, and was normal in length. On cyclic hormone therapy she had withdrawal bleeding.

Laparotomy revealed that the pelvis contained a uterus of relatively normal size, together with two normal fallopian tubes and two gonads in the normal position (Figures 4, 5). The gonads were symmetrical in size, 1.0 × 0.7 × 3.5 cm, and were represented by two parts: the upper part was a white streak while the lower part was edematous and reddish.

On histological examinations of serial sections at the center of bilateral gonads, a dysgenetic gonadal ridge consisting of gonadal stroma and hilar structure, and corpus albicans-like tissues accompanied with calcified nodules was found (Figure 6).

Fibrous tissue is the major component of the gonadal stroma, and is suggestive of normal ovarian stroma. The surface of the gonadal streak was covered with a layer of low cuboidal cells. In the stroma, no structure resembling primary germ cells or follicular apparatus was detected in these sections. In the hilar zone (Figure 7), a tubular structure which was indistinguishable from the ovarian rete, and a few nests of hilar cells were seen. Some hilar cells contained yellowish-brown pigments in the cytoplasm, although typical crystalloids were not detected. In the deep part of the streak tissue, corpus albicans-like structures

## 症　例

本例は，生産児10名中の第８女であり，同胞のうちで男１人および女４人は新生児期に死亡した（図１）．本例は，その表現型は女性であり（図２），31歳の時に原発性無月経の検査のために入院した．出生時における父親は，年齢43歳で，異常がなく，健康であった．母親は，40歳で，健康であり，妊娠中に薬物を服用したことはなかった．本例には，幼児期に麻疹および肺炎の，７歳の時に頭部打撲の，13歳の時に淋疾の，また30歳の時に癲癇の既往歴があった．23歳で結婚したが，妊娠したことはない．身長 163.8 cm，体重52.0kg，指極間径 176 cm．外観はやや男性的で，乳房の発達は軽度であり，腋毛および恥毛は比較的少ない．翼状頚も外反肘もなく，陰門部および陰核の発達は正常である（図３）．その他の全身検査所見は正常．大陰唇にも鼠径部にも性腺を触れない．膣は，２指が入り，長さは正常である．周期的なホルモン療法によって，消退性出血が認められた．

開腹してみると，骨盤内に比較的正常な大きさの子宮があり，正常な卵管２本と正常な位置に性腺２個があった（図４，５），性腺は，左右同大，1.0 × 0.7 × 3.5 cm であり，二つの部分から成っていた：上部は白色索状であり，下部は浮腫状で赤色を帯びていた．

両側における性腺中心部の連続切片についての組織学的検査では，性腺間質，門部構造ならびに石灰化性小結節を伴う白体様の組織から成る形成不全性の性腺隆起が認められた（図６）．

この性腺間質は，主として線維組織から成り，正常な卵巣間質を示唆している．性腺索状部の表面は，短い立法形細胞の層でおおわれていた．これらの切片では，原始卵細胞あるいは洋胞に似た構造が間質に認められなかった．卵巣門部には（図７），卵巣索とは区別できないところの管状構造ならびに門細胞巣が少数みられた．門細胞は，細胞質内に黄褐色の色素を有するものもあるが，定型的な結晶状構造は検出できなかった．索状部組織の深

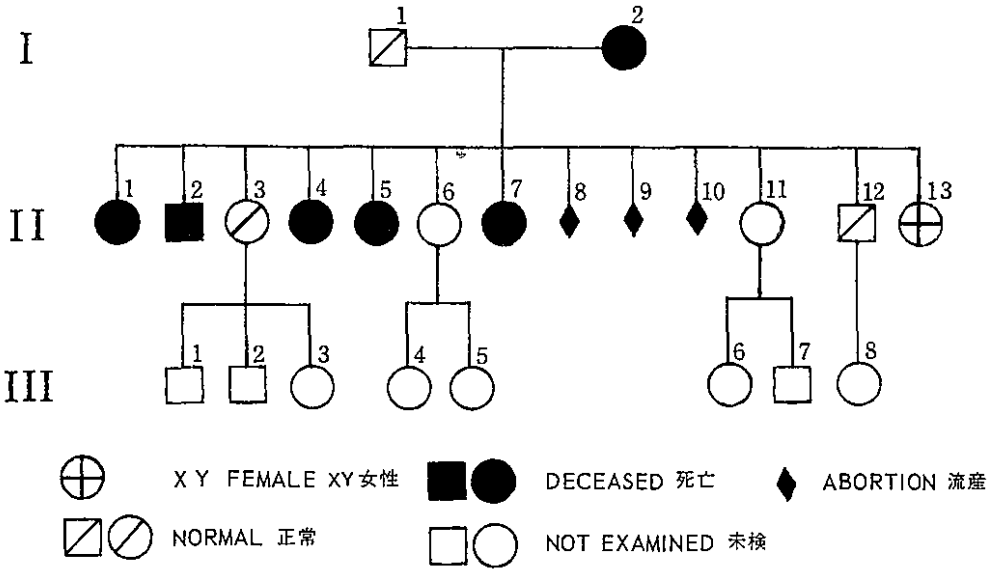



*FIGURE 1 Family pedigree of XY female with ovaries*

図1　卵巣を有するXY女性の家系

were present (Figure 8), and calcified nodules, whose original structure was unidentifiable, were scattered in or near the corpus albicans-like tissues. Neither testicular tissues nor areas suggesting neoplasm were detected on either side of the gonad. These histological observations may be interpreted to indicate that this patient has dysgenetic gonads.

X-ray and hysterosalpingographic examinations demonstrated the presence of normal kidneys, uterus, and fallopian tubes. No bony abnormality was seen by X-ray examination of the hands, femora, lumbar spine, and pituitary fossa.

The results of hormone assays of the urine are shown in Table 1. It is interesting to note that the estrogen value of urinary excretion was slightly elevated from the normal range, while the gonadotropin value remained within normal limits. These findings were unusual for this condition and cannot be explained. Patient's clinical appearance especially scant breast development and eunuchoid features were compatible with hypoestrinism.

Functional tests of the endocrine glands were essentially normal: $^{131}I$ uptake was 21.5% in 24 hours, and a thyroid scan was normal; the Thorn test showed a decrease of eosinophiles of 51.4%; water loading test showed normal ADH responsiveness. Responses to ACTH and Metopiron were normal. Fasting blood sugar was 74.0 mg/100 ml, and a glucose tolerance test was normal.

部には，白体様の構造があり（図８），この白体様組織の中および近くには，いずれの組織から由来したか不明の石灰化小結節が散在していた．性腺のいずれの側にも精巣組織あるいは新生物を示唆する部分は認められなかった．これらの組織学的所見は，本例が性腺形成不全であることを示すものと解釈できる．

X線検査および子宮卵管造影法検査の結果，腎臓，子宮および卵管は正常と認められた．手，大腿骨，腰椎および脳下垂体窩のX線検査では，なんらの骨性異常も認められなかった．

尿中のホルモン分析の結果を表１に示す．尿中エストロゲン排泄値が正常範囲よりも高いのに対し，ゴナドトロピン値が正常範囲内であることは興味深い．本疾患にこのような所見のみられることは珍しく，かつその説明はできない．本例の臨床的外観，特に軽微な乳房発達と類宦官症様の特徴を示したことは，低エストロゲン症に一致していた．

内分泌腺機能検査所見は本質的に正常であった：$^{131}I$ 摂取率は24時間に21.5%，また，甲状腺スキャニングは正常；Thorn 試験で好酸球減少率は51.4%；水負荷試験でADH反応は正常．ACTHおよびメトピロンに対する反応は正常．空腹時血糖値は74.0mg／100 ml，また糖負荷試験は正常．

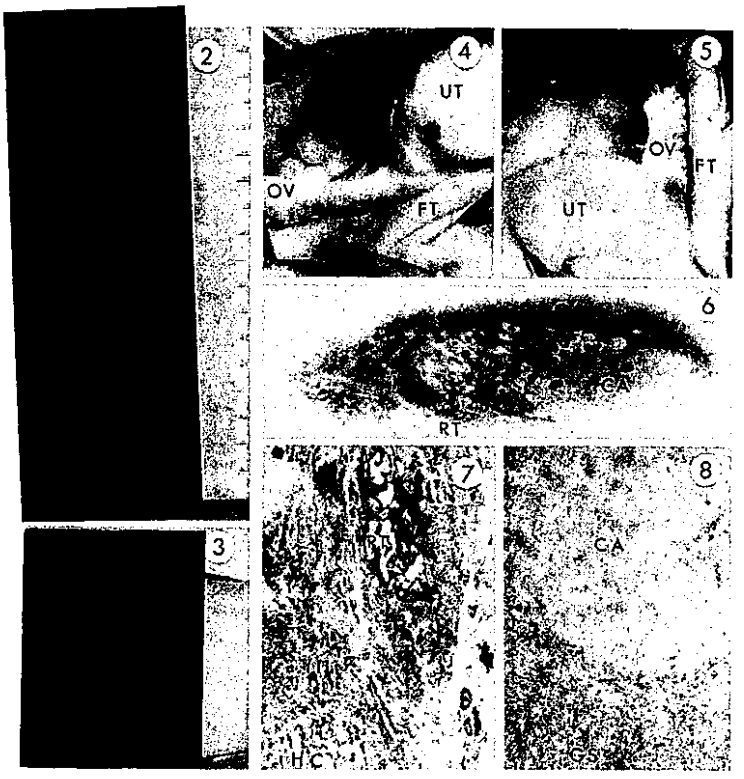



*FIGURE 2 Photograph of the patient.*
図2　患者

*FIGURE 3 Photograph of the external genitalia.*
図3　外陰部

*FIGURE 4, 5. Surgical findings, showing the internal genital organs of the patient. Figure 4 shows right side, and Figure 5 shows left side. UT, Uterus; OV, Ovary; FT, Fallopian tube.*
図4，5　開腹所見，本例の内性器を示す．図4は右側，図5は左側．UT：子宮，OV：卵巣，FT：卵管

*FIGURE 6 Low-power photomicrograph of a cross section of the right ovary. HC, Nest of hilar cells: GS, Gonadal stroma: CA, Corpus albicans-like structure; RT, Rete tubules.*
図6　右側卵巣の断面の低倍率顕微鏡写真．HC：門細胞巣，GS：性腺間質，CA：白体様構造，RT：卵巣索

*FIGURE 7 Section through the hilar zone showing the rete tubules (ovarian rete) and a nest of hilar cells. RT, Rete tubules; HC, Nest of hilar cells*
図7　卵巣門部の断面．卵巣索および門細胞巣がみられる．RT：卵巣索，HC：門細胞巣

*FIGURE 8 Photomicrograph of gonadal stroma and corpus albicans-like structure. CA, Corpus albicans-like structure; GS, Gonadal stroma.*
図8　性腺間質および白体様構造の顕微鏡写真．CA：白体様構造，GS：性腺間質

TABLE 1 COMPARATIVE DATA ON ENDOCRINE STUDY

表1　内分泌検査成績の比較

| Urinary Excretion 尿中排泄 | | Normal Range 正常範囲 | Present Case 本例 |
|---|---|---|---|
| Estrogen エストロゲン | /day 1日当たり | 2-30 μg | 39.0 μg |
| Pregnanediol プレグナンジオール | /day 1日当たり | 0.5-3 mg | 0.25 mg |
| Gonadotropin ゴナドトロピン | /day 1日当たり | 4-16 mouse unit | 8 mouse unit |
| 17-KS | /day 1日当たり | 4-8 mg | 3.0 mg |
| 17-OHCS | /day 1日当たり | 1.5-4 mg | 0.7 mg |

Her intelligence was that of an imbecile as shown by the WAIS-test score of 65; and the Tanaka-Binet test score of 67.7.

知能検査の結果は，WAIS 試験の成績が65；Tanaka-Binet試験成績が67.7であって，魯鈍ということになった．

## CHROMOSOME STUDIES

Aceto-orcein-stained squash preparations from material derived from the buccal mucosa, both ovaries, fallopian tubes, endometrium, appendix, and skin were examined for the presence of sex chromatin. From each tissue 500 nuclei were examined and no sex chromatin masses were seen.

Chromosome studies were carried out on leukocytes cultured according to the method of Moorhead et al[9] with a minor modification, as well as on monolayer cultures derived from the ovaries, fallopian tubes, endometrium, appendix, and skin (for details, see Kadotani et al[10]). Slides were made according to the routine air-dry method.

Chromosome counts based on 20 or more cells of each specimen described above indicated that, of a total of 334 metaphases, 307 had a normal chromosome number of 46 (Table 2). Microscopical examinations showed, in every 46-cell, one small chromosome in an unpaired state. Further, detailed karyotype analyses were performed on 10 to 30 cells from each tissue, and all cells showed 15 chromosomes in group C6-X-12, as well as the presence of one small chromosome which ranked in length between the E18 and F19-20 autosomes (Figure 9). Morphologically, the small chromosome was found to be identical to the normal male Y chromosome on the basis of the following features; an indistinct centromere which is totally heteropycnotic; a secondary constriction in the middle part of the long arm; a narrow chromatid divergence; a rather diffuse and faintly stained configuration of the distal part of the long arm; showing no satellite association with D13-15 and G21-22 autosomes.

## 染色体検査

口内粘膜，両側の卵巣，卵管，子宮内膜，虫垂および皮膚から入手した材料についてアセト・オルセイン染色押潰標本による性染色質検査を行なった．それぞれの組織についての細胞核500個の検査では，性染色質は認められなかった．

染色体調査は，Moorhead らの方法[9]に軽度の改変を加えた白血球培養，ならびに卵巣，卵管，子宮内膜，虫垂および皮膚から入手した材料の単層組織培養（詳細については角谷ら[10]を参照）について行なわれた．標本は通常の空気乾燥法によって作成した．

上記の各標本について20個またはそれ以上の細胞において染色体数を調べた結果，合計334個の分裂中期細胞のうち307個は，正常な46の染色体数を示した（表2）．顕微鏡検査では，対になっていない小さな染色体1個が，染色体数46の細胞のすべてに認められた．それぞれの組織について10ないし30個の細胞の詳細な核型分析を行なったところ，すべての細胞においてC6－X－12群に15個の染色体が認められ，かつ長さがE18とF19—20常染色体との中間に相当する小さな染色体1個が認められた（図9）．形態的には，この小さな常染色体は次のような特徴を示すので，正常な男子Y染色体に一致すると考えられた：着糸点は，不明瞭で，全体に異常凝縮を呈す；長腕の中央部に第二次狭窄がある；染色分体の開きが少ない；長腕末端部の形状は，その染色性がやや瀰漫性で淡い；D13—

TABLE 2 CHROMOSOME-NUMBER DISTRIBUTION OF CULTURED CELLS DERIVED FROM A CASE WITH AFOLLICULAR OVARIAN DYSGENESIS

表2　無卵胞性卵巣形成不全例の培養細胞における染色体数の分布

| Specimen 標本 | | Days in Culture 培養日数 | Cells Counted 計算細胞数 | Chromosome Number 染色体数 <44 | 45 | 46 | 47 | 48+ | Cells Karyotyped 核型分析細胞数 |
|---|---|---|---|---|---|---|---|---|---|
| Leukocytes 白血球 | 1 | 3 | 59 | 1 | 1 | 57 | | | 22 |
| | 2 | 3 | 66 | 1 | 2 | 62 | 1 | | 10 |
| Skin 皮膚 | | 30 | 17 | 2 | | 15 | | | 5 |
| | | 60 | 19 | 3 | 2 | 14 | | | 6 |
| Appendix 虫垂 | | 30 | 21 | 2 | 1 | 18 | | | 13 |
| Fallopian Tube 卵管 | | 17 | 24 | | 1 | 23 | | | 16 |
| Endometrium 子宮内膜 | | 18 | 27 | 1 | 1 | 25 | | | 14 |
| Right ovary 右側卵巣 | | 17 | 49 | 2 | 3 | 44 | | | 18 |
| Left ovary 左側卵巣 | | 20 | 52 | | 3 | 49 | | | 22 |
| Total 合計 | | | 334 | 12 | 14 | 307 | 1 | | 126 |

Cells with 45 chromosomes showed no karyotypic constancy, with the random absence of any one of chromosomes.

Cultured leukocytes from the subject's father, brother, and sister (Figure 1) had normal chromosome complements. Since the length of the Y chromosome was an inheritable character,[11,12] relative ratio in the length of the Y to the G21-22 chromosomes of the patient were compared to that of her father and brother. Relative values were 1.42 ± 0.12 in the patient, 1.42 ± 0.13 in her father and 1.62 ± 0.17 in her brother, respectively. The results showed that the Y chromosome in the patient is equivalent in size to that of her father and brother.

The chromosome replicating pattern at the end of the DNA synthesis period was studied in cultured leukocytes by an autoradiographic procedure (Sofuni and Sandberg[13]). It is well established that most labeled metaphases of normal female cells have one late-replicating X chromosome.[14,15] The present specimens, however, had no cells showing a late-replicating chromosome in group C6-X-12, based on 60 labeled metaphases suitable for analysis. The Y chromosome of the patient was late replicating, in striking contrast to the replicating pattern of the G21-22 chromosomes (Figure 9), and its autoradiographic behavior was virtually identical to that of the Y chromosome in male cells.

Recently, fluorescent staining technique for identifying the Y chromosome has been developed.[16,17] This technique confirmed the presence of the Y chromosome in this patient. Slides were prepared from leukocytes cultures of the patient, normal

15およびG21—22常染色体との付随体連合は認められない．染色体数45の細胞は，核型が一定でなく，いずれかの染色体1個が不特定に欠如している．

本例の父親，兄および姉（図1）よりの培養白血球における染色体構成は正常であった．Y染色体の長さは遺伝する性質のものであるので，[11,12] 本例におけるY染色体のG21—22染色体に対する長さの相対的比率を父親および兄のそれと比較検討した．その相対的比率は，本例が1.42±0.12，父親が1.42±0.13，兄が1.62±0.17であった．本例におけるY染色体の長さは，父親や兄のそれと同じであると認められた．

培養白血球におけるDNA合成後期の染色体複製をオートラジオグラフィー法によって調べた（Sofuni およびSandberg[13]）．正常な女性では，標識された分裂中期細胞の大部分においてX染色体の一つがおそくまで複製を続けることが立証されている．[14,15] しかし，今回の標本においては，分析に適当な分裂中期細胞の60個を検査したところ，C6—X—12群におそくまで複製を示す染色体はみられなかった．本例におけるY染色体は，おそくまで複製を示し，G21—22染色体の複製様式と著しく対照的であり（図9），そのオートラジオグラフィー所見は，男性細胞のY染色体とほとんど同じであった．

最近，Y染色体を同定するための蛍光染色法が開発されている．[16,17] この技法により，本例においてY染色体の存在を確認しえた．本例および正常な男女の培養白血球

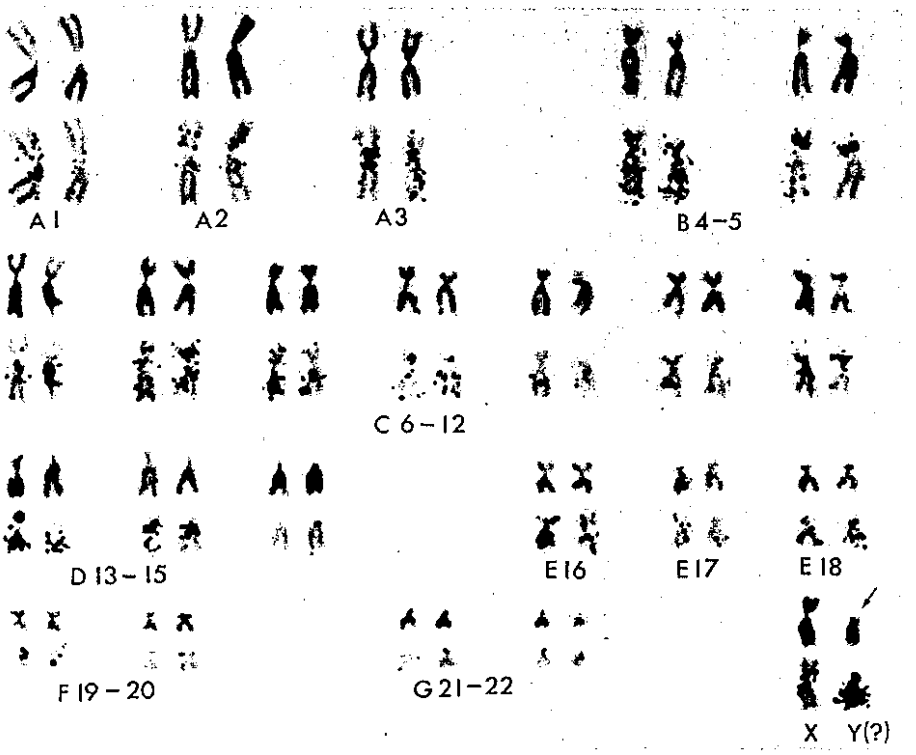
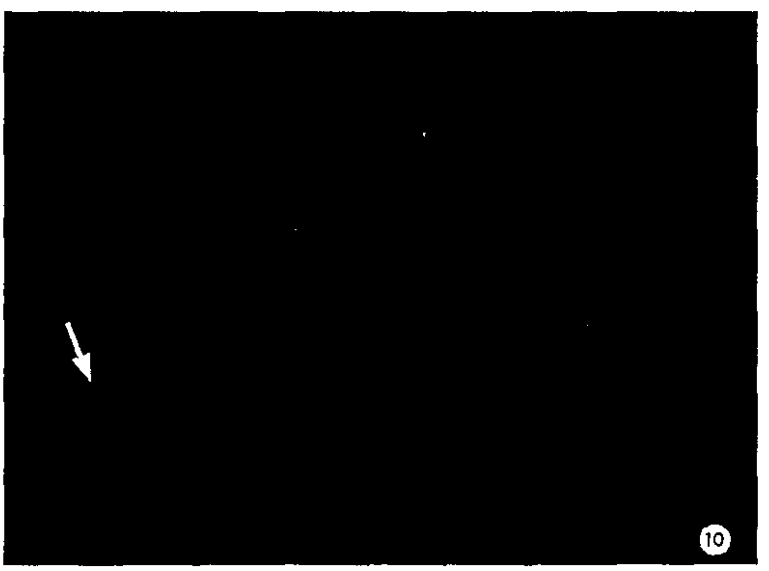



*FIGURE 9 Karyotype from the proband. The chromosomes were photographed before and after autoradiography. Arrow indicates the Y chromosome, showing heavy labeling.*

図9　発端者の核型．オートラジオグラフィー前後において染色体の撮影を行なった．矢印は，強度に標識されたY染色体を示す．



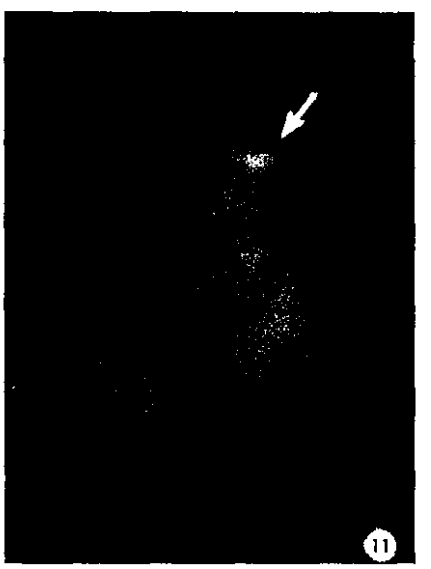




*FIGURE 10 & 11 Photographs of cultured leukocytes from the proband, stained with a fluorescent acridine derivative. Figure 10 shows a metaphase with a brightly fluorescing Y chromosome (arrow), and Figure 11 shows an interphase nucleus having single fluorescent body (arrow).*

図10，11　蛍光性のアクリジン誘導体で染色した発端者の培養白血球．図10は，明るい蛍光性を示すY染色体（矢印）を有する分裂中期細胞であり，図11は，静止期の細胞核における単一の蛍光性の小体（矢印）である．

males and females. The slides were kept in MacIlvaine's citric acid-phosphate buffer (pH 4.1) for 5 minutes, then in freshly prepared 0.5% aqueous solution of quinacrine hydrochloride ("Atabrine", Winthrop Lab. N.Y.) for 5 minutes, washed and mounted in buffer for observation under a Nikon fluorescence microscope, using BV exciter filter and Y51 and Wratten 2B barrier filter.

In the preparations from normal males, almost all metaphases showed that the distal half of the long arm of the Y chromosome fluoresced the largest and brightest. A small brightly fluorescent body was observed in interphase nuclei, and the proportion of cells showing this "male chromatin body" was about 30%. No similar fluorescent properties were observed in female cells.

The cells of the propositus had the characteristic staining property identical to normal male cells; a brightly fluorescing chromosome was observed in all of 50 metaphases (Figure 10), and a small fluorescent body was also recognized in interphase nuclei (Figure 11). These results demonstrate that this female patient has an XY sex-chromosome constitution.

## DISCUSSION

The patient, who was hospitalized because of primary amenorrhea, was diagnosed as a female with afollicular ovarian dysgenesis. The major clinical features are: female phenotype, normal stature, presence of vagina, hormonally responsive uterus, bilateral fallopian tubes and afollicular ovaries, and the absence of testis as well as any of the stigmata of Turner's syndrome. On cytogenetic examination she evidently had a normal male chromosome complement (46, XY), on the basis of the following findings: (1) sex-chromatin test was negative; (2) the chromosome identified as Y had morphologic features, late DNA-replication pattern and fluorescent staining characteristic identical to the Y chromosome in normal male cells.

It has been generally accepted that the Y chromosome carries strong masculinizing factors. Notwithstanding the occurrence of the Y chromosome, this case showed a striking development of internal and external female characteristics. The possibility that the Y chromosome was a deleted X produced probably as a result of a long arm deletion may be excluded with reasonable confidence on the evidence described above.

Occurrence of masked mosaicism, such as XY/XO, though not completely ruled out, is unlikely in

から標本を作成した．標本は，まずMacIlvaineのクエン酸—燐酸塩緩衝液（pH 4.1）に5分間保ち，次に塩酸キナクリン（New York, Winthrop 研究所製の「Atabrine」）の新鮮な0.5%水溶液に5分間浸しておいた後に水洗し，緩衝液に封入し，ニコン蛍光顕微鏡でBV励起フィルターならびにY51およびWratten 2B接眼フィルターを用いて検査した．

正常な男性よりの標本では，ほとんどの分裂中期細胞のY染色体長腕の下半分は蛍光度が最も強く，明るい．また，静止期の細胞核には，強い蛍光を有する小体がみられ，この「男性染色質小体」を有する細胞の割合は約30%であった．女性の細胞には，このような蛍光性の特徴は認められなかった．

発端者の細胞は，正常な男性の細胞と同様の特徴的な染色性を示した；分裂中期細胞50個の全部に蛍光度の明るい染色体があり（図10），静止期の細胞核に蛍光性の小体が認められた（図11）．この結果は，本例の性染色体構成がXYであることを示すものである．

## 考　察

原発性無月経で入院した本例は，無卵胞性卵巣形成不全と診断された．おもな臨床所見は次のとおりであった：表現型は女性であって，外観正常，膣は存在し，ホルモンに反応する子宮と両側の卵管は認められるが，卵巣は無卵胞性で，精巣はなく，ターナー症候群の徴候もない．細胞遺伝学的調査では，次の所見が認められ，正常な男性の染色体構成（46, XY）を示すものと考えられた：(1) 性染色質検査結果は陰性；(2) Yと同定された染色体は，正常な男性の細胞におけるY染色体と同様の形態的特徴，おそくまで続くDNA合成様式および蛍光染色性を示した．

一般に，Y染色体は，強力な男性化因子を保有すると考えられている．本例では，Y染色体があるにもかかわらず，女性内性器および外性器の著しい発達を示した．このY染色体は，あるいは長腕欠失の結果生じたX染色体欠失であるかもしれないという可能性は，前記の所見によってかなりの確信をもって否定できるであろう．

XY／XOなどの潜在的なモザイクの出現の可能性は完全には否定できないが，本例の内胚葉（虫垂），中胚葉（白血

this case, because the cultured cells from the endoderm (appendix), mesoderm (leukocytes, bilateral ovaries and fallopian tubes, and endometrium), and ectoderm (skin), all had a normal 46, XY complement. Since the cells with 45 chromosomes showed the random loss of any one of chromosomes, this is further evidence against the possibility of XY/XO mosaicism.

It has been shown that the short arm of the Y chromosome carries testis-determining genes[18] and that the X and Y associate with each other at the distal end of the short arm during meiosis.[19,20] The possibility exists that testis-determining genes of the Y may be lost as a result of the XY crossing over in paternal meiosis.

Recently, Sasaki and Kamada[21] reported that a case of phenotypically normal female golden hamster, with apparently functional ovaries, showed an XY sex-determining mechanism. They offered two tentative interpretations: one is the loss of male factors in the Y chromosome, caused by the interchange of the X and the Y during meiosis, or alternatively a partial short arm deletion of one of the two X chromosomes. They also point out that the chance of an interchange between the X and the Y chromosomes might be expected to occur less frequently in the human than in the golden hamster, since the X and the Y are seen associated end-to-end without forming chiasma in the human male, whereas in the golden hamster chiasma formation between the X and the Y has been observed during male meiosis.

On histologic examination of tissues from the patient, no germinal cells were found in serial sections through the midportion of both gonads, but gonadal stroma and hilar structures were seen which were indistinguishable from the same components of normal human ovary. However, it was difficult to account for the histogenesis of corpus albicans-like structure accompanied by calcified nodules in the absence of germ cells. The former structure bore a close morphological resemblance to normal, but old, corpus albicans. If it were true corpus albicans, however, evidence of germ cells and follicular apparatus would be expected. The original structure from which the calcified nodules were derived could not be identified microscopically, although small arteries and corpus albicans itself were considered as possibilities.

The subject was mentally deficient. This may be unrelated to the gonadal syndrome under discussion since other reported cases have had normal intelligence.[8,26] This may be a real though uncommon component.

球，両側の卵巣と卵管，子宮内膜）および外胚葉（皮膚）の組織培養では，すべての細胞は正常な46，XY構成を示しており，その可能性は少ない．染色体数が45の細胞でいずれかの染色体1個の欠失が不特定であったことは，XY／XOモザイク型の可能性を否定するいま一つの証拠である．

Y染色体短腕が精巣決定遺伝子を保有し，[18] 減数分裂の際にXおよびYは短腕の端部で接合することが認められている．[19,20] 父親における減数分裂の時に，XY交叉の結果，Yの精巣決定遺伝子が消失する可能性もあると考えられる．

最近，SasakiおよびKamadaは，[21] 機能的な卵巣を有するように思われ，かつ表現型が正常の雌のゴールデンハムスターの1例においてXYの性染色体構成を認めたと報告した．これについて暫定的に二つの解釈をあげている：一つは，減数分裂におけるXとYの交換によるY染色体における男性因子の消失であり，他の一つは，2個のX染色体のうちの一つにおける短腕の部分的欠失である．また，ヒトでは，XおよびY染色体の交換の生ずる機会がゴールデンハムスターに比べて少ないであろうとかれらは指摘している．すなわち，ヒトの場合は，男性におけるXとYは端部接合し，キアズマ形成がないのに対して，雄のゴールデンハムスターにおける減数分裂ではXとYとのキアズマ形成が認められている．

本例から入手した組織についての組織学的検査の結果，両側の性腺中央部の連続切片に卵細胞は全く認められなかったが，正常な女性の卵巣におけると同様の性腺間質および門部構造がみられた．しかし，卵細胞がないにもかかわらず，石灰化した小結節を伴った白体様の構造が発生していたことの説明は困難であった．この構造の形態は，正常な古い白体にきわめて類似していた．しかし，真の白体であれば，卵細胞および泙胞の形跡が認められることが予想される．石灰化性小結節の起源は，顕微鏡検査で確認できなかったが，小動脈および白体自体に由来する可能性も考えられた．

本例は精神薄弱であった．他の例では，知能が正常であることが報告されているので，[8,26] この所見は，ここで取り上げている性腺症候群と無関係であるかもしれない．しかし，これは実際には本症の一部であることがまれにはあるかもしれない．

Jones et al[22] and Greenblatt et al[23] reviewed previous reports of gonadal dysgenesis, and concluded that the pathologic findings in the ridge were similar, regardless of the cytogenetic findings. The multiplicity of reported cytogenetic findings makes it difficult to understand the interrelations between chromosome constitution and pathologic findings as well as to understand embryological events in ovarian dysgenesis. Jones et al[22] proposed the hypothesis that the development of ovarian agenesis was due to the failure of primitive germ cells to migrate into germ ridge. They also suggested that a pair of X chromosomes was necessary for normal development of the ovary.

Jost[24] has shown that rabbits, whether genetically male or female, develop female internal and external genitalia, if gonadectomy is performed during early intrauterine development. This finding suggests that the testis-determining genes on the Y chromosome act only at a critical period as a trigger to start the differentiation of the medulla into testis. In other words, if a genetic male fails to differentiate the testis at a critical stage, its gonads begin to differentiate into ovaries in a succeeding stage.[1,24,25]

If the above assumption is applied to the present case, the occurrence of the XY female may be explained as follows: the testis-determining effect of the Y chromosome was adversely affected by some environmental factor (i.e. anoxia, infection, maternal hormonal imbalance, etc.), resulting in the development of both internal and external female genitalia.

Recently, Sternberg et al[8] and Espiner et al[26] have reported the familial occurrence of XY females with pure gonadal dysgenesis. They suggested a possibility that an abnormal gene or genes, which are X-linked or carried on an autosome, may suppress the male-determining capacity of the Y chromosome, thus leading to female development and pure gonadal dysgenesis, with an XY-sex constitution. Their assumption may be applicable for the explanation of the genesis of the present XY female. The present study was, however, unable to confirm the possibility proposed by Sternberg et al,[8] because of imcomplete familial investigation.

Jones ら[22] および Greenblatt ら[23] は，性腺形成不全に関する以前の報告を再検討し，細胞遺伝学的所見の違いにもかかわらず，性腺隆起における病理学的所見はいずれも同様であったと結論した．報告されている細胞遺伝学的所見が多様であることのために，染色体構成と病理所見との関係については理解が困難であるとともに，卵巣形成不全では胎生期にいかなることが起こるかの理解も困難である．Jones らは，[22] 卵巣形成不全が起こるのは，原始卵細胞の性腺隆起への移動がないためであるという仮説を提案している．また，卵巣の正常な発達のためには，2個のX染色体が必要であることを示唆している．

Jost は，[24] ウサギでは，遺伝学的に雄であるか雌であるかにかかわらず，胎生期の早期に性腺切除を行なった場合，女性内性器と外性器の発達が起こることを認めた．この所見は，Y染色体上の精巣決定遺伝子が重要な時期においてのみ，髄質の精巣への分化を開始するための引き金として作用することを示すものである．すなわち，遺伝的に男性である者において重要な時期に精巣の分化が起こらなければ，その後の段階で性腺の卵巣への分化が生ずるのである．[1,24,25]

本例に上記の推測を当てはめてみると，XY女性の発現は次のように説明できるであろう：Y染色体の精巣決定因子がなんらかの環境要因(たとえば，酸素欠乏，感染症，母体のホルモン不均衡など)の悪影響を受けた結果，女性内性器および外性器がともに発達するに至った．

最近，Sternberg ら[8] および Espiner ら[26] は，純粋な性腺形成不全を有するXY女性の家族的発生を報告している．かれらは，Xまたは常染色体上に保有される異常な遺伝子あるいは遺伝子群によってY染色体の男性決定能が抑制され，そのために女性的な発達および純粋な性腺形成不全がもたらされるという可能性を示唆した．その推測によって，今回のXY女性の発現が説明できるかもしれない．しかし，今回の研究では，家族の調査が不完全であるため，Sternberg ら[8] のあげた可能性は確認できなかった．

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