

Case Report

Coexistence of Gonadal Dysgenesis and Mullerian Agenesis with Two Mosaic Cell Lines 45,X/46,X,del(X)(p22.2)

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Key Words

gonadal dysgenesis;
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Turner's syndrome;
X chromosome

Gonadal dysgenesis and Mullerian agenesis both are common causes of primary amenorrhea. Coexistence of gonadal dysgenesis and Mullerian agenesis has been previously described as a rare event. The karyotypes, 45,XO, 45,X/46,XX, 45,X/46,X,dic(X), 46,XX, and 46,XY, have been reported in the literature. A 22-year-old woman presented with primary amenorrhea and normal intelligence. Her physical examination confirmed the absence of breast development and axillary hair. The woman weighed 43 kg and was 150 cm tall. Scoliosis of the thoracic spine was noted on a chest X-ray film. Also, her pelvic examination revealed a vaginal introitus with a vaginal depth of 7 cm, measured by sounding. Her external genitalia were female but lacked pubic hair. The rectal examination failed to reveal a uterus. Pelvic ultrasound revealed the absence of uterus and ovaries, and her serum gonadotropin levels were in the menopausal range (FSH, 118.59 IU/L; LH, 38.94 IU/L). Estradiol was less than 10 pg/ml. Two mosaic cell lines, 45,X (50%) and 46,X,del(X)(p22.2)(50%), were found in the chromosomal study. Laparoscopic evaluation confirmed the absence of uterus and ovaries with normal fallopian tubes. Coexistence of gonadal dysgenesis and Mullerian agenesis is a rare event. The two mosaic cell lines 45,X/46,X,del(X)(p22.2) in this combination have not been reported before. In patients with this condition, estrogen will initiate and sustain maturation and function of secondary sexual characteristics, and lifelong hormone therapy will protect against osteoporosis and cardiovascular disease. [*Chin Med J (Taipei) 2002;65:450-452*]

Gonadal dysgenesis and Mullerian agenesis both are common causes of primary amenorrhea. Coexistence of gonadal dysgenesis and Mullerian agenesis has been previously described as a rare event. Gonadal dysgenesis includes gonadal developmental anomalies associated with X-chromosome monosomy (45,X) and related disorders in which fragments of the other X or Y chromosome are preserved in the karyotype.¹ The rudimentary ovaries form streak gonads, and the female genital organ is usually normal. Mullerian agenesis includes an absence of uterus; the

karyotype is normal female, and the ovarian function is normal.²

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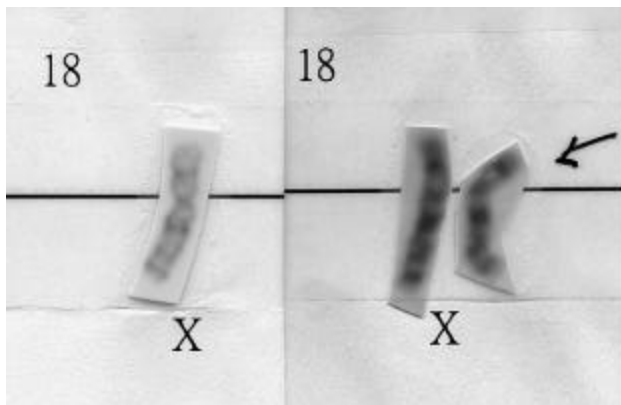


Fig. 1. One X chromosome missing in one cell line and had a terminal deletion over its short arm at band Xp22.2 in the other cell line.



Fig. 2. Laparoscopic examination showed streak gonads, uterine aplasia, and rudimentary fallopian tubes.

noted on a chest X-ray film. Her pelvic examination revealed a vaginal introitus with a vaginal depth of 7 cm, measured by sounding. Her external genitalia were female but lacked pubic hair. The rectal examination failed to reveal a uterus. Pelvic ultrasound disclosed the absence of uterus and ovaries, and her serum gonadotropin levels were in the menopausal range (FSH, 118.59 IU/L, LH, 38.94 IU/L). Estradiol was less than 10 pg/ml. Chromosomal study was performed on G-banded metaphase chromosomes from a culture of PHA-stimulated peripheral blood lymphocytes. Among 20 cells examined, 10 showed an abnormal karyotype that was missing 1 sex chromosome

some (45,X). The remaining 10 cells also showed an abnormal karyotype with 1 X chromosome having a terminal deletion over its short arm at band Xp22.2 (Fig. 1). Laparoscopic findings included streak gonads and uterine aplasia (Fig. 2); both rudimentary fallopian tubes met in the midline, where a thin, tubal structure had replaced the uterus. The gonad consisted of a white, elongated structure and lay parallel to the oviduct. A gonadal biopsy was not done.

Estrogen replacement therapy was begun to promote the development of secondary sexual characteristics. Conjugated estrogen, 0.625 mg, was given every day.

Discussion

Gonadal dysgenesis is the most frequent cause of primary amenorrhea and is characterized by elevated gonadotropin levels and absence of secondary sexual development. These patients may have a 45,XO, 45,X/46XX, 45,X/46,X,dic(X), 46,XX, or 46,XY karyotype. Congenital absence of the uterus has been reported coincidentally in these karyotypes.³⁻⁸ Mosaic Turner syndrome may have double or triple cell lines.⁹ We found a karyotype, 45,X/46,X,del(X)(P22.2), not reported in the literature before.

Gonadal dysgenesis and short stature are in variably present in all cases of Turner's syndrome. Pure gonadal dysgenesis patients are of normal height and do not show any other stigmata of Turner's syndrome. The patient mentioned had the feature of short stature, 150 cm, for which the success of growth hormone treatment is recognized and accepted in the literature.¹⁰ In this case, the woman had been diagnosed when she was 22 years old, however, it was too late to receive the growth hormone treatment before epiphyseal closure. Early diagnosis and growth hormone treatment before age 12 would improve this growth impairment.

When ovaries are absent in individuals being reared as female either with uterus or not, either because of surgery or streak gonads, hormone treatment will be necessary at puberty, and thereafter, estrogen will initiate and sustain the maturation and function of

secondary sexual characteristics and then promote the achievement of full height potential. For patients with genetic shortness in stature, estrogen treatment is not started until bone age is greater than 12 to avoid epiphyseal closure and allow a longer period of time for long bone growth. Life long hormone therapy will protect against osteoporosis and cardiovascular disease.

The presence of a Y chromosome in the karyotype requires excision of the gonadal areas because the presence of any medullary (testicular) component within the gonad is a predisposing factor to tumor formation and to heterosexual development (virilization). Fully staining and banding the karyotype continues to be the best method to detect the presence of testicular tissue or other mosaic combinations. This patient possessed a karyotype, 45,X/46,X,del(X)(P22.2), without an obvious Y chromosome. For cases with karyotype 46,XY,⁶ surgical removal of gonadal tissue should be completed as soon as the diagnosis is made. Mosaic Turner syndrome is associated with anterior segment dysgenesis, so a full ophthalmological assessment has been suggested.¹¹

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