Case Report

Coexistence of Mayer-Rokitansky-Küster-Hauser Syndrome and Turner Syndrome: A Case Report

Agnieszka Białka MD [1], Aneta Gawlik MD, PhD [2], Agnieszka Drosdzol-Cop MD, PhD [1,*], Krzysztof Wilk MD, PhD [1], Ewa Małecka-Tendera MD, PhD [2], Violetta Skrzypulec-Plinta MD, PhD [1]

[1] School of Health Sciences in Katowice, Medical University of Silesia, Katowice, Poland
[2] Department of Pediatrics and Pediatric Endocrinology, Medical University of Silesia, School of Medicine in Katowice, Katowice, Poland

A B S T R A C T

Background: Turner syndrome is a common chromosomal disorder, with an incidence of 1 in 2000 live-born female infants. Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) affects 1 in 4500 female births and, rarely, it might be associated with gonadal dysgenesis.
Case: A 17-year-old girl was referred to our clinic with short stature and primary amenorrhea. The patient was diagnosed with Turner syndrome and underwent estrogen therapy. At the age of 24 years, just after the patient's sexual initiation, the first complete gynecological examination was performed. A blind-ending vagina was revealed and the patient was diagnosed with MRKH.
Summary and Conclusion: Early diagnosis of coexistence of MRKH and Turner syndrome, although very difficult, might prevent patients from developing serious complications.
Key Words: Mayer-Rokitansky-Küster-Hauser syndrome, Turner syndrome, Gonadal dysgenesis

Introduction

Turner syndrome is a common chromosomal disorder resulting from complete or partial absence of the second sex chromosome, with or without cell line mosaicism.[1–3] Its incidence has been estimated as 1 in 2000 live-born female infants.

Mayer-Rokitansky-Küster-Hauser syndrome (MRKH) is defined as a congenital aplasia of the uterus and upper two-thirds of the vagina in women with 46, XX karyotype.[4] It affects one in 4500 female births.

Case

A 17-year-old girl was referred to the Department of Pediatric Endocrinology and Diabetes at the Medical University of Silesia in Katowice, Poland for evaluation of short stature and primary amenorrhea.

The characteristics of the patient's height, weight, and body mass index are presented in Table 1. According to the Tanner staging system for puberty, the patient's breast development and pubic hair development were both at stage 3 (Tanner B3P3, no menarche). Her bone age, estimated according to the Greulich and Pyle method, corresponded with the normal range for girls aged 13-14 years.

On examination, the patient had discrete dysmorphic facial features, convergent strabismus, cubitus valgus, pes planus, and kyphoscoliosis of the thoracolumbar spine. A number of psoriatic lesions were observed on her body. An abdominal ultrasound scan and echocardiography revealed no abnormalities. Her blood pressure was 100/70 mm Hg in both arms. Plasma levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) were increased (FSH: 123 mIU/mL [normal range for follicular phase: 2.8-11.3 mIU/mL, for luteal phase: 1.2-9.0 mIU/mL], LH: 30.5 mIU/mL [normal range for follicular phase: 1.1-11.6 mIU/mL, for luteal phase 0-14.7 mIU/mL]), and estradiol level was low ($<$73.4 pmol/L [normal range for follicular phase: 0-587.0 pmol/L, for luteal phase 101.0-905.0 pmol/L]).

An ultrasound scan of the thyroid revealed diffuse low echogenicity and heterogeneous echotexture with micronodules scattered throughout the parenchyma, suggestive of chronic thyroiditis. The levels of thyroid hormones and thyroid-stimulating hormone were normal; however, the levels of thyroid antibodies were increased: thyroglobulin autoantibodies was 71.6 IU/mL (normal range, 0-40 IU/mL), and antithyroid peroxidase antibody was 787 IU/mL (normal range, 0-35 IU/mL).

A pelvic ultrasound revealed hypoplastic uterus (corpus uteri 8 $\times$ 28 mm, with invisible endometrium, 13 mm cervix) and ovaries (right ovarian volume 1.5 mL, left ovarian volume 2.0 mL). A subsequent magnetic resonance imaging scan showed hypoplastic uterus (23 $\times$ 8 $\times$ 9 mm). Adequate for age structure of the ovaries could not be visualized.

A dual-energy x-ray absorptiometry scan showed a reduced z-score rate (L1-L4 spine z-score, $-$3.2; total body z-score, $-$4.2), and normal calcium and phosphorous levels; further observation of low bone mineral density was necessary.

In view of the clinical features, a standard 30-cell karyotype analysis was performed. This showed one normal X chromosome and an isochromosome of the long

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* *Address correspondence to*: Agnieszka Drosdzol-Cop, MD, PhD, Woman's Health, Medical University of Silesia, ul Medyków 12, 40-752 Katowice, Poland; Phone 0-048 32 20 88 752
E-mail address: cor111@poczta.onet.pl (A. Drosdzol-Cop).

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Table 1
General Characteristics of the Patient's Height, Weight, and BMI

Variable	Patient's Result
Height	137 cm (16.5 cm < the third percentile on a standard growth chart)
Growth rate	1.2 cm per year
Standard deviation score (hSDS) for the healthy female population	−4.87
Standard deviation score (hSDS) for females with Turner syndrome	−0.82
Weight	36.3 kg
BMI	19.34 (between the 10th and 25th percentile on a standard chart)

BMI, body mass index; hSDS, height standard deviation score.

arm of the X chromosome (46, X, and (X) (q10)), thus confirming the diagnosis of Turner syndrome. The patient started growth hormone therapy, and was referred to the Endocrinology Outpatient Clinic.

During the next hospitalization, which was performed to improve diagnostic, at the age of 19, the patient's height was 141.3 cm (12.7 cm < the third percentile), height standard deviation score was −4.15, weight was 44.0 kg, and body mass index was 22.04. Signs of spontaneous puberty were observed (according to the Tanner staging system: breast: stage 3/4 and pubic hair: stage 4). Pelvic ultrasound revealed a uterus (8 × 24 × 22 mm) and ovaries (right ovary: 14 × 7 mm, left ovary: 18 × 8 mm). Despite the spontaneous signs of puberty, because of the increased levels of FSH and LH (FSH: 81.7 mIU/mL; LH: 20.9 mIU/mL), estrogen therapy was initiated. The patient remained under the supervision of the Endocrinology Outpatient Clinic.

At the time of her next visit to the Endocrinology Outpatient Clinic, the patient was 20 years old. On physical examination, her height was 141.5 cm, height standard deviation score was −4.19, weight was 47.6 kg, and pubic hair and breast development were at Tanner stage 4 (Tanner B4P4). The patient continued estrogen therapy: transdermal estradiol at a dose of 50 μg/d, which was increased gradually, first to 100 μg/d and finally to 150 μg/d.

At subsequent visits, physical examination revealed no changes. Despite the continuous estrogen therapy, there was no menstrual bleeding. At 24 years of age, the patient was referred to the Gynecological Outpatient Clinic to broaden the diagnostic scope.

The patient had her first complete gynecological examination at the age of 24 years, just after sexual initiation because before that patient and her mother (when the patient was underage) did not agree to examination. The examination revealed a blind-ending vagina (approximately 3-4 cm in length). A transvaginal ultrasound scan showed a blind vaginal pouch; the uterus and ovaries could not be visualized. Computed tomography confirmed the blind-ending vagina with a length of approximately 4.8 cm. On the right side, along the posterolateral wall, a longitudinal structure (with a maximum width of 9 mm) was visualized. Its morphology was similar to the structure of the pelvic ligament. Bilateral tissue structures corresponding to ovaries (on the left side: 26 × 11 mm; right side: difficult to determine) were seen along the iliac vessels. The patient was diagnosed with MRKH.

Summary and Conclusion

Patients with Turner syndrome have a characteristic phenotype related to structural abnormalities of one of the sex chromosomes. Multiple medical problems might be associated with Turner syndrome. The most serious include cardiovascular abnormalities, the most common being bicuspid aortic valve and aortic coarctation. Congenital malformations of the urinary system, such as collecting-system malformations and horseshoe kidneys, coexist in 30%-40% of individuals. Other abnormalities refer to the eyes (including epicanthal folds, ptosis, hypertelorism, upward slanting palpebral, strabismus, and hyperopia), hearing (chronic otitis media and ear malformations), and autoimmune disorders (autoimmune thyroiditis and celiac disease). Two of the most characteristic clinical features are short stature (with short neck, cubitus valgus, genu valgum, and short fourth metacarpals) and absent pubertal development. More than 90% of patients have gonadal failure and only 2%-5% conceive naturally.[1]

There are two types of MRKH. In both, the first and main symptom is primary amenorrhea. In patients who present before puberty, as in the case of our patient, this can cause considerable problems with diagnosis. The first type of MRKH consists of isolated uterovaginal aplasia, and the second, known as MURCS association (Mullerian duct aplasia, unilateral renal aplasia, and cervicothoracic somite dysplasia), consists of incomplete aplasia associated with other malformations. In 40% of patients in the latter category, abnormalities concern the upper urinary tract (mainly unilateral renal agenesis, ectopia of 1 or both kidneys, renal hypoplasia, horseshoe kidney, and hydronephrosis). Associations with skeletal anomalies refer to the spine (for example scoliosis, isolated vertebral anomalies, Klippel-Feil association [ie, fusion of at least 2 cervical segments, short neck, low hairline, restriction of neck motion, and/or Sprengel deformity—a rare congenital malformation of the scapula]) and less commonly to the face and limbs. Auditory defects or deafness and less frequent heart malformations (aortopulmonary window, atrial septal defect, pulmonary

Table 2
Review of Example Features of Coexistence of Mayer-Rokitansky-Küster-Hauser Syndrome With Abnormal Gonadal Development and Various Forms of Dysgenesis, including Turner Syndrome, in the Literature[7]

Feature	Patient, n	References
Ovaries		
Absent in both sides	10	9–18
Dysgenetic in both sides	9	16,19–26
Absent and/or dysgenetic in 1 side	3	11,18,27
Uterus		
Absent	14	10,13,14,17–22,24–28
Hypoplastic	7	9,11,13,15,16,20,23
Fallopian tubes		
Normal	3	14,21,22
Hypoplastic or rudimentary	11	9,11,13,16,18–20,23–25,28
Abnormalities		
Urological	4	13,18,27,28
Skeletal	6	9–11,13,23,24
Alopecia	4	9,17,21,24
Karyotype		
Normal 46, XX	15	9,11,13,15,16,18–23,25,27–29
Turner syndrome; mosaicism	5	10,13,14,17,24