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Case Report

A case of 45,X/47,XXX mosaic Turner syndrome with limb length discrepancy

Nozomi Hishimura-Yonemaru[1#], Koji Okuhara[1], Nobuhiro Takahashi[1], Hidefumi Tonoki[1], Susumu Iizuka[1], and Toshihiro Tajima[2]

[1]*Sapporo Tenshi Hospital, Hokkaido, Japan*

[2]*Jichi Children's Medical Center Tochigi, Tochigi, Japan*

[#]*Present: Department of Pediatrics, Sapporo City General Hospital, Hokkaido, Japan*

Abstract. Patients with Turner syndrome (TS) frequently show short stature and skeletal deformities, such as kyphosis and scoliosis. However, to the best of our knowledge, limb length discrepancy (LLD) has not yet been reported in patients with TS. The case of a 12-yr-old girl with 45,X/47,XXX mosaic TS showing LLD is herein presented. She was on GH therapy for short stature and was noted to have scoliosis in the standing position at a regular examination; however, the scoliosis became less evident in the supine position, which is indicative of LLD. The length of the left leg was 5.0 cm shorter than that of the right leg when measured. She was referred to orthopedics and underwent right distal femoral and right proximal tibial staple epiphysiodesis to shorten the abnormally long limb at 10 yr 6 mo of age. One year after the operation, the LLD decreased from 5.0 to 1.5 cm. During this period, GH was continued. LLD is a rare complication in TS, but when patients with TS show scoliosis in the standing position, re-evaluation for scoliosis in the supine position should be performed and the lengths of both legs should be measured.

Key words: Turner syndrome, GH, limb length discrepancy

Introduction

Patients with Turner syndrome (TS) frequently show short stature (1, 2). In addition, it is known that patients with TS have skeletal deformities, such as cubitus valgum, genu valgum, short metacarpals, an abnormal upper to lower segment ratio, short neck, kyphosis, and scoliosis (3–5), but limb length discrepancy (LLD) has rarely been reported. A case of a Japanese patient with 45,X/47,XXX mosaic TS showing LLD is herein reported.

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Corresponding author: Nozomi Hishimura-Yonemaru, MD, Department of Pediatrics, Sapporo City General Hospital, N11, W13, Kita-Ku, Sapporo 060-8604, Japan
E-mail: gwenon-doubt@kha.biglobe.ne.jp

Case Report

A 12-yr-old Japanese girl was born after 37 wk of gestation by a normal vaginal delivery and was the first child of nonconsanguineous parents. The patient had no siblings, and her parents were healthy. Her father's height was 168 cm and her mother's height was 156 cm. Her birth

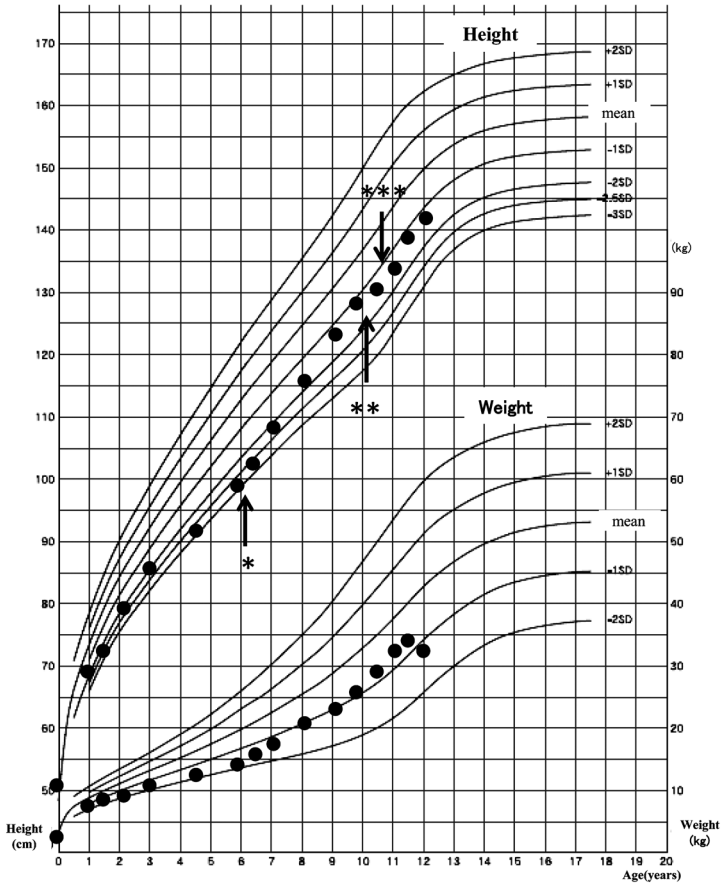
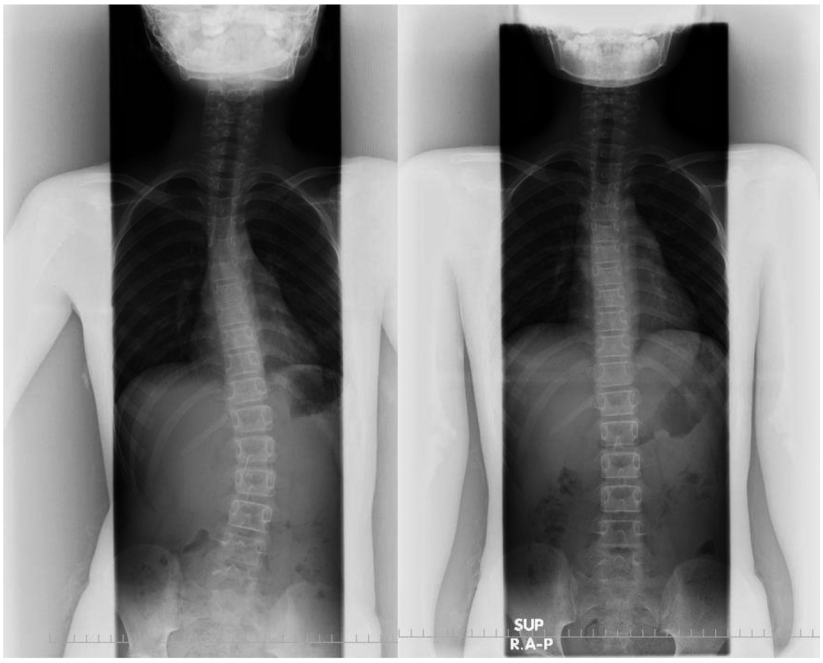


Fig. 1. Growth chart of the patient. *, Start of GH treatment; **, Withdrawal of GH treatment; ***, Restart of GH treatment.

weight was 2,868 g (+ 0.9 SD from the mean for normal Japanese girls) and her length was 46 cm (–0.6 SD from the mean for normal Japanese girls). Her short stature was noted (Fig. 1) and she was referred to our hospital. At referral, her height was 73.8 cm (–2.0 SD from the mean for normal Japanese girls) and her weight was 8,190 g. Clinical examination did not show any stigmata of TS. Laboratory investigation showed normal blood and comprehensive metabolic panel examinations. At this time, informed consent for chromosomal analysis was not obtained from her parents. She was then followed regularly at the outpatient clinic. Since her height did not catch up, as shown in Fig. 1, her chromosomal analysis was done after informed consent was obtained. One hundred metaphase cells were examined from peripheral blood cells. Her karyotype was found to be 47,XXX[93]/45,X[7] and the diagnosis of Turner syndrome was made. Further evaluation showed no urinary tract or cardiac malformations. Her mental development was normal. GH treatment was initiated at this time, to which she responded well (Fig. 1). At 9 yr 10 mo of age, she was noted to have scoliosis in the standing position at a regular examination (Fig. 2A), but the scoliosis became less evident in the supine position (Fig. 2B), which is indicative of LLD. The length of the left leg was 5.0 cm shorter than that of the right leg when measured. The radiographs of the lower limbs showed that the left femur was 1.0-cm shorter than the right femur and the left tibia was 2.4-cm shorter than the right tibia (Fig. 3A).



(A) (B)

Fig. 2. Radiography of the spine of the patient. (A) Scoliosis is evident in the standing position. (B) In the supine position, the scoliosis is improved.

She was referred to orthopedics and underwent right distal femoral and right proximal tibial staple epiphysiodesis to shorten the abnormally long limb at 10 yr 6 mo of age. At that time, GH was stopped. The effect of GH therapy on staple epiphysiodesis was not clear, but she and her parents hoped to restart GH therapy. Therefore, GH therapy was restarted one month after the operation. At 1 yr after the operation, the LLD had decreased from 5.0 to 1.5 cm (Fig. 2B). At the time of writing, the patient was 12 yr old, her height was 142.1 cm (–1.19 SD from the mean for normal Japanese girls), and her weight was 31.95 kg. Her secondary sexual characteristics were at Tanner stage III for breast development and stage II for pubic hair. Menarche had not yet occurred. Her serum LH and FSH levels were 0.6 mIU/ml and 13.5 mIU/ml, respectively, with a serum estradiol level of 13.4 pg/ml. Since the LLD had further decreased to 0.5 cm, removal of the staples was planned.

Discussion

Since the incidence of scoliosis is higher in patients with TS than in normal girls, regular examination of posture is usually done (5). However, to the best of our knowledge, LLD has not been previously reported in patients with TS. In LLD, scoliosis is seen in the standing position, but it improves in the supine position. Therefore, if a patient with TS shows scoliosis in the standing position, careful examination in the supine position and measurement of the lengths of both legs should be performed. Furthermore, radiographs of the spine and legs should be taken.

Papenhausen *et al.* (6) reported a 45,X/46,XY mosaic boy with asymmetric leg growth. According to the report, the lymphocytes demonstrated mosaic 45,X/46,XY in a ratio of 14:25. However, skin fibroblast cultures of the thigh and calf from the short leg showed

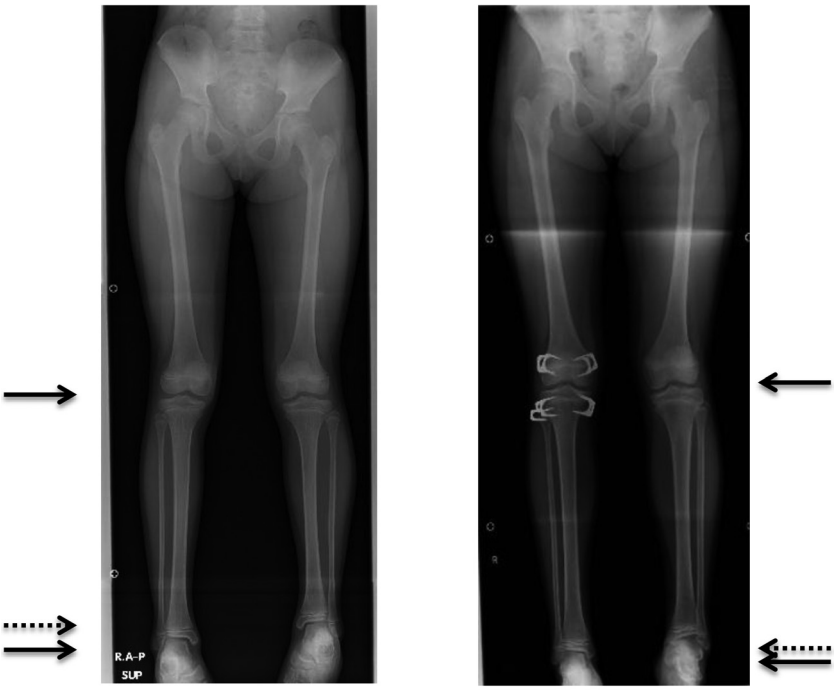


Fig. 3. Radiography of the lower limbs of the patient. (A) The radiographs show that the left leg is shorter than the right leg. (B) Six months after the operation, the LLD has not yet decreased.

100% 45,X and 80% 45,X, respectively. On the other hand, both skin fibroblast cultures of the thigh and calf from the long leg were 100% 46,XY. Similar to this case, LLD could be explained by the dominant distribution of the 45,X cell lineage in the short leg. In the present case, cytogenetic study was performed only for lymphocytes. Females with 47,XXX usually show tall stature and long legs (7). The main reason for these features is that in trisomy X, although two of the three X chromosomes are inactivated, genes in the pseudoautosomal regions that escape X-inactivation are expressed from the three X chromosomes. In the present case, chromosomal analysis of skin fibroblasts of the legs was not done, but the 47,XXX cell line may be predominant in the long leg, with the 45,X cell line predominating in the short leg.

There is a possibility that GH treatment may accelerate scoliosis in TS patients (8); in that context, LLD could be worsened by GH treatment. In addition, GH may affect staple epiphysiodesis. Moreover, estrogen is known to exacerbate Madelung deformity in SHOX deficiency (9).

Although the inequality of right and left limbs has not been aggravated by GH treatment and the development of secondary sex characteristics in the present patient, careful follow-up of the LLD is required.

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