

A rare of Turner syndrome with a special karyotype: a case report

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Summary

Turner syndrome (TS) is a gonadal dysgenesis caused by absence or structural abnormalities of sex chromosome. Isochromosome Mosaic TS is a structurally abnormal X chromosome consisting of either two short or two long arms, with only an 8-9% prevalence among women with TS based on international studies. The present report describes a 30-year-old female with isochromosome mosaic karyotype TS. The patient had no menarche so far. G-banding chromosome analysis indicated mosaic 45,X[3]/46,X,i(X)(q10)[79]/47,X,i(X)(q10),i(X)(q10),i(X)(q10)[3]/49,X,i(X)(q10),i(X)(q10),i(X)(q10),i(X)(q10)[79]. Both clinical and cytogenetic investigations proved this patient to be a special isochromosome Xq Mosaic TS with autoimmune hypothyroidism and hyperlipidemia.

Key words: Primary amenorrhea; Turner Syndrome; Karyotype; Mosaic Isochromosome Xq; Autoimmune hypothyroidism.

Introduction

Turner Syndrome (TS) is a common chromosomal disorder caused by numerical or structural aberrations of sex chromosomes occurring in 1:2, 000 to 1:2,500 liveborn females [1]. 45,X monosomy karyotype accounts for 50-60% of TS cases. Most mosaicism karyotypes (as 45,X/46,X,X), and partial 45, X with a second structurally abnormal X chromosome consisting of either two short or two long arms [2, 3]. The clinical manifestations of TS include short stature, gonadal dysgenesis resulting from delayed puberty, primary amenorrhea, and infertility [4-6].

TS patients produce autoantibodies due to the abnormal X chromosome, which may lead to autoimmune diseases. TS patients also have concurrent diseases, such as hypothyroidism, renal abnormalities, neurocognitive disorders, and congenital/acquired cardiovascular diseases [7, 8]. The relationship between thyroid and TS has been reported previously [9].

It has been suggested that there might be a casual relationship between aberrations of the X-chromosome and the risk of autoimmune hypothyroidism. Autoimmune hypothyroidism is common, with an annual incidence of 3.2% in TS. It is suggested that the thyroid function should be checked regularly in TS patients [10].

The aim of this case report presentation is to describe a mosaic 45,X/46,X,i(X)(q10)/47,X,i(X)(q10),i(X)(q10)/49,X,i(X)(q10),i(X)(q10),i(X)(q10),i(X)(q10) with TS, accompanied by a high incidence of autoimmune hypothyroidism.

Case Report

The patient was hospitalized due to infertility. She was 30-years-old, with a stature of 152 cm. Her intelligence quotient (IQ) was below average, and she had not experienced menarche so far. Through transvaginal ultrasonography, her uterus was visualized 3.8×3.5×2.5 cm³, and bilateral ovaries (left: 1.7×1.4 cm² and right: 1.6×1.1 cm²). These results showed that the dimensions of two ovaries were under normal size. The sex hormone levels were detected via peripheral blood, with results of follicle stimulating hormone (FSH) 35.68 mIU/ml (normal range: 1.79-22.51), luteinizing hormone (LH) 15.78 mIU/ml (normal range: 1.2-12.86), progesterone (P) 0.28 ng/ml (normal range: 0.31-18.56), Luteinizing hormone releasing hormone (LHRH) stimulation testing showed abnormal gonadotropic hormones, and the levels of FSH and LH levels were high at different time points of baseline (0.5, 1, 2, and 3-hour post-stimulation) (Table 1). Serum insulin (12.65 IU/mL) levels were within normal range. In addition, her total thyroxine (TT4: 79.76 nmol/L) and total triiodothyronine (TT3: 1.34 ng/mL) were normal, while thyroid-stimulating hormone (TSH: 11.41 uIU/mL) was higher along with high levels of anti-thyroglobulin antibodies (TGAb: 954.3 IU/mL) and autoantibody to thyroid per-oxidase (TPOAb: 566.5 IU/mL) (Table 2). The total cholesterol level (6.34 mmol/L) and serum LDL-cholesterol (4.25 mmol/L) were also higher than normal range. Karyotyping was performed following peripheral blood lymphocyte culture. A total of 100~200 metaphase cells were analyzed by the Gbanding method. Chromosomal analysis revealed that the mosaic status for the isochromosome formation in the long arm of X, i(Xq). Her karyotype is mosaic 45,X[3]/46,X,i(X)(q10)[79]/47,X,i(X)(q10),i(X)(q10)[3]/49,X,i(X)(q10),i(X)(q10), i(X)(q10), i(X)(q10) [79] (Figure 1). This is consistent with a rare Isochromosome Xq Mosaic TS with four karyotypes. High-throughput sequencing indicated an abnormal female karyotype. It showed that a 45.28Mb deletion in Xp22.31-p11.22, a 3.16 Mb deletion in Xp22.33-p22.32, and a 92.36Mb

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Table 1. — Results of LHRH stimulation test.

Hormone	0.5 hour	1 hour	2 hours	3 hours
FSH (mIU/ml)	49.67	57.47	52.93	46.88↑
LH (mIU/ml)	47.79	44.98	33.76	26.36↑

LHRH: gonadotropin-releasing hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone. ↑ indicates that the value is above the normal range.

mosaic repeated fragment in Xp11.22-q28, respectively.

Discussion

This is a rare special karyotype case of TS with autoimmune hypothyroidism with mosaic 45,X[3]/46,X,i(X)(q10)[79]/47,X,i(X)(q10),i(X)(q10)[3]/49,X,i(X)(q10),i(X)(q10),i(X)(q10),i(X)(q10)[79]. In addition, it is the first report of a mosaic case of four karyotypes in a TS case. The cause of infertility in this patient is primary amenorrhea relating to the abnormalities of the X chromosome. The severity of the phenotypic manifestations of TS mostly depends on the proportion of chromosomally compromised cells in each patient [11, 12]. Generally, the higher proportion of cells with an abnormal karyotypes includes more severe clinical symptoms, but with an earlier diagnosis. The phenotypes in TS varies, follicular development, and the potential for fertility can be maintained in some TS with chromosomal mosaicism [13].

This TS patients phenotypes were closely related with previously reported ones, such as 45,X/46,X,i(X)(q10) or Mosaic 45,X/46,X,i(X)(q10)/47,46,X,i(X)(q10),i(X)(q10) isochromosome Xq karyotype [14, 15]. In this case, the TS patient was also diagnosed with autoimmune hypothyroidism, evidenced by lower levels of TT4 and TT3, higher levels of TSH, and higher levels of autoantibody to TPO. The patient had a high titer of thyroid autoantibodies: TPOAb and TgAb, which are involved in the process of thyroid gland follicular cells' autoimmune disorder, causing permanent damage of thyroid tissue cells and resulting in hypothyroidism, and the incidence rate of autoimmune thyroid diseases in TS patients is 13%~55% [16].

Women with an isochromosome-X karyotype were also

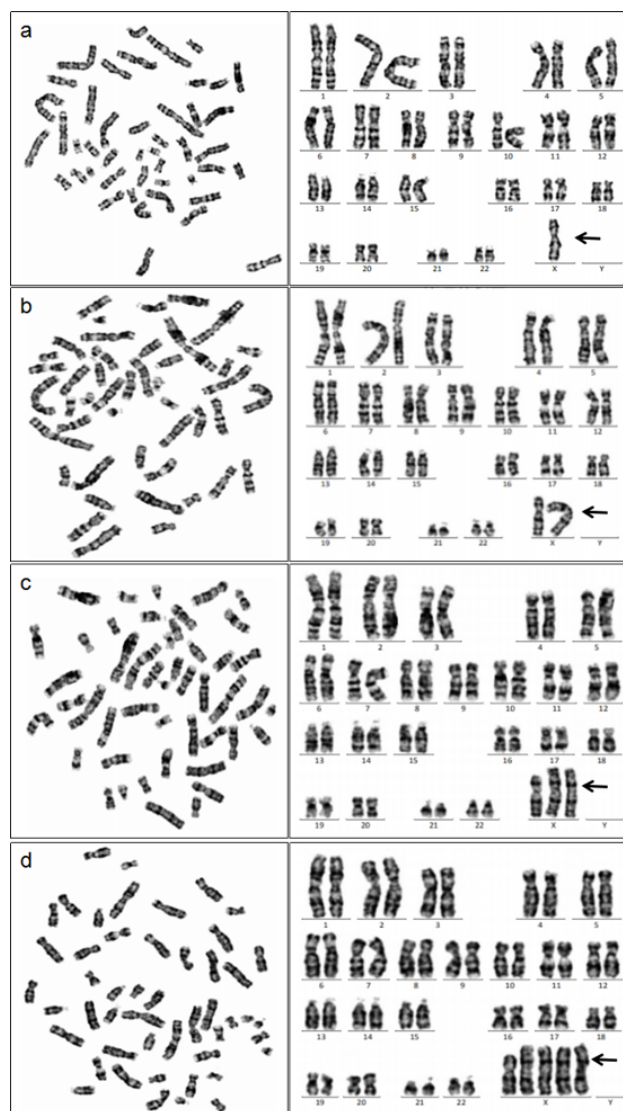


Figure 1. — Results of routine karyotyping. (a) Routine karyotyping 45,X. (b) Routine karyotyping 46,X,i(X)(q10). (c) Routine karyotyping 47,X,i(X)(q10)×2. (d) Routine karyotyping 49,X,i(X)(q10)×4. The abnormal chromosomes locations are indicated by arrows. Scale bars = 100 μm.

Table 2. — Results of thyroid data and blood lipids test.

Test item	Numerical value	Reference range
Total thyroxine (T4)(nmol/L)	79.76	66-181
Total triiodothyronine (T3)(ng/mL)	1.34	0.8-2.0
Serum free thyroxine (FT4)(ng/dL)	0.96	0.93-1.7
Serum free triiodothyronine (FT3)(pg/mL)	3.27	2.0-4.4
Serum thyroid-stimulating hormone (TSH)(uIU/mL)	11.41↑	0.27-4.2
Anti-thyroglobulin antibodies(TG-Ab)(IU/mL)	954.3↑	<115
Anti-thyroid peroxidase antibody (TPO-Ab)(IU/mL)	566.5↑	<34
Serum total cholesterol (mmol/L)	6.34↑	0-5.17
Serum triglycerides (mmol/L)	1.6	0-2.3
Serum HDL-cholesterol (mmol/L)	1.43	1.29-1.55
Serum LDL-cholesterol (mmol/L)	4.25↑	0-3.37

↑ indicates that the value is above the normal range.

significantly more likely to develop hypothyroidism compared to other karyotypes, and it is speculated that some genes located on the long arm of the X chromosome (Xq) may play an important pathogenetic role in the development of autoimmune thyroid disease [17, 18]. On the contrary, some research showed that the high rate of autoimmune thyroid disease in TS patients was independent on the isochromosome-X karyotype, which indicates that the karyotype 45,X of TS patients also has a high rate of autoimmune thyroid disease [19-22]. The mechanism of the autoimmune thyroid disease and TS need to be further studied.

Conclusion

This is a rare case of TS with 4 karyotypes. Patients had primary amenorrhea, with normal size of ovaries, and had autoimmune hypothyroidism. The thyroid function should be checked regularly in TS patients. Moreover, prevention other complications should be included.

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