**Case Report**

**Turner Syndrome with Ulcerative Colitis**

Hiromi Hyodo¹, Yuichiro Tomita¹, Kohta Hirai¹, Hitoshi Hirakawa², Shigeru Ueno², and Hiroyuki Ishiguro¹

¹Department of Pediatrics, Tokai University School of Medicine, Kanagawa, Japan
²Department of Pediatric Surgery, Tokai University School of Medicine, Kanagawa, Japan

**Abstract.** Turner syndrome is a chromosomal disease frequently associated with autoimmune disorders including diabetes mellitus, thyroid disease and inflammatory bowel disease (IBD). Although the etiology of IBD has not been fully elucidated, genetic analysis has recently revealed several susceptibility genes. Recently, cases with Turner syndrome associated with IBD have been reported. We report here a 13-yr-old girl with Turner syndrome associated with ulcerative colitis. The patient was undergoing growth hormone treatment and presented with abdominal discomfort and bloody diarrhea. Her karyotype pattern was 46,X,i(Xq). Barium enema revealed punctate collections of barium suggesting microulcerations in the descending and sigmoid colon with loss of haustra. Flexible sigmoidoscopy showed that the mucosa was erythematous and friable upon touch and that the wall had frank hemorrhage and inflammatory polyp formation from the anal verge through the splenic flexure. Histologically, mucosal and submucosal inflammation was prominent, suggesting cryptitis and crypt abscess formation. Based on these findings, she was diagnosed as having ulcerative colitis, and 5-aminosalicylic acid, prednisolone and dietary therapy were initiated. Our observations in this patient suggest that X chromosome abnormality may influence the development of IBD and that screening for gastrointestinal disease in patients with Turner syndrome may help lengthen life expectancy in these patients.

**Key words:** Turner syndrome, ulcerative colitis, 46,X,i(Xq)

**Introduction**

Turner syndrome is a common genetic disorder resulting from partial or complete absence of one sex chromosome and occurring in approximately 1 per 2,500 live-born females (1, 2). The association of Turner syndrome with strong susceptibility to autoimmune disorders, including diabetes mellitus, hypothyroidism and inflammatory bowel disease (IBD) (3), especially in a subgroup with a chromosomal structural abnormality, has recently been well established (2, 4).

IBD is comprised of two major disorders, Crohn's disease (CD) and ulcerative colitis (UC). Approximately 20 percent of patients with IBD develop symptoms in childhood or adolescence. The development of IBD early in life has implications that are not encountered in adults. UC is a chronic inflammatory disorder of the intestine characterized by dysregulated mucosal immune response. Although the etiology of UC
has not been fully clarified, genetic analysis has recently revealed several susceptibility genes for IBD (5).

Although an association between Turner syndrome and IBD has been described (3, 4), the incidence of Turner syndrome with IBD is rare (6), and the pathogenic mechanism linking Turner syndrome with IBD has not been elucidated.

We describe here a patient with a 46,X,i(Xq) karyotype pattern who developed UC during growth hormone therapy.

**Case Report**

A 10-yr-old Japanese female was referred to our pediatric endocrinology clinic for evaluation of short stature. The prenatal course was uncomplicated, and she was born after full-term gestation with a birth weight of 3,000 g and a birth height of 47.8 cm. The results of newborn mass screening for metabolic abnormalities and endocrinological disorders were negative. Her developmental milestones were normal. On physical examination at 10 yr old, her height was 122.2 cm (–3.1 SD for a normal 10-yr-old Japanese female and +1.4 SD for a 10-yr-old). Turner syndrome female without genital bleeding and her weight was 32.8 kg (–0.5 SD for a normal 10-yr-old Japanese female); a high arched palate and cubitus valgus were noted (Fig. 1). Notably absent were the webbing of the neck, low hairline, shield chest with widely spaced nipples and facial features characteristic of Turner syndrome. Her breasts and pubic hair were Tanner stage I. Endocrinological evaluation revealed growth hormone deficiency according to insulin tolerance test (peak GH: 4.37 ng/ml) and hypergonadotropic hypogonadism. Her bone age by the RUS method was 10.4 yr old. Diabetes mellitus and thyroid dysfunction were not detected. Chromosomal analysis of peripheral lymphocytes disclosed a 46,X,i(Xq) karyotype pattern. Turner syndrome was diagnosed on the basis of her physical examination, endocrinological evaluation and karyotype. Growth hormone treatment (0.35 mg/kg/wk) was initiated at age 11 yr old.

At the age of 13 yr and 9 mo, she presented with intermittent abdominal discomfort and mucoid bloody diarrhea. She had lost her appetite and had moderate tenderness in her lower abdomen. The cramping abdominal pain gradually worsened over the following 3 mo, and the frequency of bloody diarrhea increased. She was admitted to our hospital with these symptoms at the age of 13 yr and 11 mo. On admission, her height was 136.3 cm (–3.6 SD for a normal 14-yr-old Japanese female and +1.0 SD for a 14-yr-old). Turner syndrome Japanese female without genital bleeding and her weight was 30.5 kg (–2.3

![Fig. 1 Longitudinal growth curve.](image-url) Longitudinal growth curve plotted against cross-sectional growth charts for Japanese female (0–18 yr) 2000. 5-ASA: (5-aminosalicylic acid).
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Her body temperature was 37.3°C, her pulse was 96 beats per minute and her blood pressure was 106/44 mmHg. Aphthous ulcers in the oral cavity and anal fistulae were not observed. An abdominal examination revealed a distended and mildly tender abdomen with hyperactive bowel sounds. The remainder of the examination was normal. Laboratory findings on admission were as follows: WBC, 5,700/µl; Hb, 9.4 g/dl; Ht, 29.7%; Plt, 34.5 × 10^4/µl; AST, 7 U/l; ALT, 5 U/l; LDH, 144 U/l; CK, 31 U/l; Amylase, 161 U/l; CRP, 0.23 mg/dl; and an erythrocyte sedimentation rate (ESR) of 22 mm/h. She was diagnosed with presumed infectious enterocolitis and was hydrated intravenously and treated empirically with antibiotics. A stool culture was negative for bacterial infection. After 7 d with minimal response to therapy, she underwent barium enema, flexible sigmoidoscopy (Fig. 2 A, B) and biopsies. Barium enema showed a diffusely reticulated pattern with superimposed punctate collections of barium in microulcerations and loss of haustra in the descending colon and sigmoid colon. Flexible sigmoidoscopy showed touch friability, frank hemorrhage, erythematous mucosa and pseudopolyps in a diffuse circumferential distribution from the anal verge to the splenic flexure. Histological features included mucosal and submucosal inflammation, cryptitis, and crypt abscess formation in the descending colon and sigmoid colon. Based on these findings, she was diagnosed as having UC. Oral administration of 5-aminosalicylic acid (5-ASA, 50 mg/kg/d) and dietary treatment were initiated. Her abdominal symptoms, frequency of bloody diarrhea, serum CRP, ESR and Hb were rapidly ameliorated by this treatment. Four weeks after initial treatment, however, her abdominal symptoms and a blood examination indicated recurrence of UC. Oral prednisolone (2 mg/kg/d) was immediately initiated. Her clinical symptoms improved as a result, and no symptoms indicating recurrence of UC were observed at discharge. She was treated with oral prednisolone for 4 mo.

Spontaneous secondary sexual development was arrested at 15 yr old, and hormone replacement therapy was started with a low dose of conjugated estrogen for induction of secondary sexual development. At 17 yr old, UC recurred.
with cramping abdominal pain and bloody diarrhea. Oral prednisolone (1.0 mg/kg/d) was immediately re-administrated to treat the recurrence of UC. Her abdominal symptoms improved dramatically within a short time after resumption of the medication and dietary treatment. Oral prednisolone was administrated for 2 mo. At the age of 17 yr and 10 mo, progesterone was added to the hormone replacement therapy for maintenance of sexual development and induction of cyclic uterine bleeding.

Discussion

The prevalence of Turner syndrome is approximately 1 per 2,500 live-born females (1, 2), while the prevalences of CD and UC are 10–50 and 30–90 per 100,000, respectively (4). Turner syndrome is associated with a strong susceptibility to autoimmune disorders, with an increased risk of developing IBD. Gravholt et al. calculated a 2-fold increase in the risk of developing IBD in women with Turner syndrome (6). However, a study by Price et al. (7) found the risk to be even greater. They reported that the prevalences of both CD and UC were 1.48% and 1.48%, respectively, in a series of 135 patients with Turner syndrome, which when compared with the general population, constituted a 30-fold and 16-fold increase, respectively (7). Gastrointestinal symptoms in IBD often develop at a young age, and the median age of onset is 16 yr old. (range 9–40 yr old) (2). Moreover, IBD is often severe in women with Turner syndrome. In the case reported here, the Turner syndrome patient also developed gastrointestinal symptoms at age 13 yr old.

Although an association between Turner syndrome and IBD has been described, the pathogenic mechanism has not been elucidated. Evidence exists suggesting a cytogenetic basis for the severity of the symptoms in Turner syndrome. The pure 45,X monosomy is the most common karyotype and is associated with the most severe symptoms. Hayward et al. estimated that 57% of patients with Turner syndrome have the karyotype 45,XO, while 17% of patients have one normal X chromosome and one isochromosome that comprises two long arms instead of one long and one short arm; this isochromosome may be observed either in all cells or as a mosaic (4). Turner mosaics usually have a less severe phenotype, and up to 40% of these individuals enter puberty spontaneously before developing gonadal failure (8). The isochromosome Xq is the most common structural abnormality and is associated with autoimmune disorders, but congenital abnormalities are conspicuously absent (9). Women with the isochromosome Xq karyotype are particularly susceptible, accounting for 52% of the reported cases of IBD in women with Turner syndrome (2). Although the causes of IBD are not fully known, immunological dysfunction is thought to play an important role. IBD, like most immune-mediated diseases, is more common in women. Additionally, the increased risk of IBD in Turner syndrome, particularly in the presence of an X isochromosome, would suggest that perhaps a gene on the long arm of the X chromosome may be associated with immune dysfunction. In our case, the patient, with karyotype 46,X,i(Xq), had a less severe phenotype, but developed ulcerative colitis at adolescence.

We have reported here a karyotype 46,X,i(Xq) Turner syndrome patient with UC. The severity of UC was moderate to severe and improved after treatment with 5-ASA, prednisolone and dietary therapy. This case supports the idea that the X chromosome partly contributes to susceptibility to UC and may modulate the severity of inflammation in this condition. Turner syndrome patients are susceptible to a number of medical problems, including cardiovascular disease, osteoporosis and other endocrine, gastrointestinal and renal disorders (10). They require long-term follow-up so that early medical intervention may reduce morbidity and improve life expectancy. IBD should be ruled out in women with Turner syndrome with unexplained abdominal discomfort and bloody diarrhea.
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