Original Article

Turner Syndrome Associated with Ulcerative Colitis

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Abstract. We report the case of a 7-yr-old girl with Turner syndrome, ulcerative colitis (UC) and coarctation of the aorta. The diagnosis of Turner syndrome was made in early infancy (karyotype analysis 45, X). Growth hormone treatment was started at 3 yr and 2 mo of age. From the age of 4 yr and 5 mo, the patient suffered from persistent diarrhea with traces of blood and intermittent abdominal discomfort. As these symptoms gradually deteriorated, she was referred to our clinic at the age of 7 yr for further evaluation. Barium enema showed aphtha and loss of the fine network pattern in the descending colon and rectum. An endoscopic examination showed ulceration, edema, friability, and erythema beginning in the rectum and extending up to the splenic flexure of the descending colon. The histology of the descending colon area showed severe stromal infiltration of inflammatory cells. These endoscopic findings and the histological findings were consistent with UC. Thus, based on these findings, the patient was diagnosed as having UC. Mesalazine therapy was initiated at this time. The patient is currently being treated with mesalazine (1,000 mg/day) and abdominal symptoms and bloody diarrhea have disappeared. GH therapy was not interrupted during the therapy for UC. Retrospectively, growth hormone improved growth velocity (9 cm/year) during the first year of treatment, however from the age of 4 yr, growth velocity decreased (4–5 cm/yr) in spite of the GH treatment. Conclusion: Patients with Turner syndrome and gastrointestinal symptoms should be investigated for inflammatory bowel diseases. Growth velocity is useful for evaluating the presence of inflammatory bowel diseases and other systemic diseases.

Key word: Turner syndrome, ulcerative colitis, growth velocity, GH therapy
A 7-yr-old Japanese girl was referred to us for evaluation of bloody diarrhea. TS was diagnosed in early infancy on the basis of short neck and lymphedema, and was confirmed by karyotype analysis, i.e. 45, X. Growth hormone (GH) treatment started at 3 yr and 2 mo of age.

On admission to our hospital, the patient's height was 106 cm (–2.2 SD for normal Japanese girl) and she weighed 18.6 kg (–1.0 SD for normal Japanese girl, obesity +7.5%). She had a low hairline and deformity of the auricules. Notably absent were shield chest, cubitus valgus, or pigmented skin lesions. Her temperature was 36.7°C, her heart rate was 88/min and her respiratory rate was 24/min. Blood pressure was 100/74 mmHg in the upper extremities, but 76/44 mmHg in the lower extremities. Grade 1/6 harsh systolic ejection murmur was audible at the 3rd to 4th left sternal border. By cardiac catheterization and an aortogram, coarctation of the aorta was diagnosed. At 4 yr and 5 mo of age, the patient began suffering from intermittent abdominal discomfort and developed persistent diarrhea containing traces of blood. Ova, parasites and bacteriologic culture were negative in stool samples. The patient lost appetite and had moderate tenderness in her lower abdomen. The abdominal pain gradually worsened in the following 5 mo and frequency of bloody diarrhea increased (4–5 times/d). Pertinent laboratory findings were: serum potassium, 4.2 mEq/l; sodium, 141 mEq/l; chloride, 108 mEq/l; RBC, 345 × 10⁴ /µl; Hb, 7.3 g/dl; Ht, 26%; WBC, 4,400 /µl; serum Fe, 144 µg/dl; UIBC, 322 µg/dl; ferritin, 4.1 ng/ml; cholesterol, 130 mg/dl; total protein, 6.4 g/dl; albumin, 3.6 g/dl; AST, 19 U/l; ALT, 11 U/l; ALP, 428 U/l; cholinesterase, 109 U/L; and an erythrocyte sedimentation rate of 36 mm/h. Thyroid antibody tests were negative.

Barium enema showed aphtha and loss of the fine network pattern in the descending colon and rectum. Endoscopic examination showed ulceration, edema, friability, and erythema beginning in the rectum and extending up to the splenic flexure (Fig. 1). Histological findings of the sigmoid colon included severe stromal
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The mucosa showed severe ulceration, severe infiltration of inflammatory macrophages, lymphocytes, a moderate number of polymorphs, and plasma cells. From these findings a diagnosis of UC was made, and mesalazine (1,000 mg/d) was started. Abdominal symptoms and bloody diarrhea have improved with this treatment. GH therapy was continued without interruption.

Growth Curve and Velocity

The patient’s growth in height has followed the −2.0 SD line of normal Japanese girls. In the growth chart of Japanese TS, her growth has followed the +1.0 SD line (Fig. 2). Initiation of GH therapy at 3 yr of age initially improved her growth velocity (9 cm/yr for the first year) (Fig. 3). However, it was profoundly suppressed after 4 yr of age when diarrhea started. In retrospect, the patient’s serum IGF-1 levels during the age of 4–7 yr were not elevated (160 to 280 ng/ml) in spite of the GH dose (0.33 mg/kg/wk). After starting mesalazine, however, her growth velocity increased to 4–5 cm/yr again.

Discussion

The prevalence of IBDs in the general population is estimated at 150–250 per 100,000...
population (6). In women with TS, Gravholt et al. calculated a 2-fold increase in the risk of developing IBD (7). Other studies have reported that the risk of this association is much higher (2.6–3%) (8). Especially, gastrointestinal symptoms in TS patients are observed at a younger age, the median age of onset being 16 yr (range 9–40 yr) (9). To our knowledge, our present case report is of the youngest TS patient with UC. Thus, we must keep in mind that UC or Crohn’s disease might be a complication even in young TS patients.

X chromosomal abnormality may cause abnormal immune functions and increase the susceptibility to IBDs (4). Therefore, we should be alert to the fact that UC or Crohn’s disease might be a complication in patients with TS developing unexplained diarrhea or gastrointestinal bleeding.

Patients with IBDs manifest growth failure, which may precede abdominal symptoms by some years. Our patient showed markedly retarded growth velocity after the onset of bloody diarrhea in spite of GH therapy. After starting mesalazine for the treatment of UC, the gastrointestinal symptoms have been well controlled and a catch-up in height velocity has been observed. Therefore, the impaired response during GH therapy in our patient might have been caused by the inflammation and malnutrition due to UC overwhelming the anabolic effect of GH. Awareness of this association has clinical importance in identifying the cause of growth failure in a child with either X chromosomal abnormality or IBDs (4).

In conclusion, we emphasize that TS patients with gastrointestinal symptoms should be investigated for the possible occurrence of IBDs. We must pay attention to growth velocity during GH treatment in TS patients, because an impaired response to GH may indicate an association with other systemic disorders including IBDs.

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