Usefulness of abdominal ultrasonography with studies of the intestinal loops in Turner syndrome patients

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Received: 25 February 2013 / Accepted: 12 March 2013 / Published online: 9 May 2013
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Abstract Turner syndrome, a chromosomal disorder caused by partial or complete absence of one of the two X chromosomes, is characterized by an increased incidence (compared with that in the normal population) of either autoimmune disorders, including chronic inflammatory bowel diseases, or angiodysplasia of the small intestine. Because ultrasonography and color Doppler ultrasound are widely used to investigate gastrointestinal disorders, we decided to carry out an ultrasound-based screening study in patients with Turner syndrome to determine whether this method might be useful in the follow-up of this population.

Keywords Turner syndrome · Ultrasonography · Color Doppler ultrasound · Inflammatory diseases · Internal chronic · Angiodysplasia

Riassunto La sindrome di Turner, patologia cromosomica dovuta a parziale o totale assenza di uno dei due cromosomi X, è caratterizzata da un'augmentata incidenza rispetto alla popolazione normale di malattie autoimmuni, tra cui le malattie infiammatorie croniche intestinali, e di angiodisplasie del tenue. In considerazione dell'attuale

ampio utilizzo dell'ecografia e dell'eco-color-Doppler nello studio diagnostico delle patologie gastrointestinali si è pensato di effettuare uno screening ecografico in una popolazione di pazienti affetti da sindrome di Turner per valutare l'utilità dell'inserimento di questa metodica nel loro follow up.

Introduction

Turner syndrome (TS) is a chromosomal disorder caused by the complete or partial absence of one of the two X chromosomes. It results in diverse anomalies, ranging from a 45,X karyotype (in approximately 50 % of the cases) to several types of mosaicism (e.g., 45,X/46,XX or 45,X/47,XXX), with a female phenotype. The condition is found in approximately 1/4,000 (between 1/2,000 and 1/5,000) live-born females and is characterized by a series of clinical alterations, the most common of which short stature and gonadal dysgenesis [1–3].

The literature reveals an increased incidence in these patients of autoimmune diseases, in particular chronic inflammatory bowel diseases (CIBD) (2.6 %) [8], such as ulcerative colitis and Crohn disease [4–9], Hashimoto thyroiditis and type 1 diabetes mellitus; increased risk of coeliac disease, juvenile rheumatoid arthritis, Addison's disease, psoriasis, vitiligo and alopecia areata have also been reported. Furthermore women with TS show high prevalence of angiodysplasia of the small intestine (incidence 7 %) [10–13].

In recent years, the potential of abdominal ultrasonography for the study of gastrointestinal diseases has increased remarkably as a result of ongoing technological advances in the equipment field and researchers' growing interest in this imaging technique [14–19]. Ultrasound study of the intestinal loops is a well-established method for evaluating the

Award for the best Poster at the SIUMB National Congress 2010.

The study was a joint collaboration between the I Internal Medicine Department and the Department of Pediatrics at the University of Pavia; G. R. Corazza and D. Larizza share the last position.

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small and large intestines, and it displays high accuracy in the diagnosis and monitoring of chronic inflammatory bowel diseases, Crohn's disease in particular [18, 19]

In this study, we evaluated the usefulness of abdominal ultrasonography (US) with study of the intestinal loops for detecting intestinal disorders in patients with TS.

Patients and methods

Sixty-six patients with TS were included in the study. Thirty-five had a 45,X karyotype, and the other 32 had structural anomalies or mosaicisms involving the X chromosome. The mean age at the time of the examination was 28 ± 10 years. Thirty patients (45.4 %) had known autoimmune disease, including autoimmune thyroiditis, which was especially common. Fifty-four percent were on growth-hormone replacement therapy, and 52 % were taking estrogen-progestin combinations. Only 18 % had experienced spontaneous puberty. As control groups, we enrolled 60 women with diagnoses of irritable bowel syndrome (IBS) (mean age 34 ± 10 years) and 60 healthy female volunteers (HV) (mean age 34 ± 10 years).

Abdominal ultrasonography with color power Doppler studies of the intestinal loops was performed on each patient included in the study. All the examinations were carried out by the same examiner using an Esaote MyLab 70 XVG ultrasound system with a 1–8 MHz convex transducer and a 4–13 MHz linear transducer. The following parameters were evaluated: intestinal loop dilatation (normal caliber < 25 mm), wall thickness (normal value < 3 mm), alterations involving parietal stratification and/or vascularization, thickening of the mesentery, and presence of mesenteric lymphadenopathy.

In the ST group, peripheral venous blood was also drawn for a complete blood count, assessment of inflammatory markers (erythrocyte sedimentation rate, C-reactive protein levels), iron status, and serological markers [anti-*Saccharomyces cerevisiae* antibodies (ASCA), perinuclear atypical antineutrophil cytoplasmic antibodies (pANCA)]. A stool specimen was also collected for measurement of fecal calprotectin levels.

Complete personal and family medical histories were recorded for each patient, with emphasis on familial cases of CIBD.

The presence of gastrointestinal symptoms (i.e., abdominal pain, changes in bowel habits, meteorism) was evaluated and scored using a visual analog scale (VAS 0–10).

Statistical analysis

Parametric data (reported as mean $\pm$ SD) were analyzed with ANOVA. Differences involving non-parametric data

were analyzed with the Fisher exact test. The data obtained in the three groups were compared using the Student *t* test and the Mann–Whitney *U* test.

Results

In 44 patients with ST (66.5 %), abnormal findings were recorded for at least one of the intestinal parameters examined with ultrasound, with no differences related to karyotype. Mean wall thickness was 3.1 ± 1.3 mm in the patients with ST (Fig. 1) and 2.9 ± 1.3 mm in the IBS group. There was no significant difference between these two values ($p > 0.05$), but both were significantly higher ($p < 0.001$ and $p < 0.01$, respectively) than the mean thickness recorded in the HV group (2.3 ± 0.6 mm). As for the other parameters, significant differences between the TS patients

Fig. 1 Sigmoid colon loop with wall thickening and hypertrophy of the submucosal layer

Fig. 2 Terminal ileum: the walls are thickened and color Doppler imaging reveals rich vascularization

Fig. 3 Terminal ileum: the walls of this loop are normal in thickness but the color Doppler study reveals intense vascularization

and HVs were observed in terms of intestinal loop vascularization ($p < 0.0001$) (Figs. 2, 3), stratification ($p < 0.0001$), and dilatation ($p < 0.015$). The same parameters were also found to be significantly different in the IBS and HV groups ($p = 0.012$, $p = 0.001$, $p < 0.0001$).

Blood chemistry and serological tests performed in the TS group revealed alterations involving inflammatory markers in nine patients, seven of whom had presented at least one alteration on the intestinal US study. Nine patients (five with intestinal alterations on US) were positive for autoantibodies against ASCA. No intestinal anomalies were observed in the patients who were positive for anti-ANCA autoantibodies. The iron status was within normal limits in all TS patients.

Examination of stool samples revealed abnormal levels of calprotectin in 8 patients, 5 of whom had abnormal findings on the intestinal US study.

As far as symptoms were concerned, only one of the TS patients had abnormal gas-related distention of the intestinal loops, and another reported recurrent abdominal pain and diarrhea. None of the patients had family histories of CIBD.

Discussion

Sonographic examination of the abdomen with color power Doppler studies of the intestinal loops revealed that most patients with TS, including those with no gastrointestinal symptoms at all, have intestinal changes similar to those seen in IBS (Figs. 1, 2, 3). It is important to recall that one of the TS patients we examined had already been diagnosed with Crohn disease and five others were known to have celiac disease. In all six cases, the US examination documented changes that were compatible with these diseases.

The fact that TS patients are at risk for developing CIBD [10–13] and angiodysplasias of the small intestine [4–9] has been well documented. Abdominal sonography with examination of the intestinal loops may prove to be a useful non-invasive method for detecting and monitoring these diseases in patients with TS. In particular US examination of gastrointestinal angiodysplasia shows increased vascularization without abnormalities of stratification and wall thickness in most of cases; instead US findings in CIBD include wall thickness, often marked, abnormal wall stratification, loop dilatation and increased vascularization, variable depending on the clinical type of CIBD. In the presence of changes in the number and/or severity of the intestinal abnormalities documented on the US examination, even in the absence of symptoms, the follow-up might be adjusted, with more frequent visits and/or additional tests, thus increasing the chances of early diagnosis of these diseases.

Acknowledgments The authors thank Dr. Riccardo Albertini (Dip. Medicina Diagnost. e Servizi) and Dr. ssa Mara De Amici (Dip. di Pediatria) of University of Pavia, Fondazione I.R.C.C.S., Policlinico San Matteo, Pavia, for their contribution in the laboratory tests.

Conflict of interest None.

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