

Sigmoid Diverticulitis in Patients with Williams–Beuren Syndrome: Relatively High Prevalence and High Complication Rate in Young Adults with the Syndrome

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In a retrospective survey of 128 adults with Williams–Beuren syndrome (age range 18–62 years) sigmoid diverticulitis was reported in 10 patients (2 f, 8 m). The diagnosis of diverticulitis had been made between the ages of 17.1 and 39.6 years. An additional four patients (age range 23.5–32.2 years) had presented with sigmoid diverticulosis. In eight patients the course of the disease was complicated, some of them having to undergo multiple surgery. Conservative therapy was successful in only one female and one male patient with diverticulitis. Thus, we conclude that there is an increased prevalence of sigmoid diverticulitis in adult patients with Williams–Beuren syndrome (8% vs. 2% in the normal population in the age group below 40 years). © 2005 Wiley-Liss, Inc.

KEY WORDS: Williams syndrome; diverticulosis; diverticulitis; perforation; abdominal pain; artificial anus

INTRODUCTION

Williams–Beuren syndrome (WBS) is a contiguous gene syndrome caused by a hemizygous micro-deletion of approximately 1.6 Mb of DNA in the long arm of chromosome 7. According to current knowledge the deleted region in 7q11.23 contains at least 23 genes [Meng et al., 1998; Scherer et al., 2003]. The prevalence of the syndrome may be as high as 1:7,500 [Stromme et al., 2002].

The main symptoms are craniofacial dysmorphism [Pankau et al., 1997], cardiovascular malformation, predominantly supravalvular aorta stenosis with peripheral pulmonary stenoses [Wessel et al., 1994], relatively short stature [Pankau et al., 1992; Partsch et al., 1999], mental retardation, and a characteristic personality profile [Gosch and Pankau, 1994].

Diverticula of the bladder have been reported in individual cases of WBS [Babbitt et al., 1979; Morris et al., 1990; Schulman et al., 1996]. Diverticulosis of the sigmoid appears to be more common and has been described in 3 out of 13 adults with WBS [Morris et al., 1990] as well as in one additional

patient [Giannotti et al., 2001]. It has been hypothesized that patients with WBS may be at increased risk of diverticulitis. We present here the first overview of frequency, age distribution, and course of sigmoid diverticulitis in adult patients with this syndrome.

CLINICAL REPORTS

The scientific advisory board of the German WBS Association reviewed the clinical findings of all 128 adult patients (53 f, 75 m) aged between 18 and 62.2 years out of their whole group of 427 WBS patients. The remaining 299 patients were under age 18. They were not studied. In the context of a retrospective survey using a questionnaire, sigmoid diverticulitis was reported in 10 patients (2 f, 8 m) who, at the time of diagnosis, were aged between 17.1 and 39.6 years (median age 25 years). Four additional patients had been diagnosed as suffering from sigmoid diverticulosis. The clinical diagnosis of WBS was confirmed in all of our 14 patients by FISH which detected a hemizygous deletion in the WBS critical region in 7q11.23. Six of the 10 patients with diverticulitis experienced perforation with accompanying peritonitis. Four received an artificial anus, which could be reversed in three patients after a few months. The youngest patient underwent surgery five times over the course of 15 months, on three occasions laparoscopically. The cause of the acute abdominal pain was diagnosed as phlegmonous appendicitis, and the 3rd laparoscopy 2 months later revealed no pathological findings. 7 months later, at age 17.5 years, sigmoid diverticulitis was diagnosed when acute abdominal pain again occurred, and conservative therapy was undertaken. Finally a sigmoid resection was performed and 3 months later, a resection of the ileus with another laparotomy. So far conservative therapy was successful in only two patients (no. 8, 10). It should be noted that one of these patients (no. 8) was treated for a prolapsed rectum with subsequent partial mucosectomy at age 33 years.

Four further patients underwent colonoscopy because of recurrent abdominal pain and/or anal bleeding. All were found to have marked diverticulosis. The patients' age distribution, clinical symptoms, therapy, and course are summarized in Table I.

DISCUSSION

Surgery is not uncommon in WBS. In our group of 427 WBS patients (128 adults, 299 children and adolescents), approximately 70% had undergone at least one operation. In most cases surgery was carried out in infancy and early childhood, with the spectrum covering cardiovascular correction, herniotomy with orchidopexy, tonsillectomy with paracentesis and adenotomy, and correction of strabism. To our knowledge, there have been only two reports to date describing four WBS

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TABLE I. Clinical Data, Findings and Treatment of WBS Patients with Sigmoid Diverticulitis and Sigmoid Diverticulosis

Patient sex (f/m)	Age at diagnosis (years)	BMI (kg/m ²)	Findings	Course and treatment
Diverticulitis				
1, m	17.9	19.5	Appendicitis, abscesses, sigmoid diverticulitis, adhaesion ileus	Sigmoid resection, adhaesiolytic, appendectomy; complications: 3 laparoscopies, 2 laparotomies
2, m	17.1	23.4	Appendicitis, perforated sigmoid diverticulitis, peritonitis, relaps of diverticulitis with fistula	Appendectomy, temporary colostomy, sigmoid resection, short bowel resection, anus praeter and reanastomosis
3, m	19.1	20.9	Perforated sigmoid diverticulitis, peritonitis, scar herniation	Sigmoid resection, anus praeter, reanastomosis, abdominal wall reconstruction
4, m	23.3	19.8	Sigmoid diverticulitis, perforation, peritonitis	Sigmoid resection, anus praeter
5, m	24.1	29.3	Sigmoid diverticulitis, perforation, peritonitis, abdominal abscess	Sigmoid resection, anus praeter, reanastomosis
6, m	25.8	33.8	Sigmoid diverticulitis, perforation, peritonitis	Sigmoid resection
7, m	31.2	24.2	Sigmoid diverticulitis	Sigmoid resection, adhaesiolytic
8, m	34.9	26.7	Sigmoid diverticulitis (rectal prolaps 2 yrs earlier)	Conservative treatment
9, f	39.6	31.1	Sigmoid diverticulitis, perforation, peritonitis	Sigmoid resection
10, f	36.1	31.6	Sigmoid diverticulitis, appendicitis	Appendectomy; conservative treatment
Diverticulosis				
11, m	32.2	25.6	Sigmoid diverticulosis	Conservative treatment
12, f	29.3	16.2	Sigmoid diverticulosis, bleeding from internal haemorrhoids	Haemorrhoids treatment, conservative treatment for diverticulosis
13, m	23.5	21.4	Sigmoid diverticulosis	Conservative treatment
14, m	23.5	21.6	Sigmoid diverticulosis	Conservative treatment

patients with diverticulitis with or without complications [Morris et al., 1990; Giannotti et al., 2001].

Colon diverticulitis is a relatively common disease of the 20th century, whereby in 95% of cases the sigmoid is affected [Krenzien and Roding, 1988; Jun and Stollman, 2002]. The prevalence of diverticulosis below age 40 years in the normal population is estimated to be 10%. Only 20% of the patients with diverticulosis develop diverticulitis [Ochsenkühn and Göke, 2002] leading to an estimation of the diverticulitis prevalence in the general population below age 40 of approximately 2%.

Diverticular inflammation is seen in 0.8% of patients undergoing elective colonoscopy without clinical evidence of acute diverticulitis [Ghorai et al., 2003]. Schweitzer et al. [2002] reported on the clinical course of acute diverticulitis in 261 patients, of whom 46 (18%) were younger than 40 years (mean age 35), and of these 72% were overweight. 35% of patients received surgery as the primary treatment. In contrast, only three of our WBS patients with diverticulitis were obese (BMI > 30 kg/m²) and all were under 40 years of age with a median age of 25 years. Conservative therapy was successful in only two WBS patients. Hernandez-Siverio et al. [1992] published the case report of a 10-year-old child with acute perforation of sigmoid diverticulitis, and pointed out that this was the first report of a patient with this illness below the age of 20. In our group, three patients were younger than 20 at the time of diagnosis. These three patients suffered the severest complications (Table I).

The frequency of sigmoid diverticula in WBS is not known. Fourteen out of our patient group of 128 adults had proven diverticulosis (10.9%). Of these 14 patients 10 developed diverticulitis (71%). This number is approximately three times higher than in the normal population. The prevalence of diverticulitis in adults with WBS is 7.8% in our patient group

compared to around 2% in the normal population below age 40 years [Ochsenkühn and Göke, 2002].

In comparison, bladder diverticula are described in the literature for this syndrome [Morris et al., 1990]. In the course of nephrological diagnostics we were also able to diagnose marked bladder diverticula in monozygous twins (patients no. 13 and 14) at age 19.5 years. As we were aware of the large number of cases of sigmoid diverticula and the patients had repeatedly complained of abdominal pains, both underwent a colonoscopy at the age of 23.5 years and diverticulosis was found.

When recurrent or acute abdominal pain occurs in young adults with WBS, the possibility of diverticulitis should always be considered in the differential diagnosis and the appropriate diagnostic work-up should be initiated [Ripolles et al., 2003; Werner et al., 2003]. This applies particularly when acute appendicitis has been ruled out as the cause, since, especially in young patients, diverticulitis is frequently more severe [Afzal and Thomson, 2002], as is clearly demonstrated in our patient group.

In conclusion, sigmoid diverticulitis is approximately three to four times more common in young WBS adults than in the normal population. The prevalence of sigmoid diverticulitis in our group of WBS patients was 7.8%. The age distribution in WBS patients is changed to a younger age compared to the normal population where the prevalence increases with age and sigmoid diverticulitis is not seen below age 20 except some single exceptional cases [Hernandez-Siverio et al., 1992]. The course of the disease is more complicated and surgery is usually necessary.

The cause of the increased prevalence of bladder diverticula and sigmoid diverticulosis can be assumed to lie in the hemizygous deletion of the elastin gene. The elastic properties of the sigmoid and colonic tissue are important to withstand

the pressure of the moving stools and the peristaltic waves. In the case that elastic properties are decreased the wall of the sigmoid colon may be distended beyond the point of return and thus allow a diverticulum to develop. The formation of diverticula in the bladder and gastrointestinal tract is also known for other disorders of connective tissue like Ehlers-Danlos syndrome [Hayakawa et al., 1982; Kahn et al., 1988] and Marfan syndrome [Suster et al., 1984]. Potential gastrointestinal abnormalities have not yet been studied in mice harbouring targeted deletion of the elastin gene.

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