Collagenous gastritis in the pediatric age

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ABSTRACT

Collagenous gastritis (CG) is an uncommon condition known in the pediatric age. It is characterized by the presence of subepithelial collagen bands (> 10 μm) associated with lymphoplasmacytic infiltration of the stomach’s lamina propria. Symptoms manifested by patients with CG may be common with many other disorders. It typically manifests with epigastralgia, vomiting, and iron deficiency during pre-adolescence. This condition’s pathophysiology remains unclear. In contrast to adults, where association with collagenous colitis and other autoimmune conditions is more common, pediatric involvement is usually confined to the stomach. Drugs of choice include proton pump inhibitors and corticoids. A case is reported of a 12-year-old girl with abdominal pain and ferritin deficiency who was diagnosed with CG based on gastric biopsy and experienced a favorable outcome.

Key words: Pediatrics. Collagenous gastritis.

INTRODUCTION

Collagenous gastritis (CG) is an uncommon condition known in the pediatric age. It was first described, in 1989, by Colleti and Trainer in a 15-year-old girl (1). It is characterized by the presence of subepithelial collagen bands in the stomach (> 10 μm) associated with lymphoplasmacytic infiltration in the lamina propria. Symptoms manifested by patients with CG may be common to many other disorders. The condition’s pathophysiology remains unclear. In the late 1980s, a hypothetical deposition of protein exudate and collagen secondary to abnormally increased vascular permeability was suggested. Later, the lymphocytic infiltration seen very early in the course of CG suggested an inflammatory condition of immune origin. Usually only the stomach is involved in contrast to adults, where an association with collagenous colitis and other autoimmune disorders is more commonly seen (2). Its unclear etiopathogenesis results in no clearly established management strategies, and both corticoids and proton pump inhibitors (PPIs) are presently the drugs of choice (3).

ABRIDGED CASE REPORT

A 12-year-old girl presented with vomiting and abdominal pain of one year’s duration, with no time predilection or association with food ingestion, which even woke her up from sleep at night. There was neither weight loss nor changes in bowel habit. Her personal history was uneventful. A CBC demonstrated hemoglobin of 12.6 g/dl, and mean corpuscular volume of 79.6 fl. The rest was normal. Furthermore, she had normal AST, ALT, and GGT values, and her renal function remained unaltered. She had iron deficiency with ferritin of 9 ng/ml (20-200 ng/ml) and no increase in acute phase reagents (C-reactive protein and erythrocyte sedimentation rate). She was screened for celiac disease by measuring total IgA, anti-transglutaminase antibodies (IgA-ATA), deamidated gliadin peptide antibodies (which were negative), and HLA DQ2-DQ8. A study of food sensitization was also ordered, including total IgE and both cow’s milk protein (CMP)-specific and egg-specific IgE, which were all negative. Following these normal results, an upper digestive endoscopy had been performed in a different site, which yielded a diagnosis of gastritis, a rapid urease test on the antral biopsy being negative for Helicobacter pylori infection. No other gastric specimens were obtained for pathology analysis. Treatment was started with high-dose proton pump inhibitors (PPIs) (2 mg/kg/day) that initially resulted in clinical improvement, but the condition recurred when PPIs were withdrawn 2 months later.
She returned to our center because of persistent symptoms and more localized, increased epigastric pain for the last month. A new upper digestive endoscopy was carried out, which only revealed a single nodular image in the gastric antrum. Samples were obtained from the antrum for a rapid urease test, which was negative for *Helicobacter pylori*, and for histological analysis. In the histological description, a gastric mucosa with moderate lymphoplasmacytic infiltration stood out, together with patchy subepithelial collagenous fibrosis, including areas greater than 10 microns in thickness, which also occurred around glands (Fig. 1). No significant intraepithelial lymphocytosis were seen, nor the presence of *Helicobacter pylori*. Esophageal and duodenal samples showed no histological changes.

With the suspicion of CG a colonoscopy was performed to exclude associated collagenous colitis, which provided a normal image and histology. Treatment was reinitiated with oral esomeprazole, 40 mg every 24 hours, combined with oral iron supplementation, and symptoms subside within a few days. At 3 months from treatment onset, PPI doses were halved, and the patient remained asymptomatic at 6 months after diagnosis.

**DISCUSSION**

CG is a rare idiopathic condition scarcely described in the pediatric age. In children, it typically develops before adolescence and predominates in females (F/M: 1.6) (4). The etiopathogenesis remains unclear. It is presumed to consist of an abnormal response to some toxic or infectious stimulus, which results in chronic inflammation associated with abnormal collagen secretion and deposition from fibroblasts (4). In a recent review by Nielsen et al. (4), proximal collagenous gastrointestinal conditions are categorized in two subtypes according to anatomical localization and symptoms: Collagenous gastritis and collagenous sprue. The former subtype, as in our case, mainly affects pediatric patients and young adults, with gastric mucosal involvement in the form of predominant nodular gastritis. The latter subtype affects primarily adult individuals, with the lesion in the proximal small bowel, and presents with watery diarrhea and weight loss from malabsorption, thus entailing a poorer prognosis. Both types may be associated with collagenous colitis, which is more common in the adult form.

Presentation in children differs from the adult form in that no association with autoimmune conditions occurs (4,5). Initial CG symptoms include abdominal, predominantly epigastric, pain, dyspepsia, vomiting, and severe anemia with iron deficiency (5-7). In contrast to adults, systemic symptoms including weight loss and diarrhea are uncommon. Anemia and severe iron deficiency are a common finding in pediatric cases in the literature, as is the case with our patient. The initial symptoms shared with other conditions should prompt the exclusion, among other disorders, of *Helicobacter pylori* gastritis, gastroesophageal reflux-related esophagitis, and eosinophilic gastrointestinal disorders, on the rise in the last few decades. Furthermore, most patients develop severe iron deficiency anemia, hence celiac disease-associated intestinal malabsorption must be ruled out. From all the above upper digestive endoscopy with biopsy taking is mandatory for diagnosis. Nodularity in the gastric antrum and body is the most characteristic endoscopic finding, but is absent in a number of patients (1,3,4). On other occasions an erythematous gastric mucosa is described accompanied by pseudopolyps, erosions, ulcers, and/or bleeding (8). Histopathology provides a definitive diagnosis based on the presence of fine subepithelial collagenous bands (> 10 μm) associated with chronic inflammatory infiltration in the gastric mucosal lamina propria.

The second phenotype described is seen in adults in association with collagenous colitis (9). It typically manifests with predominant watery diarrhea. In addition to collagenous colitis, adult CG is frequently accompanied by other autoimmune conditions, hence both phenotypes are believed to have a different etiopathogenesis. The colonic mucosa usually has a normal appearance (9). An edematous colonic mucosa with pseudopolyps is not uncommon in collagenous colitis. Histopathology reveals areas of subepithelial collagenous fibrosis sharing the characteristics seen in the stomach. Etiology is unknown. An immune or autoimmune origin has been posited as the cause for the development of a fibroinflammatory disorder, together with environmental stimuli such as dietary antigens, reactions to chemicals, and more recently an increase in IgG4 within the gastrointestinal lamina propria (3,4).

The disorder usually has a benign course, and its chronic nature usually requires an individualized approach to management, which is scarcely standardized given the sparse available literature. To date no reports on CG have dealt
with malignant transformation, but the condition’s natural history remains unknown.

As regards treatment in the pediatric age, PPI use is most commonly accepted, followed by corticoid therapy (5-10). Treatment with PPIs at a dose of 1 mg/kg/day results in variable responses. Some authors prolong therapy for one year, and for others duration depends on clinical outcome. Clinical improvement is usually significant within a few months of treatment onset. Oral corticoids have also been used, and are better accepted for CG associated with colitis (3,4). Pediatric cases have been reported where budesonide was used as the treatment of choice for the management of collagenous colitis (8,11). It is for this reason that colonoscopy with biopsy taking is recommended for patients diagnosed with CG, as drug therapy may differ. Endoscopic lesions persist in most cases despite clinical improvement (9,10). Also, oral iron supplementation is advisable for patients with ferropenic anemia, who usually respond favorably (12). In the last few years, tumor necrosis factor inhibitors (infliximab) have been tried for patients with refractory collagenous colitis, but further studies are needed (13).

To conclude, collagenous gastritis is a rare condition in the pediatric age that manifests with nonspecific symptoms, and is diagnosed based on the histopathological exam of biopsy samples from the gastric antrum, as rapid urease testing alone is inadequate. Its chronic, benign nature requires treatment on an individual basis.

REFERENCES