CASE REPORT

Juvenile Polyposis Complicated with Protein Losing Gastropathy

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Abstract

A male patient with chronic bloody stool was diagnosed as juvenile polyposis at the age of 28. He had thirty to forty colonic polyps and some were removed endoscopically, while gastric polyps were too numerous to intervene. As the polyposis advanced gradually, the patient developed intractable anemia and serious hypoproteinemia. Albumin scintigram revealed protein losing gastropathy due to progressive gastric polyposis. Total gastrectomy was carried out at the age of 34 and the patient has achieved remarkable and sustainable improvement.

Key words: juvenile polyposis, protein losing gastropathy

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Introduction

Juvenile polyposis (MIM 174900) is a rare hamartomatous syndrome characterized by dozens or hundreds of juvenile polyps of the gastrointestinal tract. The incidence is estimated to be around 1 in 100,000 to 160,000, and autosomal dominant inheritance with variable penetrance has been observed in about 40% of patients (1). Recently, SMAD4 (2) and BMPRIA (3), both involved in the TGF beta signaling pathway, have been identified as the causative genes of juvenile polyposis. Histologically, abundant lamina propria with inflammatory cell infiltration and edema that cause distortion or cystic dilatation of the epithelial glands is the hallmark of this disease. The most frequently affected site is the colon (98%), followed by the stomach (14%) and small intestine (7%) (4). Although uncommon, juvenile polyposis limited or predominant to the stomach has also been reported, in which hypoproteinemia due to protein losing gastropathy is prevalent (5). Here we present a sporadic case of stomach-predominant juvenile polyposis developing intractable anemia and protein losing gastropathy that were successfully treated by total gastrectomy.

Case Report

A 28-year-old Japanese man complaining of occasional bloody stool for months was referred to our hospital because polyposis syndrome was suspected. His past history included urolithiasis and idiopathic hearing loss while there was no family history of gastrointestinal polyposis or cancer. The patient had neither hair loss nor skin lesions, indicative of Cronkhite-Canada syndrome. Laboratory data showed anemia (hemoglobin 9.2 g/dL), mild hypoproteinemia (total protein 6.1 g/dL, albumin 4.0 g/dL) and positive fecal occult blood test. Colonoscopy revealed thirty to forty sessile and pedunculated polyps throughout the entire colon and rectum (Fig. 1). Upper gastrointestinal endoscopy exhibited hundreds of polyps predominantly in the body and fundus of the stomach (Fig. 2) while the gastric antrum, esophagus and duodenum were preserved. Both serum anti Helicobacter pylori antibody and rapid urease test were negative. Double contrast barium study revealed no polyps in the small intestine. As biopsy specimens from the gastric and colonic polyps were pathologically inconclusive, we carried out endoscopic mucosal resection (EMR). Both gastric and colon polyps consisted of marked inflammation with edema

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throughout the lamina propria mucosa, dilated glands with occasional cystic change, and the epithelium without dysplasia (Fig. 3). We diagnosed this case as juvenile polyposis and performed germline mutation analysis of genes associated with polyposis syndrome. Mutation of SMAD4, SKT11, PTEN and APC were all negative by direct sequencing.

After the diagnosis, the patient had started oral iron supplementation and additional six colon polyps were removed endoscopically at the age of 32. In spite of these treatments, hemoglobin, total protein and albumin levels were gradually lowered to 6.6, 3.9 and 2.1 g/dL respectively, causing fatigue and intractable systemic edema. Follow-up endoscopy revealed the gastric polyps have grown and sprawled to the antrum affecting the entire stomach (Fig. 4). Colon polyps also grew, but less remarkably than the gastric polyps. Technetium-labeled albumin scintigraphy exhibited that protein was lost mainly through the stomach, suggesting protein losing gastropathy due to progressive gastric polyposis (Fig. 5). Polypectomy for seventeen colon polyps and total gastrectomy were carried out in April 2007 at the age of 34, six years from the initial presentation. The consequence was significant, such that the hemoglobin and albumin level recovered to the normal range on the 20th day after the surgery without transfusion. Numerous gastric polyps through
Figure 5. Technetium-labeled albumin scintigraphy (two hours after injection) showed a pool of isotopes along the greater curvature of the stomach (arrowheads), suggesting albumin leak through the stomach.

Figure 6. The total gastrectomy specimen. Nearly the entire stomach was covered with numerous polyps. Arrows denote the large pedunculated polyp of the antrum causing ball valve syndrome.

Figure 7. Microscopically, the gastric polyp consisted of prominent edema and inflammatory cell infiltration (×100, Hematoxylin and Eosin staining, panel A). A part of the large polyp of the antrum showed dysplastic change (×200, Hematoxylin and Eosin staining, panel B).

Discussion

Sachatello et al (6) classified juvenile polyposis into three categories (i) juvenile polyposis of infancy, (ii) juvenile polyposis coli, and (iii) generalized juvenile polyposis. Juvenile polyposis of infancy is the most serious phenotype diagnosed in infancy, characterized by massive polyposis throughout the gastrointestinal tract, congenital abnormality and a poor prognosis. Juvenile polyposis coli is the most common type in which polyps are limited to the colon. If juvenile polyposis are found outside as well as in the large intestine in adolescent or adult patients, it is termed generalized juvenile polyposis. In addition, juvenile polyposis of the stomach was recently proposed as the fourth category of juvenile polyposis (5). In juvenile polyposis of the stomach, polyposis should be limited to the stomach, at least at the initial presentation. Since the first case of juvenile polyposis of the stomach was reported in 1979 (7), twelve cases have been reported and Hizawa et al (5) summarized them. Seven patients had hypoproteinemia and 10 patients required gastrectomy because of refractory protein losing gastropathy or gastric cancer. The results of gastrectomy were satisfactory, but four patients thereafter developed colonic lesions including juvenile polyp, adenoma, and cancer. Although the current case might be categorized as generalized juvenile polyposis, the stomach-predominance and the clinical course resembled juvenile polyposis of the stomach. It is still controversial whether juvenile polyposis of the stomach is a distinct entity and should be distinguished from generalized juvenile polyposis. The present case suggests, however, that so-called ‘juvenile polyposis of the stomach’ might be a subtype of generalized juvenile polyposis.

Germline mutations of SMAD4 and BMPR1A are observed in a subset of juvenile polyposis cases, and the prevalence of each mutation is estimated at 20% (8). To date there is no known genotype-phenotype correlation in juvenile polyposis. Although Friedl et al (9) suggested an association between massive gastric polyposis and SMAD4
germline mutation in comparison with \textit{BMPR1A} mutation or no mutation, there is no subsequent study supporting this hypothesis and the present case does not harbor germline mutation of the gene. Mutation analysis in further generalized juvenile polyposis cases might resolve the conundrum of whether juvenile polyposis of the stomach is an independent category.

When the present patient developed significant anemia and hypoproteinemia during the course, there was a debate about treatment strategy. As there were hundreds of gastric and dozens of colonic polyps, we thought total gastrectomy and polypectomy for the large colonic polyps would be reasonable. An alternative was total gastrectomy and subtotal colectomy because (i) the anemia might be due to colon polyps, (ii) removing all colonic polyps seemed impossible, and (iii) the patient carries an increased risk of colon cancer. However, simultaneous gastrectomy and colectomy was too invasive and a future colectomy is feasible, if necessary. We believe that close follow-up and colon polypectomy will prevent advanced colon cancer and sustain an excellent condition.

\textbf{References}