Cap Polyposis with Protein-Losing Enteropathy

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Case Report

A 56-year-old male with a history of mild mental retardation, non-insulin-dependent diabetes mellitus, and hypertension presented with diarrhea and lower extremity edema of several months’ duration. The patient’s symptoms started with mild, intermittent diarrhea; several months later, his diarrhea became persistent, and he was admitted to a hospital. The patient was given metronidazole (Flagyl, Pfizer); when he did not respond to this treatment, a sigmoidoscopy was performed, revealing large inflammatory polyps with marked congestion and granulation tissue. Due to worsening symptoms, the patient underwent a left hemicolectomy, during which multiple inflammatory polyps were noted. The intervening colonic mucosa showed mild crypt distortion, which was suggestive of inflammatory bowel disease. The patient’s symptoms subsided immediately after surgery; however, 8 months later, his diarrhea recurred and began to increase in frequency. At this time, the patient’s diarrhea was explosive and consisted of a large volume of liquid. A subsequent colonoscopy revealed polyps similar to those seen during the patient’s previous colonoscopy, and the intervening mucosa showed mild crypt distortion with foci of cryptitis, which was suggestive of inactive ulcerative colitis.

One year after his initial presentation, the patient was transferred to our institution with a 30-lb weight loss from baseline, up to 24 bowel movements per day, blood in his stool, and severe lower extremity edema. On laboratory examination, the patient had a hemoglobin level of 10.5 g/dL (normal, 13.5–17.5 g/dL), mean corpuscular volume of 78 fl (normal, 80–100 fl), and iron level of 60 µg/dL (normal, 65–175 µg/dL). The patient also had a protein level of 2.9 g/dL (normal, 6–8 g/dL) and albumin level of 1.5 g/dL (normal, 3.5–5.5 g/dL). Results of 3 Clostridium difficile toxin assays were negative, and enteric organisms did not grow in the patient’s stool cultures.

A colonoscopy performed at our institution showed multiple large inflammatory polyps with overlying mucoid exudates (Figure 1). Histologically, these polyps were similar to those seen at the previous hospital, and the intervening mucosa did not show evidence of inflammatory bowel disease. Gastric biopsies did not reveal any evidence of polyps, gastritis, or neoplasia. The patient underwent a right colectomy, which showed slightly edematous, nonulcerated, nonerythematous mucosa with preserved folds and approximately 65 colonic polyps ranging in size from 0.2 cm to 2.7 cm (Figure 2). The majority of these polyps had a combination of white or yellow fibrinous exudates and hemorrhagic patches on their surfaces.

Figure 1. A large polyp in the left colon.
Figure 2. A right colectomy specimen with 65 polyps.

Figure 3. Polyps with overlying cap exudates.

(Figure 3). Histologically, the bases of the polyps had elongated, corkscrew-like glands, and the luminal surfaces had “caps” comprised of granulation tissue and exudates, with a moderate amount of chronic inflammation (Figures 4 and 5). A CD31 stain highlighted the vascularity of the overlying cap (Figure 6). Results of a D2-40 stain were negative, ruling out the presence of lymphatic channels in the overlying cap (Figure 7). A smooth muscle actin stain demonstrated obliteration of the lamina propria by smooth muscle fibers (Figure 8).

Discussion

Cap polyposis is a rare intestinal condition that was first described by Williams and associates in 1985 in a case series of 15 patients. These patients had distinctive inflammatory polyps without a significant family history or strong associations with other major colorectal diseases. From 1985 to 2004, 17 additional cases of cap polyposis were reported in the English language medical literature. Because of the rarity of this condition, these polyps are sometimes misdiagnosed as pseudopolyps in ulcerative colitis. In 2004, the second largest case series to date was published by Ng and colleagues, which included 11 cases of cap polyposis reported from 1993 to 2002. Our case study is the ninth reported case in the English language medical literature since 2003 (Table 1).

A review of the literature shows that cap polyposis tends to affect individuals of any age, at a median age of 52 years (range, 12–76 years). This finding is consistent with the average age of patients with cap polyposis reported over the past 7 years (52.8 years; range, 33–76 years). A case series conducted by Ng and coworkers showed that males are primarily affected by this condition; however, previous studies have found that females are affected more often than males (11%).

Common symptoms of cap polyposis are mucous diarrhea, tenesmus, and rectal bleeding. Mucous diarrhea in these patients can be severe, resulting in excessive protein loss. A direct loss of protein from cap polyposis was confirmed in a 54-year-old woman via scintigraphy of technetium 99m-labeled diethylenetriaminepentaacetic acid complexed to human serum albumin. There have also been reports of lower limb edema as a result of protein-losing enteropathy from cap polyposis. Likewise, approximately half of patients experience habitual straining during defecation and have chronic constipation.

Endoscopically, cap polyps are small, red, sessile or semipedunculated, and range in size from several millimeters to 2 cm. The number of polyps varies from
Figure 4. A hematoxylin and eosin stain of a polyp with a cap comprised of granulation tissue and exudates (2× magnification).

Figure 5. A hematoxylin and eosin stain of a polyp cap comprised of granulation tissue and exudates with chronic inflammation (10× magnification).

Figure 6. A CD31 stain highlighting the vascularity of the granulation tissue cap (10× magnification).

Figure 7. A D2-40 stain highlighting the absence of lymphatic channels in the polyp cap (10× magnification).

Figure 8. A smooth muscle actin stain showing muscle fibers in the lamina propria at the base of the polyps (4× magnification).
### Table 1. Cases of Cap Polyposis Published in the Literature Since 2003

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age (years)/gender</th>
<th>Presenting symptoms</th>
<th>Laboratory results</th>
<th>Colonoscopy findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ohkawara T, et al</td>
<td>67/female</td>
<td>Chronic constipation for &gt;20 years and mucous and bloody diarrhea &gt;10 times per day for 8 months</td>
<td>Hemoglobin level: 11.2 g/dL; protein level: 6.0 g/dL; albumin level: 3.2 g/dL</td>
<td>&gt;20 reddish, sessile polyps found from the distal rectum to the sigmoid colon</td>
<td>Improved without treatment</td>
</tr>
<tr>
<td>Bookman ID, et al</td>
<td>36/female</td>
<td>Abdominal pain, bloody and mucous diarrhea, urgency, tenesmus, and 20-lb weight loss</td>
<td>Normal hemoglobin level; negative test results for <em>Clostridium difficile</em> toxin assays and stool cultures</td>
<td>20 sessile polyps with caps of exudates found at the rectosigmoid junction, extending to 35 cm of the anal verge</td>
<td>Infliximab</td>
</tr>
<tr>
<td>Akamatsu T, et al</td>
<td>33/female</td>
<td>Mucous and bloody stools for 2 years and pretibial edema; diagnosed with mucosal prolapse syndrome</td>
<td>Protein level: 4.8 g/dL; albumin level: 2.8 g/dL; negative test results for stool cultures; positive test results for <em>Helicobacter pylori</em> infection</td>
<td>Multiple sessile polyps found in the rectum with mucosal adhesions</td>
<td>Rabeprazole, amoxicillin, and clarithromycin</td>
</tr>
<tr>
<td>Akamatsu T, et al</td>
<td>50/female</td>
<td>Mucous and bloody stools, tenesmus, and 8-kg weight loss; diagnosed with ulcerative colitis</td>
<td>Protein level: 5.2 g/dL; albumin level: 3.3 g/dL; negative test results for stool cultures; positive test results for <em>H. pylori</em> infection</td>
<td>Multiple sessile polyps found in the rectum and sigmoid colon; recurrence found at the anal side</td>
<td>Resection of colon; following recurrence 6 months later, treatment with lansoprazole, amoxicillin, and clarithromycin</td>
</tr>
<tr>
<td>Akamatsu T, et al</td>
<td>53/female</td>
<td>Mucous and bloody stools, watery diarrhea, and pretibial edema for 17 years; diagnosed with ulcerative colitis</td>
<td>Protein level: 5.2 g/dL; albumin level: 3.4 g/dL; negative test results for stool cultures; positive test results for <em>H. pylori</em> infection</td>
<td>Variform protruding lesions found in the rectum and sigmoid colon</td>
<td>Lansoprazole, amoxicillin, and clarithromycin</td>
</tr>
<tr>
<td>Chinen T, et al</td>
<td>52/female</td>
<td>3 weeks of bloody and mucous diarrhea</td>
<td>Low protein levels 2 years later; negative test results for stool cultures</td>
<td>Initially, 3 pedunculated polyps were found; 2 years later, multiple edematous lesions were found from the proximal rectum to the sigmoid colon</td>
<td>Polypectomy</td>
</tr>
<tr>
<td>Konishi T, et al</td>
<td>76/female</td>
<td>Mucous and bloody stools</td>
<td>Anemia and hypoproteinemia</td>
<td>30 polyps were found throughout the entire colon; 5 villous adenomas were found in the sigmoid colon</td>
<td>Laparoscopic sigmoid colectomy for adenomas only; improved without additional treatment</td>
</tr>
</tbody>
</table>

1 to more than 100, and polyps are usually located at the apices of the mucosal folds, with normal intervening mucosa. The rectum and rectosigmoid colon are the most commonly affected sites, whereas the entire colon and stomach are rarely affected. Cap polyps are often covered with a thick layer of fibrinopurulent exudates. Performing a complete colonoscopy is important because cap polyposis has been reported to extend as far as the cecum. Polypectomy should be attempted for all polyps; however, it may not be possible to attain this goal if there are numerous polyps. In this scenario, adequate biopsies should be taken for histologic examination.
Histologically, these polyps consist of elongated, distended, tortuous, and hyperplastic crypts that become attenuated toward the mucosal surface. The surfaces of these sessile polyps are ulcerated and covered by a thick layer of fibrinopurulent exudates, hence the term “cap polyps.” The lamina propria of the polyps also contains a large number of inflammatory cells.2

Morphologically, polyps associated with cap polyposis are distinct. Patients with cap polyposis are often misdiagnosed with ulcerative colitis or another inflammatory bowel disease (in 44.4% of cases over the past 8 years). Although inflammatory pseudopolyps in inflammatory bowel disease can have granulation tissue, the intervening mucosa has changes classically associated with inflammatory bowel disease. In contrast, the intervening mucosa is normal in cap polyposis. Due to the large numbers of polyps in these patients, a diagnosis of familial adenomatous polyposis is often considered; however, histologically, the polyps in cap polyposis are not adenomatous. Finally, due to the variable presence of protein-losing enteropathy, Cronkhite-Canada syndrome can also be considered; however, the polyps in cap polyposis are not hamartomatous.

The exact etiology of inflammatory polyps in cap polyposis is still unknown.2 Buisine and associates found that the mucus in cap polyposis differs from that of the normal colon in terms of ultrastructural characteristics and composition.11 However, the exact cause of protein loss has not been reported. In an attempt to investigate the presence of lymphatic channels in these polyps—which could lead to protein loss—a D2-40 stain was performed in this case, yielding negative results. Immunohistochemical stains proved the presence of vessels in the cap.

The exact cause of polyps with fibrinopurulent caps is also unknown; however, many researchers attribute these polyps to abnormal colonic motility and repeated trauma to the colonic mucosa caused by straining during defecation. Similar histologic features are present in conditions such as prolapsing mucosa, solitary rectal ulcer syndrome, inflammatory cloacogenic polyps, and gastric antral vascular ectasia. Along with cap polyposis, these conditions comprise “mucosal prolapse syndrome” and are all caused by chronic straining at stool.2 In our case report, Figure 8 demonstrates the obliteration of the lamina propria by smooth muscle fibers.

The clinical course of cap polyposis has not yet been elucidated. This condition may, at times, have a self-limiting course, whether or not polypectomy is performed. However, complete polypectomy should be performed whenever possible, as it may be curative in some patients.2,6 Patients are advised to avoid straining during defecation if they have a history of difficult defecation or chronic constipation. Various medical treatments have been advocated, including metronidazole, immunosuppressive agents, and Helicobacter pylori eradication therapy.2 Numerous studies throughout the years have shown complete resolution of cap polyposis following therapy for H. pylori infection. Over the past 8 years, 4 of 9 (44.4%) cases were effectively treated with antibiotics commonly used for H. pylori infection.5,6 The role of met-
ronidazole in treating cap polyposis may be related to its anti-inflammatory effect rather than its antibiotic action; by acting as a radical scavenger, it can inhibit leukocyte emigration and adherence. Finally, 1 study found that a course of metronidazole resulted in a marked decrease in the amount of inflammatory infiltrate in cap polyps and the subsequent resolution of this condition.2

If the disease persists or recurs despite medical management, surgical resection of the affected colon and rectum is generally indicated. The optimal time for surgery is unknown. However, every patient should be given a trial of medical management before proceeding to surgery. A repeat colonoscopy should be performed prior to surgery to confirm the presence and extent of disease. Cap polyposis has been reported to progress proximally; thus, colonoscopy helps to plan the extent of the required resection. Intraoperatively, examination of the resected specimen is necessary to ensure that the entire diseased colon is resected with adequate margins. Recurrence after surgery is not uncommon and can be the result of inadequate surgery or abnormal colonic motility affecting the entire colon. When recurrence occurs after surgery, repeat surgery is recommended.2

Summary

This case study is the ninth case reported since the last large series in 2003. Before establishing the diagnosis of cap polyposis, 4 of the 9 patients were initially diagnosed with ulcerative colitis and 1 patient was diagnosed with mucosal prolapse syndrome. Upon treatment, 4 of the 9 patients were treated for H. pylori infection, which resulted in the eradication of their gastritis and polyps. Resolution of cap polyposis was experienced after infiximab (Remicade, Centocor) in 1 patient, polypectomy in another patient, and total colectomy in a third patient; a fourth patient experienced complete resolution without any treatment. Many researchers attribute cap polyposis to mucosal prolapse syndrome; however, the exact mechanism of the underlying cause and the appropriate treatment strategy have not yet been elucidated.

References


Review

A Multidisciplinary Approach to the Diagnosis and Management of Multiple Colorectal Polyps

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Encountering numerous colorectal polyps during a colonoscopy should prompt consideration of several potential diagnoses, which may have very different treatment strategies. The case report by Gallegos and associates, which describes a patient with cap polyposis, offers an opportunity to review the multiple steps required in the diagnostic evaluation of patients with multiple colorectal polyps.1

Endoscopic Examination

An endoscopic examination is often the first opportunity for gathering data. Although finding multiple polyps during an endoscopy may be startling, the endoscopist should make every effort to document the following polyp
characteristics in as much detail as possible, as this information will guide medical and/or surgical management.

**Neoplastic Polyps (Sessile Serrated Polyps, Adenomas, and Carcinomas)**
Adenomas are potentially premalignant lesions and are at risk for progression to adenocarcinomas. Adenomas may be classified as tubular, villous, tubulovillous, or serrated. Adenomas that are villous, have high-grade dysplasia, and/or measure at least 10 mm in size are considered to be advanced adenomas. The presence of multiple (>20) colorectal adenomas should raise suspicion of a genetic polyposis syndrome.

**Hyperplastic Polyps**
As hyperplastic polyps are generally considered to be non-neoplastic, small polyps do not require additional evaluation. However, hyperplastic polyps that are large in size (≥10 mm) or number (>30) may be associated with an increased risk of colorectal cancer. It is recommended that large, right-sided hyperplastic polyps be managed in the same way as adenomas.

**Hamartomatous Polyps**
Juvenile polyps and Peutz-Jeghers polyps are the predominant types of hamartomatous lesions and have unique histologic features. If 5 or more hamartomas are detected in a child or adult, the presence of a genetic syndrome should be considered. Hamartomatous polyps can also be a feature of Cronkhite-Canada syndrome, which often presents with systemic symptoms (including protein-losing enteropathy) and does not have a genetic etiology.

**Inflammatory Polyps**
Inflammatory polyps occur most commonly in inflammatory bowel disease and are often referred to as pseudopolyps. They can also develop in the setting of chronic colonic inflammation, as occurs in infectious or ischemic colitis, chronic mucosal prolapse, Cronkhite-Canada syndrome, and cap polyposis.

**Other Mucosal and Submucosal Lesions**
Several “benign” entities can produce polyp-like lesions; however, other neoplasms can also present with the appearance of polyposis (such as lymphoma). If the endoscopist still has questions regarding the histologic diagnosis of a polyp, it may be helpful to obtain a second opinion from an institution with expertise in gastrointestinal pathology.

**Clinical Management**

**Additional Endoscopic Evaluation**
Often, the initial colonoscopy does not provide sufficient data or tissue to establish a definitive diagnosis. A repeat
colonscopy may be necessary to document the extent of colonic involvement and/or to biopsy or resect additional polyps. Patients with multiple colorectal adenomas or hamartomas should undergo an upper endoscopy to rule out polyps in the upper gastrointestinal tract. Individuals with Peutz-Jeghers–type polyps may also benefit from endoscopic or radiologic imaging to exclude small-bowel polyps. If a polyposis syndrome is diagnosed, the endoscopist should consider whether the polyp burden can be best managed through repeat endoscopies or surgical resection of the colon. If a patient has adenomas that can be cleared endoscopically, the patient should be followed closely with frequent endoscopic surveillance.7

**Medical Treatment**

If polyps are inflammatory, disease-focused medical treatment should be initiated. The first step should be to rule out infectious etiologies. If a systemic inflammatory process—such as inflammatory bowel disease, Cronkhite-Canada syndrome, or cap polyposis—is suspected, corticosteroids may be considered. If polyps are dysplastic or at risk for neoplastic transformation—or if inflammatory symptoms are refractory to medical management (as in many cases of cap polyposis)—surgical options should be considered.

**Genetic Evaluation**

Genetic evaluation is recommended for individuals who have more than 20 cumulative colorectal adenomas, more than 5 gastrointestinal hamartomas, or a family history of cancer or polyps suggestive of a genetic syndrome.6 Diagnosis of genetic polyposis syndromes is important for appropriate treatment and surveillance of both the patient and the patient’s family members. Genetic testing is available for a number of different hereditary syndromes associated with colorectal polyposis. As diagnosis and management of patients with hereditary cancer syndromes can be complicated, it is often helpful to refer these individuals to specialized centers that have expertise in genetic evaluation and counseling.

**Surgical Management**

Surgery should be considered in the setting of genetic polyposis syndromes when polyps are not amenable to endoscopic management. If symptoms of diarrhea or protein-losing enteropathy are refractory to medical management—as in the case of cap polyposis reported by Gallegos and coworkers—surgical treatment should be considered.1 The diagnosis of adenocarcinoma or advanced dysplasia, particularly in the setting of other neoplastic polyps or inflammatory bowel disease, is a strong indication for surgical resection.

### Genetic Polyposis Syndromes

#### Adenomatous Polyposis Syndromes

**Familial Adenomatous Polyposis**

Familial adenomatous polyposis (FAP) is implicated in 1% of colorectal cancer cases.7 Patients with classic FAP have hundreds to thousands of adenomas carpeting the colon. Patients with attenuated FAP have fewer than 100 polyps, and these polyps tend to develop later in life. Classic FAP is associated with a nearly-100% lifetime risk for developing colorectal cancer if the colon is not removed. There is an associated increased risk of thyroid, stomach, and small intestinal tumors, as well as bone and soft tissue tumors (Gardner syndrome) and brain tumors (Turcot syndrome). Approximately 90% of patients with classic FAP carry mutations in the APC tumor suppressor gene. Colorectal screening starts at 10–12 years of age for carriers of APC gene mutations and other at-risk individuals. Colectomy is recommended once polyps become too numerous to remove endoscopically. Most individuals with classic polyposis require total proctocolectomy. Individuals who have attenuated polyposis with rectal sparing may consider subtotal colectomy with continued surveillance of the rectal remnant every 6–12 months. Upper endoscopy, including examination of the ampulla, is recommended every 1–3 years for surveillance of duodenal and ampullary adenomas; in addition, annual surveillance of the thyroid is recommended.

**MUTYH-Associated Polyposis**

The clinical phenotype of MUTYH-associated polyposis (MAP) may be similar to attenuated or classic FAP. MAP is caused by biallelic mutations in the MUTYH gene and demonstrates autosomal recessive inheritance. Screening recommendations are generally similar to those associated with FAP.8

#### Hamartomatous Polyposis Syndromes

**Juvenile Polyposis Syndrome**

Juvenile polyposis syndrome (JPS) can be associated with autosomal dominant mutations in 1 of several genes (SMAD4, BMPRIA, and ENG), which encode proteins involved in the transforming growth factor–β signaling pathway.9 Patients often present in childhood with gastrointestinal bleeding or obstruction and have an increased risk of gastrointestinal malignancy.

**Peutz-Jeghers Syndrome**

Patients with Peutz-Jeghers syndrome (PJS) typically have multiple Peutz-Jeghers hamartomas, characteristic mucocutaneous pigmentation, and an increased risk for various gastrointestinal and other malignancies (including breast, lung, pancreatic, and sex cord tumors). PJS is caused by an autosomal
dominant mutation in the *STK11* tumor suppressor gene. Surveillance recommendations include upper and lower endoscopy, evaluation of the small intestine with radiographic tests and/or capsule endoscopy, and breast and gynecologic cancer screening.\(^{10}\)

**Cowden Syndrome** Cowden syndrome is caused by an autosomal dominant mutation in the *PTEN* tumor suppressor gene. Although gastrointestinal hamartomas are described in some of these patients, the risks for early-onset breast, thyroid, and endometrial cancer are higher than the risk for colorectal cancer. Surveillance includes screening for colorectal, breast, thyroid, and endometrial cancer.

**Conclusion**

The cap polyposis case reported by Gallegos and colleagues illustrates the importance of having a systematic plan for evaluating patients with multiple colorectal polyps.\(^1\) In this case report, the endoscopic examination provided sufficient tissue to determine that the polyps were inflammatory, and the normal biopsies of the intervening colorectal mucosa excluded other inflammatory conditions, such as inflammatory bowel disease and Cronkhite-Canada syndrome. Although the diagnosis of cap polyposis is rare, most endoscopists encounter patients with multiple colorectal polyps. A systematic and multidisciplinary approach to evaluation of such patients is necessary, as the differential diagnosis for colorectal polyposis encompasses genetic syndromes and underlying inflammatory conditions that often require coordinated endoscopic, medical, and surgical management.

**References**