Crohn's-like clinical and pathological manifestations of giant inflammatory polyposis in IBD: A potential diagnostic pitfall☆

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Abstract

Background & aims: Giant inflammatory polyposis (GIP), characterized by mass-like agglomerations of inflammatory polyps, is a rare complication of inflammatory bowel disease (IBD). We reviewed a series of cases of GIP to determine its diagnostic impact on the clinical and pathologic distinction between ulcerative colitis (UC) and colonic Crohn's disease (CD).

Methods: All colons with GIP resected over a 13-year period were identified prospectively and the corresponding clinical and pathologic records were reviewed.

Results: Twelve cases of GIP were identified, accounting for 0.8% of colectomies for IBD during the same time interval. Preoperatively, 6 (50%) patients were diagnosed with UC, 2 (17%) with CD and 4 (33%) with indeterminate colitis (IC). Postoperatively, 6 of the diagnoses (50%) were revised based on strict histopathologic criteria: all 4 diagnoses of IC to UC, one diagnosis of CD to UC, and one diagnosis of UC to CD, for a total of 10 diagnoses of UC (83%) and two of CD (17%). Significantly, 7 of 10 cases with postoperative diagnoses of UC (70%) had Crohn's-like transmural inflammation exclusively within the polyposis segments attributed to fecal entrapment and stasis and accounting for the Crohn's-like clinical complications in these cases.

Conclusions: This case series of GIP, the largest reported from a single center, highlights the high rate of Crohn's-like clinical and pathological manifestations of GIP and their potential to...
1. Introduction

The development of post-inflammatory polyps, or pseudopolyps, in patients with inflammatory bowel disease (IBD) is a common phenomenon occurring in 10% to 20% of cases. In rare instances post-inflammatory polyps can form mass-like agglomerations of worm-like projections each measuring over 15 mm, an entity known as giant inflammatory polyposis (GIP) or giant filiform polyposis. Cases of GIP have been reported in patients with both ulcerative colitis (UC) and Crohn’s disease (CD), although the exact incidence in each is not known. Patients with GIP may present with a variety of non-specific clinical symptoms including anemia, abdominal pain, rectal bleeding or frank obstruction. Endoscopic or radiographic findings of a localized mass may suggest inflammatory obstruction due to CD or elicit unfounded concern for malignancy. The size, segmental distribution and diverse clinical manifestations of GIP may therefore present challenges to clinicians in arriving at an accurate diagnosis and tailoring appropriate disease-specific management of patients with UC and CD. The diagnostic impact of GIP on the clinical and pathological classification of patients with IBD is not known. Accordingly, we carried out a review of our institutional experience with GIP based on cases identified prospectively over a 13-year period.

2. Materials and methods

All colectomy specimens diagnosed pathologically as GIP or filiform polyposis at The Mount Sinai Medical Center between 1994 and 2006 were identified prospectively by a gastrointestinal pathology subspecialist (N.H.) based on the presence of mass-like agglomerations of long, finger- or leaf-like mucosal fronds of at least 15 mm length distributed within single or multiple colonic segments. A comprehensive review of the patients’ clinical and pathology records and pathology slides was performed. Abstracted clinical data included patient demographics, disease history and duration, clinical presentation and symptoms, endoscopic and radiological findings, as well as preoperative clinical diagnoses.

The pathologic gross descriptions, macroscopic photographic images and histologic slides were reviewed jointly by two pathologists. The histological features of the polyposis segments and non-polyposis segments (areas of colitic mucosa lacking pseudopolyposis) were evaluated separately. Strict attention was paid to the classical diagnostic criteria of UC and CD in the non-polyposis segments and to any pathologically discordant features confined to the polyposis segments such as fistulae, superficial or deep fissuring ulcers, lymphoid aggregates, granulomas, transmural inflammation, neural hypertrophy or “skip” lesions.

3. Ethical considerations

This study was approved by the Institutional Review Board of The Mount Sinai Medical Center.

4. Results

4.1. Demographics and clinical features

The 12 colectomies with GIP accounted for 0.8% of colectomies for IBD performed at this institution during the same interval. The patients’ clinical features are summarized in Table 1. They ranged from 16 to 67 years of age (median, 39 years), were predominantly male (10 male, 2 female), and were of mixed ethnicity (one African-American, five Caucasian/non-Jewish, six Caucasian/Jewish). Disease duration ranged from 1 to 12 years (median, 3 years). The most common clinical presentations were bloody diarrhea (8 of 10 patients; 80%), abdominal pain (8 of 10 patients; 80%) and self-reported weight loss (6 of 10 patients; 60%). Clinical data were incomplete for two patients. Colonoscopic data were available for 9 patients but was insufficiently detailed for inclusion in this study.

The common disease complications included penetrating disease (entero-enteric fistulae in 3 of 9 patients; 33%), suppurative complications (intra-abdominal abscess in 4 of 9 patients; 44%), colonic obstruction (2 of 9 patients; 22%), frank colonic perforation (3 of 9 patients; 33%), and dysplasia (1 of 9 patients; 11%). Disease complications were unavailable for three patients.

The indications for surgery in this group of patients were varied, including 5 cases (63%) of urgent surgical intervention for complications of IBD (obstruction, perforation, or abscess) attributed to the presence of GIP. Of the remaining 7 patients, 6 were operated on for medically refractory disease, not clearly associated with GIP, and one for a diagnosis of dysplasia.

Based on all available data accrued prior to surgery the preoperative clinical diagnoses, summarized in Table 2, were UC in 6 patients (50%), CD in 2 patients, and indeterminate colitis (IC) in 4 patients. The patients classified as IC had clinical and endoscopic features of colitis but also rectal sparing in 2 cases and apparent penetrating disease in the other 2 patients. The two patients initially diagnosed with CD had penetrating complications and both suffered colonic perforation requiring emergent operative management.

4.2. Pathological features

Gross anatomical descriptions and/or photographs were available for 11 colectomy specimens. (Table 2) The gross distribution of colitis was universal in 8 cases (73%) and segmental in 3 (27%). GIP was limited to 1 or 2 separate colonic segments in 6 cases (55%) and involved multiple
segments contiguously in 5 (45%). Microscopically, 10 colons exhibited diffuse mucosal-based colitis that extended to the rectum and fulfilled the classical histopathologic criteria for UC (Figs. 3 & 4).4,5

The inflammatory polyps had varied configurations ranging from finger- or leaf-like to fused bridging formations. Microscopically, they were lined along most of their lengths by reactive, sometimes goblet-cell-rich, mucosa that frequently gave way to granulation tissue and acute inflammatory exudates at the apical surfaces.

The spaces intervening between agglomerated GIPs were occupied by abscess-like cystic cavities filled with acute inflammatory exudates, fecal matter, "dirty" mucin or combinations thereof. The mucosa at the base of the spaces was commonly ulcerated or fissured, some fissures extending deeply into the muscularis mucosa and accompanied by Crohn’s-like lymphoid aggregates, hypertrophic nerves and chronic serositis. Based on the context of these Crohn’s-like features and their complete absence from regions of colon with absent or less crowded inflammatory polyps, they were not given diagnostic weight in arriving at the final pathological diagnoses.

GIP-associated Crohn’s-like features occurred in 7 of the 10 colons diagnosed as UC (70%). The specific features included deep fissures (4), intramural lymphoid aggregates (2), pericolonic chronic serositis (2) and neural hypertrophy (1). Only 5 of these cases had concordant preoperative diagnoses of UC whereas 4 had preoperative diagnoses of IC and 1 of CD. Conversely, 1 case with a preoperative diagnosis of UC was revised to CD based on the presence of characteristic non-necrotizing granulomas.

In all, 6 of 12 diagnoses (50%) were revised based on the pathologic findings, the final diagnoses being UC in 10 patients (83%) and CD in 2 (17%) patients. Of the 8 patients with a final diagnosis of UC and adequate postoperative follow-up (mean 6 years, range 1–9 years) none had their diagnosis revised to CD (Table 2).

### 5. Discussion

The relapsing and remitting nature of intestinal inflammation that characterizes the course of IBD predisposes patients to numerous clinical consequences one being the
development of post-inflammatory polyps, or pseudopolyps which represent islands of regenerative mucosa in a sea of inflammation, ulceration and scarring. These remnant mucosal projections are elongated by traction from the fecal stream and subsequently form polypoid lesions. While pseudopolyps are common in IBD occurring in 10% to 20% of cases, the phenomenon of giant inflammatory polyposis (GIP), defined as lesions greater than 15 mm in height or diameter, is quite rare. In the most recent review by Maggs et al. only 81 cases were identified in the literature with a nearly even distribution between UC and CD.

The most common clinical presentations of GIP are hematochezia, abdominal pain, weight loss and frank obstruction. Other, less typical presentations including intussusception and protein losing enteropathy have also been reported. These symptoms are non-specific and frequently occur in patients with IBD. Therefore, the diagnosis of GIP is made via colonoscopy or imaging. The characteristic endoscopic finding is of a mass lesion with finger-like projections and mucosal bridges across the colonic surface. Superficial mucosal biopsies of the lesions are typically normal reflecting re-epithelialization of the surface. Cross-sectional imaging in GIP often reveals an intraluminal mass and asymmetric bowel wall thickening (Figs. 1 & 2). While these findings in a patient with IBD naturally raise concern for malignancy, pseudopolyps are almost exclusively benign with only one case of a

### Table 2 Histopathologic data and final diagnoses for 12 cases of IBD complicated by GIP.

<table>
<thead>
<tr>
<th>Case</th>
<th>age/sex</th>
<th>Extent of colitis</th>
<th>Extent of GIP</th>
<th>Crohn’s-like features</th>
<th>Clinical diagnosis</th>
<th>Pathologic diagnosis</th>
<th>Diagnosis changed</th>
<th>Follow-up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>22/M</td>
<td>Universal</td>
<td>Diffuse</td>
<td>Deep fissures, lymphoid aggregates, transmural inflammation, neural hypertrophy</td>
<td>UC</td>
<td>UC</td>
<td>No</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>28/M</td>
<td>Universal</td>
<td>Diffuse</td>
<td>Deep fissures, fistula</td>
<td>UC</td>
<td>UC</td>
<td>No</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>43/F</td>
<td>Universal</td>
<td>Diffuse</td>
<td>Deep fissures, fistula</td>
<td>UC</td>
<td>IC</td>
<td>Yes</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>58/M</td>
<td>Universal</td>
<td>Descending col</td>
<td>Lymphoid aggregates, granulomas, transmural inflammation</td>
<td>UC</td>
<td>CD</td>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>5</td>
<td>67/F</td>
<td>Universal</td>
<td>Diffuse</td>
<td>Lymphoid aggregates, transmural inflammation, strictures, fistula</td>
<td>IC</td>
<td>UC</td>
<td>Yes</td>
<td>n/a</td>
</tr>
<tr>
<td>6</td>
<td>21/M</td>
<td>Universal</td>
<td>Transverse col</td>
<td>Deep fissures</td>
<td>IC</td>
<td>UC</td>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>39/M</td>
<td>Segmental</td>
<td>Diffuse</td>
<td>Strictures</td>
<td>IC</td>
<td>UC</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>8</td>
<td>16/M</td>
<td>Segmental</td>
<td>Transverse col</td>
<td>None</td>
<td>UC</td>
<td>UC</td>
<td>No</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>62/M</td>
<td>Universal</td>
<td>Transverse col</td>
<td>None</td>
<td>UC</td>
<td>UC</td>
<td>No</td>
<td>n/a</td>
</tr>
<tr>
<td>10</td>
<td>32/M</td>
<td>Segmental</td>
<td>Segmental</td>
<td>Deep fissures</td>
<td>UC</td>
<td>CD</td>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>41/M</td>
<td>Universal</td>
<td>Sigmoid col</td>
<td>Deep fissures, strictures</td>
<td>CD</td>
<td>UC</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>34/M</td>
<td>n/a</td>
<td>Transverse col</td>
<td>None</td>
<td>CD</td>
<td>UC</td>
<td>No</td>
<td>3</td>
</tr>
</tbody>
</table>

n/a = not available.

Figure 1 Barium study of patient with giant inflammatory polyposis (GIP). The mass-like nature of GIP mimics an obstructive tumor.
The presence of GIP may pose diagnostic challenges to both clinicians and pathologists. In this case series, the largest single-center experience to our knowledge as of the time of this writing, we describe the potential diagnostic pitfalls associated with GIP in IBD.

The demographic distribution of our 12 patients (83% male; median age 39) was similar to that of the most recent comprehensive literature review compiling 81 reported cases of GIP (68% male, median age 37). A larger proportion of our cases had multiple giant inflammatory polyps in multiple colonic segments (73%), which may account for the high rate of urgent surgical intervention (55%) in our series (Fig. 3).

An unexpected finding was the degree of discordance between the clinical and final pathologic diagnoses in our patient cohort. The preoperative clinical diagnoses were UC in 6 patients (50%), CD in 2 patients, and indeterminate colitis (IC) in 4 patients. Based on pathologic findings, 6 of 12 diagnoses (50%) were revised. Five patients initially diagnosed with CD (1) or IC (4) had their diagnoses revised to UC. This finding is consistent with prior studies noting that the majority of patients initially diagnosed with IC ultimately have a diagnosis of UC. One patient initially diagnosed with UC had his diagnosis revised to CD. Thus a final diagnosis of UC was made in 10 of 12 patients (83%) and CD in two of 12 patients (17%). The predominance of GIP in UC seen in this series is contrary to the findings of the literature review by Maggs et al. who reported that just over half of cases occurred in UC (54%).

The disparity between the clinical and pathologic diagnoses in this series highlights that the presence of GIP may lead to Crohn’s-like features in UC patients. The...
macrophscopic Crohn's-like features in our 12 patients included penetrating disease (2), skip lesions and segmental colitis (3), and rectal sparing (2). Similarly, histopathologic findings often demonstrated Crohn's-like features including deep fissures involving muscularis propria (4), transmural chronic inflammation (2), pericolonic lymphoid aggregates (2), and neural hypertrophy (1). (Fig. 4) It is important to note that these features were confined exclusively to the polyposis segments, whereas the remainder of colon showed typical features of UC. Typical Crohn's-like features within agglomerations of inflammatory polyps likely result from fecal entrapment and prolonged stasis leading to segmental transmural inflammation attributed to the presence of the polyposis itself rather than an underlying diagnosis of CD.

The propensity of GIP to cause inflammatory and penetrating features that mimic CD highlighted here has been noted in prior studies.7 Thus, our findings confirm the concept of the formation of segmental Crohn's-like features attributed exclusively to the presence of GIP in patients with otherwise histologically confirmed UC. We put forward that a diagnosis of UC should therefore not be amended to CD based on the findings of the polyposis segment alone. For the clinician establishing a precise diagnosis has therapeutic implications since surgical outcomes may differ in patients with CD, UC and IC.12

In conclusion, GIP is a rare complication of IBD that can lead to diagnostic pitfalls for both the clinician and the pathologist. In our institutional experience, most cases of GIP occur in patients with UC and contain localized features within the polyposis segment that mimic CD clinically and pathologically. Therefore, a diagnosis of UC should not be amended to CD based on the findings of the polyposis segment alone. Recognition of the diagnostic pitfalls posed by GIP may help avoid misdiagnosis and improper medical and surgical management.

Conflict of interest statement

The authors confirm that there are no known conflicts of interest associated with this research and there has been no significant financial support for this work that could have influenced its outcome.

Acknowledgments

SN carried out data analysis and drafted the original manuscript. MW and XG carried out data analysis. TU participated in study design and revision of the manuscript. NH conceived of the study, participated in its design and helped to draft the manuscript. All authors read and approved the final manuscript.

References