Prevalence of Gastroduodenal Polyps in Children With Familial Adenomatous Polyposis

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Abstract

Objective: To assess the prevalence of upper gastrointestinal adenomatous polyps in a cohort of pediatric familial adenomatous polyposis (FAP) patients to determine if early screening is warranted.

Study Design: All 11 pediatric FAP patients diagnosed in Manitoba between January 2012 and December 2019 were recruited. Patient records were examined and data on age of diagnosis, gene mutation, age of first screening endoscopy, number of endoscopies, number of gastric and colonic polyps, associated pathology, medications, symptoms and FAP-related surgeries were extracted and descriptive statistics reported.

Results: A total of 11 children were diagnosed with FAP over the study period with a mean age at diagnosis of 6.3 ± 3.2 years with 72.3% males and median follow-up of 4.8 years. The mean age at first gastroscopy was 10.9 ± 2.9 years and 10.8 ± 3.0 years at colonoscopy. Eight patients (72%) had upper gastrointestinal polyps, with adenomatous changes seen in seven of them on pathology. No patients had invasive carcinoma or high-grade dysplasia. All patients developed tubular adenomas on colorectal polyp pathology. Four (36%) patients underwent surgical colectomy.

Conclusions: Early-onset upper gastrointestinal adenomatous polyps in a pediatric FAP are common. Our study provides further data to support consideration of further, large-scale research into the benefit of early endoscopic screening for upper gastrointestinal malignancy in FAP patients.

Keywords: FAP; Gastric polyps; Tubular adenoma; Pediatric; Endoscopic screening

Introduction

Familial adenomatous polyposis (FAP) syndrome is a familial inherited autosomal-dominant polyposis syndrome. FAP predisposes affected individuals to a significant polyp burden at a young age, significantly increasing the risk of colorectal cancer before the age of 30 years. Furthermore, these patients can also suffer from a variety of other malignancies, including duodenal, thyroid, brain and pancreas (1). Studies examining incidence rates of gastric and duodenal neoplasia in FAP are rare; however, one large prospective study of 368 FAP patients reported a 90% incidence of duodenal adenoma by age 70, with an overall cumulative neoplastic rate of 4.5% (2). Other studies have reported duodenal neoplasia incidences of 3% to 5% (1,3). Data on gastric cancer in patients with FAP are also rare, with a previously reported lifetime risk of 0.6% (4). However, recent reports have shown a concerning increased incidence of gastric cancer...
in Western FAP patients with certain endoscopic criteria, with one Japanese study of 80 FAP patients reporting a 28% yield of gastric neoplasm after upper endoscopy (5,6). While data on pediatric upper gastrointestinal polyps and malignancy are less robust, studies in recent years have also reported an increased detection of gastric and duodenal polyps in this population as high as 52% (7).

Guidelines suggest upper gastrointestinal screening with esophagogastroduodenoscopy (EGD) beginning at the age of 20 to 25 years, with follow-up intervals determined based on Spigelman classification criteria (1,8,9). Screening for gastric polyps with upper endoscopy has been suggested to occur at a later age based on previous evidence suggesting a low incidence of high-risk gastric pathology at an early age (1,9). Early guidelines suggesting this reported only on case reports of gastric cancer in FAP patients, however with more recent registry data suggesting an increase in gastric malignancies, further research to determine when cancerous or precancerous changes are seen and if these are present at an increasing rate in the pediatric population is important (10).

METHODS

Data Source

In this retrospective case series, medical record reviews were performed for all patients diagnosed with FAP between January 1, 2012 and December 1, 2019 in our tertiary-care referral hospital. Inclusion criteria included patients <18 years of age with confirmed FAP who were assessed in the pediatric FAP clinic and underwent endoscopy for routine screening. Colonoscopy performed was for screening purposes, and EGD was performed due to the presence of upper gastrointestinal symptoms. All EGDs were performed using a standard front-viewing gastroscope and were performed by an expert pediatric endoscopist under anesthesia/deep sedation. Endoscopic findings were documented in an operative report dictated by the primary endoscopist, and pathology specimens of abnormal looking polyps were obtained at time of endoscopy and later interpreted by three experienced pathologists to confirm histologic diagnosis. A diagnosis of FAP was established by both documented adenomatous polyposis coli (APC) gene mutation and a positive family history. Data on age of diagnosis, gene mutation, mutation site, age and indication of first screening endoscopy, total number of endoscopies, number of gastric and colonic polyps, pathology of polyp biopsies, any associated pathology, medications, symptoms, surgeries and other routine investigations (e.g., video capsule endoscopy [VCE]) were extracted. Descriptive data for each patient were then reported, including mean age at diagnosis, mean number of endoscopies, mean age at initial endoscopy, mean age of colectomy of the proband (if known) and mean age at VCE. Descriptive analysis was performed using Excel Version 14.7.0 for Mac (2011).

Ethical Consideration

The study protocol was approved by the local research ethics board.

RESULTS

A total of 11 children and young adults from 7 different families were identified and fulfilled our inclusion criteria. The mean age at diagnosis of FAP was 6.3 years (standard deviation [SD] 3.2, range 2 to 14) with 72.3% boys (n = 8). All 11 tested positive for the APC gene, and all had a positive family history for FAP. Five (n = 5) patients had further data on the specific APC gene mutations: two (n = 2) patients had mutations at codon 1061–1063 and 1309–1311, one (n = 1) at codon 1744, one (n = 1) at codon 3927 and 3931 and one at exon 50. Six patients exhibited paternal inheritance (54.5%). The mean age at first colonoscopy was 10.8 years (SD 3.0, range 6.5 to 14.9 years), while the mean age at first EGD was 10.9 (SD 2.9, range 6.5 to 14.9 years). One patient in the cohort underwent colonoscopy only at the time of first screening, with EGD performed at the next screening endoscopy the following year, as they had no symptoms initially. Other indications for EGD included the presence of nonspecific symptoms such as abdominal pain, anemia, nausea or inability to verify the type and age of presentation of the index case (i.e., first family member diagnosed). Mean number of EGDs over the study period was 3.2 scopes while mean number of colonoscopies was 3.7. VCE was performed to screen for small bowel polyps at least once in all patients, with mean age at first VCE of 12.8 years (SD 2.5, range 7.3 to 13.8 years). A total of 15 studies were performed, with conclusive results in nine patients over 12 studies. Three patients had inconclusive studies initially due to poor prep and visualization of the small bowel, with one patient undergoing repeat VCE with conclusive, normal findings. The remaining two patients with initial inconclusive studies did not undergo repeats. In total, four patients had repeat VCE performed; one due to high burden (>100) of gastric polyps seen on EGD (Patient A), one at the discretion of the ordering physician, and two due to the first study being inconclusive. No patients were found to have small bowel pathology on capsule imaging. One patient was taking a multivitamin, with no others reporting medication use. Patients were followed up for a median duration of 4.8 years (IQR 3.2 to 5.6).

At the end of follow-up, four (n = 4) patients had undergone surgical bowel resection (Table 1).

Gastric Polyposis

Eight patients (72%) had upper gastrointestinal polyps with adenomatous changes seen in seven (63.6%) of them on pathology. Table 2 provides the description of gastric polyps for each patient. Two patients (Patient B and patient F) had 40 to 50 gastric polyps on initial EGD. By the age of 15 years, seven patients (A, B, C, D, F, G and H) were found to have numerous
no patients developed adenocarcinoma or high-grade dysplasia treated and eradicated on follow-up endoscopy and pathology. Two patients (Patient H and I) had pylori on histology. Two patients (Patients B, C and D; at mean age 12.9 years, range 12.2 to 13.7 years), with one (Patient B) showing tubular adenoma.

Ten (91%) patients had endoscopic evidence of colonic polyps with tubular adenomas on pathology were diagnosed

discussion

We report a case series of 11 pediatric patients with hereditary FAP, with 63% developing early-onset upper gastrointestinal adenomatous polyps on routine endoscopic screening. Current guidelines suggest lower gastrointestinal screening with colonoscopy by age 10 to 11 in patients with a documented genetic mutation and family history of FAP to identify malignancy and plan for prophylactic colectomy. While it has been reported that gastric adenomas have a lifetime prevalence of 7% to 14%, with duodenal adenomas approaching 20% to 100%, the timing at which to begin upper endoscopic screening has been controversial with many current guidelines suggesting beginning at age 20 to 25 (1–3,9–13). Conversely, a recent guideline published by the ESPHGAN Polyposis Working Group argues that upper gastrointestinal screening should not begin before the age of 25 (14). Given the variability in guidelines from differing working groups and associations, the authors feel that further research examining the pathology of pediatric gastrointestinal polyps is important. Previous studies have reported gastric cancers in adult FAP patients, supporting the notion to screen for gastric polyps. Only one patient (Patient E) did not have tubular adenomas, with pathology showing only mild chronic inactive gastritis and eosinophils. Patient E had less than 50 polyps on screening, all of which had tubular adenomas. Fundic gland polyps (FGP) were seen in two patients (Patient B and C), with low-grade adenomatous changes seen in a FGP biopsied from Patient B. Duodenal polyps were diagnosed in three (27%) patients (Patients B, C and D; at mean age 12.9 years, range 12.2 to 13.7 years), with one (Patient B) showing tubular adenoma on histology. Two patients (Patient H and I) had Helicobacter pylori gastritis on initial endoscopy, which was successfully treated and eradicated on follow-up endoscopy and pathology. No patients developed adenocarcinoma or high-grade dysplasia over the follow-up period (Table 2).

Colonic Polyposis

Ten (91%) patients had endoscopic evidence of colonic polyps at initial screening with only one patient (Patient E) with no polyps on initial colonoscopy (10.9 years); however, colonic polyps with tubular adenomas on pathology were diagnosed on the following screening colonoscopy 1 year later. All 11 patients developed tubular adenomas before the age of 15 years. The youngest patient with tubular adenoma was 6.5 years old (Patient H), who also presented with bleeding per rectum and significant polyp burden resulting in the inability to biopsy the entire colon, and subsequently underwent colectomy at the age 7.5 years. One patient (Patient I) had tubulovillous adenoma (high-grade dysplasia) at the age of 14.9 years and underwent colectomy at 16.5 years (Table 2). The remaining two patients who had surgical colectomies were older than 18 years at time of surgery. Patient B, who had multiple gastric and duodenal polyps consistent with tubular adenoma (Figure 1B), was also found to have a significant burden of tubular adenomatous colonic polyps. Interestingly, the one patient (Patient E) who never had more than 30 gastric polyps, none of which were tubular adenomas, also had a low polyp burden on colonoscopy (Figure 1A and C).

| Table 1. Description characteristics of pediatric FAP cohort |
|---------------------------------------------------------------|
| Demographics                                                  | Result                              |
| Age at diagnosis, mean (SD); range                           | 6.3 years (3.2); range 2–14 years   |
| Male sex, % (n)                                               | 72.3% (8)                           |
| APC gene mutation, % (n)                                      | 100% (11)                          |
| Paternal inheritance pattern, % (n)                          | 54.5% (6)                           |
| Age of proband colectomy, mean (SD); range                   | 20.9 years (5.5); range 8–27 years |
| Age at first colonoscopy, mean (SD); range                   | 10.8 years (3.0); range 6.5–14.9 years |
| Age at first EGD, mean (SD); range                           | 10.9 years (2.9); range 6.5–14.9 years |
| Number of colonoscopies, mean                                | 3.8                                 |
| Number of EGD, mean                                           | 3.3                                 |
| VCE, total                                                    | 15                                  |
| Normal VCE                                                    | 12                                  |
| Inconclusive                                                  | 3                                   |
| Age at first VCE, mean (SD); range                           | 12.8 years (2.48); range 7.3–13.8 years |
| Symptoms                                                      |                                     |
| Abdominal pain                                                | 54.5% (6)                           |
| Blood per rectum/hematochezia                                | 27.2% (3)                           |
| Nausea/reduced appetite                                       | 18.1% (2)                           |
| Anemia                                                        | 9.0% (1)                            |

| APC, Adenomatous polyposis coli; EGD, Esophagogastroduodenoscopy; VCE, Video capsule endoscopy. |

gastric polyps. Only one patient (Patient E) did not have tubular adenomas, with pathology showing only mild chronic inactive gastritis and eosinophils. Patient E had less than 50 polyps on screening. Five patients (Patient A [Figure 1A], B, C, F and G) had 40 to 50 polyps at a mean age of 13.3 years (SD 1.7) on screening, all of which had tubular adenomas. Fundic gland polyps (FGP) were seen in two patients (Patient B and C), with low-grade adenomatous changes seen in a FGP biopsied from Patient B. Duodenal polyps were diagnosed in three (27%) patients (Patients B, C and D; at mean age 12.9 years, range 12.2 to 13.7 years), with one (Patient B) showing tubular adenoma on histology. Two patients (Patient H and I) had Helicobacter pylori gastritis on initial endoscopy, which was successfully treated and eradicated on follow-up endoscopy and pathology. No patients developed adenocarcinoma or high-grade dysplasia over the follow-up period (Table 2).
### Table 2. Description of gastric and colonic polyps

| Patient, age (years) | Gastric Findings | Colonic Findings |
|----------------------|------------------|------------------|
|                      | Endoscopic description | Number of polyps | Pathology | Endoscopic description | Number of polyps | Pathology | Colectomy |
| A                    |                    |                  |           |                      |                  |          |           |
| 11.1                 | Sessile           | 7                | Mild focal gastritis | Sessile | 5-10 | Tubular adenoma, hyperplastic | No |
| 12.2                 | Sessile           | 20               | Normal    | Sessile | 10-20 | Tubular adenoma | |
| 13.2                 | Sessile           | 10-20            | Adenomatous | Sessile | 20-30 | Tubular adenoma | |
| 14.0                 | Sessile           | 20-30            | Mild chronic gastritis | Sessile | 20-30 | Tubular adenoma | |
| 15.0                 | Sessile           | 50               | Tubular adenoma | Sessile | 50 | Tubular adenoma | |
| B                    |                    |                  |           |                      |                  |          |           |
| 11.3                 | Sessile           | 40-50            | Normal    | Sessile | 100-200 | Tubular adenoma | No |
| 12.7                 | Sessile, FGP      | 50-100           | FGP, Tubular adenoma | Sessile | 40 | Tubular adenoma | |
|                      | 5 duodenal        | Tubular adenoma  | Pedunculated | 3 | | |
| 13.7                 | Sessile           | 150-200          | FGP with low grade adenomatous changes, tubular adenoma | Sessile | 200 | Tubular adenoma | |
|                      | 8 duodenal        | Tubular adenoma  | Pedunculated | 8 | | |
| 14.7                 | Sessile           | Numerous         | Tubular adenoma | | * | * | * |
| C                    |                    |                  |           |                      |                  |          |           |
| 7.3                  | -                 | -                | -         | Not described | 3 | Tubular adenoma | No |
| 8.3                  | Sessile           | 5                | Normal    | Sessile | 5-10 | Tubular adenoma | |
| 9.5                  | Sessile           | 5-10             | Normal    | Sessile | 40-50 | Mucosal lymphoid aggregate | |
| 13.9                 | FGP               | 4                | Normal    | Not described | Multiple | Tubular adenoma | |
|                      | 2 duodenal        | Tubular adenoma  | Normal    | | | |
| 15.3                 | Sessile           | Numerous         | Tubular adenoma | Not described | 100-150 | Tubular adenoma | No |
| D                    |                    |                  |           |                      |                  |          |           |
| 6.6                  | None              | None             | Normal    | Sessile | 1 | Normal | No |
| 12.1                 | Sessile           | Multiple         | Normal    | Not described | Multiple | Tubular adenoma | |
|                      | 1 duodenal        | Normal           | | | | |
| 13.5                 | Sessile           | Multiple         | Tubular adenoma | Not described | >50 | Tubular adenoma | |
| E                    |                    |                  |           |                      |                  |          |           |
| 10.2                 | Sessile           | <5               | Normal    | None | None | Normal | No |
| 12.2                 | Normal            | Normal           | Normal    | Sessile | <5 | Tubular adenoma | |

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| Patient, age (years) | Endoscopic description | Number of polyps | Pathology | Endoscopic description | Number of polyps | Pathology | Colectomy |
|---------------------|------------------------|------------------|-----------|------------------------|------------------|-----------|-----------|
| 13.3                | Sessile                | 5-10             | Mild chronic inactive gastritis | Sessile           | 5-10             | Tubular adenoma | No        |
| 14.2                | Sessile                | 20-30            | Eosinophils | Sessile             | 5-10             | Normal     |           |
| 15.5                | Sessile                | 30-40            | Normal     | Sessile             | 5-10             | Tubular adenoma |           |
| F                   |                        |                  |           |                       |                  |            |           |
| 10.6                | Sessile                | <100             | Tubular adenoma | Sessile           | 1               | Flat adenoma |           |
| 11.9                | Sessile                | 40-60            | Tubular adenoma | Sessile           | 5-10             | Tubular adenoma |           |
| 12.9                | Sessile                | 10-20            | Tubular adenoma | Sessile           | 5-50             | Tubular adenoma |           |
| 13.9                | Sessile                | <50              | Normal     | Sessile             | 5-10             | Normal     |           |
| 14.8                | Sessile                | <50              | Tubular adenoma | Sessile           | 20-30            | Tubular adenoma |           |
| 16.2                | Sessile                | 50-100           | Tubular adenoma | Sessile           | 50-100           | Normal     |           |
| G                   |                        |                  |           |                       |                  |            | No        |
| 10.9                | None                   | None             | Normal    | None                 | None             | None       | None      |
| 12.3                | Sessile                | <20              | Tubular adenoma | Sessile           | <5              | Tubular adenoma |           |
| 14.1                | Sessile                | 50-100           | Tubular adenoma | Sessile           | 2               | Flat adenoma |           |
| H                   |                        |                  |           |                       |                  |            | Yes       |
| 6.5                 | None                   | None             | Normal    | Sessile             | Extensive, unable to survey colon | Tubular adenoma |           |
| I                   |                        |                  |           |                       |                  |            | Yes       |
| 14.9                | Sessile                | 10               | Tubular adenoma | Sessile           | >50             | Tubulovillous adenoma |           |
| 16.5                | None                   | None             | Normal    | -                    | -               | -          |           |
| J                   |                        |                  |           |                       |                  |            | Yes       |
| 14.1                | None                   | None             | H. pylori | Sessile             | 5               | Normal     |           |
| 15.9                | None                   | None             | Normal    | Sessile             | 20              | Tubular adenoma |           |
| 17.7                | -                      | -                | -         | Sessile             | Multiple        | Tubular adenoma |           |
| 18.8                | -                      | -                | -         | Sessile             | Multiple        | Tubular adenoma |           |
| K                   |                        |                  |           |                       |                  |            | Yes       |
| 14.1                | None                   | None             | H. pylori | Sessile             | 10-20           | Tubular adenoma |           |
| 15.9                | None                   | None             | Normal    | Sessile             | 20-30           | Tubular adenoma |           |
| 17.7                | -                      | -                | -         | Sessile             | Multiple        | Tubular adenoma |           |
| 18.8                | -                      | -                | -         | Sessile             | Multiple        | Tubular adenoma |           |

FGP, Fundic gland polyp.
*Patient refused colonoscopy.
- Procedure not performed.
adenocarcinomas is still unknown and given the increasing incidence reported, the authors propose more frequent endoscopic examination in patients with high-risk features, which has previously been defined as polyps >10 mm, antral polyps, carpeting of gastric polyps, presence of polypoid mounds, size of solitary polyps and polyp histology (10). The data on pediatric gastric polyposis and the risk of malignancy are currently lacking. Gutierrez Sanchez et al. reported duodenal adenomas with low-grade dysplasia in 52% of pediatric patients with FAP who underwent EGD for screening purposes in a cohort of 69 patients (7). After combining their results into a systematic review with other upper gastrointestinal findings in pediatric FAP patients, a duodenal adenoma detection rate of 42% was reported. Gastric adenomas were less common, with adenomas being reported in only 7.2% of the studied cohort and in 8.7% in the systematic analysis. While no adenocarcinomas were detected in either pediatric population, the authors conclude that further research into the natural progression of these lesions is necessary (7).

We report gastric polyps in 8 out of 11 (72%) pediatric patients before the age of 15 years with 63.6% (n = 7) demonstrating adenomatous changes before the age of 15 years. One large retrospective review by Attard et al. (15) reported upper gastrointestinal endoscopic findings in 24 pediatric patients with FAP (mean age 13.5 [4.4] years and most common indication for endoscopy was screening in an asymptomatic patient). Seventy-five per cent (n = 18) had multiple fundic gland polyps, with 42% (n = 10) showing low-grade dysplasia at a mean age of 14.8 years. High-risk features were found in three patients, all of whom had antral polyps with adenomatous changes. Duodenal polyps were found in another 10 patients, with one showing tubulovillous adenoma on histology (15). Another review reported duodenal adenocarcinoma development in pediatric patients with FAP to be as high as 12% (15). Coffey et al. (16) retrospectively analyzed gastric fundic polyps in a pediatric database of 8527 gastric biopsies, reporting five patients with FAP, 40% (n = 2) showing dysplastic changes on histology (median age 17.7 years, range 15.4 to 19.5). While our series is smaller than the study by Attard et al. and Sanchez et al., 73% (n = 8) patients in our study had gastric polyps, with 63.6% (n = 7) demonstrating tubular adenomas before the age of 15, a much higher rate of gastric low-grade dysplastic lesions. We also report two (n = 2, 18.2%) patients with FGP seen on EGD, one of which showed low-grade adenomatous changes on histology. The reported prevalence of FGP in the pediatric FAP population has been variable, with one study reporting a prevalence of 24% and others as high as 75%, and have been reported at a median age of 17.7 years (14,16). Given the oldest age of our cohort was just over 16 years, it is possible our data reflect the lower range of FGP prevalence. The finding of FGP with low-grade adenomatous changes has been previously reported, although this is a less common finding in FGP (16). Gastric adenocarcinoma and proximal polyposis syndromes (GAPPS) have recently been described as a unique variant of FAP manifesting as a gastric polyposis syndrome (17,18). Worthley et al. (18) first reported the syndrome in 2011, with the youngest affected offspring diagnosed at age 10. In a study by Repak et al. (17) of three affected family members, one offspring died after being diagnosed with GAPPS at age 26, with the subsequent two members undergoing gastrectomy at age 23 and 30. In both series, this rare variant was diagnosed in patients who would not have otherwise been included in many of the current screening guidelines, further supporting the rationale to screen all pediatric FAP patients with upper endoscopy.

VCE was performed a total of 15 times. In total, nine patients had conclusive findings, with the remaining two patients having inconclusive findings on the first VCE and not undergoing a repeat. In total four patients underwent repeat VCE: one due to a high burden of gastric polyps, two due to the first study being inconclusive, and one at the discretion of the ordering physician. The literature on pursuing VCE in pediatric FAP patients is lacking and very few studies exist commenting on its utility. Iaquinto et al. examined the small bowel of 23 adult patients (range 18 to 51 years) with FAP with VCE, reporting a 30% polyp detection rate (19). All polyps were small (<5 mm) and the authors report a poor correlation with duodenal and periampullary detection rates on VCE (n = 4) as compared to visualization by a side viewing gastroscope (n = 11). However, the presence of duodenal adenomas was associated with the detection of more distal small bowel polyps. As far as we are aware, there have been no large-scale studies examining polyp detection rates of VCE in the pediatric FAP population. We report no patients with distal small bowel pathology seen on VCE. Given the low rates of sinister distal small bowel pathology reported in adult FAP patients, the authors would argue that further research would be necessary to justify pursuing routine VCE on pediatric FAP patients.

All patients had a documented mutation in the APC gene. Data on the genetic site of mutation were available in four patients. It has previously been reported that certain mutation locations on the APC gene are predictive of FAP severity, with mutations between codon 1250 and 1464 predicting severe colonic disease (14). Patient E and F both had mutations in codons 1309–1311. While both had colonic tubular adenomas documented by the age of 12, one patient had a relatively low burden of colonic polyps (5 to 10) as compared to the other (50 to 100; Table 2). The data on mutations associated with severity of upper gastrointestinal polyps are less robust, although it has been reported that mutations in Exon 15 are associated with more severe duodenal involvement (20). Given the lack of further data on specific location mutations, the authors cannot make any conclusions on mutation site and disease severity in our cohort.
Figure 1. (A) Gastric body polyps (Patient A).

Figure 1. (B) Gastric, duodenal and colonic polyps (Patient B) i. Duodenum.

Figure 1. (B) Gastric, duodenal and colonic polyps (Patient B) ii. Cardia (retroflexion).

Figure 1. (B) Gastric, duodenal and colonic polyps (Patient B) iii. Colon.

Figure 1. (B) Gastric, duodenal and colonic polyps (Patient B) iv. Colon.

Figure 1. (C) Gastric and colonic polyps (Patient E) i. Gastric polyps.
Our findings support previous research reporting a high burden of colonic polyps that can occur at an early age (1,12,21). The oldest age at follow-up in the study was 20 years, with two patients undergoing colectomy as children and the remaining two at 19 years. While a large European database showed very low rates of colorectal cancer in pediatric patients (0.2% incidence of colorectal cancer between the age of 11 and 15 years), we report two patients with high-risk features for development of colorectal malignancy (21). One patient (Patient H) had extensive burden of colonic polyps showing tubular adenoma, and as a result of the inability to biopsy all the polyps with the very young age of colectomy in the proband, had an early colectomy at age of 7.5 years. The second patient (Patient I) underwent colectomy at age 16 years after pathology showed evidence of high-grade tubulovillous adenoma.

While the findings of our study are novel and important especially with the currently available limited data, we recognize the limitations of our study, most importantly the small sample size, absence of those with de novo mutation, and retrospective analysis, which also limited our ability to classify the polyps visualized by standard classification systems (i.e., Paris classification). We also identify that in our cohort, no high-grade dysplasia or adenocarcinoma was seen that would prompt early intervention or gastrectomy. However, we report a high incidence of adenomatous changes in patients <15 years with numerous gastric and duodenal polyps, suggesting a possible trend to early precancerous changes. With an increasing prevalence of gastric cancers now seen in an adult Western population and increasing rates of upper gastrointestinal adenomatous changes in pediatric FAP patients as reported by Gutierrez Sanchez et al., we feel this study adds to the literature that screening FAP patients for these lesions at an earlier age may be necessary. Given variable reported prevalence and the uncertainty around the progression of these lesions in a young cohort, we strongly feel that our results suggest a need for more large-scale studies on upper gastrointestinal screening in pediatric patients with the intent of better understanding if there has also been a shift in the natural history and pathology of pediatric polyposis (10,22). The increasingly reported variant of GAPPS seen worldwide furthers the argument for, at minimum, addition of upper gastrointestinal screening in pediatric FAP patients at time of diagnosis. These results should warrant further large-scale research into the true prevalence of high-risk lesions in pediatric FAP patients to further understand if there is a benefit to performing EGD at a younger age than it is currently recommended (1,9).

CONCLUSION
Our study reports a high burden of gastric polyposis with adenomatous changes in a pediatric cohort with FAP. Given the increasing incidence of gastric cancer in adult FAP patients and high rates of upper gastrointestinal adenomatous polyps recently reported in pediatric patients, in addition to the ongoing lack of research in adenomatous changes in upper gastrointestinal lesions in pediatric FAP patients, early screening for upper gastrointestinal malignancies should be further studied for consideration. Long-term prospective longitudinal research including larger sample size is needed to determine the rates of upper gastrointestinal malignancy in patients with documented early-adenomatous changes of the upper GI tract.

DISCLOSURES
J.K.S. has nothing to disclose. W.El-M. has nothing to disclose. C.N.B. has been on advisory boards for Abbvie Canada, Ferring Canada, Janssen Canada, Shire Canada, Takeda Canada, Pfizer Canada, consulted to Mylan Pharmaceuticals, has received educational grants from Abbvie Canada, Pfizer Canada, Shire Canada, Takeda Canada, Janssen Canada and has been on the speaker’s panel for Janssen Canada, Medtronic Canada, Takeda Canada and Shire Canada. H.S. has been on the advisory board of Takeda Canada, Pendopharm, Ferring Merck Canada and Guardant Health, Inc. and has received educational grant from Ferring and research funding from Merck Canada.

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