Inflammatory Fibroid Polyp of the Gastrointestinal Tract: A Systematic Review for a Benign Tumor

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Abstract. *Background/Aim:* Inflammatory fibroid polyp (IFP) is a rare, usually solitary and intraluminal polypoid benign tumor that can affect any part of the gastrointestinal (GI) tract, although in the majority of cases it affects the

stomach. This lesion is characterized by proliferation of highly vascular fibrous tissue and infiltration by a variable number of different inflammatory cells. Its etiology is unknown. Our aim was to describe all the reported data concerning IFP. *Materials and Methods:* An extensive search of the PubMed Index was performed for publications with titles or abstracts containing the terms: "inflammatory fibroid polyp" with/without "Vanek". Results were filtered for publications in English and concerning only humans. One hundred and twenty-four publications were finally included in this review. *Results:* IFP has a female predominance. It affects patients in their 5th decade of life, although there are cases of patients from 4 to 84 years of age. IFP usually affects the stomach and more specifically the gastric antrum but can be detected throughout the GI tract. A significant number of cases remain asymptomatic but

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Figure 1. PRISMA flow for the current literature review.

the most frequent presentations of IFP are abdominal pain, acute abdomen and GI bleeding. Most cases are treated by endoscopic resection of the lesion. No recurrence nor IFP-specific complications have been reported. Histopathology of IFP varies. Conclusion: It is relatively safe to conclude that both the etiology and the timing of diagnosis might change the histopathology, immunohistological staining and tissue structure of IFP. Suggested theories should be taken into consideration with caution as the etiology and pathophysiological mechanisms of IFP are unknown.

Inflammatory fibroid polyp (IFP) was first described by Vanek in 1949 as a 'submucosal granuloma with eosinophilic

infiltration' (1). IFP is a rare, usually solitary and intraluminal polypoid benign tumor that can affect any part of the gastrointestinal (GI) tract, although in the majority of cases it affects the stomach. This lesion is characterized by proliferation of highly vascular fibrous tissue and infiltration by a variable number of different inflammatory cells. The term IFP has gained wide acceptance since its first use in a 1953 publication by Helwig and Ranier (2). A plethora of different names have been suggested to describe IFP, such as eosinophilic granuloma, granuloblastoma or gastric fibroma with eosinophilic infiltration, granuloma with eosinophils, hemangiopericytoma, inflammatory fibroid tumor, and inflammatory pseudotumor (3, 4). The great number of

Figure 2. Macroscopic view of Inflammatory fibroid polyp (IFP). A: Gastroscopy demonstrating a reddish IFP of the antrum. B: Colonoscopy demonstrating a pedunculated and reddish IFP of the cecum. C: Pedunculated IFP of the rectum.

Figure 3. Abdominal computed tomography demonstrating an inflammatory fibroid polyp of the lesser curvature of the stomach. A: Coronal section; B: transverse section; C: sagittal section.

possible names reflects our ignorance on the exact mechanism of IFP development and the different hypotheses on the etiology of IFP. Local infection, allergic reaction, autoimmune processes or excessive host response to an unknown stimulus have all been described as possible causes of IFP development (5, 6). Due to its unknown etiology, the malignant potential of what is otherwise described as a benign tumor is currently under debate. Familial occurrence or concomitant development of IFP and other GI malignancies show that some malignant potential might be present, although it is infrequent (7-10). Immunohistologically, IFPs are characterized by spindle cells with unclear origin, positive for CD34 and vimentin, and negative for CD117 (11, 12). The overexpression of platelet-derived growth factor receptor alpha

(PDGFRA) and oncogenic *PDGFRA* mutations in the majority of analyzed IFP suggests that this tumor might develop through activated PDGFRA (13, 14). A variety of clinical signs and symptoms are linked to IFP, mainly GI bleeding or abdominal pain, but the clinical presentation may significantly vary, and it mimics other pathology.

This article aims to provide an extensive review of the available English literature on IFP.

Materials and Methods

An extensive search of the PubMed Index was performed for publications with titles or abstracts containing the terms: “inflammatory fibroid polyp” with/without “Vanek”. In order to include most of the existing literature in this review, no starting or

Table I. Gastrointestinal location of recorded inflammatory fibroid polyps in the included studies.

Location	Number of cases	Percentage of total
Stomach	278	66.7%
Cardia	5	
Corpus	4	
Fundus	1	
Antrum	178	
Prepyloric	7	
Pylorus	2	
Unspecified	81	
Esophagus	8	1.7%
Small bowel	88	21.1%
Ileum	40	
Distal ileum	11	
Proximal ileum	1	
Jejunum	12	
Ileocecal valve	3	
Unspecified	21	
Gallbladder	1	0.2%
Duodenum	2	0.5%
Large bowel	35	8.4%
Cecum	11	
Transverse	4	
Descending	4	
Sigmoid	2	
Rectum	5	
Unspecified	9	
Appendix	3	0.7%
Ileo-anal pouch	1	0.2%
Total	417	100%

Table II. Number of patients presenting with specific symptoms and signs.

Presenting symptom or sign	Number of patients
Acute intestinal obstruction, peritonitis, acute abdomen	52
Abdominal pain	63
Epigastrium	11
Right lower quadrant	5
Lower abdomen	3
Unspecified	44
Nausea	20
Vomiting	29
Hematemesis	3
Dysphagia	4
Melena	5
Fever	8
Lower gastrointestinal bleeding	17
Occult gastrointestinal bleeding	4
Abdominal cramping, Distention	13
Anemia	13
Indigestion	5
Weight loss	10
Diarrhea	6
Constipation	9
Other	10
Pneumoperitoneum	1
Loss of appetite	4
Cholecystitis	1
Lower urinary tract symptoms	1
Arthralgia	1
Chest discomfort	1
Epigastric discomfort	
Asymptomatic	26

ending search date were selected. Results were filtered for publications in English and concerning only humans. All references from the identified publications were searched for other non-indexed cases.

Out of 222 publications, 133 were finally included in this review (Figure 1) (3, 8, 15-19, 20-145). A large number of publications (n=72) prior to 1990 could not be electronically retrieved and were excluded. Seventeen were also excluded as they were irrelevant, earlier reviews of the literature, hypotheses, medical images or other types.

Results

One-hundred and thirty-three publications reported on 417 patients; 158 males (37.9%), 211 females (50.6%) and 49 of unreported gender (11.8%). The median age of the patients was 53 years (range=4-84 years).

The esophagus was affected by IFP in eight cases (1.7%) and most of these cases also involved the cardia or the sphincter. In 66.7% of all cases, IFP affected the stomach (n=278) (Figure 2). In approximately two-thirds of these cases, the antrum was affected (n=178) (Figure 3A), followed by the prepyloric segment, the cardia, the corpus,

the pylorus and finally the fundus (Table I). The duodenum was rarely affected (n=2, 0.5%). The small bowel was affected in 21.1% (n=88) of all cases. In these cases, the IFP was frequently located in the ileum (n=52), followed by the jejunum (n=12). The ileocecal valve was affected in three cases. The large bowel was affected in 8.4% of cases (n=35) and cecum was the most frequent location of an IFP (n=11) (Figure 3B) followed by the rectum (Figure 3C). There were only two cases of IFP in the appendix (0.7%). Other parts of the GI tract were even more rarely affected.

Patient presentation was recorded as close as possible to the original authors' wording; therefore, some symptoms and signs might overlap each other. Pain was recorded to be the most frequent symptom (17.0%), closely followed by acute abdominal symptoms (12.8%). Other frequent symptoms were vomiting (7.8%), nausea (5.4%), lower GI bleeding (4.5%), abdominal distension (3.5%) and anemia (3.5%). A number of patients (7.0%) were asymptomatic and in 10 cases (2.4%) findings were incidental. The number of

Figure 4. Endoscopic polypectomy. A: Resection of an inflammatory fibroid polyp of the antrum; B: Resection of an inflammatory fibroid polyp of the cecum.

patients presenting with a given symptom can be seen in Table II. No information was given on the presenting complaints of 233 patients (55.9%).

Endoscopic polypectomy (Figure 4) was the method of treatment in 85 cases (20.4%). Laparotomy and laparoscopy were performed in 49 cases (11.8%), followed by further surgical treatment depending on the pathology discovered. Small bowel resection was performed in 35 cases (8.3%). Partial or total gastrectomy was performed in 16 cases (3.8%). Further information on the procedures performed are shown in Table III. There was no information on the treatment method of 238 patients (57.1%).

In most cases, histopathology reports were typical of IFP. In a small number of cases, there were significant differences from the expected IFP histopathology and in some of these cases other concomitant malignancy or other GI pathology was present (10, 15-19). The majority of pre-1990 publications share limited data on the histopathology of the tissue excised during surgery or biopsied by endoscopy. Immunohistochemical reports varied significantly regarding the staining for CD34, CD117, actin, human foreskin fibroblast 35 (HHF-35), CD68 (KP1), macrophage marker antibody (Mac 387), human melanoma black 45 (HMB-45), phosphoglucomutase 1 (PGM1), vimentin, desmin, H-caldesmon, epithelial membrane antigen (EMA), anaplastic lymphoma kinase (ALK1), stem cell factor (SCF), B-cell lymphoma 2 (BCL2), CD21, CD23, human herpesvirus 8 (HHV8), and Epstein-Barr virus (EBER). In the majority of the cases, eosinophils were present in the tissue. Eosinophilia was not present or reported in most cases. CD34 staining was positive in most samples, with a varying intensity.

Table III. Procedure and therapy of inflammatory fibroid polyps.

Procedure	Number of patients
Endoscopic polypectomy, endoscopic mucosal resection, endoscopic submucosal resection, endoscopic resection, radical endoscopic resection	85
Laparotomy, laparoscopy	49
Segmental resection of ileum, jejunum, unspecified	36
Partial or subtotal gastrectomy	10
Total gastrectomy	6
Right hemicolectomy	6
Conservative or medical treatment	5
Open polypectomy	4
Ileocecal valve resection	4
Appendectomy	3
Refused treatment	2
Anterior partial fundoplasty	1
Billroth II	1
Roux-en-Y	1
Antrectomy with gastroduodenostomy	1
Rectal excision	1
Segmental resection of transverse colon	1
Segmental resection of duodenum	1
Laparoscopic cholecystectomy	1
Laparoscopic atypical gastrectomy	1
Esophagectomy	1
Laparoscopic transgastric polypectomy	1

Helicobacter pylori infection was recorded in four cases (0.96%) and it was treated in all of them (16, 72, 75, 114); the remaining studies either reported negative *H. pylori* test or did not report any data on this kind of infection.

Figure 5. Histological characteristics of inflammatory fibroid polyp (IFP) of the colon (A-C) and stomach (D- I). A: IFP of the colon arising in the submucosa and expanding to the mucosa (hematoxylin-eosin, original magnification $\times 40$). B: IFP of colon consisting of a loose fibromyxoid background, inflammatory cells and variably sized blood vessels (hematoxylin-eosin, original magnification $\times 100$). C: Bland spindle-shaped mesenchymal cells and heavy inflammatory infiltrate consisting mainly of eosinophils and secondarily of lymphocytes and plasma cells (hematoxylin-eosin, original magnification $\times 200$). D: Submucosal tumor under low-power examination (hematoxylin-eosin, original magnification $\times 20$). E, F: The tumor shows a prominent vasculature, large numbers of inflammatory cells, especially eosinophils, and concentrically arranged polygonal to spindle tumor cells around vessels (hematoxylin-eosin, original magnification $\times 100$ and $\times 200$, respectively). G: Multinucleated tumor cells are rarely seen (hematoxylin-eosin, original magnification $\times 400$). H: Spindle-shaped tumor cells are positive for CD34 but negative for C-KIT (CD34, original magnification $\times 200$). I: Scattered mast cells are depicted (C-KIT, original magnification $\times 200$).

Discussion

This review follows what has been described in the relevant bibliography (5, 6, 11-13, 146-150).

IFP affects women more frequently (1.3:1 female to male ratio). The median age of patients is - as expected - in the fifth decade of life but a wide range of ages are affected (4-84 years).

The data from the 417 patients included in our review also confirm that the most commonly affected site of the GI tract is the antrum. In general, the stomach was affected in two-

thirds of all cases (67%). The small bowel was the second most affected organ (21%) and colon was the third (8%). The rest of the GI tract was very rarely affected (<3% in total). The few cases of esophageal IFP seem to have involved the lower third of the esophagus and almost always the lower esophageal sphincter or the cardia to some degree.

Despite the fact that some patients remain asymptomatic, IFP tends to present with a variety of different symptoms mimicking other pathology. The asymptomatic cases might be the result of smaller lesions, especially in larger organs (e.g. stomach) where it might take longer for an IFP to cause any

symptoms. In most cases, patients with IFP presented with either abdominal pain or the clinical picture of acute abdomen in 63 and 52 cases, respectively. Abdominal pain is one of the symptoms of acute abdomen, but in our review these two terms must be distinguished as we tried to follow the authors' description of symptoms. Abdominal cramping and distension were also separately reported in 13 cases. Abdominal pain and acute abdomen were frequently the result of small bowel or ileo-cecal intussusception. Vomiting and nausea were also frequent symptoms in 29 and 20 cases, respectively. Lower GI bleeding and anemia were also frequent in 17 and 13 cases, respectively. In some cases, symptomatic or exuberant anemia was the alerting sign for patients to seek medical advice and discover the underlying cause of IFP. Other symptoms, including atypical ones, were less frequently reported.

Regarding the treatment, patients treated with an endoscopic IFP resection were 85 in total, including all endoscopic methods mentioned in the original texts. In 49 cases, laparotomy was performed, followed by a wide variety of open procedures depending on the localization of the IFP. Despite the fact that the stomach was the most affected organ, gastrectomy of any type was performed in 17 cases, which can be explained by the hypothesis that gastric IFP can often be removed endoscopically. On the other hand, resection of a small bowel segment was more often performed despite the small bowel being affected in a smaller number of cases. This might be the result of technical difficulty of IFP resection during lower GI endoscopy and it is reported that in some cases the polyps - especially the larger ones - had to be cut into small pieces in order to be removed or it was impossible for them to be threaded through the endoloop. Table III describes the therapeutic procedures. In all cases, no recurrence was recorded and after initial treatment, no further treatment was necessary (3, 8, 15-19, 20-145).

It is already described in the literature that IFP can be categorized into four histopathological groups: Classical fibrovascular, nodular, sclerotic, and edematous (147). A fifth category of IFP was suggested, that of nuclear pleomorphism, but it is rather atypical. Other authors considered the edematous form as simply a result of edema of the small bowel due to intussusception (148). The natural history of IFP is still unknown but from the wide range of reported polyp sizes and its asymptomatic nature it might be assumed that IFP demonstrates a long and slow growth. During this long period of time, the histology of IFP might change. Smaller lesions have a more marked onion-like distribution of spindle-shaped cells and, as the lesion becomes larger, the tissue architecture changes through the different existing types; furthermore, different histological types can co-exist within the same IFP (148). All the above may explain why histopathology reports from the included studies report a typical IFP picture but they still differ from each other

(Figure 5). Furthermore, not all IFPs stain similarly for CD34, desmin, vimentin, CD117 and other expressed proteins. Although the majority of recorded IFP cases were found to be positive for CD34, still this is not a rule that can exclude IFP from other possible diagnoses. The same is also valid for other protein staining, such as vimentin and CD117 (147, 149, 150). Based on different tissue staining, some authors conclude that there are different histological varieties of IFP. To make things more complicated, some authors suggest that IFPs have a malignant potential, as malignant processes have been found near or within some IFP (10, 114). On the other hand, no well-based evidence exists that confirms this theory.

Even though both epidemiology and the presenting clinical picture have been described in previous publications, this study confirms them, as it includes all the reported data concerning IFP, however, a number of questions remain, including the etiology and the histopathology of IFP. A possible weak point of this literature review is the large number of cases that could not be retrieved and included.

Conclusion

This study confirms what is already known of the epidemiology and the presenting clinical picture of IFP. From all the above, it is relatively safe to conclude that both the etiology and the timing of diagnosis might change the histopathology and tissue structure of the IFP.

Conflicts of Interest

All the Authors declare that there are no conflicts of interest.

Authors' Contributions

NG, CD and AG designed the study and wrote the article. NG, CD, AG, VEG, ED, PF, EV, AS, AP and AS collected the data. NT performed the statistical analysis. SS and AL performed the histopathological evaluations. GS performed the radiological evaluations. AA performed the endoscopy. DS, EAA, KK and DD offered scientific advice. NG, CD and AG revised the article. DD critically revised the article and was the supervisor.

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