

Vanek's tumor of the small bowel in adults

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Abstract

Inflammatory fibroid polyps (IFPs), or Vanek's tumor, are one of the least common benign small bowel tumors. IFP affects both sexes and all age groups, with a peak of incidence in the fifth and seventh decades. They can be found throughout the gastrointestinal tract but most commonly in the gastric antrum or ileum. The underlying cause of IFPs is still unknown. Genetic study of IFP showed mutations in platelet derived growth factor alpha in some cases. At the time of diagnosis most IFPs have a diameter of 3 to 4 cm. The lesions have always been recorded as solitary polyps. Symptoms depend on the location and the size of the lesion, including abdominal pain, vomiting, altered small bowel movements, gastrointestinal bleeding and loss of weight.

IFPs arising below the Treitz ligament can present with an acute abdomen, usually due to intussusceptions. Abdominal computed tomography is currently considered the most sensitive radiological method to show the polyp or to confirm intussusceptions. Most inflammatory fibroid polyps can be removed by endoscopy. Surgery is rarely needed. Exploratory laparoscopy or laparotomy is frequently recommended as the best treatment for intussusceptions caused by IFP. The operation should be performed as early as possible in order to prevent the intussusceptions from leading to ischemia, necrosis and subsequent perforation of the invaginated bowel segment. This report aims at reviewing the diagnosis, etiology, genetics, clinical presentation, endoscopy, radiology, and best treatment of IFP.

Key words: Small bowel; Inflammatory fibroid polyps; Abdominal pain; Intussusception; Computed tomography scan; Surgery

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Core tip: Inflammatory fibroid polyps, or Vanek's tumor, are one of the least common benign small bowel tumors. Abdominal computed tomography is currently considered the most sensitive radiological method to show the polyp or to confirm complications. This report aims at reviewing the etiology, diagnosis, and treatment options of this entity, with emphasis on the success rate of radiologic investigations, the need for laparoscopic diagnosis and the role of surgery. The debate arises over the importance of the differential diagnosis. Moreover, if surgery is performed, consideration needs to be given to what operation should be undertaken and in which patients.

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INTRODUCTION

Inflammatory fibroid polyps (IFPs), or Vanek's tumor, are one of the least common benign small bowel tumors. They fall under the classification of submucosal connective tissue tumors. IFP affects both sexes (with slight predominance of the condition in men) and all age groups, with a peak of incidence in the fifth and seventh decades^[1-11]. The mean age of patients with gastric tumors is significantly higher compared with IFP of the small bowel (72 years vs 53 years). IFP account for 0.1%-3.0% of all gastric polyps^[11]. They can be found throughout the gastrointestinal (GI) tract-most commonly in the gastric antrum or ileum, but rarely in the duodenum and jejunum. The underlying cause of IFPs is still unknown. Many have suggested etiologies possibly related to chemical, physical, or metabolic triggers. Genetic study of IFP showed mutations in platelet derived growth factor alpha (PDGFRA) in some cases^[12-16]. At the time of diagnosis most IFPs have a diameter of 3 to 4 cm; however, there is also a report of a case with an IFP 20 cm in size^[3]. The lesions have always been recorded as solitary polyps. Symptoms depend on the location and the size of the lesion, and include abdominal pain, vomiting, altered small bowel movements, GI bleeding, loss of weight and intestinal intussusceptions. Abdominal computed tomography (CT) is currently considered the most sensitive radiological method to show the polyp or to confirm intussusceptions^[17,18]. Most inflammatory fibroid polyps can be removed by endoscopy. Only rarely is surgery necessary. IFPs arising below the Treitz ligament can present with an acute abdomen (obstructive ileus) usually due to intussusceptions. Exploratory laparoscopy or laparotomy is frequently recommended as the best treatment for intussusceptions caused by IFP. The operation should be performed as early as possible in order to prevent the intussusceptions from leading to ischemia, necrosis and subsequent perforation of the invaginated bowel segment^[19-21].

DEFINITIONS

IFPs are rare, idiopathic, localized, pseudotumor, benign neoplastic lesions originating in the submucosa of the gastrointestinal tract. The disease was first described in the stomach by Vanek in 1949^[4] as a benign, non-encapsulated, submucosal granuloma, composed mainly of loose connective tissues, vessels and with an eosinophilic inflammatory component. At the same time the German pathologist Franz Bolck noticed these lesions, too, and referred to them as granuloblastoma of the stomach. The involvement of the small intestine and colon by IFPs is rare^[4-9]. Various names for IFPs have been suggested, including eosinophilic granuloma, submucosal fibroma, hemangiopericytoma, inflammatory pseudotumor and fibroma. However, the term IFP first proposed by

Helwig and Ranier^[22] in 1953 for gastric polyps has gained acceptance for similar lesions throughout the GI tract. Since then several hundred reports, mainly case series and reports on single cases, have been published which predominantly focused on clinical and morphologic aspects. Notably, inflammatory fibroid polyps have been regarded as reactive lesions for decades. In 2008, however, the neoplastic nature of IFP became evident by the detection of activating PDGFRA mutations in these tumors^[14]. IFPs can develop in many different locations in the GI tract. The most common site is the gastric antrum (66%-75%), followed by the small bowel (18%-20%), colorectal region (4%-7%), gallbladder (1%), esophagus (1%), duodenum (1%), and appendix (< 1%). However, the ileal segment is the most common site where these polyps cause intussusception^[22-35].

GENETICS

The gene *PDGFRA* is located at 4q12.

The first genetic study of IFP showed mutations in *PDGFRA*^[14]. The frequency of mutations among case series ranges from 21.7% to 69.6%. Activating *PDGFRA* mutations occur in exons 12, 14 and 18. A genotype-phenotype correlation could be established in terms of tumor location as gastric IFP harbors significantly more frequent exon 18 mutations. Exon 12 mutations are, however, associated with small bowel lesions. So far, only two cases with exon 14 mutations have been described, one originating from the small bowel the other from the stomach^[12-16].

ETIOLOGY

Historically, IFP have been thought to represent a reactive inflammatory lesion. It was assumed that IFP might be associated for example with *Helicobacter* infection or type A gastritis. After discovery of activating *PDGFRA* mutations^[14] in these tumors it became apparent that IFP represent true neoplasms which are obviously driven by activating mutations in the *PDGFRA* gene. The precise etiopathogenesis of IFPs remains unknown, but trauma, allergic reaction, genetic tendency, bacterial, physical, chemical and even metabolic stimuli have been suggested as initiators of the process. For some authors, it could be a consequence of chronic irritation and inflammation or a consequence of extreme reaction of the body to an intestinal trauma or a localized variant of eosinophilic gastroenteritis, given that it has a marked eosinophilic infiltration. The more common occurrence of these lesions in the stomach, with its coarse food content and active muscular contractions, supports a traumatic etiology, but it is difficult to account for lesions in the lower ileum on this basis^[2]. Some cases of association between IFP and Crohn's disease were reported^[36-38].

HISTOLOGY

IFP are benign. So far local recurrences have been described only anecdotally. No convincing case with invasive growth or aggressive outcome has been reported. It was suggested that IFP with concentric stromal proliferation may originate from a population of dendritic interstitial cells. Macroscopically, these tumors are pedunculated or sessile, measure 0.2-20 cm in diameter^[39-42] and project into the bowel lumen. The mucosal surface is usually ulcerated and pale. Histologically IFP arise from the submucosa and are characterized by vascular and fibroblast proliferation and an inflammatory response, dominated by eosinophils. Microscopically, it is composed of mononuclear, spindle-shaped cells, which are characteristically arranged in whorls or in an onion skin like fashion around blood vessels or mucosal glands, forming a confused or whirl-like structure. The inflammatory infiltration also includes blood vessels, eosinophils, lymphocytes, macrophages, and mastocytes. The matrix consists of fine fibrillar collagen but might also be collagen-rich. The "classic" (or gastric) type which was originally described by Josef Vanek is characterized by a heavy inflammatory infiltrate which is rich in eosinophilic granulocytes. These lesions show many spindle cells but only little collagen. Some authors have shown that there is another morphological subtype ("intestinal type") which, in contrast, is paucicellular and collagen-rich. Both cellular elements, fibroblastic spindle cells and inflammatory infiltrate, are less numerous. These tumors tend to be larger than those of the gastric type^[15]. Outside of ulcerations no necroses are found. There is no considerable proliferative activity as mitoses of the spindle cell are almost never seen and Ki67 is below 1%. Immunohistochemically, the spindle cells are mostly positive for CD34 but this feature may be absent especially in the intestinal type. PDGFRA expression is frequently found^[14]. Immunostains for KIT, DOG-1, S100 and EMA are consistently negative. This may be important in the differential diagnosis of gastrointestinal stromal tumors, perineurioma and other spindle cell lesions of the gastrointestinal tract. IFP are clearly distinct from gastrointestinal stromal tumors by their morphology, submucosal origin and clinical behavior, although both entities share common mutational subtypes of the PDGFRA gene^[16]. An immunohistochemical study of IFP showed a strong positivity for vimentin and the absence of staining for macrophages (HAM-56) expression in all cases evaluated, which suggests a major component of spindle cells best recognizable as fibroblasts. Further immunohistochemical analysis can demonstrate variable reactivity for actin, CD34, desmin, CD117 and S100^[23,43-46].

CLINICAL PRESENTATION

IFPs are usually asymptomatic, remain undiagnosed

for a long time or are incidental findings at endoscopy and laparotomy. When they are symptomatic, the clinical symptoms depend on the location and size of the tumor^[2]. Abdominal pain is the main symptom in patients with lesions in the stomach. Intussusception and obstruction are the most frequent initial symptoms when the polyp is located in the small intestine^[8,47-61]. Other GI symptoms, such as vomiting, diarrhea, bloody stools (larger polyps tend to erode and ulcerate superficially), tenesmus, and alterations in bowel habits, are also seen although their frequencies are low. Patients with IFPs in the small bowel are most likely to present with chronic episodes of colicky abdominal pain, lower GI bleeding, anemia and, more rarely, intestinal obstruction due to episodes of intestinal intussusception and rarely with necrosis and perforation^[58,62-67]. Although malignant diseases represent the major causes of intussusceptions in adults, there are few reports of intestinal obstruction and perforation caused by IFPs. Pre-operative diagnosis of intussusceptions is rare but can occur in finding a palpable mass on the abdomen or with the use of imaging techniques.

DIAGNOSIS

An accurate diagnosis is based on a good medical history, thorough physical examination, and specific imaging modalities, such as X-ray, ultrasonography (US), CT, magnetic resonance imaging (MRI), enteroclysis, endoscopic procedures, angiography, and capsule endoscopy^[17,18,69-72]. Diagnostic laparoscopy (DL) may assist in the diagnosis of intussusception in cases in which the diagnosis is suspected but not confirmed by preoperative workup. Moreover, DL can help to establish the cause and is less traumatic than an exploratory laparotomy^[48].

RADIOLOGICAL APPEARANCE

Typically, abdominal X-ray examination^[2,17,18] is the first diagnostic tool used, because obstructive symptoms dominate the clinical picture in most cases. Barium enema was the gold standard for diagnosis of intussusception until the mid-1980s. Around the same time, it was found that air could be used to diagnose and treat intussusception. Today, enteroclysis is rarely used in the diagnosis of intussusception. This invasive double-contrast imaging method is performed under fluoroscopy, MRI, or CT imaging. Although enteroclysis shows not only the inside of the lumen but also has high sensitivity and specificity for revealing small and mucosal lesions, its invasive nature limits its use. US is considered a useful tool in the diagnosis of intussusceptions. The primary imaging modality of choice is ultrasound scanning, which enables the diagnosis or exclusion of intussusception with a sensitivity of 98% and 100%, respectively, a specificity of 88%, and a negative predictive value

of 100%. Its classical imaging features include the target or doughnut sign in the transverse view and the pseudokidney, sandwich, or hayfork sign in longitudinal view. However, obesity and the presence of a large amount of air in the distended bowel loops can limit image quality and subsequent diagnostic accuracy^[70,71]. Abdominal CT is currently considered the most sensitive radiological method for confirming intussusception, with a reported diagnostic accuracy of 58%-100%. In contrast to US, CT is unaffected by the presence of gas in the bowel lumen. With CT scan the mean sensitivity, specificity, positive predictive value, and negative predictive value for diagnosing surgical enteroenteric lesions using a measured lesion length of > 3.5 cm were 100%, 57.3%, 5.7,% and 100%, respectively. Similarly, the figures for polyps with a measured axial diameter > 3 cm were 100%, 32.9%, 3.7% and 100%, respectively. MRI can contribute to the radiological diagnosis of intussusception by demonstrating the "bowel-within-bowel" or "coiled-spring" appearance. A polyp can be detected as a leading point using a combination of breathing-independent T2-weighted MRI and gadolinium-enhanced breath-hold T1-weighted imaging. A study comparing MRI and CT for the diagnosis of intestinal obstruction showed that the cause of obstruction was correctly diagnosed by CT in 71% and by MRI in 95% of cases. The sensitivity, specificity and accuracy for MRI imaging was 95%, 100% and 96%, respectively as compared to 71%, 71% and 71% for helical CT^[17,18,48,50,69-72].

ENDOSCOPIC EVALUATION

The gastric IFP may be diagnosed and treated by gastroscopy^[73]. Double-balloon enteroscopy, also known as "push-and-pull" enteroscopy, can be used to examine approximately 70-150 cm of the small bowel, and double balloon enteroscopy can examine the full length of the small bowel, both antegrade and retrograde^[74]. Capsule endoscopy and digital balloon endoscopy are newer means of diagnosing various gastrointestinal disorders. Capsule endoscopy is a noninvasive diagnostic test used to locate the source of gastrointestinal bleeding and to identify the causes of other intestinal disorders, including intussusception and various tumors. On capsule endoscopy, intussusception has been reported to appear as a mass lesion of the small bowel. Although obstructive symptoms are contraindicated for capsule endoscopy, this new method for evaluating the small bowel could be helpful in cases with long-standing abdominal pain and negative results on radiological examination, CT, or barium studies, to exclude the possibility of malignancy. Colonoscopy is useful only in cases in which colonic involvement is strongly suspected, and it allows the lesion to be diagnosed and biopsied. On colonoscopy, intussusception is seen as an intraluminal mass directed centrally and distally. However, diagnosis

is rarely made by colonoscopy, and the diagnosis is usually made during surgery^[2,48].

DIFFERENTIAL DIAGNOSIS

The underlying cause in most cases of enteroenteric intussusceptions was benign, whereas it was mostly malignant in the ileocolic and colocolic cases. That is, the potential for malignancy increased from proximal to distal intussusception. Causes of intestinal obstruction in adult patients include adhesion bands, malignant tumors and hernia in descending order of appearance. Most lead points in the GI tract involve primary or metastatic malignancy, lipomas, leiomyomas, adenomas, neurofibromas, postoperative adhesions, Meckel's diverticulum, foreign bodies, vascular anomalies, lymphoid hyperplasia, trauma, celiac disease, cytomegalovirus colitis, lymphoid hyperplasia secondary to lupus, Henoch-Schönlein purpura, Wiskott-Aldrich syndrome, appendiceal stump, or IFP. The etiologies of intussusceptions in the small bowel and the colon are quite different. In the small intestine there is a predominance of benign processes, with up to 90% of cases including hamartomas, lipomas, leiomyoma neurofibromas, adenomas, Peutz-Jeghers syndrome, IFP, adhesions, Meckel's diverticulum, lymphoid hyperplasia, trauma, celiac disease, intestinal duplication, Henoch-Schönlein purpura, appendiceal stump, and tuberculosis and more rarely IFPs. The ileum segment is the most common site where these polyps cause intussusception. Malignant lesions (either primary or metastatic) account for 14%-47% of cases of intussusception in the small intestine. On the other hand, intussusception occurring in the large bowel is more likely to have a malignant etiology and accounts for 43%-80% of cases^[2,40,48]. Colon adenocarcinoma is the most important cause of malignant large bowel intussusception. Benign lesions provoking large bowel intussusception include lipomas, leiomyomas, adenomatous polyps and endometriosis. IFPs can mimic several other tumor and non-tumor processes of the gastrointestinal tract. Differential histopathological diagnoses include spindle cell lesions, such as inflammatory fibrosarcoma, spindle-cell carcinoids, and gastrointestinal stromal tumors (GISTs). Differentiation can be difficult, especially between IFPs and GISTs. GISTs are common in the stomach and frequently present as polypoid masses. In the intestine, these tumors can present with intussusception similar to IFP. Immunohistochemistry is used to distinguish between IFPs and GISTs. Both tumors are positive for CD34 and vimentin, but GISTs are positive for CD117, while IFPs are not^[2].

TREATMENT AND PROGNOSIS

Most inflammatory fibroid polyps can be removed by endoscopy (endoscopic submucosal dissection is required)^[73,75]. Only rarely is surgery necessary.

Inflammatory fibroid polyps are benign and do not recur nor metastasize. Exploratory laparoscopy or laparotomy is frequently recommended as the best treatment for intussusceptions caused by IFP. The lesion seems to lack malignant potential and recurrence of the polyp has been reported very rarely. The operation should be performed as early as possible in order to prevent the intussusceptions from leading to ischemia, necrosis and subsequent perforation of the invaginated bowel segment. When surgery is delayed and intestinal perforation with peritonitis occurs, there is a considerable increase in morbidity and mortality. The appropriate management of adult intussusceptions remains controversial, with the debate focusing mostly on the issue of primary *en bloc* resection vs initial reduction followed by more limited resection. Thus, the most important factors in the surgical decision process in an adult patient without a histopathological diagnosis in the preoperative period and intussusception was detected during a surgical operation, and are the location and size of the mass and viability of the invaginated segment^[2,47-50]. Reduction by surgery before resection may theoretically permit more limited resection; however, the risk of potential intraluminal seeding or venous tumor dissemination during the manipulation of a malignant lesion should also be taken into consideration. The incidence of malignancy as the cause of small intestinal intussusceptions ranges from 1% to 47%, and the majority of lesions are metastatic. Therefore, recent reports have recommended initial reduction of externally viable small bowel prior to resection. The likelihood of cancer in ileocolic and colocolic intussusception is 43%-100%. The vast majority of these lesions arise as a primary lesion, in which resection without reduction is recommended^[47-50].

CONCLUSION

The debate arises over the importance of the differential diagnosis. Moreover, if surgery is performed, consideration needs to be given to what operation should be undertaken and in which patients.

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