

Review Article

Capsule Endoscopy for Ileitis with Potential Involvement of Other Sections of the Small Bowel

Hyun Seok Lee¹ and Yun Jeong Lim²

¹Department of Internal Medicine, Kyungpook National University School of Medicine, Colon Cancer Center, Kyungpook National University Medical Center, 807 Hoguk-ro, Buk-gu, Daegu 41404, Republic of Korea

²Department of Internal Medicine, Dongguk University, College of Medicine, Dongguk University Ilsan Hospital, 27 Dongguk-ro, Ilsandong-gu, Goyang 10326, Republic of Korea

Correspondence should be addressed to Yun Jeong Lim; drlimyj@gmail.com

Received 26 May 2015; Revised 11 August 2015; Accepted 23 August 2015

Academic Editor: Andrew S. Day

Copyright © 2016 H. S. Lee and Y. J. Lim. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Ileitis is defined as inflammation of the ileum. This condition includes ulcers, aphthous ulcers, erosions, and nodular or erythematous mucosa. Various etiologies are associated with ileitis. Crohn's disease, ulcerative colitis, medications such as nonsteroidal anti-inflammatory drugs, infectious conditions, neoplasms, infiltrative disorders, vasculitides, spondyloarthritis, endometriosis, and radiation therapy-related conditions involve the ileum. However, the differential diagnosis of terminal ileitis can be difficult in many cases. Video capsule endoscopy (VCE) has become a useful tool for the diagnosis of a variety of small bowel lesions. This review describes each of the various conditions associated with ileitis and the diagnostic value of VCE for ileitis, which may help identify and evaluate these conditions in clinical practice. Based on the information provided by VCE, a definitive diagnosis could be made using the patients' medical history, clinical course, laboratory and ileocolonoscopy findings, radiologic imaging findings, and histologic findings.

1. Introduction

Intubation and observation of the terminal ileum have become a standard procedure during routine screening colonoscopy, as well as in the evaluation and management of patients suspected or known to have lesions of the small bowel, including the ileum. During ileocolonoscopy, some individuals may present with various mucosal lesions of the terminal ileum. These may be limited only to the terminal ileum or manifest as part of other small bowel lesions [1, 2].

Ileitis is defined as inflammation of the ileum [3] and includes ulcers, aphthous ulcers, erosions, and nodular lesions and edematous or erythematous mucosa (Figure 1) [4, 5]. Crohn's disease (CD) affects any part of the gastrointestinal tract, and involvement of the terminal ileum is frequent [1]. Many studies on ileitis have focused on CD. However, CD does not cause all cases of ileitis. Multiple other etiologies are associated with ileitis. These include various infections, vasculitis, spondyloarthritis, and drug-related factors such as

nonsteroidal anti-inflammatory drugs (NSAIDs) (Table 1). The diagnosis of the cause of ileitis is important because patients require appropriate treatment for their condition, and misdiagnosis may delay patient management and worsen their condition [3, 5].

Video capsule endoscopy (VCE) has become a useful tool for the diagnosis of a variety of small bowel lesions. VCE is a noninvasive method for complete visualization and assessment of the mucosal surface. It is a safe technique without any reported mortalities. One of the risks associated with VCE is retention of the capsule. Patients with suspected CD have approximately 1 percent retention rate [6]. Careful consideration is necessary before performing VCE on any patient with the potential for capsule retention. Cases of capsule retention can often be managed conservatively, resulting in spontaneous passage of the capsule. If the capsule does not pass spontaneously after conservative medical therapy, it may be retrieved by device-assisted enteroscopy (DAE). Although conservative approaches or attempts at endoscopic capsule

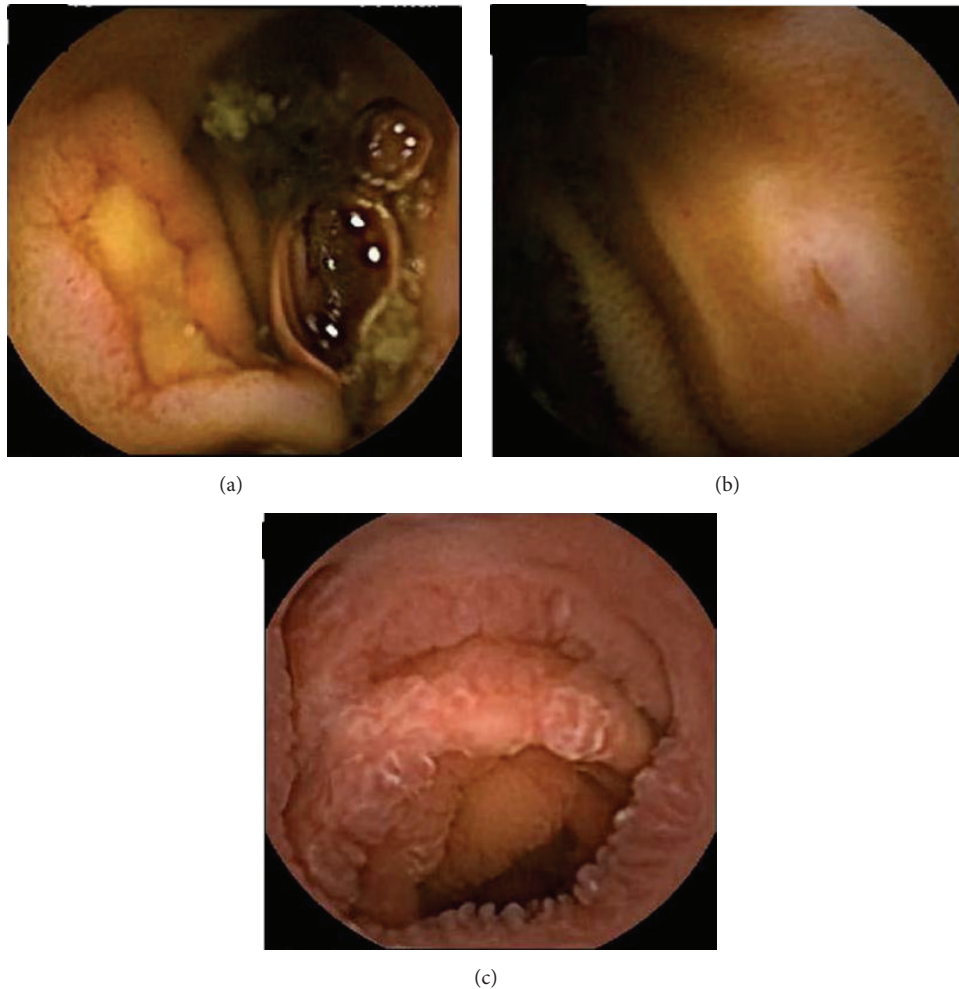


FIGURE 1: (a–c) Video capsule endoscopy findings for ileitis: (a) ulcer, (b) erosion, and (c) edematous mucosa.

retrieval are unsuccessful in some cases, only a minority of patients will need to undergo surgery in order to retrieve a retained capsule. This surgical intervention not only removes the capsule but also could be used for the treatment of the underlying cause of the retention, such as a stricture or tumor [7–10].

The clinical implications of these ileal lesions that were identified during ileocolonoscopy and the guidelines for their management remain uncertain. This review describes each of the various conditions associated with ileitis, which may have involved only the ileum or other small bowel lesions (Table 1), and the role of VCE for ileitis, which may help identify and evaluate these conditions in clinical practice.

2. Differential Diagnoses and the Role of the VCE in Patients with Ileitis in Clinical Practice

2.1. Inflammatory Bowel Disease. VCE has been widely used for the diagnosis and monitoring of patients with inflammatory bowel disease (IBD), principally CD. About 30% of

the patients with CD have exclusive small bowel involvement [11], and their diagnosis is often missed if the decision is based solely on ileocolonoscopy findings. VCE is now considered an important technique for monitoring small bowel CD and has also been employed in the management of patients with unclassified IBD [12]. A previous prospective study evaluated the diagnostic accuracies of VCE, magnetic resonance enterography (MRE), and computed tomography enterography (CTE), in 93 patients with suspected or newly diagnosed CD compared to that of ileocolonoscopy [13]. The sensitivities and specificities for the diagnosis of CD in the terminal ileum were 100% and 91% by VCE, 81% and 86% with MRE, and 76% and 85% for CTE, respectively. VCE is therefore more accurate for diagnosing subtle small bowel lesions than any other modality. VCE could be the first-line modality for the detection of ileal CD that is beyond the reach of colonoscopy [12, 13].

IBD cannot be classified as CD or ulcerative colitis (UC) using ileocolonoscopy and pathologic criteria in 10–15% of the patients. At least 30% of these patients with unclassified IBD will be reclassified as having CD during the course of their diseases, usually after identification of small bowel

TABLE 1: Causes of ileitis based on ileocolonoscopy findings.

Inflammatory bowel disease
Crohn's disease
Backwash ileitis in ulcerative colitis
Drug-related ileitis
Nonsteroidal anti-inflammatory drug enteropathy
Other drugs
Ileitis of uncertain clinical significance
Nodular lymphoid hyperplasia
Infection
<i>Actinomyces israelii</i>
<i>Anisakis</i> spp.
<i>Clostridium difficile</i>
<i>Cytomegalovirus</i>
<i>Histoplasma capsulatum</i>
<i>Mycobacterium avium</i> complex
<i>Mycobacterium tuberculosis</i>
<i>Salmonella</i> spp.
<i>Yersinia</i> spp.
Neoplasms
Lymphoma
Adenocarcinoma
Leiomyosarcoma
Carcinoid tumor
Metastatic cancer
Infiltrative disorders
Eosinophilic enteritis
Amyloidosis
Sarcoidosis
Vasculitides
Behcet's disease
Systemic lupus erythematosus
Henoch-Schonlein purpura
Other vasculitides
Spondyloarthritis
Ankylosing spondylitis
Nonradiographic axial spondyloarthritis
Undifferentiated spondyloarthritis
Reactive arthritis (Reiter syndrome)
Spondyloarthritis associated with psoriasis or psoriatic arthritis
Endometriosis
Radiation enteritis

lesions [14, 15]. Several studies have evaluated the utility of VCE for reclassification of patients with unclassified IBD. A study on the diagnostic yield of VCE in patients with UC or unclassified IBD was conducted on 120 individuals. Overall, 19 out of 120 patients (15.8%) had VCE findings consistent with the diagnosis of CD. Among these 19 patients with positive findings on VCE, 18 had also previously undergone

a small-bowel follow-through study and only one showed findings consistent with CD [16]. Another multicentric study evaluated the value of VCE in increasing diagnostic accuracy in patients with unclassified IBD. Thirty patients with unclassified IBD were included in the study. Among them, 5 were diagnosed with CD. However, interestingly, CD was diagnosed on repeated ileocolonoscopy with biopsies, in 6 out of 25 VCE-negative patients. VCE is a potentially clinically useful tool for categorizing patients with unclassified IBD [17].

Backwash ileitis refers to inflammation of the terminal ileum in patients with UC. Although the term "backwash" indicates exposure of the mucosa to the reflux of cecal contents, the precise pathogenesis is not well understood [3]. The mucosal inflammation patterns of the cecum, ascending colon, and terminal ileum are often similar to one another. The severity of ileal inflammation paralleled the severity of colonic inflammation and was more common in patients with pancolitis and cecal involvement compared to those with left-sided colitis [18, 19]. Backwash ileitis can be distinguished endoscopically from the ileitis observed in CD, on the basis of the absence of distinct ulcers in the terminal ileum [20]. Mucosal biopsies may help distinguish CD from UC in patients with backwash ileitis. The presence of granulomatous inflammation on histology also indicates ileitis in CD patients [3]. However, in the absence of granulomata or indistinguishable ileitis in IBD patients, VCE may be useful. Although VCE may not play a significant additional role in the diagnosis or management of backwash ileitis itself, as identified by ileocolonoscopy, it may provide useful information for reclassifying unclassified IBD with ileitis or altering the indeterminate current diagnosis (UC or CD). In a retrospective cohort analysis of patients with previously diagnosed IBD, 4 out of 5 patients with IC and 1 of 2 patients with unclassified IBD had their disease reclassified to CD based on newly diagnosed small bowel mucosal lesions [21].

2.2. Drug-Related Ileitis. Most drugs may cause a diffuse small bowel lesion that includes the ileum. Ulcerations due to NSAIDs can occur in the stomach and duodenum. The small bowel and colon are also susceptible to the adverse effects of NSAIDs [22]. NSAID enteropathy is usually subclinical, although some patients may present with various NSAID-induced injuries, such as ulcers, erosions, strictures, and perforations in the small bowel, including the ileum [23]. The pathogenesis is believed to involve the inhibition of intestinal prostaglandin synthesis [24].

Diagnosis may be made using direct visualization methods, such as VCE, ileocolonoscopy, and DAE. NSAID enteropathy, including ileitis, is suspected in patients with a history of NSAID use. Both elderly patients and those taking long-term NSAIDs tend to be at higher risk of NSAID enteropathy [24]. Endoscopic and VCE findings in these patients include ulcerations, erosions, and strictures. These symptoms or endoscopic findings should improve following the withdrawal of NSAIDs [3].

NSAIDs frequently lead to ileitis or colitis resembling CD. They also exacerbate preexisting CD. NSAID-induced enteropathy is often misdiagnosed as CD because of the

pathological similarity between these two diseases. Since CD usually causes long, thick inflammatory strictures rather than thin, fibrotic diaphragms and presents with ulcers that are often deeper, longitudinal, and more irregular than the sharply demarcated lesions of NSAID enteropathy, the two conditions can be distinguished from each other on this basis. Furthermore, a cobblestone appearance, inflammatory polyps, and histologic findings of granulomas, crypt abscesses, or crypt distortion suggest CD instead of NSAID enteropathy [3, 5].

Small bowel diaphragm disease is a relatively recent clinical entity, which presents with short, symmetric ileal strictures and focal bowel wall thickening. The most common cause is the long-term use of NSAIDs, which inhibit cyclooxygenase-1. Cyclooxygenase-1 inhibition results in reduced microcirculatory blood flow, localized ischemia, and ulcers. The strictures and mucosal diaphragms developed from circumferential mucosal ulceration with subsequent contractions of scar tissue rings [25]. A recent VCE study identified mucosal diaphragms in 2% of 120 patients taking long-term NSAIDs [26]. Other conditions that can result in mucosal diaphragms include potassium intake, celiac disease, eosinophilic gastroenteritis, and radiation injury [27]. Pathologically, diaphragms appear as a disk of tissue protruding circumferentially into the intestinal lumen, reducing the lumen to a small diameter. The most common presenting symptoms are abdominal pain and anemia [25, 28].

NSAID-induced small bowel injury has been retrospectively assessed using a small bowel VCE database registry [29]. The lesions were located in the jejunum (52.8%) and ileum (27.9%) in 140 patients. The most prominent findings after performing VCE were multiple ulcerations (58.6%) and erosions or aphthous ulcers (22.9%) [29].

Several other drugs rarely cause inflammation that is confined to the ileum. Localized ulceration, fibrosis, and stenosis of the ileum with obstruction occurred in patients who ingested tablets with a combination of enteric-coated potassium chloride and hydrochlorothiazide [30]. Parenteral gold therapy is associated with inflammation with edema and ulceration that is limited to the ileum. This rare complication can develop after being treated with gold therapy for rheumatoid arthritis [31]. Other types of drug-related ileitis without diffuse small bowel lesions are associated with the use of oral contraceptives and digoxin [3, 32, 33].

2.3. Ileitis of Uncertain Clinical Significance. Some asymptomatic individuals may present with ileitis, such as aphthous ulcers or small ulcerations in the terminal ileum, which are unaccompanied by lesions in the ileocecal valve or colon [2]. Advances in VCE have increased the detection of small bowel lesions in healthy, asymptomatic individuals, as well as in patients with small bowel disease [2]. Some studies on VCE have reported that small bowel mucosal breaks are found in 5% to 10% of healthy individuals [34–36], although other studies have failed to detect these lesions in healthy subjects [2, 37, 38].

These isolated terminal ileal ulcerations may be one of the earlier manifestations of serious diseases, such as CD and

intestinal tuberculosis. Some patients with aphthous ulcer-type CD later develop typical ulcer-type CD. In these patients, progression from aphthous ulcer lesions to overt CD requires a relatively long period. In other patients, aphthous ulcer lesions disappear or remain unchanged on follow-up visits [2, 39]. A recent study reported that CD is unlikely to develop in asymptomatic individuals with isolated ileitis [40].

2.4. Nodular Lymphoid Hyperplasia. Nodular lymphoid hyperplasia (NLH) of the ileum may cause ileitis. NLH of the ileum is a benign reactive process, which is also known as terminal lymphoid ileitis. It can present as an asymptomatic disease in most patients and is a rare condition in adults. Published literature on NLH mainly includes case reports and a small series of patients [1, 41, 42]. A previous study reported the case of a 13-year-old boy with a stricture of the ileum that was diagnosed as CD on small bowel follow-through. The lesion did not resolve on steroid therapy, and the patient required surgical resection of the terminal ileum. Histopathology of this region showed focal lymphoid hyperplasia instead of CD [43].

NLH of the gastrointestinal tract is characterized by the presence of multiple small nodules, which are normally between 2 and 10 mm in diameter. NLH is more commonly distributed in the small bowel and mainly involves the terminal ileum, although it may also be found in the stomach, colon, or rectum [44]. The pathogenesis is largely unknown. NLH can occur in all age groups, but it is primarily diagnosed in children and can also affect adults with or without immunodeficiency. Some patients have associated diseases, such as common variable immunodeficiency disease, selective IgA deficiency, *Giardia lamblia* infection, human immunodeficiency virus (HIV) infection, celiac disease, or *Helicobacter pylori* infection [41]. NLH in a defunctionalized colon was reported in an adult immunocompetent patient who underwent ileostomy because of localized regional ileitis [45].

A diagnosis of NLH is established by endoscopy, VCE, or small bowel barium studies and confirmed histologically. The condition is defined histologically by markedly hyperplastic, mitotically active germinal centers, and well-defined lymphocyte mantles found in the lamina propria or in the superficial submucosa [46]. A retrospective study was conducted to test the ability of MR enterography to differentiate NLH of the ileum from CD. NLH altered both subjective and quantitative MRI parameters, including the T2 signal, contrast enhancement, and mural thickness. NLH was erroneously diagnosed as CD in a blinded assessment, among four out of nine cases (44%), whereas all cases of CD were correctly classified. NLH of the ileum may be indistinguishable from CD on MR enterography [47]. When NLH is involved in the small intestine, VCE is important for the diagnosis, in order to exclude complications such as lymphoma and to determine the extent of the disease in the small bowel [41]. Treatment is directed towards associated conditions because the disorder itself generally requires no intervention. NLH is a risk factor for both intestinal and very rarely extraintestinal lymphoma. Since there is a risk of malignant transformation, surveillance VCE and small bowel

series are recommended by some authors, in patients with small bowel involvement of the NLH [41, 48].

2.5. Ileitis Caused by Intestinal Infection. Intestinal infections usually present with an acute episode of diarrhea, which resolves spontaneously. As a result, an endoscopic assessment is not needed in most patients. In contrast to acute diarrhea, patients with persistent or chronic diarrhea require further evaluation. Endoscopy is the main diagnostic procedure as it facilitates the examination of the mucosa. Biopsy specimens can also be obtained in order to identify the causal pathogens. Biopsies are frequently performed during ileocolonoscopy. These procedures have a limited range of examination because a large part of the small intestines is excluded. As a result, VCE is an extremely useful tool, since it allows assessments of the intestinal mucosa with a high diagnostic yield and can have a direct impact on the management of such patients. VCE can detect erosions or ulcers involving the intestinal mucosa in patients with a variety of bacterial infections, viruses, fungus, or parasites (Table 1). Moreover, the lesions detected by VCE can be subsequently confirmed by biopsies obtained during DAE [49].

Although intestinal infections by many pathogens can involve the ileum, *Yersinia* and abdominal tuberculosis infections may specifically involve the ileum. The ileocecal region is the most common site of intestinal tuberculosis caused by a *Mycobacterium tuberculosis* infection [50]. Ileocolonoscopy findings of intestinal tuberculosis may include ulcers, strictures, pseudopolyps, nodules, fistulas, or deformed ileocecal valves. The main differential diagnosis of ileocecal tuberculosis at endoscopy is CD [3, 51]. Biopsy for culture and histopathological evaluation can be useful in definitively distinguishing between these two disorders. Longitudinal ulcers, skip lesions, anorectal lesions, aphthous ulcers, and a cobblestone appearance were significantly more frequent in patients with CD than in those with intestinal tuberculosis. Transverse ulcers, a patulous ileocecal valve, scars or pseudopolyps, and the involvement of fewer than four segments were more commonly observed in patients with intestinal tuberculosis than in those with CD [52].

Yersinia enterocolitica infection occurs mainly in the terminal ileum and ileocecal valve and causes mucosal ulceration and thickening of the ileal wall. The diagnosis is made most directly by ileocolonoscopy with biopsy and culture. Endoscopic features of *Yersinia* infection include round or oval elevations with ulcerations in the terminal ileum, and small ulcers may be detected on the ileocecal valve and the cecum. In contrast to CD ulcers, *Yersinia* ulcers are mostly uniform in size and shape [1, 53].

Although VCE can detect erosions or ulcers involving the intestinal mucosa in patients with an intestinal infection, VCE may not have a significant role in the diagnosis and management of these conditions because they usually are treated with empirical agents and supportive measures in actual clinical practice.

2.6. Neoplasms. Ileitis presents with ulcers, erosions, nodular lesions, and edematous or erythematous mucosa of the

ileum. Small bowel neoplasms may also manifest as the appearance of ileitis when the small bowel lesions include the ileum or only involve the ileum. Small bowel malignancy may represent less than 2% of all malignant tumors of the gastrointestinal tract. VCE enables a more detailed inspection of the small bowel. A registry-based series of 67,843 patients with small bowel tumors was reported to the National Cancer Database. In these patients, the distribution of primary tumors in the small intestine included carcinoid tumors (45%), lymphomas (21%), adenocarcinomas (13%), and sarcomas of the ileum (15%) [54]. These lesions usually manifest as wall thickenings, areas of luminal narrowing, and small ulcers and erosions that resemble ileitis.

The utility of VCE in the diagnosis of small bowel neoplasm was demonstrated in a retrospective analysis of the records of 562 patients who underwent VCE for a variety of indications, including obscure gastrointestinal bleeding and persistent abdominal pain [55]. Fifty patients (8.9%) were diagnosed with small bowel tumors, and 48% of these were malignant lesions. The types of tumors diagnosed by VCE included 8 adenocarcinomas (1.4%), 10 carcinoids (1.8%), 4 gastrointestinal stromal tumors (0.7%), 5 lymphomas (0.9%), and 3 inflammatory polyps as well as one of each of lymphangioma, lymphangiectasia, hemangioma, hamartoma, and tubular adenoma. This incidence of small bowel tumors suggests an important role for VCE in the diagnosis of patients with suspected small bowel lesions. VCE may lead to the earlier detection and treatment of small bowel tumors, including those with ileum involvement [55].

2.7. Infiltrative Disorders. Ileitis includes ulcers, erosions, and nodular lesions, as well as edematous or erythematous mucosa of the ileum. Infiltrative disorders may also manifest as ileitis when the small bowel lesions involve the ileum.

2.7.1. Eosinophilic Enteritis. The entire gastrointestinal tract from the esophagus to the colon can be affected in patients with eosinophilic gastroenteritis, an inflammatory disorder characterized by eosinophilic infiltration of the gastrointestinal tract. Endoscopic findings of eosinophilic ileitis include erythema, polypoid lesions, erosion, or ulceration. The diagnosis is established by the presence of an elevated number of expected eosinophils on microscopic examination of biopsies of the ileal mucosa [56]. Although the cutoff value for the definition of a pathological infiltration of eosinophils is still debated, the threshold of 20 eosinophils per high power field ($\times 400$) is used for the diagnosis of eosinophilic enteritis [57, 58].

2.7.2. Amyloidosis. Amyloidosis refers to the extracellular tissue deposition of fibrils composed of low molecular weight subunits of a variety of proteins. Amyloid deposition in the gastrointestinal tract is greatest in the small intestine. Patients with gastrointestinal amyloidosis usually present with bleeding, malabsorption, protein-losing gastroenteropathy, or gastrointestinal dysmotility [59]. Endoscopic findings in the ileum in these patients include erosions, ulcerations, friability, and wall thickening. The diagnosis of gastrointestinal

amyloid requires a tissue biopsy with positive staining of the amyloid with Congo red or the presence of amyloid fibrils on electron microscopy [60].

2.7.3. Sarcoidosis. Sarcoidosis is a systemic granulomatous disease of unknown etiology, which is characterized by the formation of noncaseating granulomas. Although the stomach is the most commonly involved portion of the gastrointestinal tract, sarcoidosis has also been described in the esophagus, small intestine, appendix, colon, rectum, pancreas, and peritoneum [61]. Endoscopy or VCE may show nodules or aphthous erosions in the small bowel, including the ileum. The diagnosis of ileal sarcoidosis is based on the presence of noncaseating granulomas in a biopsy of the affected lesion [62].

2.8. Vasculitides. Vasculitides may manifest as ileitis when small bowel lesions involve the ileum and are defined by the presence of inflammatory leukocytes in vessel walls with reactive damage to the mural structures. Vasculitides involving the gastrointestinal tract are usually part of a systemic process and only rarely cause ileitis. The most common vasculitides with gastrointestinal involvement include Behcet's disease, systemic lupus erythematosus, and Henoch-Schonlein purpura [3]. Discrete ulcerations are most often seen in the terminal ileum, cecum, ascending colon, and esophagus in patients with Behcet's disease [63].

Endoscopy should be performed with caution in patients with suspected gastrointestinal involvement of vasculitis because of the increased risk of perforation of the edematous, ischemic bowel. VCE may be a useful tool for the diagnosis of ileal vasculitis because noninvasive visualization of small bowel mucosal lesions, such as irregular erosions and ulcerations, is possible [64].

2.9. Spondyloarthritis. Ileitis has been observed in association with various features of spondyloarthritis. The clinical features of spondyloarthritis are inflammation of the axial joints, asymmetric oligoarthritis, dactylitis, and enthesitis. Spondyloarthritis includes ankylosing spondylitis, nonradiographic axial spondyloarthritis, undifferentiated spondyloarthritis, reactive arthritis (Reiter syndrome), spondyloarthritis associated with psoriasis or psoriatic arthritis, and spondyloarthritis associated with CD and UC [65]. Additional features of spondyloarthritis include bowel inflammation. There is a strong relationship between active peripheral arthritis and histological gut inflammation. Up to two-thirds of patients with spondyloarthritis have histologic signs of bowel inflammation. Two types of lesions have been identified. An acute lesion, which resembles acute bacterial ileitis and chronic ileitis, is often indistinguishable from CD [66]. Spondyloarthritis was diagnosed in 36% of patients with IBD [67]. VCE enables visualization of small bowel lesions consistent with CD in 33% of these patients [12].

2.10. Endometriosis. Ileal involvement of endometriosis is rarely associated with ileitis. Endometriosis is the presence of endometrial glands and stroma at extrauterine sites. Bowel

endometriosis is most commonly found on the rectosigmoid colon. In a case series of 168 patients who underwent surgical treatment of endometriosis of the bowel, the terminal ileum was involved in 1% [68]. Ileal endometriosis may present with diarrhea, constipation, abdominal pain, or bloating, which may mimic CD. Although abdominal imaging techniques can identify some bowel lesions, they are unable to differentiate between endometriosis and other conditions. These lesions can be more reliably detected and evaluated via laparoscopy [68, 69].

2.11. Radiation Enteritis. Injury to the intestine can occur following radiation therapy for a malignant lesion and may affect the ileum, sigmoid colon, and rectum in the radiation field. Radiation enteritis tends to involve specific areas depending on the radiation ports. Chronic radiation injury is characterized by telangiectasia, a plethora of neovascularity, and spiraled vessels with ulcerated epithelium. The diagnosis is usually established by suggestive radiologic findings in patients with compatible clinical features who have a history of radiation exposure. Abdominal CT may show nonspecific thickening or stricture of bowel segments. Deep insertion into the ileum with retrograde DAE may be disturbed by abdominal adhesion. VCE can be used to identify these lesions, despite their diminutive size. A case of a patient with radiation enteritis was reported in 2007. In that patient, colonoscopy revealed normal colonic mucosa and blood passing through the ileocecal valve, but the colonoscope could not be passed into the terminal ileum. VCE indicated that the bleeding was from edematous, fissured mucosa in the ileum [70]. Another study reported the case of a middle-aged woman who received radiotherapy after surgical resection of a uterine leiomyosarcoma. She presented with severe anemia, loose stools, and abdominal pain. Abdominal CT was normal and colonoscopy revealed fresh blood and small clots on normal mucosal in the colon. The VCE demonstrated mucosal atrophy, villous edema, and stricture, as well as diffuse bleeding from the terminal ileum, and radiation enteritis was diagnosed [71]. The largest study, which involved 15 patients, concluded that VCE can safely and effectively diagnose small intestinal radiation enteritis. No episodes of capsule retention were identified [72]. In a recent case series of three patients who were treated with pelvic radiation therapy, abdominal CT and enteroclysis did not show stenosis of the small bowel and the bleeding point remained unknown. DAE could not reach the causal lesion due to the pelvic adhesion. They subsequently underwent VCE, which revealed diffuse ileitis with multiple angioectasias. Active bleeding from radiation enteritis was diagnosed with VCE without retention in each of three patients [73]. A thick wall or strictured segment of the ileum may suggest possible VCE retention, but the risk of retention is sometimes difficult to predict. If radiation enteritis is suspected as the cause of small bowel bleeding and DAE may not accomplish deeper insertion into the ileum, VCE is recommended as the initial tool for diagnosing radiation enteritis when small bowel stenosis has not been previously detected. Most of all, the risk of retention should be assessed using abdominal CT or enteroclysis before performing VCE [73].

3. Conclusions

Various conditions are associated with ileitis. The utility of VCE has been established in the diagnosis of CD. VCE may provide important clinical information for patients with many other conditions that cause ileitis because of its excellent visualization of the entire small bowel mucosa, including the ileum, its excellent tolerability, and safety profile. One limitation of the VCE is its lack of the tissue sampling ability. VCE has the advantage directing DAE to identify the correct location in order to obtain biopsies. The differential diagnosis of ileitis can be difficult in many cases. Based on the information provided by VCE, a definitive diagnosis can often be made using the patient's medical history, clinical course, laboratory and ileocolonoscopy findings, radiologic imaging results, and histologic findings.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- [1] D. Bojic and S. Markovic, "Terminal ileitis is not always Crohn's disease," *Annals of Gastroenterology*, vol. 24, no. 4, pp. 271–275, 2011.
- [2] H.-S. Chang, D. Lee, J. C. Kim et al., "Isolated terminal ileal ulcerations in asymptomatic individuals: natural course and clinical significance," *Gastrointestinal Endoscopy*, vol. 72, no. 6, pp. 1226–1232, 2010.
- [3] S. Dilauro and N. F. Crum-Cianflone, "Ileitis: when it is not Crohn's disease," *Current Gastroenterology Reports*, vol. 12, no. 4, pp. 249–258, 2010.
- [4] S. H. Jeong, K. J. Lee, Y. B. Kim, H. C. Kwon, S. J. Sin, and J. Y. Chung, "Diagnostic value of terminal ileum intubation during colonoscopy," *Journal of Gastroenterology and Hepatology*, vol. 23, no. 1, pp. 51–55, 2008.
- [5] H. A. Park, S. Y. Nam, S. K. Lee et al., "The Korean guideline for gastric cancer screening," *Journal of the Korean Medical Association*, vol. 58, no. 5, p. 373, 2015.
- [6] A. S. Cheifetz, A. A. Kornbluth, P. Legnani et al., "The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease," *American Journal of Gastroenterology*, vol. 101, no. 10, pp. 2218–2222, 2006.
- [7] J. H. Cheon, Y.-S. Kim, I.-S. Lee et al., "Can we predict spontaneous capsule passage after retention? A nationwide study to evaluate the incidence and clinical outcomes of capsule retention," *Endoscopy*, vol. 39, no. 12, pp. 1046–1052, 2007.
- [8] E. J. Despott and C. Fraser, "Small bowel endoscopy in inflammatory bowel disease," *Best Practice and Research: Clinical Gastroenterology*, vol. 26, no. 3, pp. 279–291, 2012.
- [9] R. Goel, J. Hardman, M. Gulati, and J. O'Donohue, "Video capsule retention in inflammatory bowel disease: an unusual presentation and discussion of retrieval methods," *Case Reports in Gastrointestinal Medicine*, vol. 2013, Article ID 607142, 4 pages, 2013.
- [10] M. Pennazio, C. Spada, R. Eliakim et al., "Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline," *Endoscopy*, vol. 47, no. 04, pp. 352–386, 2015 (Chinese).
- [11] J. Cosnes, C. Gowerrousseau, P. Seksik, and A. Cortot, "Epidemiology and natural history of inflammatory bowel diseases," *Gastroenterology*, vol. 140, no. 6, pp. 1785–1794, 2011.
- [12] U. Kopylov and E. G. Seidman, "Role of capsule endoscopy in inflammatory bowel disease," *World Journal of Gastroenterology*, vol. 20, no. 5, pp. 1155–1164, 2014.
- [13] M. D. Jensen, T. Nathan, S. R. Rafaelsen, and J. Kjeldsen, "Diagnostic accuracy of capsule endoscopy for small bowel Crohn's disease is superior to that of MR enterography or CT enterography," *Clinical Gastroenterology and Hepatology*, vol. 9, no. 2, pp. 124.e1–129.e1, 2011.
- [14] M. Guindi and R. H. Riddell, "Indeterminate colitis," *Journal of Clinical Pathology*, vol. 57, no. 12, pp. 1233–1244, 2004.
- [15] R. Eliakim, "The impact of wireless capsule endoscopy on gastrointestinal diseases," *Southern Medical Journal*, vol. 100, no. 3, pp. 235–236, 2007.
- [16] S. Mehdizadeh, G. Chen, P. J. Enayati et al., "Diagnostic yield of capsule endoscopy in ulcerative colitis and inflammatory bowel disease of unclassified type (IBDU)," *Endoscopy*, vol. 40, no. 1, pp. 30–35, 2008.
- [17] V. Maunoury, G. Savoye, A. Bourreille et al., "Value of wireless capsule endoscopy in patients with indeterminate colitis (inflammatory bowel disease type unclassified)," *Inflammatory Bowel Diseases*, vol. 13, no. 2, pp. 152–155, 2007.
- [18] A. S. Abdelrazeq, T. R. Wilson, D. L. Leitch, J. N. Lund, and S. H. Leveson, "Ileitis in ulcerative colitis: is it a backwash?" *Diseases of the Colon and Rectum*, vol. 48, no. 11, pp. 2038–2046, 2005.
- [19] E. R. Paine, "Colonoscopic evaluation in ulcerative colitis," *Gastroenterology Report*, vol. 2, no. 3, pp. 161–168, 2014.
- [20] J. A. Leighton, B. Shen, T. H. Baron et al., "ASGE guideline: endoscopy in the diagnosis and treatment of inflammatory bowel disease," *Gastrointestinal Endoscopy*, vol. 63, no. 4, pp. 558–565, 2006.
- [21] S. A. Cohen, I. M. Gralnek, H. Ephrath et al., "Capsule endoscopy may reclassify pediatric inflammatory bowel disease: a historical analysis," *Journal of Pediatric Gastroenterology and Nutrition*, vol. 47, no. 1, pp. 31–36, 2008.
- [22] I. Bjarnason, J. Hayllar, A. J. Macpherson, and A. S. Russell, "Side effects of nonsteroidal anti-inflammatory drugs on the small and large intestine in humans," *Gastroenterology*, vol. 104, no. 6, pp. 1832–1847, 1993.
- [23] P. Y. Kwo and W. J. Tremaine, "Nonsteroidal anti-inflammatory drug-induced enteropathy: case discussion and review of the literature," *Mayo Clinic Proceedings*, vol. 70, no. 1, pp. 55–61, 1995.
- [24] G. R. Gibson, E. B. Whitacre, and C. A. Ricotti, "Colitis induced by nonsteroidal anti-inflammatory drugs. Report of four cases and review of the literature," *Archives of Internal Medicine*, vol. 152, no. 3, pp. 625–632, 1992.
- [25] K. T. Flicek, A. K. Hara, G. De Petris, S. F. Pasha, A. D. Yadav, and C. D. Johnson, "Diaphragm disease of the small bowel: a retrospective review of CT findings," *American Journal of Roentgenology*, vol. 202, no. 2, pp. W140–W145, 2014.
- [26] L. Maiden, B. Thjodleifsson, A. Seigal et al., "Long-term effects of nonsteroidal anti-inflammatory drugs and cyclooxygenase-2 selective agents on the small bowel: a cross-sectional capsule enteroscopy study," *Clinical Gastroenterology and Hepatology*, vol. 5, no. 9, pp. 1040–1045, 2007.

- [27] G. De Petris and J. I. López, "Histopathology of diaphragm disease of the small intestine: a study of 10 cases from a single institution," *American Journal of Clinical Pathology*, vol. 130, no. 4, pp. 518–525, 2008.
- [28] I. Sarantitis, A. D. Gerrard, R. Teasdale, and S. Pettit, "Small bowel diaphragm disease mimicking malignancy," *BMJ Case Reports*, vol. 2015, 2015.
- [29] K. N. Shim, E. M. Song, Y. T. Jeon et al., "Long-term outcomes of NSAID-induced small intestinal injury assessed by capsule endoscopy in Korea: a nationwide multicenter retrospective study," *Gut and Liver*, 2014.
- [30] D. J. Buchan and C. S. Houston, "Small bowel ulceration associated with enteric-coated potassium chloride and hydrochlorothiazide," *Canadian Medical Association Journal*, vol. 92, pp. 176–179, 1965.
- [31] D. Geltner, M. Sternfeld, S. A. Becker, and M. Kori, "Gold-induced ileitis," *Journal of Clinical Gastroenterology*, vol. 8, no. 2, pp. 184–186, 1986.
- [32] R. K. Kurup and P. A. Kurup, "Hypothalamic digoxin, hemispheric chemical dominance, and inflammatory bowel disease," *International Journal of Neuroscience*, vol. 113, no. 9, pp. 1221–1240, 2003.
- [33] J. P. Wright, "Factors influencing first relapse in patients with Crohn's disease," *Journal of Clinical Gastroenterology*, vol. 15, no. 1, pp. 12–16, 1992.
- [34] D. Y. Graham, A. R. Opekun, F. F. Willingham, and W. A. Qureshi, "Visible small-intestinal mucosal injury in chronic NSAID users," *Clinical Gastroenterology and Hepatology*, vol. 3, no. 1, pp. 55–59, 2005.
- [35] J. L. Goldstein, G. M. Eisen, B. Lewis, I. M. Gralnek, S. Zlotnick, and J. G. Fort, "Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo," *Clinical Gastroenterology and Hepatology*, vol. 3, no. 2, pp. 133–141, 2005.
- [36] T. Matsumoto, T. Kudo, M. Esaki et al., "Prevalence of non-steroidal anti-inflammatory drug-induced enteropathy determined by double-balloon endoscopy: a Japanese multicenter study," *Scandinavian Journal of Gastroenterology*, vol. 43, no. 4, pp. 490–496, 2008.
- [37] L. Maiden, B. Thjodleifsson, A. Theodors, J. Gonzalez, and I. Bjarnason, "A quantitative analysis of NSAID-induced small bowel pathology by capsule enteroscopy," *Gastroenterology*, vol. 128, no. 5, pp. 1172–1178, 2005.
- [38] H. Endo, K. Hosono, M. Inamori et al., "Incidence of small bowel injury induced by low-dose aspirin: a crossover study using capsule endoscopy in healthy volunteers," *Digestion*, vol. 79, no. 1, pp. 44–51, 2009.
- [39] T. Matsumoto, M. Iida, S. Nakamura, K. Hizawa, T. Yao, and M. Fujishima, "Crohn's disease of aphthous type: serial changes in intestinal lesions," *British Journal of Radiology*, vol. 73, no. 874, pp. 1046–1051, 2000.
- [40] E. L. Courville, C. A. Siegel, T. Vay, A. R. Wilcox, A. A. Suriawinata, and A. Srivastava, "Isolated asymptomatic ileitis does not progress to overt Crohn disease on long-term follow-up despite features of chronicity in ileal biopsies," *The American Journal of Surgical Pathology*, vol. 33, no. 9, pp. 1341–1347, 2009.
- [41] A. Albuquerque, "Nodular lymphoid hyperplasia in the gastrointestinal tract in adult patients: a review," *World Journal of Gastrointestinal Endoscopy*, vol. 6, no. 11, pp. 534–540, 2014.
- [42] D. C. Schwartz, C. E. Cole, Y. Sun, and R. F. Jacoby, "Diffuse nodular lymphoid hyperplasia of the colon: polyposis syndrome or normal variant?" *Gastrointestinal Endoscopy*, vol. 58, no. 4, pp. 630–632, 2003.
- [43] I. Ganly and P. J. Shouler, "Focal lymphoid hyperplasia of the terminal ileum mimicking crohn's disease," *British Journal of Clinical Practice*, vol. 50, no. 6, pp. 348–349, 1996.
- [44] M. Ranchod, K. J. Lewin, and R. F. Dorfman, "Lymphoid hyperplasia of the gastrointestinal tract. A study of 26 cases and review of the literature," *The American Journal of Surgical Pathology*, vol. 2, no. 4, pp. 383–400, 1978.
- [45] A. D. Shiff, D. G. Sheahan, and S. S. Schwartz, "Nodular lymphoid hyperplasia in a defunctionalized colon," *Gastrointestinal Endoscopy*, vol. 19, no. 3, pp. 144–145, 1973.
- [46] J.-C. Rambaud, P. De Saint-Louvent, R. Marti et al., "Diffuse follicular lymphoid hyperplasia of the small intestine without primary immunoglobulin deficiency," *The American Journal of Medicine*, vol. 73, no. 1, pp. 125–132, 1982.
- [47] A. A. Plumb, D. A. Pendsé, S. McCartney, S. Punwani, S. Halligan, and S. A. Taylor, "Lymphoid nodular hyperplasia of the terminal ileum can mimic active crohn disease on MR enterography," *American Journal of Roentgenology*, vol. 203, no. 4, pp. W400–W407, 2014.
- [48] Y. Bayraktar, O. Ersoy, and C. Sokmensuer, "The findings of capsule endoscopy in patients with common variable immunodeficiency syndrome," *Hepato-Gastroenterology*, vol. 54, no. 76, pp. 1034–1037, 2007.
- [49] G. Gay, M. Delvaux, and M. Frederic, "Capsule endoscopy in non-steroidal anti-inflammatory drugs-enteropathy and miscellaneous, rare intestinal diseases," *World Journal of Gastroenterology*, vol. 14, no. 34, pp. 5237–5244, 2008.
- [50] L. S. Farer, A. M. Lowell, and M. P. Meador, "Extrapulmonary tuberculosis in the United States," *American Journal of Epidemiology*, vol. 109, no. 2, pp. 205–217, 1979.
- [51] J. F. Alvares, H. Devarbhavi, P. Makhija, S. Rao, and R. Kottoor, "Clinical, colonoscopic, and histological profile of colonic tuberculosis in a tertiary hospital," *Endoscopy*, vol. 37, no. 4, pp. 351–356, 2005.
- [52] Y. J. Lee, S.-K. Yang, J.-S. Byeon et al., "Analysis of colonoscopic findings in the differential diagnosis between intestinal tuberculosis and Crohn's disease," *Endoscopy*, vol. 38, no. 6, pp. 592–597, 2006.
- [53] T. Matsumoto, M. Iida, T. Matsui et al., "Endoscopic findings in *Yersinia enterocolitica* enterocolitis," *Gastrointestinal Endoscopy*, vol. 36, no. 6, pp. 583–587, 1990.
- [54] K. Y. Bilimoria, D. J. Bentrem, J. D. Wayne, C. Y. Ko, C. L. Bennett, and M. S. Talamonti, "Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years," *Annals of Surgery*, vol. 249, no. 1, pp. 63–71, 2009.
- [55] G. M. Cobrin, R. H. Pittman, and B. S. Lewis, "Increased diagnostic yield of small bowel tumors with capsule endoscopy," *Cancer*, vol. 107, no. 1, pp. 22–27, 2006.
- [56] M. Lee, W. G. Hodges, T. L. Huggins, and E. L. Lee, "Eosinophilic gastroenteritis," *Southern Medical Journal*, vol. 89, no. 2, pp. 189–194, 1996.
- [57] G. Pineton de Chambrun, P. Desreumaux, and A. Cortot, "Eosinophilic enteritis," *Digestive Diseases*, vol. 33, no. 2, pp. 183–189, 2015.
- [58] M.-J. Chen, C.-H. Chu, S.-C. Lin, S.-C. Shih, and T.-E. Wang, "Eosinophilic gastroenteritis: clinical experience with 15 patients," *World Journal of Gastroenterology*, vol. 9, no. 12, pp. 2813–2816, 2003.

- [59] S. Petre, I. A. Shah, and N. Gilani, "Review article: gastrointestinal amyloidosis—clinical features, diagnosis and therapy," *Alimentary Pharmacology and Therapeutics*, vol. 27, no. 11, pp. 1006–1016, 2008.
- [60] S. Tada, M. Iida, A. Iwashita et al., "Endoscopic and biopsy findings of the upper digestive tract in patients with amyloidosis," *Gastrointestinal Endoscopy*, vol. 36, no. 1, pp. 10–14, 1990.
- [61] D. M. Warshauer and J. K. T. Lee, "Imaging manifestations of abdominal sarcoidosis," *American Journal of Roentgenology*, vol. 182, no. 1, pp. 15–28, 2004.
- [62] E. C. Ebert, M. Kierson, and K. D. Hagspiel, "Gastrointestinal and hepatic manifestations of sarcoidosis," *American Journal of Gastroenterology*, vol. 103, no. 12, pp. 3184–3193, 2008.
- [63] J. W. Griffin Jr., H. B. Harrison, F. J. Tedesco, and L. R. Mills, "Behcet's disease with multiple sites of gastrointestinal involvement," *Southern Medical Journal*, vol. 75, no. 11, pp. 1405–1408, 1982.
- [64] B. Stancanelli, A. Vita, M. Vinci, A. Magnano, and F. Purrelloprof, "Bleeding of small bowel in Henoch-Schönlein syndrome: the successful diagnostic role of video capsule endoscopy," *American Journal of Medicine*, vol. 119, no. 1, pp. 82–84, 2006.
- [65] H. Zeidler and B. Amor, "The Assessment in Spondyloarthritis International Society (ASAS) classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general: the spondyloarthritis concept in progress," *Annals of the Rheumatic Diseases*, vol. 70, no. 1, pp. 1–3, 2011.
- [66] F. De Keyser, D. Baeten, F. Van den Bosch et al., "Gut inflammation and spondyloarthropathies," *Current Rheumatology Reports*, vol. 4, no. 6, pp. 525–532, 2002.
- [67] C. Stolwijk, M. Pierik, R. Landewé, A. Masclee, and A. Van Tubergen, "Prevalence of self-reported spondyloarthritis features in a cohort of patients with inflammatory bowel disease," *Canadian Journal of Gastroenterology*, vol. 27, no. 4, pp. 199–205, 2013.
- [68] R. M. A. Pereira, A. Zanatta, C. D. L. Preti, F. J. F. de Paula, E. L. A. da Motta, and P. C. Serafini, "Should the gynecologist perform laparoscopic bowel resection to treat endometriosis? Results over 7 years in 168 patients," *Journal of Minimally Invasive Gynecology*, vol. 16, no. 4, pp. 472–479, 2009.
- [69] R. K. Yantiss, P. B. Clement, and R. H. Young, "Endometriosis of the intestinal tract: a study of 44 cases of a disease that may cause diverse challenges in clinical and pathologic evaluation," *American Journal of Surgical Pathology*, vol. 25, no. 4, pp. 445–454, 2001.
- [70] Y. Kopelman, G. Groissman, and Z. Fireman, "Radiation enteritis diagnosed by capsule endoscopy," *Gastrointestinal Endoscopy*, vol. 66, no. 3, p. 599, 2007.
- [71] J. Schembri, M. Azzopardi, and P. Ellul, "Small bowel radiation enteritis diagnosed by capsule endoscopy," *BMJ Case Reports*, vol. 2014, 2014.
- [72] H. M. Kim, Y. J. Kim, H. J. Kim, S. W. Park, S. Bang, and S. Y. Song, "A pilot study of capsule endoscopy for the diagnosis of radiation enteritis," *Hepato-Gastroenterology*, vol. 58, no. 106, pp. 459–464, 2011.
- [73] M. Nakamura, Y. Hirooka, O. Watanabe et al., "Three cases with active bleeding from radiation enteritis that were diagnosed with video capsule endoscopy without retention," *Nagoya Journal of Medical Science*, vol. 76, no. 3-4, pp. 369–374, 2014.