

Primary colorectal lymphoma: computed tomography and double-contrast barium enema examination findings with histopathological correlation in 19 patients

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Background: Primary colorectal lymphoma (PCL) is a rare disorder, the accurate imaging diagnosis of which remains a clinical challenge. This study aimed to characterize the imaging features of PCL by double-contrast barium enema (DCBE) examination and computed tomography (CT) and correlate them with histopathological findings.

Methods: DCBE (n=6) and CT (n=19) findings for 19 pathologically proven PCLs were evaluated and compared with histopathological findings in this retrospective analysis.

Results: Non-Hodgkin lymphoma was present in all patients, and the most common histological type was diffuse large B-cell lymphoma (63.2%, 12/19). The most common site was the ileocecum (84.2%, 16/19). CT revealed circumferential infiltrative lesions (68.4%, 13/19), polypoid masses (26.3%, 5/19) and ulcerative lesions (5.3%, 1/19). Most (94.7%, 18/19) lesions appeared as moderate enhancements. Fourteen (73.7%, 14/19) patients had serous membrane infiltration presenting as a poorly defined serous membrane and focal opacities in the pericolonic fat. Regional lymph node involvement was observed in twelve (63.2%, 12/19) patients who presented with aggregated nodules or masses. Frequent findings of the DCBE exam included a filling defect and niche with slight mucosal destruction, mild luminal narrowing and preserved peristalsis. The imaging appearance reflected the gross pathological findings well, although the preoperative diagnostic accuracy was low.

Conclusions: The imaging features of PCL have a relatively characteristic appearance but are still, at times, hardly differentiated from carcinoma. Familiarity with the radiological features of PCL on DCBE and CT can help ensure a correct diagnosis.

Keywords: Computed tomography (CT); double-contrast barium enema (DCBE); primary colorectal lymphoma (PCL)

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Introduction

Primary colorectal lymphoma (PCL) is a rare disorder that has been reported to occur in 0.4% of all colorectal malignancies (1). The colon and rectum are also uncommon sites for lymphoma compared with the rest of the gastrointestinal tract, accounting for 10-20% of all cases of gastrointestinal lymphoma (2-6). The diagnostic criteria of PCL were initially established by Dawson et al. (7) in 1961. A diagnosis of PCL requires histological confirmation of a lymphoma fulfilling the following strict criteria: no superficial enlarged lymph nodes on first examination of the patient; chest radiographs showing no obvious enlargements of the mediastinal nodes; total and differential white blood cell counts within normal limits; laparotomy showing only regional nodes affected by disease; and tumor-free liver and spleen. Subsequently, the criteria were extended in the modern era to encompass a few wider ranges of manifestations, including all patients who present with lymphoma that apparently originated from a colorectal site (5,8,9), in accord with the alternative definition of extranodal lymphoma (10,11).

The imaging features of PCL are rarely described. Double-contrast barium enema (DCBE) and computed tomography (CT) are the two main radiographic procedures used to diagnose and evaluate colon lymphoma. In this article, we describe the spectrum of PCL via a retrospective evaluation of the imaging features and histopathological findings in 19 patients with pathologically proven PCL.

Methods

This study was approved by the Institutional Review Board at Cancer Hospital, Chinese Academy of Medical Sciences. Because the study was retrospective and the data were analyzed anonymously, the need for written informed consent was waived.

Patients

Patients who presented with predominant colorectal lesions were defined as having PCL according to the definition for primary gastrointestinal tract lymphoma proposed in previous reports (5,8,9). A search of the pathology files of colorectal neoplasms (n=17,108) at our institution revealed that PCL was diagnosed in nineteen patients with imaging (DCBE or CT) between January 2005 and December 2018. All these patients received histopathologic diagnosis

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of lymphoma and subtypes were classified according to immunohistochemical staining. Twelve patients were male, and seven were female (age range, 17–75 years). Sixteen patents underwent surgical resection; the other three patients only underwent colonoscopic biopsy. All 19 patients had undergone CT examination; seventeen patients underwent enhanced CT examination, and two patients underwent nonenhanced CT examination. Six patients also had undergone DCBE examination.

Image acquisition and review

The CT equipment and scan parameters were as follows: GE lightspeed 64-VCT: 120 kV, 450 mAs, thickness 5 mm, spacing 5 mm, reconstruction thickness 1.25 mm, reconstruction spacing 0.8 mm; GE lightspeed Ultra 8-MDCT: 120 kV, 450 mAs, thickness 5 mm, spacing 5 mm, reconstruction thickness 1.25 mm, reconstruction spacing 0.8 mm; Toshiba Aquilion 64-MDCT: 120 kV, 380 mAs, thickness 5 mm, spacing 5 mm, reconstruction thickness 1 mm, spacing 0.8 mm. Enhanced CT examinations commenced following a 65-s delay after intravenous injection with 85 mL of contrast medium (300 mg/mL) using a power injector at a rate of 2.5 mL/s. DCEB images were obtained using the following equipment: a Toshiba Mec ADR-100A digital gastrointestinal apparatus; and a Shimadzu DAR-3000 digital gastrointestinal apparatus.

The CT and DCBE findings were retrospectively reviewed in consensus by two radiologists who were aware of the diagnosis. The CT findings included the location and extent of the lesion, morphological patterns, presence of necrosis, characteristics of enhancement, dissemination of pericolonic fat, presence of regional lymph node enlargement and another organ involvement. The evaluation of the DCBE findings included the presence of a niche, filling defect, mucosal destruction, luminal narrowing, peristalsis, and ileocecal deformity. The large intestinal lymphoma pattern was classified into four types: a circumferential infiltrative form, an ulcerinfiltrative form, a focal/localized polypoid form, or a mesenteric nodal form (12-15). These findings were correlated with those of a colonoscopy and an examination of gross resected specimens.

Results

Clinical and pathological features of PCL

Clinical presentations included abdominal pain and

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Case no.	Sex/age (years)	Lesion location			Gross findings characteristics		
			Pathological exam	Histology	Туре	Penetrating to serous membrane	
1	F/22	Terminal ileum, ileocecum	Surgery	PTCL, NOS	Ulceroinfiltrative	Yes	
2	F/33	lleocecum, appendix	Surgery	DLBCL	Polypoid mass	Yes	
3	M/75	Terminal ileum, ileocecum, ascending colon	Surgery	DLBCL	Ulceroinfiltrative	Yes	
4	M/59	Rectum	Microscopy	DLBCL	Polypoid mass	NA	
5	M/23	Terminal ileum, ileocecum, ascending colon	Surgery	B-cell unclassified	Surgery after chemotherapy	NA	
6	M/61	Terminal ileum, ileocecum, ascending colon	Surgery	DLBCL	Circumferential infiltrative	No	
7	M/39	Terminal ileum, ileocecum	Surgery	DLBCL	Circumferential infiltrative	Yes	
8	M/49	Terminal ileum, ileocecum, ascending colon	Surgery	DLBCL	Circumferential infiltrative	Yes	
9	M/68	Terminal ileum, ileocecum	Surgery	DLBCL	Circumferential infiltrative	Yes	
10	F/55	Terminal ileum, ileocecum, ascending colon	Surgery	DLBCL	Circumferential infiltrative	Yes	
11	F/50	Terminal ileum, ileocecum	Surgery	DLBCL	Circumferential infiltrative	No	
12	F/60	Descending colon, transverse colon	Surgery	MALT	Polypoid mass (multiple)	Yes	
13	M/27	Terminal ileum, ileocecum, ascending colon	Surgery	MALT	Polypoid mass	Yes	
14	M/67	lleocecum, ascending colon	Surgery	DLBCL	Circumferential infiltrative	Yes	
15	F/74	Terminal ileum, ileocecum, ascending colon	Surgery	MALT	Polypoid mass (multiple)	No	
16	M/42	sigmoid colon	Surgery	MALT	Circumferential infiltrative	No	
17	M/17	Terminal ileum, ileocecum, ascending colon	Surgery	DLBCL	Circumferential infiltrative	Yes	
18	F/58	Terminal ileum, ileocecum, ascending colon	Microscopy	DLBCL	Polypoid mass	NA	
19	M/65	lleocecum	Microscopy	MCL	Polypoid mass	NA	

Table 1 Clinical and pathological characteristics of PCL in 19 patients

PCL, primary colorectal lymphoma; PTCL, peripheral T-cell lymphoma; NOS, not otherwise specified; DLBCL, diffuse large B-cell lymphoma; MALT, B-cell lymphoma arising from mucosa-associated lymphoid tissue; MCL, mantle cell lymphoma; NA, not applicable.

discomfort in nine patients, bloody stools in five, and altered bowel habits in four; PCL was detected in one patient without any clinical symptoms by a health examination. According to the Ann Arbor staging scheme (16,17), seven patients had disease confined to the colon (stage IE, 36.8%), eleven had regional lymph node involvement (stage IIE, 57.9%), and one had adjacent organ and tissue involvement (stage IVE, 5.3%).

Pathologically, non-Hodgkin lymphoma (NHL) was present in all patients. The histological details are presented in *Table 1*. Immunohistochemical staining revealed diffuse large B-cell lymphoma (DLBCL) in 12 patients (63.2%), B-cell lymphoma arising from mucosa-associated lymphoid tissue (MALT) in 4 patients (21.1%), unclassified B-cell

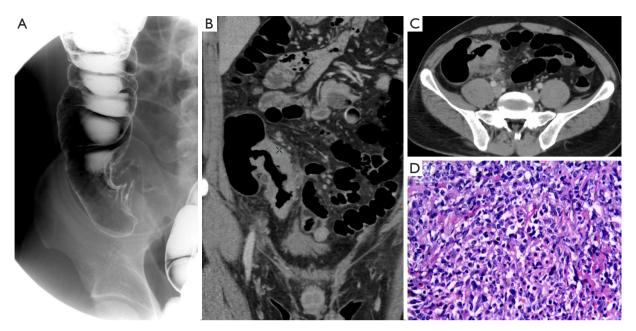


Figure 1 A 39-year-old male patient (case no. 7) with diffuse PCL in the terminal ileum and ileocecum. (A) DCBE image showing an irregular filling defect, ileocecal deformation and mild narrowing with a smooth mucosal surface. (B) Contrast-enhanced coronal CT reconstruction and (C) axial CT images showing circumferential diffuse bowel wall thickening with moderate enhancement. (D) The histopathology of the lesion was suggestive of DLBCL (HE, ×400). DCBE, double-contrast barium enema; DLBCL, diffuse large B-cell lymphoma; PCL, primary colorectal lymphoma.

lymphoma in 1 patient (5.3%), peripheral T-cell lymphoma, not otherwise specified (PTCL, NOS) in 1 patient (5.3%), and mantle cell lymphoma (MCL) in 1 patient (5.3%).

Imaging features of PCL

Forty-four colorectal segments were involved; sixteen lesions were located in the ileocecum, thirteen in the terminal ileum, ten in the ascending colon, one in the rectum, one in the descending colon, one in the transverse colon, one in the sigmoid colon and one in the appendix.

The CT findings indicated a circumferential infiltrative form presenting wall thickening (n=12) (*Figures 1,2*), a focal polypoid mass form (n=6) (*Figure 3*), and a cavitary/ ulceroinfiltrative form (n=1) (*Table 2, Figure 4*). Two cases presented as aneurysmal dilatation (*Figure 4*). Of seventeen patients who underwent enhanced CT, two lesions exhibited central low attenuation with necrosis, while the other fifteen lesions manifested as homogeneous soft-tissue masses with mild or moderate enhancement (similar to the psoas muscle within the same slice). Fifteen lesions extended into the serous membrane or pericolonic fat, characterized by stranding or linear soft-tissue density in the pericolonic fat area. Regional lymphadenopathy, including bowel wall lymph nodes, pericolorectal lymph nodes, and mesentery root lymph nodes, was found in twelve patients; one case showed enclosure of the mesenteric vessels without invasion (*Figure 3*). Direct involvement of both the ovaries and diaphragm was evident in one patient. Intussusception of the terminal ileum was seen in one patient.

Six patients underwent DCBE examination (*Table 3*). A filling defect was found in all patients, a flat niche in four (*Figure 2*), mild mucosal destruction in three, luminal narrowing in all patients with slight luminal narrowing in three, and ileocecal deformation in three (*Figure 1*). Peristalsis was preserved in five patients.

Comparison of imaging and pathological findings

Among these 19 patients, the preoperative CT diagnoses were colon carcinoma in ten patients, lymphoma in five patients and undefined in four patients. Among the six patients who underwent DCBE, the preoperative diagnosis was lymphoma in two and colon carcinoma in four. The preoperative diagnostic accuracies of PCL were 26.3% (5/19) with CT and 33.3% (2/6) with DCBE.

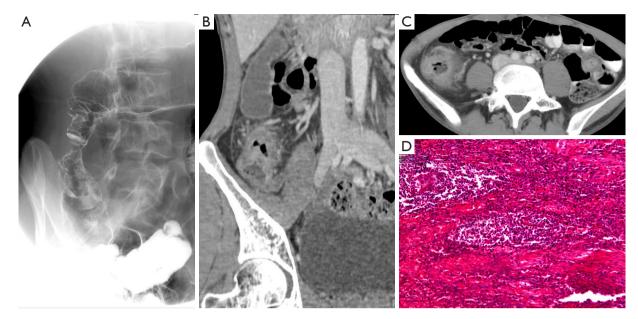


Figure 2 A 27-year-old male patient (case no. 13) with diffuse PCL in the terminal ileum, ileocecum and ascending colon. (A) DCBE image showing circumferential narrowing of the descending colon with a smooth mucosal surface. (B) Contrast-enhanced coronal CT reconstruction and (C) axial CT images showing circumferential diffuse bowel wall thickening with moderate enhancement. Stranding or linear soft-tissue densities in the pericolonic fat space characterized the extension into the serous membrane and pericolonic fat. (D) The histopathology of the lesion was suggestive of MALT lymphoma (HE, $\times 200$). DCBE, double-contrast barium enema; MALT, mucosa-associated lymphoid tissue; PCL, primary colorectal lymphoma.

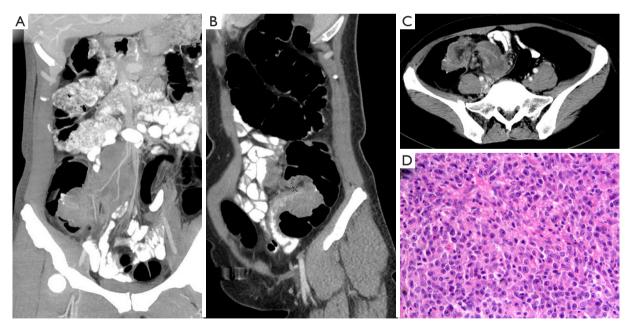


Figure 3 A 33-year-old female patient (case no. 2) with focal PCL in the ileocecum. (A) Contrast-enhanced coronal CT MIP reconstruction image; (B) sagittal CT reconstruction and (C) axial CT images showing a focal mass on one side of the bowel wall, which caused eccentric luminal narrowing. A large fused lymph node was observed in the mesenteric root of the ileocecum, showing minimal enhancement and enclosure of the mesenteric vessels without invasion; (D) the histopathology of the lesion was suggestive of DLBCL (HE, ×400). PCL, primary colorectal lymphoma; MIP, maximum intensity projection; DLBCL, diffuse large B-cell lymphoma.

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Case no.	Туре	Serosal extension	Necrosis	Enhancement	Regional lymph node enlargement	Distant lymph node enlargement	Another organ involvement
1	Circumferential infiltrative	Yes	NA	NA	Yes	No	No
2	Polypoid mass	Yes	No	Moderate	Yes	No	No
3	Ulceroinfiltrative	Yes	Yes	Moderate	No	No	No
4	Polypoid mass	Yes	NA	NA	No	No	No
5	Circumferential infiltrative	Yes	No	Moderate	Yes	No	No
6	Polypoid mass	No	No	Moderate	Yes	No	No
7	Circumferential infiltrative	Yes	No	Moderate	Yes	No	No
8	Circumferential infiltrative	Yes	No	Moderate	No	No	No
9	Circumferential infiltrative	Yes	No	Moderate	No	No	No
10	Circumferential infiltrative	Yes	No	Moderate	Yes	No	No
11	Circumferential infiltrative	No	No	Moderate	No	No	No
12	Polypoid mass (multiple)	Yes	No	Moderate	Yes	Yes	Yes
13	Circumferential infiltrative	Yes	No	Moderate	No	No	No
14	Circumferential infiltrative	Yes	No	Moderate	Yes	No	No
15	Circumferential infiltrative	Yes	No	Moderate	Yes	Yes	No
16	Circumferential infiltrative	No	No	Moderate	Yes	No	No
17	Circumferential infiltrative	Yes	No	Mild	Yes	No	No
18	Polypoid mass	Yes	Yes	Moderate	Yes	No	No
19	Polypoid mass	No	No	Moderate	No	No	No

Table 2 CT findings of primary colorectal lymphoma in 19 patients

NA, not applicable.

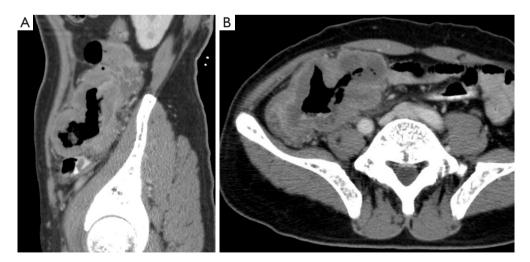


Figure 4 A 75-year-old male patient (case no. 3) with PCL in the terminal ileum, ileocecum and ascending colon. (A) Contrast-enhanced sagittal CT and (B) axial CT images show ulceroinfiltrative lesions with aneurysmal dilatation of the lumen. The histopathology of the lesion was suggestive of DLBCL. PCL, primary colorectal lymphoma; DLBCL, diffuse large B-cell lymphoma.

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Case no.	Niche	Filling defect	Mucosal destruction	Luminal narrowing	Peristalsis	lleocecal deformity
7	No	Yes	Slight	Mild	Yes	Yes
8	Yes	Yes	Yes	Yes	Yes	Yes
9	Yes	Yes	Slight	Mild	Yes	Not displayed
13	Yes	Yes	Slight	Mild	Yes	Not displayed
16	Yes	Yes	Yes	Yes	No	Not displayed
19	No	Yes	Yes	Yes	Yes	Yes

Table 3 DCBE findings of primary colorectal lymphoma in six patients

DCBE, double-contrast barium enema.

Colonoscopy (n=3) or colectomy specimens (n=16) were available for all 19 patients. However, one patient received preoperative chemotherapy, and the pathological changes were obscure. According to the gross findings (n=18), two lesions manifested as ulcerative masses, seven as focal masses, and nine as diffuse thickness of the colorectal wall. The accuracy of CT classification was 83.3% (15/18). Both ulcerative lesions exhibited giant ulcerations with an irregular, elevated bottom; one lesion was located in the ileocecum, and the other involved the ileocecum and part of the ascending colon. CT demonstrated only one ulcerative lesion. According to surgical pathological findings (n=15), four lesions were limited to the superficial myometrium of the colorectal wall, while the other eleven lesions infiltrated the serous membrane and pericolorectal fat, which was 93.3% (14/15) consistent with the prospective CT diagnosis of whether the lesion infiltrated the serous layer.

Discussion

Clinical and pathological features of PCL

The incidence of PCL is greatest among those aged 50 to 70 years, with a mean age at presentation of between 50 and 55 years in Eastern Asian reports (18). In our study, the age range was wide (17–75 years old); five patients were younger than 40 years old. This finding may be correlated with a trend of tumors occurring in younger people. Our study shows a slight male predominance (male: female =12:7), which correlates well with the results of most previous studies (19-22). The most common presenting symptoms were abdominal pain and weight loss or changes in bowel habits, as previously reported in the literature (20-22). In our study, clinical symptoms included abdominal pain and discomfort in six patients, altered bowel habits in

three patients, and bloody stools in three patients. None of the patients experienced weight loss, which may be correlated with most of our patients being diagnosed at an early stage (92.4% stage I or II). In turn, this phenomenon may be because of improved diagnostics, increased health awareness, or racial differences between Eastern and Western individuals.

In our study, NHL was present in all 19 patients. T-cell lymphoma was present in 1 (5.3%), and B-cell lymphoma was present in 18 (94.7%), including DLBCL in 12 patients (63.2%), MALT in 4 patients (21.1%), unclassified B-cell lymphoma in 1 patient (5.3%), and MCL in 1 patient (5.3%). DLBCL was the most common subtype of PCL, which correlates well with the results of most studies (20,23). MALT of the gastrointestinal tract most commonly affects the stomach, and colorectal involvement is uncommon. Such tumors are characterized by an indolent course with little evidence of dissemination outside the gut, but these tumors can transform into intermediate or highgrade lymphoma (24-26). In our series, the lesions of two MALT cases both infiltrated the serosal membrane and perienteric tissues; one of these patients manifested multiple lesions involving the transverse and descending colons and infiltrating the paracolic tissues and organs. T-cell lymphoma is usually very aggressive with a poor prognosis (27,28). Perforation of the bowel frequently occurs (29-32). In our series, T-cell lymphoma manifested pathologically as a diffuse lesion and deep ulceration.

Imaging features of PCL

PCL is likely to involve multiple segments of the colon. In our series, there was Forty-four colorectal segments were involved in 19 patients. According to previous studies in the literature, the most common location for colorectal lymphoma is the ileocecum, occurring in 30-60% of cases, probably because more lymphoid tissue is present in this region (2,22,33-35). Our study showed a higher rate, with 84.2% (16/19) of the lesions located in the ileocecum; among these, thirteen involved the terminal ileum. The ascending colon was the next most common site of occurrence (52.6\%, 10/19) in our series. Some studies have shown that the rectum is another common site of PCL; however, there was only one (5.3%) case of rectum involvement in our study.

In our study, a circumferential lesion with colorectal wall thickening was the most common morphological pattern (68.4%, 13/19). These lesions presented as concentric wall thickening with a structure integrated with the intestinal wall on CT and circumferential narrowing of the colon with a smooth mucosal surface on DCBE. The smooth mucosal surface is caused by the submucosal infiltration of lymphoid cells rather than mucosal ulceration. Lymphoma does not elicit a desmoplastic response, and submucosal lymphoid infiltration weakens the muscularis propria of the bowel wall. Therefore, although PCL lesions are often long and circumferential, severe luminal narrowing is uncommon, and signs of aneurysmal dilatation can even occur in some cases, as in three cases in this study. Aneurysmal dilatation of the lumen is a characteristic sign and may be due to replacement of the muscularis propria and destruction of the autonomic nerve plexus by lymphoma (36).

Polypoid masses have been reported to be the most frequent form of PCL (1). However, focal polyploid masses were detected in 5 (26.3%) patients in this study; single, large polypoid masses on one side of the bowel wall were observed in three patients, while multiple focal polyploid masses in the colon were found in one patient. The differential diagnosis of this form of lymphoma is colon carcinoma or large colonic polyps. PCL manifests as larger masses than colon carcinoma. Additionally, PCL can extend beyond the colon wall and form a large peritoneal mass (1). In our series, focal polypoid masses were less common than circumferential lesions. The characteristic finding of this form is an eccentric mass.

Previously, it was believed that colon lymphoma has no or minimal mucosal ulceration. According to radiological studies in the literature (28), peripheral T-cell lymphoma of the colon manifests as either a diffuse or a focal segmental lesion and shows extensive mucosal ulceration on DCBE examination. This differentiation of this form from inflammatory bowel disease is difficult. In our study, the only case of T-cell origin lymphoma manifested as circumferential infiltration without ulceration on CT, while pathology revealed ulceration, which may have been because such pathological ulcerations are more difficulty to detect on CT images than on DCBE images.

According to a previous view, PCL with serosal or pericolonic fat extension was less common than colorectal carcinoma (36). However, in our study, there were eleven cases (73.3%, 11/15) pathologically proven and twelve cases (78.9%, 15/19) on CT with serosal extension or pericolonic fat extension. Therefore, serosal or pericolonic fat extension may not be a characteristic radiographic feature of colon carcinoma compared with PCL. The extension manifested as stranding densities in the pericolonic fat with an unclear serosal membrane or stripe-like opacities parallel to the bowel wall on CT. Compared with the appearance of colon carcinoma, these opacities were less acute and had fewer nodules on the bowel wall (37).

Twelve (63.2%) patients had regional lymph nodal involvement, which manifested as aggregated nodules or masses in the pericolonic fat space or lymph drainage area characterized by homogeneous soft-tissue lesions without necrosis, moderate enhancement and characteristic enclosure of the mesenteric vessels without invasion. When CT reveals the presence of an infiltrative process accompanied by enlarged lymph nodes in the abdomen or pelvis, lymphoma should be the primary consideration in the differential diagnosis and must be excluded by endoscopic biopsy.

Comparison of imaging and pathological findings

The diagnostic accuracy of PCL was 26.3% (5/19) with CT and improved to 33.3% (2/6) when combined with DCBE. Combining DCBE and CT examinations may offer improved diagnostic accuracy in difficult cases. In this study, all imaging misdiagnosed cases were diagnosed as colorectal cancer. The imaging features of PCL on DCBE included giant mucosal rugae, superficial submucosal filling defects, and changing lesion forms with compression on fluoroscopy compared to colorectal cancer. However, these imaging signs are usually subtle, non-specific and overlap with colorectal cancers. We suggested that this is the main cause for PCL imaging misdiagnosis, in addition to the very low prevalence of PCL. Although the CT diagnostic accuracy of PCL is even lower, the diagnostic ability of lesion morphological classification (83.3%) and serosal or pericolonic fat extension (93.3%) is satisfactory. As opposed to diagnosis, the value of CT is that it reveals the location

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and extent of the lesion and the involvement of adjacent organs and tissues as well as distant metastasis. Therefore, CT is very crucial for PCL staging and is currently performed as a routine exam in clinical practice.

Conclusions

PCL is a relatively rare malignant disease. The most common histological subtype of colorectal lymphoma is DLBCL. PCL usually presents circumferential or polyploid lesions in the ileocecum and cecum, with slight mucosal destruction and mild luminal narrowing on DCBE, along with moderate and homogeneous enhancement on CT. Aneurysmal dilatation of the lumen is sometimes observed. Although the imaging features of PCL overlap with those of other colon pathologies, such as carcinoma and inflammatory disease, CT is valuable in the evaluation of invasion extent and lymphadenopathy. Familiarity with the radiological features of PCL on DCBE and CT can help ensure correct diagnosis.

Acknowledgments

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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