

# Clinical diagnosis and treatment of primary small intestinal lymphoma

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## Abstract

**Background:** To report experiences in the diagnosis and treatment of primary lymphoma of the small intestine (PSIL).

**Method:** The clinical data of 15 patients with PSIL treated from January 2015 to July 2019 at Guangzhou First People's Hospital were investigated retrospectively. Among the 15 patients, 9 were male, and 6 were female, with ages ranging from 18 to 73 years, with a median age of 51.6 years. Data relating to gender, age, clinical manifestation, laboratory examination, imaging, diagnosis, and treatment of the patients were reviewed.

**Results:** The most common clinical manifestations were abdominal pain, abdominal lump, bowel obstruction, gastrointestinal hemorrhage, and atrepsy. Serum tumor markers were checked and found to be normal. In all 15 cases, tumors were found by spiral computed tomography (CT), and 12 cases were diagnosed as PSIL. Eleven cases were given barium meal examinations, and positive results were found in 4 cases, with only 1 case considered to be PSIL. All 15 patients underwent surgery. All patients were diagnosed as having non-Hodgkin lymphoma by postoperative pathology (8 patients with diffuse large B-cell lymphoma, 5 with mucosa associated lymphoid tissue type B-cell lymphoma and 2 with enteropathy-type intestinal T-cell lymphoma). There were no cases of perioperative deaths. Ten patients received adjuvant chemotherapy with the CHOP (cyclophosphamide, epirubicin, vincristine, and prednisone) regimen after the operation. Fourteen cases were followed up for a mean duration of 30 months (range of 6-52 months). The 1- and 3-year survival rates were 85.7% and 57.1%, respectively.

**Conclusion:** PSIL has no specific clinical manifestations. The diagnostic rate with barium study is low, whereas spiral CT is a promising diagnostic method for PSIL. Surgery combined with chemotherapy is important for the treatment of PSIL.

**Keywords:** Lymphoma, non-Hodgkin, primary small intestine lymphoma (PSIL), diagnosis, therapy

## Introduction

Primary small intestinal lymphoma (PSIL) is a rare malignant tumor of the gastrointestinal tract. Due to its insidious onset and lack of specific clinical manifestations, it is easily misdiagnosed. We aimed to explore the diagnosis and clinical treatments of PSIL by analyzing the clinical manifestations and computed tomography (CT) characteristics of 15 patients who were admitted to our hospital between January 2015 and July 2019.

## Materials and methods

### General clinical information

There were 15 cases in this group, comprising 9 men and 6 women. This study was approved by the Ethics Review Committee at Guangzhou First People's Hospital, and we obtained the clinical information of the patients after obtaining their informed consent. The age of PSIL onset ranged from 18 to 73 years, and the median age was 51.6 years. Eleven cases (73.3%) were over the age of 40 years. The patients' history of symptoms ranged from 1 week to 1.5 years. The main clinical manifestations included abdominal pain, abdominal mass, intestinal obstruction, gastrointestinal bleeding, and wasting. Serum tumor indexes (carcinoembryonic antigen, CA19-9) were normal in all patients. All cases met the Dawson diagnostic criteria as follows [1]:

(1) There was no pathological superficial lymph node en-

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largement when the patient was first seen.

(2) Chest X-rays did not show any mediastinal lymph node enlargement.

(3) There were no naive or abnormal cells in the peripheral blood.

(4) The tumor was mainly located in the small intestine or invaded nearby lymph nodes via lymphatic vessels.

(5) There was no invasion of the liver or spleen (except for the direct spread of adjacent lesions).

This study was approved by the Ethics Review Committee at Guangzhou First People's Hospital, and we obtained the clinical information of the patients after obtaining their informed consent.

### Spiral CT examination

All 15 cases were examined by abdominal spiral CT, and the findings included intestinal wall thickening, intestinal luminal mass, and mesenteric lymph node enlargement. Secondary manifestations included intussusception, intestinal obstruction, and small amounts of peritoneal effusion. The intestinal lumen was in an "aneurysm-like" dilated state in 9 cases, and the lumen of the intestine was mildly stenosed with incomplete intestinal obstruction in 1 case. Fifteen cases showed soft tissue density on the CT scan, irregular low-density necrotic areas were seen within the lesion, and the lesion was mildly enhanced on enhanced scans. The fat surrounding the intestinal wall disappeared in 7 cases. The CT findings of 9 cases showed mesenteric lymphadenopathy. There were 15 cases diagnosed by CT, of which 12 cases were accurately diagnosed (Figure 1: a-c), 1 case was misdiagnosed as intestinal adenocarcinoma, and 1 case was misdiagnosed as a stromal tumor; the diagnosis of 1 case was still uncertain.

### Barium meal examination of the digestive tract

Before surgery, 11 cases underwent barium gastrointestinal examination. One case exhibited the disappearance of mucosal folds in the intestinal wall and dilatation of the intestinal lumen, which was suggestive of lymphoma. One case exhibited disappearance of mucosal folds in the intestinal wall, and multiple fine niches were seen, which led to a misdiagnosis of limited enteritis. Two cases had results suggestive of external pressure changes, and seven patients had no obvious abnormalities on the barium gas-

trointestinal examination.

### Tumor site

Of the 15 patients, 5 cases had tumors in multiple sites, 3 had tumors in the ileocecal region, 1 had tumors involving both the stomach and duodenum, 1 had tumors involving both the duodenum and jejunum, 7 had tumors involving the ileum, 2 had tumors involving the jejunum, and 1 had tumors involving the duodenum. Ileal lymphoma was defined as a lesion involving the terminal ileum and the ileocecal valve, cecum, or appendix.

### Surgical modality and adjuvant treatment

All patients received surgical treatment, including 9 cases who underwent radical resection, 3 cases who underwent tumor reduction surgery due to the discovery of extensive metastases in the abdominal cavity, and 3 cases who underwent short-circuiting and biopsy due to severe abdominal adhesions or tumor with invasion of the large retroperitoneal vessels. After surgery, 11 cases received 4 to 8 cycles of adjuvant chemotherapy with the CHOP (cyclophosphamide, epirubicin, vincristine, and prednisone) regimen.

## Results

### Histological type

The 15 PSIL patients were confirmed by pathological examination to have non-Hodgkin lymphoma (NHL). Eight (53.3%) patients were classified as having diffuse large B-cell lymphoma (DLBCL), 5 (33.3%) as having mucosa-associated lymphoid tissue B-cell lymphoma (33.3%), and 2 (13.4%) as having enteropathy-associated T-cell lymphoma.

### Follow-up and prognosis

We followed up with 14 patients for a mean duration of 30 months (range 6-52 months). One case of stress ulcer occurred after the operation, and there were no perioperative deaths. However, 6 patients died due to tumor metastasis or recurrence. The 1- and 3-year survival rates were 85.7% and 57.1%, respectively.

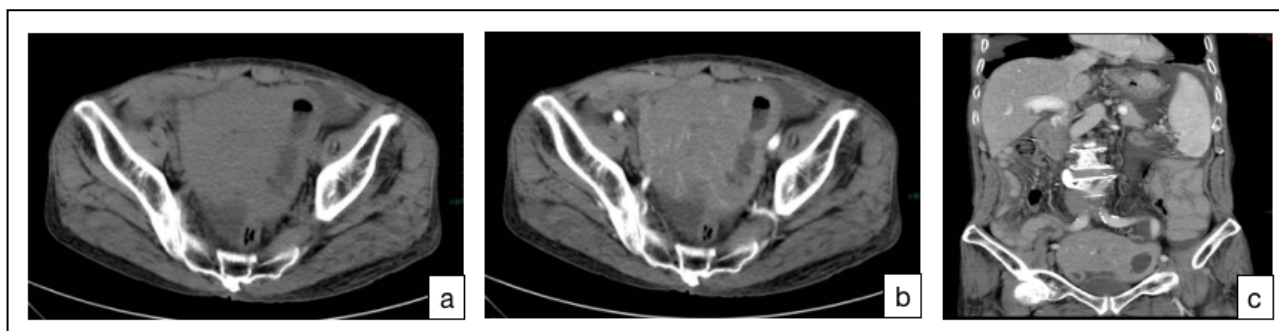


Figure 1. (CT images (a-c) of a 74-year-old man who was considered as possibly having small intestinal lymphoma because his small intestine wall was evidently unevenly thickened and soft tissue masses had formed. a: CT non-contrast enhanced scan. b: CT contrast enhanced scan. c: coronal reconstruction.).

## Discussion

Primary small intestinal lymphoma (PSIL) is a rare malignant tumor of the gastrointestinal tract, which accounts for 19% to 38% of malignant tumors of the small intestine, and 20% to 30% of all primary gastrointestinal lymphomas [2, 3]. Small intestinal lymphomas can be classified as primary or secondary. The former occurs in the submucosal lymphatic tissue of the small intestine, which grows as solitary nodules and does not infiltrate the surrounding tissues for a long time; the prognosis of primary small intestinal lymphoma is good. The secondary type refers to small bowel disease as a component of systemic lymphoma, and autopsies have revealed that 50% of lymphoma patients had small bowel invasion [4]. The causes of PSIL are not exactly known, but research has reported that it is related to environmental factors, viral infections, genetics, immunodeficiency, some intestinal diseases, and drugs [5, 6]. PSIL can occur in any part of the small intestine, but the lymphatic-rich distal ileum has the highest incidence. PSIL often manifests as intermittent abdominal pain, abdominal masses, unexplained gastrointestinal bleeding and obstruction, and decline of body mass, but has no specific clinical manifestations [7]. Therefore, patients with the above clinical manifestations should undergo a small bowel examination.

The clinical manifestations of PSIL are unspecific, and it is hard to diagnose by endoscopic and barium meal examination. In the past, PSIL was diagnosed by postoperative pathological examination [8]. With the popularity of multi-slice computed tomography (MSCT) and the development of 3D reconstruction technology, these have become the most important and valuable examination methods for the current-day diagnosis of small bowel tumors [9].

PSIL originates from the lamina propria of the small intestine mucosa or lymphatic tissue in the submucosa. It often grows in the lamina propria or submucosa along the long axis of the organ, and then invades into and out of the cavity, and the lesions can be widespread or multiple in the early stage. Barium meal examination can only show lesions in the intestinal cavity and indirect signs of extracavitary lesions, and it is often not easy to detect smaller mucosal lesions. When PSIL is accompanied by ulceration, it is often difficult to distinguish it from adenocarcinoma. Therefore, barium meal examination, as well as enteroscopy, lacks specificity for its diagnosis. When small intestinal lymphoma is not accompanied by ulceration, it is difficult to make a correct diagnosis, as endoscopic lesions are not clear, and they often show generalized inflammation and erosion. The diagnostic rate of pathological biopsy is low, as the biopsy often does not extend deep into the mucosa, and it is also greatly limited in its ability to diagnose tumor infiltration of extracavity tissue.

The performance of spiral CT in diagnosing PSIL is mainly characterized by its ability to identify different forms of intestinal wall thickening, and the following characteris-

tics can provide an important basis for diagnosis:

(1) The intestinal wall is thickened, and the intestinal cavity is dilated. Normal small intestinal wall thickness is <3 mm, and the normal intestinal cavity width is <30 mm. This standard can be used as a reference for intestinal wall thickening and expansion, which can manifest as symmetrical or eccentric thickening. The thickening of the intestinal wall is mainly due to thickening of the submucosa and muscle layers thickening. Most of the intestinal tube is above 3/4 weeks of diameter.

(2) Analysis of the images of the same level of lesions in different phases shows that most of the lesions have variable intestinal morphology and still maintain a certain degree of expansion and flexibility. This may be related to the absence of factors that induce fibroblast responses in lymphoma.

(3) The lesions are less invasive.

(4) Analysis of the enhancement CT values of each stage reveals that the difference before and after enhancement is 20–35 HU, suggesting that PSIL is a mildly or moderately enhanced tumor. PSIL needs to be differentiated from small-bowel adenocarcinoma and small-bowel Crohn's disease when the main manifestation is thickening of the bowel wall. MSCT and its post-processed images can not only show intra-intestinal lesions, but also submucosal and extraintestinal lesions. It has unique advantages in the diagnosis of PSIL and is a better diagnostic method.

Malignant lymphoma is a tumor that is sensitive to radiotherapy and chemotherapy. The current consensus is that malignant lymphoma should be treated surgically followed by the use of adjuvant treatment [10, 11]. The surgical resection and the scope of lesion cleanup should be based on the tumor location, tumor size, and the range of its invasiveness. It is easier to separate and remove the tumor from the surrounding tissues during surgery, as intestinal lymphoma normally grows non-invasively. We advocate active radical surgery for intestinal malignant lymphoma if it cannot be cured to prevent complications such as perforation and bleeding during chemotherapy; palliative surgery should be considered. Early diagnosis is vital for improving the prognosis of PSIL. Hence, to avoid delays in the timing of surgery, an exploratory laparotomy should be performed decisively for patients who have surgical indications.

## Declarations

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## References

1. Dawson I M, Cornes J S, Morson B C. Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis. *British Journal of Surgery*, 1961, 49: 80-89.
2. Tamura H, Ogata K, Kondo A, et al. Double balloon endoscopy as a useful tool for the diagnosis and treatment of four cases of primary small intestinal lymphoma. *Rinsho Ketsueki*, 2007, 48(6): 510-513.
3. Foukas P G, de Leval L. Recent advances in intestinal lymphomas. *Histopathology*, 2015, 66(1): 112-136.
4. Nakamura S, Matsumoto T, Iida M, et al. Primary gastrointestinal lymphoma in Japan: a clinicopathologic analysis of 455 patients with special reference to its time trends. *Cancer*, 2003, 97(10), 2462-2473.
5. Grande B M, Gerhard D S, Jiang A, et al. Genome-wide discovery of somatic coding and noncoding mutations in pediatric endemic and sporadic Burkitt lymphoma. *Blood*, 2019, 133(12): 1313-1324.
6. Terai S, Iijima K, Kato K, et al. Long-term outcomes of gastric mucosa-associated lymphoid tissue lymphomas after *Helicobacter pylori* eradication therapy. *The Tohoku Journal of Experimental Medicine*, 2008, 214(1): 79-87.
7. Feng L, Zhang G, Hu Z, et al. Diagnosis and treatment of 81 patients with primary gastrointestinal lymphoma. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*, 2009, 34(7): 582-588.
8. Kobayashi H, Nagai T, Omine K, et al. Clinical outcome of non-surgical treatment for primary small intestinal lymphoma diagnosed with double-balloon endoscopy. *Leukemia & Lymphoma*, 2013, 54(4): 731-736.
9. Yang C B, Yu N, Jian Y J, et al. Spectral CT Imaging in the Differential Diagnosis of Small Bowel Adenocarcinoma From Primary Small Intestinal Lymphoma. *Academic Radiology*, 2019, 26(7): 878-884.
10. Beaton C, Davies M, Beynon J. The management of primary small bowel and colon lymphoma--a review. *International Journal of Colorectal Disease*, 2012, 27(5): 555-563.
11. Gonzalez Q H, Heslin M J, Dávila-Cervantes A, et al. Primary colonic lymphoma. *American Surgeon*, 2008, 74(3): 214-216.

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