**The Clinical Diagnosis and Treatment of Primary Small Intestinal Lymphoma**

**Abstract: Objective:** To report the experiences of 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 was investigated retrospectively. Of the 15 cases, 9 patients were male and 6 were female, the average age was 51.6 years(range, 18-73 years). Data of gender, age, clinical manifestation, laboratory examination, imageology examination, diagnosis and treatment of the patients was reviewed．**Results:** The most common clinical manifestations were as follow: abdominal pain, abdominal lump, bowel obstruction, gastrointestinal hemorrhage and athrepsy. Serum tumor markers were checked normal. A1l the 15 cases were found with tumor by spiral CT, and 12 cases were diagnosed as PSIL. 11 cases were given Ba-meal examinations, and positive results was found in 4 cases, and only l case was considered to be PSIL. All the 15 patients received operation. All the patients were diagnosed as non-Hodgkin lymphoma(NHL) by postoperative pathology (8 patients as diffuse large B-cell lymphoma, 5 as mucosa associated lymphoid tissue type B cell lymphoma and 2 as enteropathy-type intestinal T cell lymphoma). No perioperative death occured. 10 patients received adjuvant chemotherapy with the regimen of CHOP (cyclophosphamide+epirubicin+vincristine +prednisone) after the operation. 14 cases were followed up for a mean time of 30 months(range, 6-52 months). The 1-and 3-years survival rate was 85.7％and 57.1％, respectively．**Conclusions:** PSIL has no specific clinical manifestations. The diagnostic rate with barium study is low, spiral CT scan is a promising diagnostic method for PSIL. Operation combined with chemotherapy is important for PSIL.

**Key words：**Lymphoma, non-Hodgkin, primary small intestine lymphoma(PSIL), Diagnosis, Therapy

**Introduction:** Primary small intestinal lymphoma (PSIL) is a rare disorder of digestive system malignant tumor, because of its onset is insidious and a lack of specific clinical manifestations, easily lead to misdiagnosis. We aimed to explore the diagnosis and clinical countermeasures of Primary Small Intestinal lymphoma (PSIL) through analyzing the clinical manifestations and CT characteristics of 15 patients, who were admitted to our hospital from January 2015 to July 2019.

  **Materials and Method**

**1.General clinical information**

There were 15 cases in this group, 9 men and 6 women. The onset age of patients was 18-73 years, and the average age was 51.6 years.11 cases (73.3%) were over the age of 40 years. The patient's history ranged from 1 week to 1.5 years.The main clinical manifestations included abdominal pain, abdominal mass, intestinal obstruction, gastrointestinal bleeding and wasting.The serum tumor indexes (carcinoembryonic antigen, CAl9-9) were normal. All cases met the Dawson diagnostic criteria.[1]

1. The patient is first seen there is no pathological superficial lymph node enlargement.
2. Chest X-ray shows no mediastinal lymph node enlargement.
3. There is no naive or abnormal cells in peripheral blood.
4. Tumor mainly located in the small intestine or invading nearby lymph nodes via lymphatic vessels.
5. There is no invasion of liver or spleen (except for direct spread of adjacent lesions).

**2. 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 includes intussusception, intestinal obstruction and small amounts of peritoneal effusion. The intestinal lumen was "aneurysm-like" dilated in 9 cases and the lumen of intestine was mildly stenosed with incomplete intestinal obstruction in 1 case. 15 cases showed soft tissue density on CT scan, and irregular low-density necrotic areas were seen within the lesion, and the lesion was mildly enhanced on enhanced scan. The fat space around the intestinal wall disappeared in 7 cases. The CT findings of 9 cases showed mesenteric lymphadenopathy. There were 15 cases diagnosed by CT, among which 12 cases were accurately diagnosed (Figure a-c), 1 case was misdiagnosed as intestinal adenocarcinoma, 1 case was misdiagnosed as stromal tumor, and the diagnosis of 1 case was still uncertain.



(The small intestine wall is obviously unevenly thickened and soft tissue masses are formed, considering the possibility of small intestinal lymphoma. **Figure a**: CT non-contrast enhanced scan. **Figure b**: CT contrast enhanced scan. **Figure c**: Coronal reconstruction.)

**3.Barium meal examination of digestive tract**

Before surgery, 11 cases underwent barium gastrointestinal examination. 1 case had disappearance of mucosal folds in the intestinal wall and dilatation of the intestinal lumen, which suggested lymphoma. one of them had disappearance of mucosal folds in the intestinal wall and saw multiple fine niches, which was misdiagnosed as limited enteritis. 2 cases suggested external pressure changes, and seven patients had no obvious abnormalities on barium gastrointestinal examination.

**4. Tumor site**

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

**5. 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 large retroperitoneal vessels. After surgery, 11 cases received 4-8 cycles of adjuvant chemotherapy with CHOP (cyclophosphamide + epirubicin + vincristine + prednisone).

  **Results**

**1.Histological type**

The 15 Primary Small Intestinal lymphoma (PSIL) patients were confirmed by pathological examination to be non-Hodgkin Lymphoma（NHL): 8 patients were classified as Diffuse large B-cell lymphoma (DLBCL) (53.3%), 5 patients were classified as mucosa-associated lymphoid tissue B-cell lymphoma (33.3%), 2 patients were classified as enteropathy-associated T-Cell Lymphoma（13.4%).

**2.Follow-up and Prognosis**

We took 14 patients follow-up after operation about 6~52 months (average 30 months): 1 case of stress ulcer occurred after operation, there was no perioperative death, and 6 cases died of tumor metastasis or recurrence. The survival rate of 1-and 3-years was 85.7% and 57.1%, respectively.

**Discussion:**Primary small intestinal lymphoma (PSIL) is a rare disorder of digestive system malignant tumor, which is 19% to 38% in malignant tumors of the small intestine, and accounts for 20% to 30% in all primary gastrointestinal lymphomas.[2, 3] The small intestinal lymphoma can be classified as primary or secondary, the former occurs in the submucosal lymphatic tissue of the small intestine, which grow as solitary nodules and do not infiltrate the surroundings for a long time. Besides, the prognosis of primary small intestinal lymphoma is good. The secondary refers to small bowel disease as a component of systemic lymphoma, and its autopsy revealed that 50% of lymphoma patients had small bowel invasion.[4] What's the causes of primary small intestinal lymphoma is not exactly known, but research has reported that it is related to environmental factors, viral infections, genetic factors, immunodeficiency, some intestinal diseases, drugs, etc. [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, decline of body mass, etc, while has no specific clinical manifestations.[7] Therefore, patients with the above clinical manifestations should take the small bowel into examination.

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

PSIL originates from the lamina propria of 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 can only show indirect signs for extracavitary lesions, and it is not easy to find smaller mucosal lesions. When PSIL is accompanied by ulcer formation, it is often difficult to identify it from adenocarcinoma. Therefore, barium meal examination lacks specificity for its diagnosis. So is enteroscopy. When small intestinal lymphoma is not accompanied by ulcer formation, it is difficult to make a correct diagnosis, endoscopic lesions are not clear, and they often show general inflammation and erosion. The positive rate of pathological biopsy is low as the biopsy is often not deep into the mucosa, and there are also great limitations in the diagnosis of tumor infiltration of extracavity tissue. The spiral CT performance of PSIL is mainly characterized by different forms of intestinal wall thickening, and the following characteristics can provide an important basis for diagnosis:1) The intestinal wall is thickened and the intestinal cavity is dilated. Normal small intestinal wall thickness <3 mm, intestinal cavity width <30 mm. This standard can be used as a reference for intestinal wall thickening and expansion, which can be manifested by symmetry thickening, it can also be eccentricity thickening. The thickening of intestinal wall is mainly act as the submucosa thickening and muscle layer thickening, most of the intestinal tube above 3 / 4 weeks of diameter; 2) Analyzing 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 response in lymphoma. 3) Less invasion of lesions. 4) Analyze the enhancement CT value of each stage, the difference between before and after enhancement is 20 to 35 HU, suggesting that PSIL is a mildly or moderately enhanced tumor. PSIL needs to be identified with small bowel adenocarcinoma and small bowel Crohn's disease when the main manifestation is bowel wall thickening. MSCT and its post-processed images can show not only 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 which is sensitive to radiotherapy and chemotherapy. The current consensus about the treatments of malignant lymphoma is surgical treatment and then the adjuvant treatment.[10, 11] And the resection of surgical and the scope of lesion clean-up should be based on the tumor location, tumor size, and size of the tumor invasion range,etc. It is easier to separate and remove it from the surrounding tissues during surgery as intestinal lymphoma is a non-invasive growth method. We advocate active radical surgery for intestinal malignant lymphoma, if it cannot be cured, in order to prevent complications such as perforation and bleeding during chemotherapy, a palliative surgery should be needed. Early diagnosis is very important to improve the prognosis of PSIL. And to avoid delays in the timing of surgery, an exploratory laparotomy should be performed decisively for patients who with surgical indications.

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