

CHINESE MEDICAL SCIENCES JOURNAL

ORIGINAL ARTICLE

Clinical Characters of Gastrointestinal Lesions in Intestinal Behcet's Disease

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Key words: Behcet's disease; gastrointestinal tract

Objective To investigate the clinical features, diagnosis methods, therapeutic principles of intestinal Behcet's disease.

Methods The clinical data of 45 patients with confirmed intestinal Behcet's disease admitted to Peking Union Medical College Hospital from August 1998 to April 2010 were retrospectively analyzed.

Results The clinical courses of patients with intestinal Behcet's disease were from 26 days to 33 years, and the average duration was 6.32 ± 1.01 years. The appearance of extra-gastrointestinal symptoms was significantly earlier than that of gastrointestinal symptoms (7.35 ± 1.39 years vs. 3.24 ± 0.82 years, $P < 0.05$). The predominant gastrointestinal manifestations were right lower quadrant pain (95.56%) and hematochezia or melena (40.00%). Misdiagnosis occurred in 17 cases. In patients without systemic medicine therapy before surgery, the incidence of postoperative infection of incision site and abdominal cavity was significantly higher than that in those undergoing systemic medicine therapy (80.00% vs. 0%, $P < 0.05$).

Conclusions Because of the diversity of gastrointestinal manifestations, intestinal Behcet's disease is easily misdiagnosed. The systemic medical therapy before surgery could decrease the incidence of infection of incision and abdominal cavity.

Chin Med Sci J 2011; 26(3):168-171

BEH CET'S disease is also called Behcet's syndrome, which was first described by a Turkish dermatologist in 1937. Behcet's disease is a rare systemic vasculitis characterized by painful mouth ulcers, genital ulcers, and eye problems. It can also

involve visceral organs such as gastrointestinal (GI) tract, joints, heart, lung, blood vessels and central nervous system.¹ Most of patients suffering from intestinal Behcet's disease first complain of GI symptoms, and the symptoms are often varied and non-specific. Therefore, this disease is prone to be undiagnosed or misdiagnosed. In this article, we analyzed the clinical features of 45 patients with intestinal Behcet's disease, admitted and treated in our hospital from August 1998 to April 2010, in order to im-

Received for publication April 21, 2011.

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prove the surgical strategies for intestinal Behcet's disease.

PATIENTS AND METHODS

Patient enrollment

A total of 45 patients with intestinal Behcet's disease treated in our hospital were enrolled into the study from August 1998 to April 2010. All the patients met the diagnostic criteria for Behcet's disease developed by the International Study Group for Behcet's Disease.²

Data analysis

Clinical data of the 45 cases were retrospectively analyzed including clinical manifestation, physical findings, laboratory test results, radiographic and pathological findings, operations and medication therapy, as well as prognosis.

Statistical analysis

SPSS 13.0 software was used for statistical analysis. The time from onset of GI symptoms to correct diagnosis was compared with that of extra-GI symptoms appearance to correct diagnosis using *t* test. The difference of incidence rate of postoperative infection between patients with systemic medical therapy before operation and ones without systemic medical therapy was analyzed by χ^2 test. $P < 0.05$ was considered as statistical significance.

RESULTS

Clinical manifestation

Of the 45 confirmed patients, 25 were male and 20 were female, and sex ratio (male/female) was 1.25:1. The ages at the time of Behcet's disease diagnosis were from 10 to 65 years old with an average age of 37.64 ± 1.90 years old. All of the patients had not family histories of intestinal Behcet's disease.

The clinical courses of the 45 cases were from 26 days to 33 years, and the average duration was 6.32 ± 1.01 years. Totally, 17 cases had been previously misdiagnosed. Of them, 6 were misdiagnosed as appendicitis, 5 as intestinal tuberculosis, 2 as GI infection, 2 as esophagitis, and 2 as superficial gastritis.

All of the 45 cases had extra-GI symptoms. All cases had recurrent oral ulcers, 37 (82.22%) cases suffered from recurrent genital ulcers, 30 (66.67%) cases manifested skin lesions (erythema nodosum-like lesions, pseudofolliculitis, papulopustular lesions, *et al*), 19 (42.22%) cases were positive for pathergy tests, 7 (15.56%) cases had eyes lesions, and 3 (6.67%) cases complained of joint pain. Besides, 23 (51.11%) patients had episodes of fever

during the clinical course. Only 2 patients got the correct diagnosis as the extra-GI symptoms showed up. In 43 (95.56%) cases, in which the diagnosis can not be ascertained after onset of extra-GI symptoms, the average time from onset of symptoms to correct diagnosis was 7.35 ± 1.39 years.

A total of 43 of 45 (95.56%) patients complained of abdominal pain, in which 26 (57.78%) patients showed right lower quadrant pain. Other GI symptoms included hematochezia or melena (18/45, 40.00% cases), nausea and vomit (11/45, 24.44% cases), diarrhea (7/45, 15.56% cases), hematemesis (2/45, 4.44% cases), retrosternal pain and heartburn (3/45, 6.67% cases), mass in the right lower quadrant (3/45, 6.67% cases), pain below xiphoid (1/45, 2.22% cases), abdominal flatulence (6/45, 13.33% cases), and body-weight loss (11/45, 24.44% cases). Only 4 cases were diagnosed as Behcet's disease as GI symptoms appeared for the first time, and 7 cases were diagnosed before appearance of GI disorders. Thirty-four cases were not definitely diagnosed after onset of GI symptoms and the average time from onset of symptoms to correct diagnosis was 3.24 ± 0.82 years, which indicated that appearance of extra-GI symptoms was significantly earlier than that of GI symptoms ($t = 2.54$, $P < 0.05$).

Physical examination showed 17 (37.78%) cases with right lower quadrant tenderness, 2 cases with rebound tenderness and muscle tonus, 4 cases with tenderness in middle to lower quadrant, and 2 with masses in right lower quadrant.

Results of laboratory tests

The complete blood count revealed white blood cells elevated in 13 (28.89%) while decreased in 7 (15.56%) patients, peripheral blood neutrophils increased in 25 (55.56%) cases, and hematocrit elevated in 24 (53.33%) cases. Of all, 37 (82.22%) cases showed abnormal erythrocyte sedimentation rate levels and 25 (46.67%) cases were with increased C-reactive protein levels. In 26 (51.00%) cases receiving HLA-B5 antigen serotype test, 8 (17.78%) were identified to be positive. Twenty-five cases were positive for stool occult blood test. Immunoserologic analyses including rheumatoid factor (RF), antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), anti-saccharomyces cerevisiae antibody (ASCA), extractable nuclear antigen (ENA) were all negative.

Results of GI tract visualization

Twenty-two cases received this examination. GI tract visualization revealed inflammatory changes and ulcer at the ileocecal junction in 9 cases.

Results of gastroscopy

Gastroscopy was performed in 25 cases. There were 14 (31.11%) cases of chronic superficial gastritis, 6 (13.33%) cases of esophageal ulcers, 3 (6.67%) cases of gastric ulcers, and 2 (4.44%) cases with no lesion.

Results of colonoscopy and pathology

Colonoscopy with biopsy was performed in 32 patients. Colonoscopy showed 27 (60.00%) of them were with ulcers at the ileocecal junction, most of which were annular with surrounding mucosal congestion and erosion. The pathology of all the 27 patients demonstrated chronic inflammation of the mucus membranes, ulcers, granulation tissue formation, small blood vessel dilation and bleeding at the ileocecal junction. Two cases formed marginal ulcer after right hemicolectomy. One case was diagnosed as colon cancer and one case as rectal cancer, respectively.

Surgical treatment

Abdominal operations were carried out in 18 patients, 5 of whom (11.11%) had twice operations, 1 (2.22%) case had 4 procedures. Six patients were found to have ileocecal mass preoperatively, 3 of whom received ileocecal resection, 2 received right hemicolectomy, and the other 1 successively received ileocecal resection and right hemicolectomy because of anastomotic stoma fistula. For 5 patients diagnosed as ileocecal perforations, 2 of them had neoplasty, 1 case had ileostomy, 1 case had ileocecal resection, and 1 case had right hemicolectomy. One patient with colon cancer underwent right radical hemicolectomy. One patient with rectal cancer received radical resection. One patient who developed colovesical fistula received colostomy. Besides, 4 patients who were considered as appendicitis and intra-abdominal abscess received appendectomy. Of them, 2 patients complicated with intestinal fistula underwent right hemicolectomy, and the other 2 cases were treated by incision and drainage of appendiceal abscess.

Complication

Of the 18 patients who received surgical therapy, 15 cases had not received any systemic medical therapy before operation, and 12 of them (80.00%) suffered from infection of incision site and abdominal cavity. Three cases with systemic medical therapy before surgery did not develop any infection after operation. The incidence of postoperative infection between patients with systemic medical therapy before operation and ones without systemic medical therapy had significant difference ($P < 0.05$).

Medical therapy

All of the 45 cases were given systemic medical therapy after definite diagnosis in our hospital, and the diseases were all effectively controlled.

Follow-up

In this cohort, 42 cases were followed up, and 3 cases were lost. All of them were alive. The median survival time of 17 cases with operation was 1792 days and that of 25 cases without operation was 1778 days. There was no significant difference between them ($P > 0.05$).

DISCUSSION

Behcet's disease involves not only mouth, eyes and genital organs but also many other organs and systems, which can be categorized as different types, such as vascular, neurological, and intestinal types.¹ The pathogenesis of Behcet's disease is not well defined and often ascribed to multiple factors, such as genetic factor, immunological factor, environmental factor, infectious pathogens and epidemic factor.^{3, 4} The GI tract is one of the common organs affected by Behcet's disease. Behcet's disease causes inflammation and ulceration throughout the digestive tract. Deep and recurrent ulcerations can cause GI tract narrowing, perforation, peritonitis and bleeding.⁵ The lesions tend to affecting the ileum and colon, especially the ileocecal junction, then the lower part of the esophagus and gastric fundus. The most of ulcerations in the lower esophagus are superficial, and those in the stomach and duodenum appear to be common gastritis or ulcers, hence it is difficult to differentiate.^{6, 7}

Diagnosing Behcet's disease is very difficult because no specific test confirms it. Usually, abdominal pain in right lower quadrant is the most common complaints. Because the symptom is very similar to symptom of other diseases of the digestive tract, careful evaluation is essential to distinguish them. Totally, 17 cases in our cohort were misdiagnosed. Intestinal involvement of Behcet's disease should be diagnosed with endoscopy. When it is quite hard to tell the differences between the diffuse lesions in the colon of intestinal Behcet's disease and those in ulcerative colitis or Crohn's disease, clinical doctors should thoroughly recognize the clinical characteristics of intestinal Behcet's disease to help distinguish Behcet's disease from other disorders.

There is no cure for Behcet's disease. Treatment typically focuses on relieving symptoms, reducing inflammations and preventing serious complications. Corticosteroid is still the main medication to treat inflammation.

Immunosuppressive drugs and NSAIDs can help control an overactive immune system. α -IFN, TNF- α and infliximab⁸ are effective alternative treatment options for patients with Behcet's disease. At acute phase, high dose corticosteroid may be necessary for patients affecting by acute severe GI tract inflammation. However, the side effects of corticosteroids are harmful to digestive organs. So that, histamine receptor antagonists and proton pump inhibitors are required to counteract those adverse effects.

Application of surgical treatment should be fully contemplated. Especially in acute phase, operations should be avoided as far as possible. Otherwise, postoperative complications significantly increased, and postoperative relapse rate could be as high as 50%, in addition, 37.5% of the patients will need a second procedure because of marginal ulcer.⁹ In all, surgical treatment should be placed at the third position even after interventional therapies are ineffective. Certainly, some severe intestinal ulcers can cause perforation and bleeding, which must require emergent surgical treatment. Even at mean time, please remember that therapies targeting primary disease should be put in important place to go with,¹⁰ which are coincident to our study results, pre-operative systemic medical therapy can obviously reduced the incidence of postoperative incision site and abdominal cavity infections. Thus, early correct diagnosis and intervention by medicine are essential for the prognosis and complication prevention of intestinal Behcet's disease.

REFERENCES

1. Dowling CM, Hill AD, Malone C, et al. Colonic perforation in Behcet's syndrome. *World J Gastroenterol* 2008; 14: 6578-80.
2. Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. *Lancet* 1990; 335: 1078-80.
3. Gbate JV, Jorizzo JL. Behcet's disease and complex aphthosis. *J Am Acad Dermatol* 1999; 40:1-18.
4. Shang YB, Han SX, Li JH, et al. The clinical feature of Behcet's disease in Northeastern China. *Yonsei Med J* 2009; 50:630-6.
5. Naganuma M, Iwao Y, Inoue N, et al. Analysis of clinical course and long-term prognosis of surgical and nonsurgical patients with intestinal Behcet's disease. *Am J Gastroenterol* 2000; 95:2848-51.
6. Hohamed HH, Imed BG, Mounis L, et al. Esophageal involvement in Behcet's disease. *Yonsei Med J* 2002; 43: 457-60.
7. Yi SW, Cheon JH, Kim JH, et al. The prevalence and clinical characteristics of esophageal involvement in patients with Behcet's disease: a single center experience in Korea. *J Korean Med Sci* 2009; 24:52-6.
8. Makoto N, Atsushi S, Tadakazu H, et al. Efficacy of infliximab for induction and maintenance of remission in intestinal Behcet's disease. *Inflamm Bowel Dis* 2008; 14: 1259-64.
9. Chou SJ, Chen VT, Jan HC, et al. Intestinal perforations in Behcet's disease. *J Gastrointest Surg* 2007; 11:508-14.
10. Altıntaş E, Senli MS, Polat A, et al. A case of Behcet's disease presenting with massive lower gastrointestinal bleeding. *Turk J Gastroenterol* 2009; 20:57-61.