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Case Report Open Access

Crohn's Disease Complicated by Gastrointestinal Non-Hodgkin's Lymphoma: Report of a Case

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Abstract

Although Crohn's Disease (CD) increases the risk of neoplasma mainly in the form of adenocarcinoma in the area of inflammation, rare cases of primary gastrointestinal non-Hodgkin's Lymphoma (NHL) have been reported in the clinical course of CD. The mechanism underlying the lymphoma that complicates CD is still unclear. In the current report, the clinicopathological characteristics of primary gastrointestinal NHL in a CD patient receiving long-term azathioprine and infliximab therapy are presented. The case report that will be discussed is believed to provide clinicians an insight into the possibility of lymphoma development and will stress the importance of obtaining a reliable histological diagnosis whenever possible.

Keywords: Crohn's disease; Non-Hodgkin's lymphoma (NHL); Gastrointestinal; Surgery

Abbreviation: CD: Crohn's Disease; NHL: Non-Hodgkin's Lymphoma

Introduction

Crohn's Disease (CD) is an inflammatory disease of the intestines that may affect any part of the gastrointestinal tract from the mouth to the anus. CD is an autoimmune disease, in which the immune system of the body attacks the gastrointestinal tract, thereby causing inflammation [1]. This disease increases the risk of neoplasma, in which gastrointestinal tract adenocarcinomas are the most common complications [2,3]. In addition, the risk for other types of neoplasmas may be increased in CD including lymphoma and carcinoid tumors [4,5].

The precise neoplasma risk data in CD are very limited. A recent published meta-analysis has shown a fourfold increased risk of Non-Hodgkin's lymphoma (NHL) in a subgroup of inflammatory bowel disease patients treated with azathioprine and/or 6-mercaptopurine [6]. The mechanism underlying the lymphoma that complicates CD still needs to be elucidated. Alterations in immune surveillance, chronic inflammatory condition, immunosuppressive therapy, exposure to radiation, and Epstein barr virus infection have all been suggested [6-11].

In the current report, a case of primary gastrointestinal NHL in a patient with CD receiving long-term azathioprine and infliximab therapy is presented.

Case Presentation

A 66 year-old man with complaints of recurrent diarrhea for 5 years and stomach ache for 1 month was hospitalized in January 2009. Five years prior to hospitalization, the patient began to suffer from diarrhea without obvious causes with 3-6 times daily defecation of about 200 ml pasty feces. The patient was diagnosed with CD after enteroscopy upon his hospitalization. He was subjected to medication, but the symptoms were not well-controlled. The patient returned to the authors' hospital for ileocecal junction resection, and the pathological examination showed that he suffered from CD. After the post-operative intensification therapy with arilin, mesalazine (Etiasa) and azathioprine were used for maintenance therapy. However, the therapeutic efficacy was not satisfactory. After infliximab was administered for the treatments in December 2008 and January 2009, the symptoms were slightly alleviated. One month before the most recent hospitalization, diarrhea recurred accompanied by stomach ache and hemafecia. The patient was hospitalized in the division of internal medicine due to CD and postoperative ileocecal junction. After he was discharged from his previous confinement, the patient was in good mental health, but his appetite was poor and his liquid intake was minimal. His sleep was normal, and he urinated normally. During the physical examination, the patient's blood pressure 80/50 mmHg, and his nutritional status was poor. He demonstrated symptoms of serious anemia. His palpebral conjunctiva was pale. Slight tenderness was detected in his right lower quadrant. Rebound tenderness was not detected, bump was not detected, bowel sounds were active, and accentuation was not found. His blood routine examination results were as follows: WBC, 2.0×10^9/L; Hb, 51g/L; albumen (hepatic function), 29.3 g/L. His routine stool examination tested positive for occult blood. Examinations on the patient's upper gastrointestinal tract using barium meal after his hospitalization revealed a descending segment of duodenum-ascending colonic fistula (Figure 1A). Gastroscopic analysis showed a descending segment of duodenum-ascending colonic fistula, considered to be induced by CD, and non-atrophic gastritis (Figure 1B). Enteroscopic analysis showed multiple ulcers in the colon. However, the nature of these ulcerations was not identified. Whether these ulcerations were due to CD or intestinal tuberculosis still required further examinations. Sinus tract formation in the ileocolon stoma was also determined from the enteroscopic analysis (Figure 1C).

The patient was then subjected to surgical operation. During the operation, a 7×8 cm bump was found in the original stoma at the upper right quadrant involving the abdominal wall, duodenum, and gastric antrum. Subsequently, the bump was opened. A 3 cm×3 cm ulcerative tumor was found in the gastric antrum and orificium fistulae with a diameter of about 1 cm in the duodenum and gastric antrum respectively. The patient underwent resections in the original

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Figure 1A: Descending segment of the duodenum-ascending colonic fistula (arrow) revealed by the X-ray barium meal.

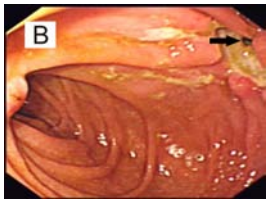

Figure 1B: Descending segment of the duodenum fistula (arrow) as determined by gastroscopy.

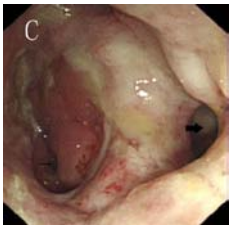

Figure 1C: Sinus tract at the ileocolon stoma (thick arrow) and the proximal segment of the sinus tract at the ileocolon stoma (thin arrow) as seen from fiberscope.

stoma, a part of his stomach, and a part of his duodenum. The terminal ileum of the pedicle flap was repaired, his gallbladder and duodenum stoma were resectioned, the biliary passage was explored, and jejunum nutrient canal insertion, as well as intestinal side-to-side anastomosis, was conducted. The excised specimens were subjected to pathological examinations. The results are shown as follows: colon, CD (Figure 2A); gastric antrum, NHL (diffusive large B cell-type) (Figure 2B); and immunohistochemical analysis CD_{20}^{+}, CD_{3}^{-}, CK^{-}, EMA^{-}, Syn^{-}, SMA^{-}, CD_{68}^{+}, and Ki_{67}^{-}. Local inflammation was detected at the duodenal orificium fistulae. Metastatic tumor was not detected in the six granules of the mesenteric lymph nodes (0/6) or in the eight granules of the gastroepiploic glands (0/8).

Leakage was detected in the position of repair in the duodenum 4 days after the operation. Thus, local sufficient drainage was performed, and the patient was healed and discharged after one month. Drug medication was not administered after the chemotherapy according to CHOP program for six cycles in a local hospital after the discharge. From the time the patient underwent chemotherapy, he no longer suffered from stomach ache, diarrhea, hemafecia, and dark stools. His appetite improved, and his body weight increased about 12 kg. Now he can work or live a normal life. Until now, no examination has monitored a relapse of CD or NHL.

Discussion

CD is a chronic granulomatous disease in the gastrointestinal tract without definite cause. The lesions mainly involve the terminal ileum, colon, proximal end of the ileum, jejunum, and other positions [1]. The causes of the disease are still unclear, but interplay of genetic environmental and immunologic factors is crucial in its pathogenesis. The primary gastrointestinal tract lymphoma is a malignant tumor originating from the lymphatic tissues below the mucosal membrane of the gastrointestinal tract, which accounts for approximately 2%-4% of the malignant tumors in the gastrointestinal tract. The pathological type is mainly NHL, which accounts for 4%-20% of the entire NHL [12]. This disease frequently invades the stomach and the small intestine, and that histological results are golden criteria for the diagnosis of this disease. The exact cause of Non-Hodgkin's lymphoma is not known, but a virus or activation of abnormal genes is believed to be involved in some cases. Some risk factors include:(1) being aged 60 and above, (2) autoimmune disease (e.g. rheumatoid arthritis) (3) exposure to pesticides, chemical solvents, and dyes, (4) exposure to some viral infections such as Epstein barr virus, (5) immunodeficiency states such as AIDS, congenital immunodeficiency, or chronic immune suppression by medications and (6) prior exposure to chemotherapy or radiation therapy. Parsonnet et al. found that primary gastric NHL is associated with previous Helicobacter pylori infection [13].

CD complicated by gastrointestinal NHL is not frequently seen and its association is a contentious issue. Lymphoma incidence rate was not significant difference between Crohn's disease and control cases in the study of Lewis et al. [14]. However, Kandiel et al. reported that Non-Hodgkin's lymphoma frequency was 4 times higher among inflammatory bowel disease patients, and the increased risk of lymphoma could be a result of the medications, the severity of the underlying disease, or a combination of the two [6]. In a previous report, a relatively long disease course was frequently manifested before the complication of lymphoma in CD [11], which may be related to Epstein barr virus infection [7], chronic inflammatory condition [8], and the utilization of immunosuppressive agents [9] or tumor necrosis factor inhibitors, such as infliximab [10]. The last two causes may play a potential triggering role in the development of NHL in our case.

Until now, there have been cases of lymphoma mimicking Crohn's disease in the literature. Given the low morbidity and scarcity

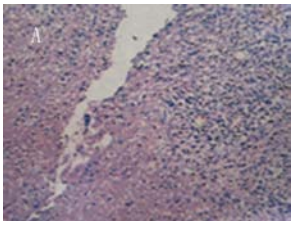

Figure 2A Histological features of CD (×100) as demonstrated by HE staining.

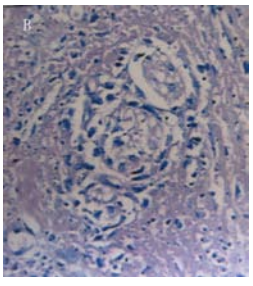

Figure 2B: Histological features of NHL (×100) as demonstrated by HE staining.

of specific clinical symptoms of gastrointestinal tract lymphoma, invasions in the digestive canal are frequently seen in primary and major manifestations, such as stomach ache, diarrhea, hemafecia, and others, which are extremely similar to the clinical manifestations in CD and other inflammatory bowel diseases. Thus, this ailment may be misdiagnosed, particularly when complicated lymphoma exists simultaneously with CD. Complicated lymphoma can be pathologically confirmed only after operational treatment on CD.

Although complicated lymphoma is rarely manifested in CD, clinical physicians should be cautious, particularly when the following symptoms are detected in patients and the possibility of complicated lymphoma is considered: (1) abdominal mass, (2) sign of ascites, (3) swelling of the celiac lymph nodes, (4) intussusceptions, and (5) loss in efficacy of the original therapeutic program. Once the possibility of lymphoma is suspected, histological examinations should be promptly performed to obtain definite diagnosis and timely treatment.

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