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## Case Report

# The Jejunum Non-Hodgkin's Diffuse Large B cell Lymphoma: an Origin of Extra-Germinal Center - @

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## ABSTRACT

**Introduction:** Diffuse Large B Cell Lymphoma (DLBCL), as a set of heterogeneous aggressive lymphoma, most commonly originated in the germinal center B lymphocytes. Rare cases were from peripheral blood B cell (outside germinal center) or from the inert lymphoma development and transformation. And such tumor with originality outside germinal center was seldom seen in the literature. Even the tumor in combination with chronic gastritis has not been reported before.

**Presentation of case:** A 51-year-old man admitted to emergency department with acute abdominal pain around the umbilicus. From the collective materials, the initial diagnosis was as chronic gastritis, cholecystitis and gall bladder small polyps. After hospital, the optimal therapy did not relieve the symptoms. Intraoperatively, a mass with a diameter of almost 5 cm originated from the distal jejunum segments neighboring the duodenum was seen. The patient was managed by segmental resection of the small intestine including the mass. Histologically, the cancerous cells are 4-5 fold larger than the normal lymphocytes. They exhibited atypical, and these heterotypic lymphocytes diffusely infiltrated in the whole layer of the digestive tract. The immunohistochemical studies showed that tumor cells expressed B cell differentiation antigen, with positivity for CD20, CD3, CD5, CD30, Ki-67 (> 80%), Bcl, MUM, and negativity for CD21, CD10, Bcl-2. So, the final pathologic diagnosis was diffuse large B lymphoma of the jejunum.

**Discussion:** Microscopic examination of the small intestine is a necessary means of diagnosis of the disease. Concomitant resection of tumoral lesions detected in the neighbor intestinal segments should be considered to diagnose and treat. For the diagnosis of this kind of tumor, immunohistochemistry pattern including positivity for CD20, CD3, CD5, CD30 etc. plays a crucial role. Therefore, detailed immunohistochemistry analysis should be constructed in suspicious cases.

**Conclusion:** Coexistence of diffuse large B lymphoma of the jejunum with chronic gastritis, cholecystitis and gall bladder small polyps is a rare event. Complete surgical excision and postoperative chemotherapy could be regarded as the main modality of such disease. Long-term follow up with serial imaging techniques is recommended.

## INTRODUCTION

Diffuse Large B Cell Lymphoma (DLBCL) is one of the most common types of cancer with a tendency toward diffuse aggressive behavior and recurrence [1-4]. It is estimated that there are over 200,000 new cases of B-Cell Non-Hodgkin's Lymphoma (B-NHL) in 2015, accounting for a predicted 4% of new cancer diagnoses and 3% of cancer deaths. For the therapy of this tumor, the first-line strategy was immune-chemotherapy, typically rituximab with CHOP for diffuse large B-cell lymphomas or with hyper-CVAD for Burkitt lymphomas [5-8], but the longer prognosis was poor. It is a reactive or inflammatory process in the lymphoid system mostly occurring in elderly patients, however, latest research shows that some cases have been reported with unusual extra-lymphoid center (originated from peripheral blood) [3]. Poor prognosis of the tumor was monitored because of an aggressive behavior with intra-abdominal and retroperitoneal diseases [4,9]. There is limited number of lymphoma cases found in the gastrointestinal tract [10]. However, such diffuse large B cell lymphoma with chronic gastrointestinal inflammation has been rarely reported before. Also, the depth and extent of surgery in such cases has not yet been studied because of the rarity of these cases. In this paper, the aim was to report a rare lymphoma occurred in jejunum of an old male patient with chronic gastroenteritis in order to provide helpful guidance for digestive physicians.

## CASE PRESENTATION

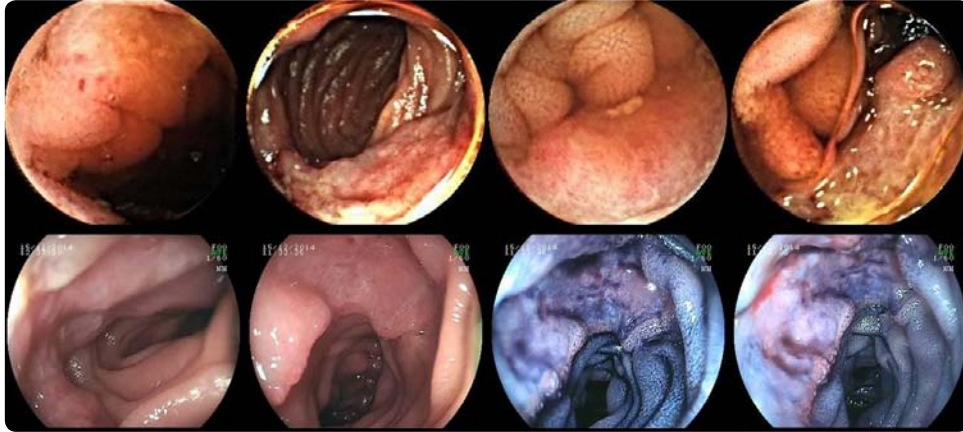
A 51-year-old man, transferred to the emergency department in our hospital on 2014-12-1, presented with drastic abdominal pain in the peripheral umbilicus direction. Pathological course was as follows: since January, 2014, there were no significant incentives, but the pain, as the durative ache, appeared mainly under the xiphoid region, and accentuated when dining, also radiated to the small of the back. Intestinal peristalsis abated with loss of appetite. Accordingly there were a series of non-specific clinical symptoms, for example, reduced gastric acid, belching, nausea, vomiting, diarrhea, chills,

fever. In the course of the disease, no obvious changes was found in the spirit, appetite, sleep of the patient, and in the urine amount, weight strength, but the color of the excreta gradually deepened. The sole evidence was with chronic gastritis in the previous history.

On admission, physical examination revealed light abdominal tenderness and small rigidity around the peri-umbilical region. It exhibited mild anemia face, general superficial lymph node enlargement, sclera and skin jaundice. No obvious abnormality was got in heart-lung auscultation. Other parameters were in normal range, including no abdominal tenderness, no rebound tenderness, no gastrointestinal type, no abdominal varicose veins, no Murphy sign, etc. Previous laboratory tests from other hospital showed normal leukocyte count and hemoglobin level. All other biochemical values were within the normal range. Heart colored ultrasonography revealed no abnormalities. MRI results in liver and spleen indicated the cholecystitis and gall bladder small polyps.

After hospital, the blood routine showed that, erythrocyte  $3.78 \times 10^{12}/L$ , hemoglobin 109g/L, red blood cells deposited 33.8%, blood sedimentation 28 mm/h; coagulant function showed that, Fib 5.27 g/L, ALT 7 U/L, TP 49.41 g/L, propagated 28.95 g/L, blood CRP is 31.54 mg/L, other parameters from the blood including renal function, blood amylase and AFP, CEA, CA199 were all in normal range. But the stool occult blood was slightly positive. Special inspection included that, one was gastroscopy, the results indicated chronic atrophic antral gastritis with debauched and chronic esophagitis; the colonoscopy showed no obvious abnormalities; the gastrointestinal barium meal showed that, the patient had chronic gastritis; small intestine microscope exhibited no obvious organic disease in the small intestine (Figure 1).

With a presumptive diagnosis of chronic gastroenteritis, cholecystitis, thereafter suppressing acid secretion, protecting stomach, spasmolysis and other symptomatic treatment were performed to the patient. In the first 3 days abdominal pain symptoms abated, but unfortunately, in the following days the clinical symptoms aggravated



**Figure 1:** The pathological site was captured by gastro scope (above) and small intestine microscope (below).

greatly. At this time, the stool occult blood emerged strong positive and the blood routine showed HGB: 106 g/L, so the consideration was that, pancreatic lesions were still not excluded, then line abdominal CT examination was conducted (Figure 2), the data still showed no abnormalities in pancreas, just a few swollen mesenteric lymph nodes were seen. Then a surgery was performed on this patient in order to confirm the abnormalities. During intraoperative process, chronic jejunum inflammation was detected. Some swollen and even melt lymph nodes were seen. Therefore, the segmental resection of the inflamed jejunum including the mass was conducted. The specimens collected were sent to pathological office for further investigation. Also, the wound recovered well at the seventh postoperative day with no inflammation, bleeding and edema. On the 3th postoperative month, he had no abdominal symptoms and neoplastic recurrence from the follow up and laboratory examinations.

## HISTOPATHOLOGY

The specimen was collected from the jejunum with a length of 10 cm after fixation in 10% neutral buffered formalin. Histopathology was concordant with chronic intestine inflammation as infiltration of the mucosa by atypical leukocytes. A serial section of the inflamed jejunum revealed a polypoid mass with a diameter of 5.5 cm. The tumor was covered with normal mucosa and it was located from the sub epithelial to subserosal planes, mostly intraluminal. Tissue serial



**Figure 2:** The picture indicated the pathological site highlighted in orange color captured by computer tomography.

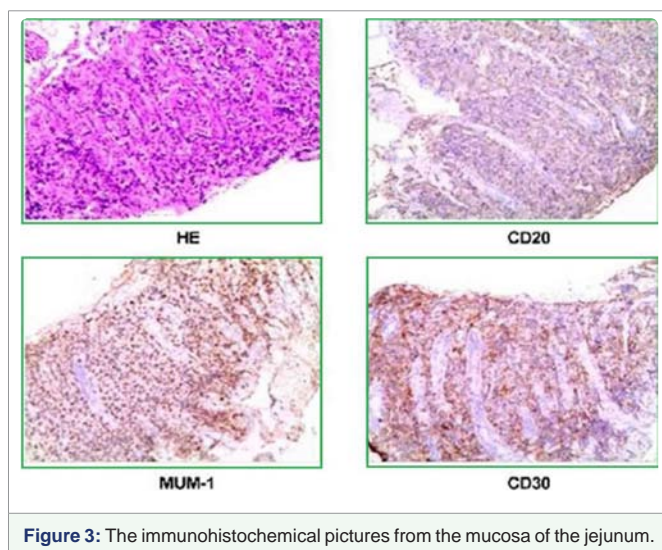
slices of the lesion showed diffuse lymphocytes appearance with no well demarcated borders in all layers of the jejunum. Perforation, necrosis, hemorrhage, calcification and ulceration were not identified macroscopically. But histologically, the tumor cells scattered in the mesenchyma surrounded degenerated or necrotic normal tissue. The immunohistochemical studies showed that tumor cells were positive for CD20, CD3, CD5, CD30, Ki-67(> 80%), Bcl, MUM. Additionally, negative results were detected for antibodies to CD21, CD10, Bcl-2 (Figure 3). Ki-67 was positive in 15% of the cells. The final pathologic diagnosis was diffuse large B lymphoma of the jejunum. Also, the written consent was taken from the patient.

## DISCUSSION

B-Cell non-Hodgkin's lymphoma is one of the most common types of cancer in the world [2,4,11]. The tumor was of invasive malignancy to the human health, and commonly occurred in the elderly male patients, and the average age was more than 60. In clinic, the manifestation of the tumor was that, the single or multiple lymph nodes grew up quickly in the short time period, even outside the nodes there was a rapid increase of the mass, progress rapidly, and damage the function of liver and spleen. Although lymph node is the most common site of the lesion, few occurrences have also been reported in extra-germinal sites including the mediastinum, gastrointestinal tract, skin, bone, brain, etc [9,10,12]. Some reporters also showed the inert lymphoma was involved in this lesion [13]. These lymphoma cells could be activated and transformed, which cause the cancerous cell diffusely invade the normal organ. Extra-germinal site lesions usually present with non-specific signs and symptoms including abdominal pain, gastric and intestinal mass with occasional obstruction and shit character change in patients. Such patients are often easy to exert misdiagnosis. The efficient test modalities are in urgent need. The small intestine microscope is of new imaging techniques developed in recent years. It can be used to confirm the site of the tumor and the condition of this lesion. Besides the equipment monitoring, concomitant resection of tumoral lesions and histopathological examination are of the essence. It has also been suggested that long-term follow up with serial imaging techniques are required [14-18]. However, the choice of the imaging test and the interval has not been determined yet. As a B lymphocyte surface marker, the CD20, CD30, MUM etc [19], should be tested commonly. Except the B cell clusters of differentiation, the Bcl-2/6, P53 and Myc gene mutations should also be investigated because of about

20-30% DLBCL has t(14;18) and the Bcl gene translocation [20-23]. As a biomarker of tumor proliferative activity, Ki-67 value may be helpful to determine the time interval for follow up [24]. Therefore, an individualized follow up should be planned for each patient. The intestine microscope and PET/CT tomography at the postoperative 3th month was evaluated as normalcy for the patient [16-18].

The clinical therapy for such tumor was far unsatisfactory. Different therapies strategies were applied in different patients. Stem cell transplantation, Mitral valve repair engineering, targeting therapy and various chemical drugs were used to cure this type of tumor. But little success was achieved [25]. Anti-CD20 monoclonal antibody (rituximab) was still the first-line chemotherapy medication [26-28]. Although a few patients were cured by the standard immune-chemotherapy, while over 50% of patients showed resistance to rituximab or tolerance against the chemotherapeutics, which caused them to relapse and then died of the disease. Drug resistance is a major challenge to the long-term efficacy of targeted cancer therapies. Recently, people began to adopt tumor autophagy to kill this tumor. Although autophagy process can degrade some unnecessary or dysfunctional cellular components via the fusion of autophagosomes and lysosomes, the role of autophagy in tumor therapy remained complex. Emerging evidences showed that this modality remains controversial: On one hand, when under severe conditions such as nutrient deprivation, commander of growth inhibition, cells tended to up-regulate autophagy for degenerating misfolded protein or damaged organelle to provide fundamental nutrients and energy for survival [29]. On the other hand, some anti-tumor drugs like arsenic could induce overreacted autophagy, leading to autophagy-dependent cell death in Acute Myelocytic Leukemia (AML) cells [30]. Recent years, some scientists tried to use the strategy of co-inhibition of autophagy and Hh pathway, but the effect was not far satisfactory. Thus, looking for better treatment and medications become the challenge of more scholars [31-33]. From the data of statistics, this tumor is sensitive to chemotherapy, the use of strengthening the MDT, about 60-80% of the patients can completely respond; about 50% of the patients can clinically recover. Anti-CD20 monoclonal antibody (Rituximab, mabthera) combining with chemotherapy can significantly improve the prognosis of patients. And it is now still the most successful biological treatment of clinical cases.



## CONCLUSION

Diffuse Large B Cell Lymphoma (DLBCL) is a set of heterogeneous aggressive lymphoma, which occurred in germinal center or extra-germinal sites of old adults. For the diagnosis of DLBCL, the intestine microscope and immunohistochemistry pattern plays a crucial role. Complete surgical excision in combination with chemotherapy might be the main modality of the therapy of diffuse large B cell lymphoma [9,11]. Long-term follow up with serial imaging techniques may be recommended for possible aggressive behavior and recurrence. Doctors firstly should pay attention to the clues of the symptoms, signs and related inspection, look for a more reasonable explanation, avoid missed diagnosis. Secondly, the advantage of intestine microscope (capsule endoscope) should attract much attention because of more comfort, longer distance and higher sensitivity. Thirdly, the usage in combination of capsule endoscopy and enteroscopy in the initial diagnosis of intestinal diseases could provide more helpful insights for the digestive physicians.

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