# Synchronous diffuse large B-cell lymphoma masquerading as jejunojejunal intussusception with unexplained pleural effusion in elderly male: A rare manifestation

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**Abstract**

The primary gastrointestinal lymphoma is uncommon. This is a confirmed case of synchronous primary diffuse large B-cell lymphoma manifested as jejunojejunal intussusception with lymph nodal and pleural metastasis. Its clinical manifestations, morphological characteristics, immunophenotypes, and molecular biological characteristics are very different, which is the biggest challenge before surgery.

## 1. INTRODUCTION

Multiple primary malignant tumors are defined as the detection of two or more malignancies in an individual person [1,2] In particular, synchronous primary malignancy is extremely rare [2-5]. The GI tract is the most common site of extra-nodal lymphoma involvement. Primary GIL is a heterogeneous entity and constitutes approximately 10-15% of all NHL and estimates 30%-40% of all extra-nodal lymphomas [2,6,7]. Primary GIL accounts for 1% to 10% of all GI malignancies and up to 90% of which are B-cell non-Hodgkin lymphoma (NHL) [2.4.8.9]. In majority of studies investigate that stomach is the commonly affected site followed by small intestine. Lymphoma of the small intestine is the most common part of the ileum, followed by the jejunum and duodenum [10]. The most common identification site is the ileocolon region [1,2,5,8,11-14]. The vast majority of GILs are NHLs, DLBCL, mucosa-associated lymphoid tissue lymphomas (MALTomas), although Hodgkin lymphoma about one-third of NHL has been reported. DLBCL is a heterogeneous entity rarely causing acute bowel obstructive symptoms and intussusceptions.2-4 Synchronous primary DLBCLs of the small intestine is extremely rare and requires careful diagnosis is suspected [2,8].

Adult intussusception accounts for 5% of all intussusceptions. About 90% of cases of intussusception in children arise from unknown causes [4,15], which include infections, anatomical factors and altered motility. Only 10% of which is secondary to specific pathological lesions such as Meckel's diverticulum, polyps, and benign or malignant tumor [1,8]. The most small bowel lead points are benign lesions, and malignant lesions account for 30% of intussusception cases [1-4].

Obstruction and perforation are rare and life-threatening complications of GIL. Multiple intestinal intussusception caused by synchronous DLBCLs of the jejunum is extremely rare [1,8,16,17]. Secondary lymphoma pleural involvement (secondary pleural lymphoma) is common and occurs in about 20% of lymphomas. Primary GI-DLBCL initially presenting with pleural effusion [15], or with intestinal perforation is very uncommon [4,6,16,18]. To our knowledge, we firstly report an 85-year old male concerns an extremely rare manifestation of synchronous primary DLBCLs of the jejunum with unexplained pleural effusion and disseminating multiple lymph nodal involvement presenting as JJ intussusception in clinically. The purpose of this

report is to remind clinicians that lymphoma should be considered when assessing the cause of unexplained pleural effusion, especially when the available examination data cannot be confirmed by clinical manifestations. To our knowledge, this is the first confirmed case of synchronous primary DLBCLs of the jejunum masquerading as JJ intussusception with lymph nodal and pleural metastasis. Learning aims of this case report, we can understand that its clinical manifestations, morphological characteristics, immunophenotypes and molecular biological characteristics are very different and important. It is indeed the biggest challenge before surgery and is not to be ignored.

## 2. PRESENTATION OF CASE

An 84-year-old man complained with an intermittent colicky abdominal pain, dyspnea, orthopnea, fatigue, pallor looking, and progressive generalized edema for one month. On admission, vital signs were BT: 37.5°C, PR:98/min, RR:19/min, BP: 86/64mmHg. Laboratory data included Hgb: 4.4 g/dl, Hct: 15.1%, MCV: 71.6 fl, MCH: 20.9 pg, MCHC: 29.1 g/dl, neutrophils: 78.9%, lymphocytes: 87.7%, monocyte: 12.2%, NT-proBNP (PBNP): 3260 pg/mL, Na+: 123mmol/L, albumin: 2.39 g/dL, and urine protein was trace. Tumor marker (CEA, PSA, CA199 and AFP) levels were within normal limits. Microcytic anemia, hypoalbuminemia, and hyponatremia were firstly considered. He had BPH post-operation and denied of allergy history. He had BPH post-operation and denied of allergy history. He was negative for hepatitis B and human immunodeficiency virus (HIV) tests. Esophagogastroduodenoscopy revealed reflux esophagitis of Los Angeles classification grade A and gastric polyp over middle body was found. Chest x-ray showed bilateral pleural effusions (Figure 1A). Chest CT scan exhibited atelactasis of LUL and LLL with bilateral pleural effusions (Figure 1B). Some small lymph nodes with less than 1 cm at mediastinum and no bony destruction of thoracic cage was detected. CT scan of abdomen and pelvis demonstrated two segments of small bowel intussusception (Figure 1C-D), and one presented abnormal enhancement of the leading point with regional small lymph nodes and small bowel tumor was considered (Figure 1C-D). No peritoneal effusion or ascites was found. Suspected jejunal tumor related to JJ intussusception. Enlargement of left para-aortic and peri-portal lymph nodes were noted. Clinical and imaging examinations showed highly suspected of jejunal intussusception and intestinal obstruction. He underwent the diagnostic laparoscopy assisted laparotomy and two areas of JJ intussusception with manual reduction of intussusception. Subsequent segmental resection of the jejunum with lymph nodes dissection were also performed.

Histopathologic examination, the resected specimen submitted was a segmental jejunum with two separated protruding ulcerative polypoid masses between 10 cm in distances were identified, measured up to 3 by 2 by 2 cm (T1) and 2.5 by 1.5 by 1 cm (T2) (Figure 2). Microscopically, both T1 and T2 intestinal polypoid masses revealed diffuse loosely cohesive sheets and nodules, marked diffuse monotonous lymphoid elements with mixtures medium to large cells displayed vesicular nuclei with prominent nucleoli. Nuclear pleomorphic or large with obscure cytoplasm seen (Figure 3A-D). Sections showed homogeneous infiltrative lymphoma cells separating fibers through the intestinal wall and periserosal adipose tissue. The lymphoma cells reached up to the serosa and was accompanied by perforation of peritonitis. Analysis of dissected lymph nodes indicated 12 out of 16 mesenteric regional lymph nodes were involved by the lymphoma and displayed similar morphology suggesting high grade lymphoid malignancy. Immunohistochemical (IHC) staining, these lymphoma cells (T1 and T2) demonstrated diffusely positive immunoreactivity for CD20 (strongly diffuse membranous staining) (Figure 4A-B), increase expression for proliferative Ki-67-labeling index with approximately 90% of involved lymphoma cells (Figure 4C-D). Lymphoma cells also presented positive for Bcl-2, MUM-1/ IRF (multiple myeloma oncogene 1, post-germinal center or activated B-like), and focal positive for Bcl-6 (B-cell lymphoma 6, germinal center marker). In contrast, tumor cells showed negative for CD3 (T-cell marker) with positive in background small lymphocytes, and negative for CD-10 (germinal center marker), pan-CK, NSE, CD30, CD4 and cyclin-D1. The feature of synchronous high-grade DLBCLs of the jejunum was diagnosed. Subsequently pleural effusion cytopathology illustrated detection of lymphoma cells. Bronchoscopy brush cytology and sputum cytology showed negative for malignant cells. Trephine needle core biopsy for bone marrow examination showed negative for lymphoma involvement. The final pathological diagnosis prompted a diagnosis of synchronous DLBCLs of the jejunum with mesenteric lymph nodal and pleural metastasis associated intestinal obstruction with perforation was concluded. The

pathological TNM stage indicated, AJCC, 8thed stage, pT3N2M1, Stage IV (associated with primary GI lymphoma stage: pT3N2M1B0).

## 3. OUTCOME AND FOLLOW-UP

After emergency surgery, the patient recovered uneventfully. He was referred to the medical oncology team for further appropriate postoperative management. Subsequently, he received standard chemotherapeutic regimens (called Rituximab-CHOP) scheduled was administrated. Unfortunately, the patient sustained acute critical conditions presented hemodynamic worsen gradually, congestive heart failure, complicated hospital bacterial infection, massive pleural effusion with acute respiratory failure and hypovolemic shock related acute kidney failure developed. The patient expired six months after surgery.

## 4. DISCUSSION

The GI tract is the most common site of extra-nodal lymphoma involvement. Primary GIL accounts for 30-40% of extranodal lymphomas and 15-20% of all non-Hodgkin's lymphomas [1,19,20]. In majority of studies, stomach is the commonly affected site followed by small intestine. Stomach (50–60%) is the commonest site followed by small intestine while colon, rectum and esophagus (<1%) account for a minority of cases [4,7]. The GILs are active aggressively and require early diagnosis and management [1,2,21]. Unusual synchronous cases of lymphoma and non-lymphoid malignancies and another cancers are well described [2,4,6,20]. The coexistence of double primary malignancies especially malignant lymphomas of the jejunum is extremely rare [4,8]. Multiple lymphomatous polyposis (MLP) is a primary GIL with a distinctive entity and rare solid lymphoma intestinal segment involvement. The Dawson criteria are identified the classic tests for diagnosis of GIL include followings as absence of palpable lymphadenopathy in clinical examination; absence of mediastinal lymphadenopathy in a chest x-ray; normal range of total WBC and differential count; disease confined to the intestine and adjacent nodes involvement; no evidence of liver or spleen involvement [11].

Intussusception in adults is usually related to the underlying pathology. In previous well-documented adult intestinal intussusception caused by benign (63%), idiopathic (23%) and malignant (14%) lesions [4.22] The most common site of small bowel lymphoma is the ileum, ileocecal region followed by the jejunum and duodenum [2,4,14,19,23]. The GI tract NHL/DLBCL is unusual pathological lead point that can cause to intussusception in older children and in adults [1,8,18,24]. Although intussusception is very common in children, a leading cause of childhood intestinal obstruction [1.3], but it accounts for 5% of all intussusception, intestinal obstruction in adults accounting for 1-5% [3]. Clinically, adult intussusception is rarely considered in the differential diagnosis of patients with abdominal discomfort. However, adult intussusception preoperative diagnosis is difficult because the typical symptoms. The incidence of average age was 55 years (range 21-79 years old), male to female ratio was 2.6: 1 [25]. A study reviewed 36 published cases of intussusception caused by lymphoma from 2000 to 2011 [1.5]. These ages of the patients ranged from 16 to 86 years old. Among 36 patients in the 16 to 24 age group, only 7 patients developed secondary NHL with intussusception [5]. The clinical features of small intestinal lymphoma are non-specific. Common clinical manifestations of adult intussusception include symptoms such as colicky abdominal cramps, nausea, vomiting, weight loss, and rarely have acute obstruction symptoms, ulceration, intussusception, intestinal perforation or diarrhea [1,4].

The simultaneous occurrence of DLBCL is even rarer in the jejunum. Synchronous primary DLBCL of the jejunum is extremely uncommon and only three cases have been reported because of JJ intussusception caused by NHL in adult [1,8,16,26]. This additional case is synchronous DLBCs and the clinical manifestations presented as JJ intussusception with intestinal perforation with multiple lymph nodes and pleural metastasis. In literatures review that have been described a first rare case of DLBCL presenting with 2 areas of JJ intussusception only once previously [8], and a similar case with one area of JJ intussusception caused by DLBCL has been reported [1,8,16,19]. The previous rare case report has been described multiple recurrent JJ and ileo-ilea intussusceptions due to multiple lymphomatous polyposis associated with high-grade DLBCL of small intestinal in a child [1]. Obstruction and perforation is uncommon and life-threatening complications of NHL, which can occur at the time of diagnosis or during treatment. Previously, reported one case of

concurrent malignant B-cell lymphoma of the jejunum and multiple synchronous colon cancers [7], and one case with synchronous perforation of primary non-Hodgkin's T-cell lymphoma (NHTL) of the jejunum and descending colon presented with perforation and peritonitis.6

Clinically, the pathophysiology of primary pleural effusion or secondary malignant (metastatic) pleural effusion must to do differential diagnosis. Primary GI-DLBCL initially presented as unexplained pleural effusion is extremely rare. Recently, this an unusual case of unilateral pleural effusion associated with primary rectal DLBCL reported [2,9]. It is indeed extremely rare that synchronous DLBCLs with multiple lymph node and bilateral pleural metastasis in the same tissue and clinically characterized by JJ intussusception is indeed extremely rare. This present case concerns considering an extremely rare manifestation of synchronous primary DLBCLs of the jejunum with disseminating multiple lymph nodal and pleural involvement presenting as intestinal obstruction with perforation associating with two areas of JJ intussusception in an elderly male in clinically. To be best our knowledge and review, there is still no same case report in the published English literature.

The non-specific clinical manifestations make preoperative diagnosis difficult. The staging of primary GI-DLBCL is completed by considering imaging examination and bone marrow aspiration and biopsy evaluation. To establish an accurate diagnosis and staging of this heterogeneous group of lymphomas, applications of different procedures have been used, including endoscopic ultrasound (EUS), endoscopic biopsies, computed tomography (CT), magnetic resonance imaging (MRI), diagnostic laparoscopy, scintigraphy, angiography, positron emission tomography (FDG-PET), and/or molecular cancer markers [1,2,4,11]. Typical imaging features of intussusception include cross-sectional target sign or donut sign, longitudinal cross-sectional false kidney sign, sandwich sign, or pitchfork sign [1,2].

For the pathological diagnosis of surgical resection specimens, in terms of pathological diagnosis, histology and morphology, high-grade DLBCL must be differentiated from epithelial carcinomas, lymphoid or hematological neoplasms and/or leukemia. Currently widely used IHC staining could to do differential diagnosis. Histopathologic and IHC examinations, the specificity and sensitivity of CD19, CD20, CD79a and PAX5 markers to detect B-cell lineage lymphoma/leukemia-derived are analyzed on the tissue microarray by IHC [2,4,18,20]. In present case, IHC detection demonstrated CD20 marker shows strong and diffuse membranous staining, transcriptional factor (MUM1/IRF4) expressed in final step of intra-germinal center B cell differentiation and in post-germinal center (late centrocytes) B cells. CD10, BCL6, and MUM1 expression in DLBCL [1,4,6,27].

Primary GIL should always be retained in the differential diagnosis of intussusception cases, especially in older age and children groups. The therapeutic strategy for gastrointestinal lymphoma depends on the patient's age, clinical condition, histological subtype, extent and burden of the disease, and comorbidities. The effective treatment strategy generally includes surgery, radiotherapy and further chemotherapy (Rituximab with cyclophosphamide, doxorubicin, vincristine, and prednisolone R-CHOP) in such our case. Surgical resection combined with chemotherapy that has been shown to improve overall survival independent intestine large B-cell lymphoma [2,26-29]. The outcomes are directly related to the stage of at the diagnosis, with long term survival rate reported is close to 75 % overall [12]. The evaluation of prognosis of synchronous primary lymphoma in the intestine correlates better with the depth of invasion, tumor size, and lymphadenopathy. It was previously reported that the prognosis of GIL is very poor. This present case was late stage of disease with complicated critical conditions with microcytic anemia, hypoalbuminemia, and hyponatremia, pleural effusion, and poor survival could be predicted. Prognostic factors include the evaluation of stage at diagnosis, the presence of perforations, tumor resectability, histological subtype and multimodal treatment [9,12,21,29]. Lymphoma perforations with involving pleural and nodes generally have higher tumor stage and poorer prognosis in such our case. DLBCL of the small intestine has significantly improved stage I and stage II survival. Previous study data showed that early stage (stage I and II) patients have a longer cumulative survival compared to stage III or IV patients [12]. Early diagnosis and further management are important to improve the prognosis of intestinal intussusception in patients with NHL-DLBCL.

## 5. CNCLUSION

Intussusception in the adult population is often associated with underlying pathology. Considering that adult intussusception is a rare entity with inaccurate medical history and clinical examination. Imaging method evaluations are needed for diagnosis. Primary small bowel DLBCL can present a variety of clinical manifestations, which shows the importance of a highly suspected clinically, which is helpful for rapid diagnosis and subsequent treatment. Thus, learning aim based on this extremely rare case report, we can learn that its clinical manifestations, morphological characteristics, immunophenotypes and molecular biological characteristics are very different and important, which is challenging to preoperative diagnosis. Clinicians and surgeons should keep this in mind in the assessment of patients with intestinal obstruction, and should always be kept in the differential diagnosis of intussusception, especially in the older age or children groups. Emergency surgery is an option to treat severe intussusception. The diagnosis for localized intestinal DLBCL is usually confirmed by histopathology and IHC examination after obtained surgical specimen. Surgery, chemotherapy, radiotherapy and or immunotherapy is a different application of its management, may be in a different combination.

## AUTHOR CONTRIBUTIONS

Junn-Liang Chang: drafting manuscript review, corresponding author, data interpretation, evaluation, information acquisition and final approval;

Kuang-Ting Liu: responsible for operating pathological tissue / specimen processing, information acquisition and final approval, concept and design, critical review and final approval.

Yueh-Ching Chang: responsible for operating pathological tissue sections, special chemical staining and immunohistochemical staining, information acquisition, critical review, and final approval.

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## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

## ETHICL STATEMENT

The authors would like to thank the patient. Ethical approval is not required, the report did not provide identification information of patients.

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**Figure Legends**

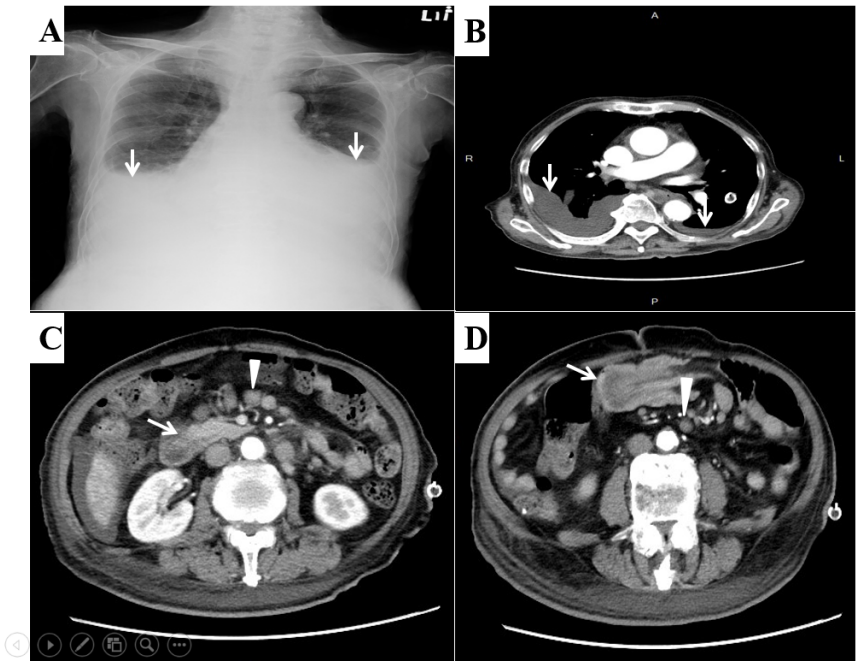


**FIGURE 1** Chest-x-ray showed bilateral pleural effusions (1A, white arrow). Chest CT scan exhibited bilateral pleural effusions (B, white arrow). Representative photographs of the CT scan of abdomen and pelvis indicated two segments of small bowel intussusception (C and D, white arrow), and one presented abnormal enhancement of the leading point with enlarged regional small lymph nodes (C and D, white arrowhead).

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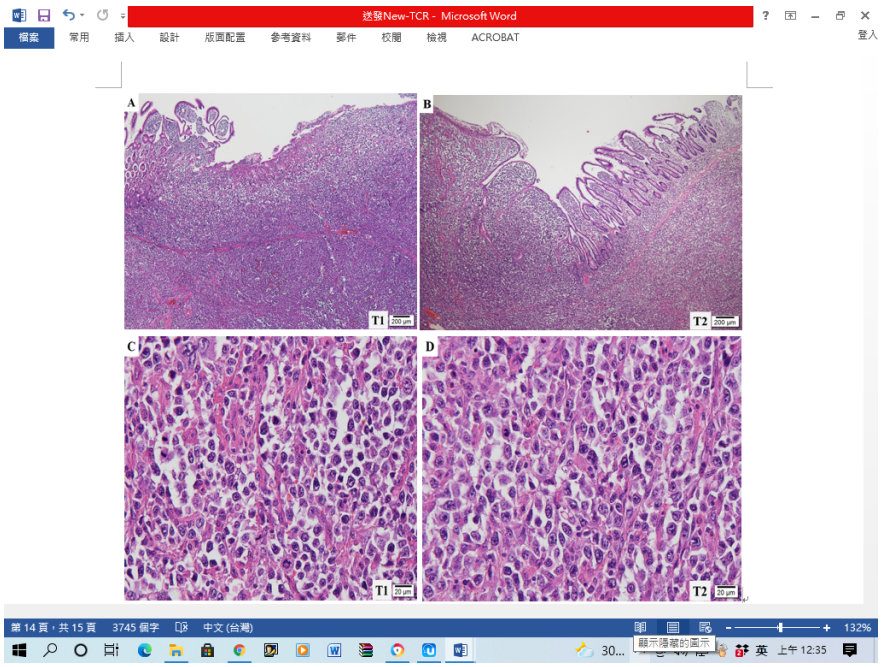
**FIGURE 2** Photograph of panoramic view displayed two separate ulcerative polypoid nodular masses of the jejunum (T1 and T2, green arrow).




**FIIGURE 3** Photographs of representative sections with hematoxylin & eosin (H&E) staining of the jejunal two separate DLBCLs (T1, A: H&E, original magnification x 40; T2, B: H&E, original magnification x 400) and (T1, C: H&E, original magnification x 400; T2, D: H&E, original magnificationx 400).

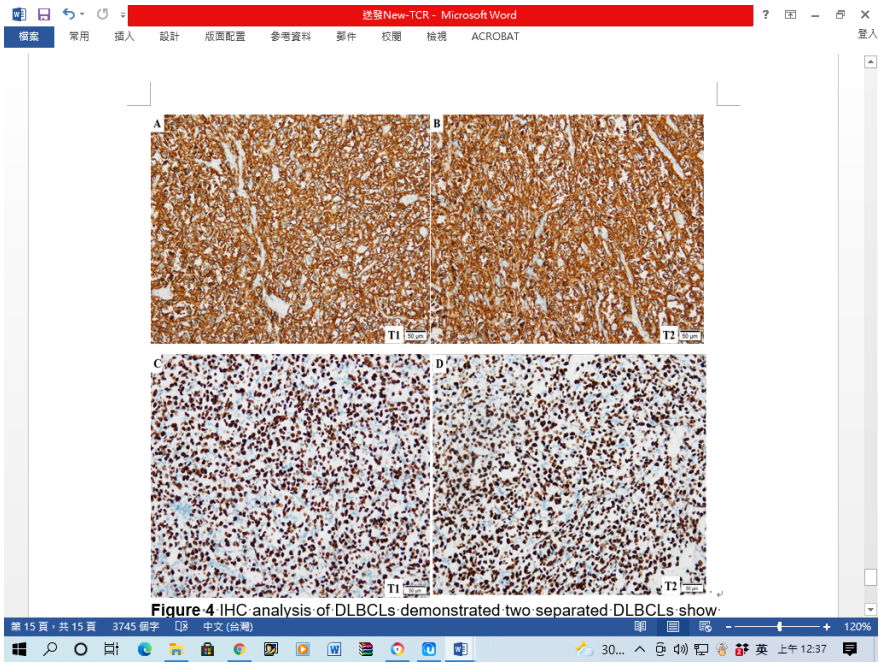



**FIGURE 4** IHC analysis of DLBCLs demonstrated two separated DLBCLs show diffusely positively for CD20 (T1, A: IHC, original magnification x 200; T2, B: IHC, original magnification x 200), and positive for proliferating Ki-67 labeling index with 90% of involvrf tumor cells (T1, C: IHC, original magnification x

200; T2, D: IHC, original magnification x 200).