Case Report

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Incidental finding of multiple diffuse large B-cell lymphomas masquerading as jejunojejunal intussusception with unexplained pleural effusion: a case report

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Introduction: Primary non-Hodgkin's lymphoma of the gastrointestinal (GI) tract is rare. It is aggressive and necessitates early diagnosis and management. Simultaneous primary GI lymphomas are unusual with rarely reported cases.

Case presentation: This novel case report describes an 84-year-old man with multiple primary diffuse large B-cell lymphomas (DLBCLs) of the jejunum with disseminating pleural and multiple regional lymph nodes involvement presenting as intestinal obstruction and segments of jejunojejunal intussusception. The patient underwent surgical intervention and adjuvant chemotherapy. Unfortunately, the patient suffered from multiple organ failure and died 4 months after surgery.

Clinical discussion: Obstruction and perforation are rare and life-threatening complications of GI lymphoma. Multiple DLBCLs of the jejunum are rare. Moreover, primary GI-DLBCL that initially presents with pleural effusion or with intestinal perforation is uncommon. This report aims 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.

Conclusion: Through this case report, the authors learn that clinical manifestations, morphological characteristics, immunophenotypes, and molecular biological characteristics are vastly different and important. This poses the biggest challenge before surgery and should not be ignored.

Keywords: diffuse large B-cell lymphoma, intussusception, jejunojejunal, Non-Hodgkin's lymphoma

Introduction

The (GI tract is the most common site of extranodal lymphoma involvement. GI lymphoma (GIL) is a heterogeneous entity and constitutes ~5–20% of all NHL and comprises 30–40% of all extranodal lymphomas[1]. Furthermore, GILs represent 1–10% of all GI malignancies[2]. The vast majority of GILs are NHLs, DLBCL, and mucosa-associated lymphoid tissue lymphomas, although Hodgkin lymphoma constitutes about one-third of reported NHL cases. DLBCL is a heterogeneous entity, rarely causing acute obstructive symptoms and intussusceptions[1,3]. About 90% of intussusception in children arises from unknown causes, including infections, anatomical factors, and altered motility and 10% is attributed to specific pathological lesions such as Meckel's diverticulum, polyp, and benign or malignant tumours[1,2]. In adults, most small bowel lead points are benign lesions, and malignant lesions account for 30% of intussusception cases[2–4].

In the literature review, we first report an unusual manifestation of multiple primary DLBCLs of the jejunum with disseminating bilateral pleural and multiple lymph nodal involvement presenting initially as pleural effusion mimicking jejunojejunal (JJ) intussusception secondary to non-Hodgkin B-cell lymphoma clinically in an elderly man. We present a rare

HIGH LIGHTS

- Primary gastrointestinal (GI) tract primary non-Hodgkin's lymphoma (NHL) is rare, aggressive, and requires early diagnosis and treatment.
- Multiple diffuse large B-cell lymphomas (DLBCLs) mimic as intestinal intussusception with unexplained pleural effusion.
- Clinical symptoms, immunophenotypes and biological characteristics differ.

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case of multiple primary jejunal DLBLCs managed by following the SCARE 2020 guideline[5].

Presentation of case

An 84-year-old man complained of intermittent colicky abdominal pain, dyspnoea, orthopnea, fatigue, and progressive generalized oedema for 1 month. On admission, vital signs were stable. Laboratory data included Hgb was 13.4 g/dl (14–18), Hematocrit was 40.1% (42–52), neutrophils was 78.9% (40–74), lymphocytes was 42.7% (19–48), monocyte was 12.2% (3.4–9.0), C-reactive protein was 1.2 mg/dl (0–0.5), Na + was 123 mmol/l (137–145), and urine protein was trace. Tumour markers included carcinoembryonic antigen, prostate specific antigen, carbohydrate antigen-199, and alpha-fetoprotein levels were within normal limits. The others showed non-contributor profile. The patient had benign prostatic hyperplasia post-operation and denied history of allergy or consuming alcoholic beverages or illegal drugs. Additionally, no drug allergies and/or adverse reactions, addictions, or B symptoms, history of smoking, chewing betel nuts, occupation, or travel in the past 3 months were reported. Furthermore, there was no contributing family history including relevant genetic information, and psychosocial history. The patient was negative for hepatitis B and HIV tests. Esophagogastroscopy showed reflux esophagitis of Los Angeles classification grade A and gastric polyp over the middle body. The chest X-ray displayed mildly homogeneous hypoechoic pleural effusion. Computed tomography (CT) scan of the chest exhibited atelectasis of left upper lobe and left lower lobe with bilateral pleural effusion (Fig. 1A, B) and small lymph nodes with short-axis less than 1 cm at mediastinum without bony destruction of the thoracic cage was found. CT scan of the abdomen and pelvis (Fig. 1C, D) demonstrated two small bowel intussusception segments while one presented abnormal leading point enhancement with regional small lymph nodes and a small bowel tumour. Enlargement of left para-aortic and periportal lymph nodes was detected. Suspected jejunum tumour-associated JJ intussusception. Consequently, a diagnostic laparoscopy-assisted laparotomy with manual intussusception reduction was undertaken with additional segmental jejunum resection and mesenteric lymph node dissection.

Gross histopathologic examination revealed a segmental jejunum with two separate protruding ulcerative polypoid masses with10 cm in between, measuring $3 \times 2 \times 2$ cm (T1) and $2.5 \times 1.5 \times 1$ cm (T2) (Fig. 2). Microscopically, both T1 and T2 intestinal polypoid masses showed obvious diffuse, monotonous lymphoid components, mixed with variably sized pleomorphic lymphocytes. The tumour cells showed large, obscure cytoplasm with pleomorphic nuclei (Fig. 3A–D). Mesenteric and regional dissected lymph nodes revealed metastases in 14 of 16 lymph nodes. In immunohistochemical (IHC) staining, these lymphoma cells (T1 and T2) demonstrated diffusely positive immunoreactivity for CD45, CD20 (Fig. 4A, B), MUM1, and focal expression for Bcl-2 and Bcl-6. Approximately 90% of tumour cells showed positive for proliferative Ki-67-labelling index for (Fig. 4C, D). However, they showed negative immunostaining for pan-CK, NSE, CD3, CD10, CD4, and cyclin D1. High-grade non-Hodgkin's B-cell

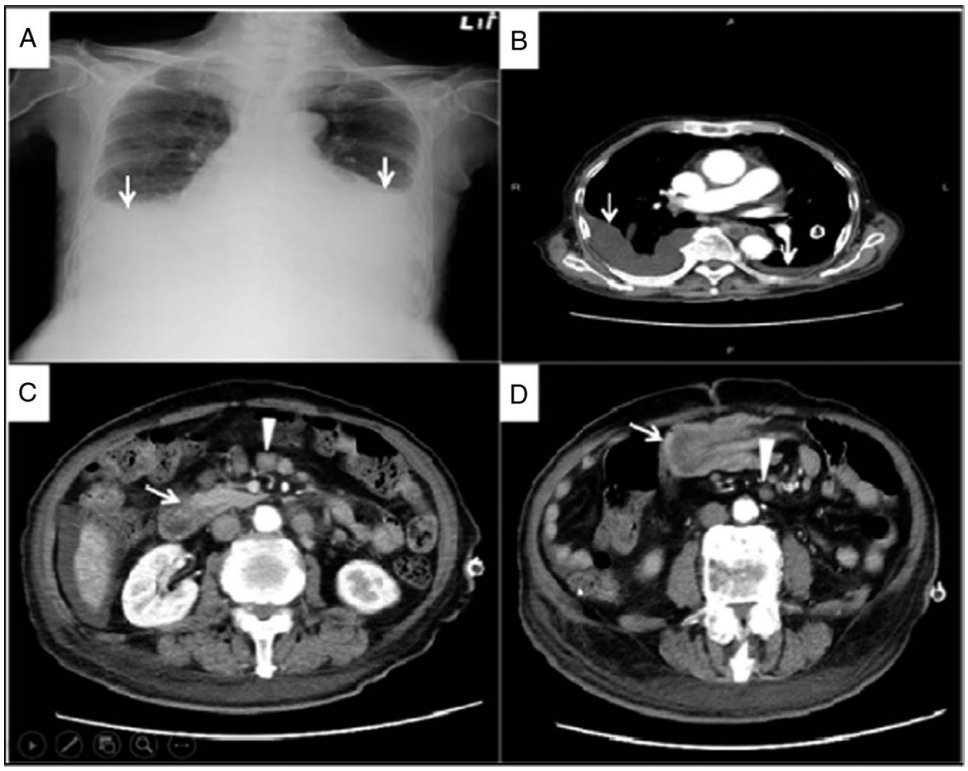

Figure 1. Chest X-ray shows bilateral pleural effusions (A, white arrow). Chest CT scan exhibits bilateral pleural effusions (B, white arrow). Representative photographs of the CT scan of abdomen and pelvis indicate two segments of small bowel intussusception (C, D, white arrow), and one presents an abnormal enhancement of the leading point with enlarged regional small lymph nodes (C, D, white arrowhead). CT, computed tomography.

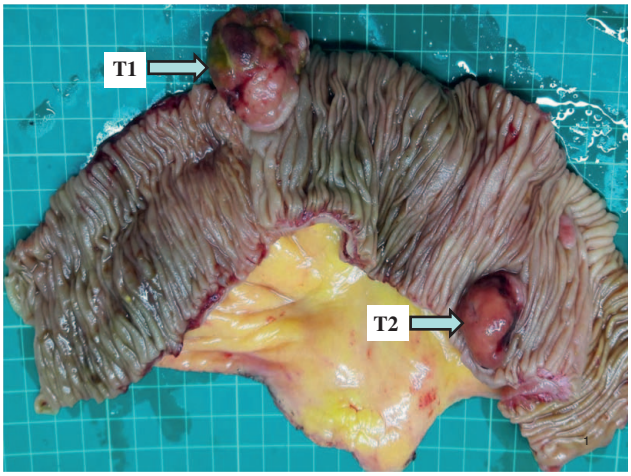

Figure 2. Photograph of a panoramic view displays two separate ulcerative polypoid nodular masses of the jejunum (T1 and T2, green arrow).

lymphoma (DLBCL) of the jejunum was diagnosed. Subsequently, pleural effusion cytopathology demonstrated positive lymphoma cell involvement. Trephine needle core biopsy for bone marrow showed negative lymphoma involvement. The final pathological diagnosis indicated multiple DLBCLs of the jejunum with mesenteric lymph nodal and pleural involvement.

IHC staining for HHV8 latency-associated nuclear antigen-1 and in-situ hybridization for Epstein-Barr virus analysis were negative. Hence, histopathological findings confirmed the diagnosis of multiple primary jejunal DLBCLs. This case report illustrated the unique manifestations of multiple primary jejunal DLBCLs. A bone marrow biopsy was recommended. Due to absence of B symptoms and family members' refusal, bone marrow biopsy for lymphoma localization was not performed. Therefore, the patient was referred to medical oncology team for postoperative management. Subsequently, adjuvant chemotherapeutic regimens (Rituximab-CHOP) schedule was administrated. Unfortunately, the patient sustained acute critical conditions such as gradual hemodynamic worsening, congestive heart failure, complicated hospital bacterial infection, massive pleural effusion with acute respiratory failure, and hypovolemic shock-related acute kidney failure. The patient expired four months after surgery.

Discussion

Though unusual synchronous cases of lymphomas and non-lymphoid malignancies are described, double primary malignancies coexistence, especially malignant lymphomas of the GI tract is rarely reported. The most common histologic types for GILs are DLBCLs. Multiple lymphomatous polyposis is a primary GI lymphoma with a distinctive entity and rare solid lymphoma intestinal segment involvement. Synchronous primary GILs especially the small intestines are extremely rare with few

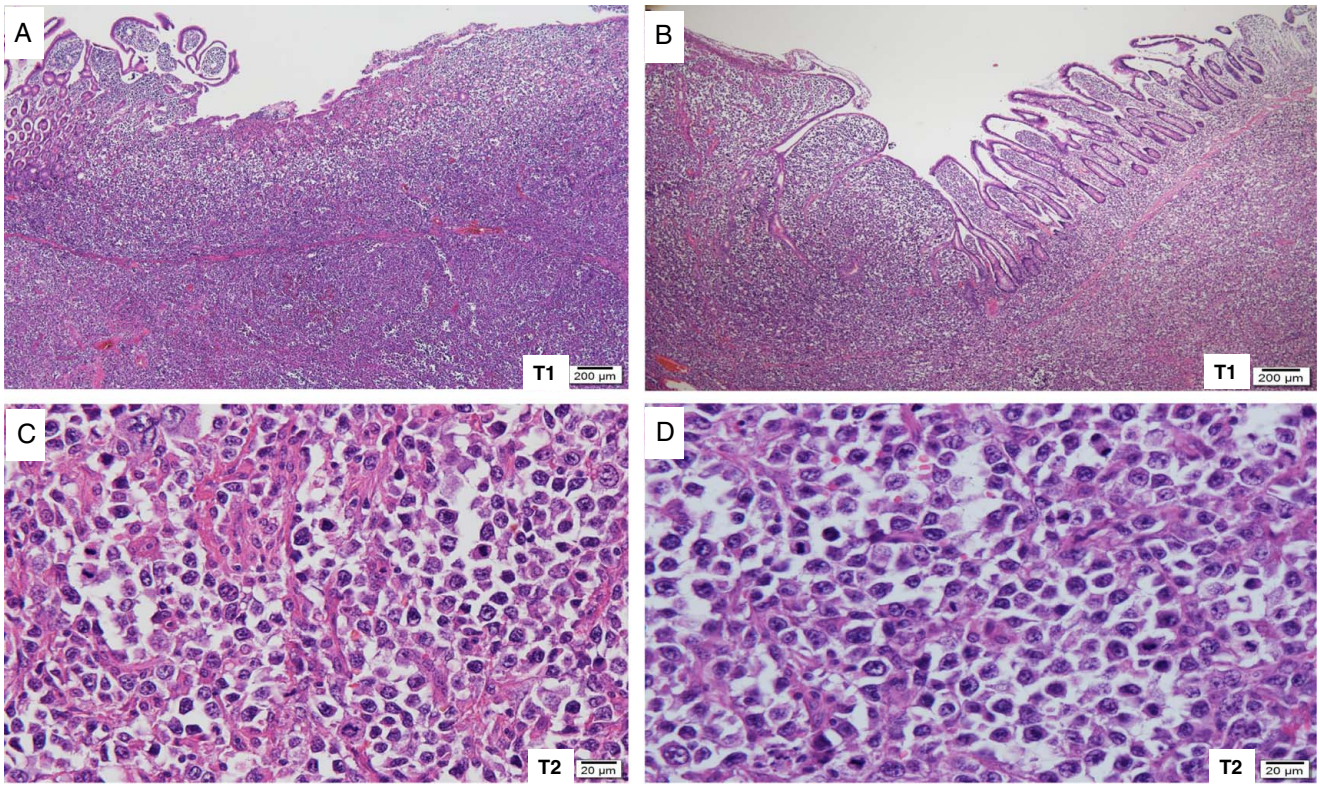

Figure 3. Photographs of representative sections with hematoxylin & eosin (H&E) staining of the jejunal two separate DLBCLs [T1, (A) H&E, original magnification × 40; T2, (B) H&E, original magnification × 400] and [T1, (C) H&E, original magnification × 400; T2, (D) H&E, original magnification × 400]. DLBCL, diffuse large B-cell lymphomas.

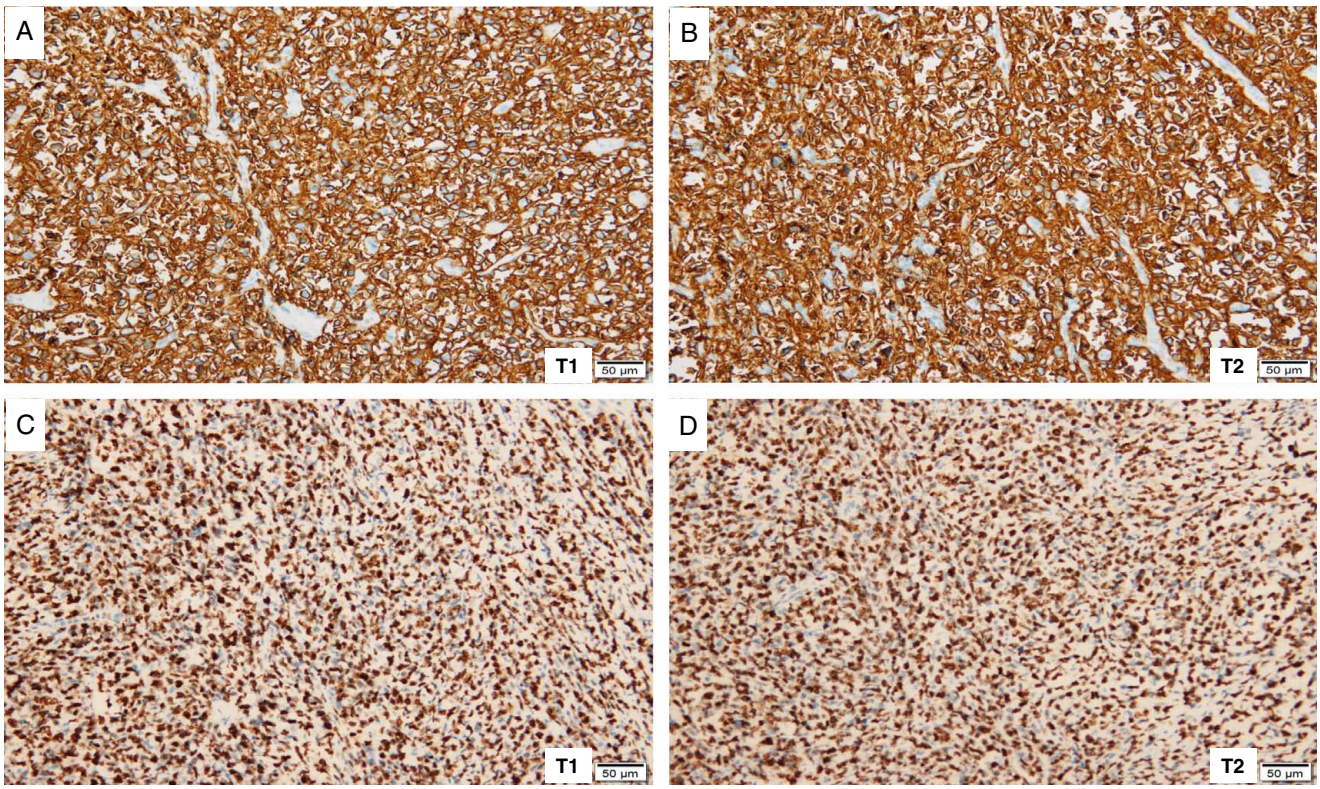

Figure 4. IHC analysis of DLBCLs demonstrates two separated DLBCLs, which are diffusely positive for CD20 [T1, (A) IHC, original magnification × 200; T2, (B) IHC, original magnification × 200], and positive for proliferating Ki-67-labelling index with 90% of involved tumour cells [T1, (C) IHC, original magnification × 200; T2, (D) IHC, original magnification × 200]. DLBCL, diffuse large B-cell lymphomas; IHC, immunohistochemical.

reports. These aggressive tumours require early diagnosis and management[1,4]. Primary multiple DLBCLs with pleural and disseminating lymph nodal involvement presenting as the JJ intussusception is extremely rare. We believe, there are no similar case reports in literature.

The GI tract is the most predominant site of extranodal lymphoma involvement. Most studies indicate stomach (50–60%) as a commonly affected site followed by small intestine while colon, rectum, and oesophagus (<1%) account for minority cases[1,4,6,7].

The Dawson criteria are the classic tests for diagnosis of gastrointestinal lymphoma. Absence of palpable adenopathy in clinical examination is evidenced by: mediastinal lymphadenopathy absence in a chest X-ray; normal total white blood cell and differential count range; disease confined to the intestine and adjacent nodes involvement; no evidence of liver or spleen involvement[8].

The criteria for multiple primary malignancy were first proposed by Warren and Gates in 1932 as; (a) tumours with definite malignant features, (b) histological distinctive tumours, and (c) ruling out the possibility of metastatic tumour of the index tumour[9].

The clinical manifestations of small bowel lymphoma are nonspecific. Patients have symptoms such as colicky abdominal cramps, nausea, vomiting, and weight loss, and rarely have acute obstruction symptoms, intussusception, perforation, or diarrhoea[2,4]. Another study reviewed 36 cases of intussusception cases caused by lymphoma. The age range of patients was 16–86 years[4].

GI tract NHL/DLBCL has unusual pathological lead pointing to intussusception in older children and adults. Adult intussusception is an extremely rare cause of intestinal obstruction, representing ~1–5% of bowel obstructions, and relates to underlying benign or malignant lesions. Intussusception from the GI tract may be caused by NHL. DLBCL, the adult intussusception cause, is an uncommon entity but well documented[1,3,4,10].

The staging of primary GI-DLBCL is completed through imaging examination and bone marrow aspiration and biopsy. To establish an accurate diagnosis and staging of heterogeneous group of lymphomas, different procedures including endoscopic ultrasound, endoscopic biopsies, CT, MRI, diagnostic laparoscopy, scintigraphy, angiography, FDG-PET, and/or molecular cancer markers are applied[2,4,7].

IHC examination, markers CD20 (B-cell marker) show strong and diffuse membranous staining, transcriptional factor (MUM1 / IRF4) expressed in final step of intra-germinal centre B-cell differentiation, and post-germinal centre (late centrocytes) B cells, CD10, BCL-6, and MUM1 expression in diffuse large B-cell lymphoma[1,2,4,5,10,11].

Primary GI lymphoma may be the differential diagnosis of intussusception cases, especially in older age and children groups. Therapeutic strategy for gastrointestinal lymphoma depends on the patient's age, clinical condition, histological subtype, extent and disease burden, and comorbidities. Varied combinations of surgery, chemotherapy, radiation therapy, and radioimmunotherapy contribute to management.

Although multiple jejunal NHLs are significant clinically, the clinical, pathological features, and prognosis are controversial. Multiple intestinal DLBCLs and single lymphoma share similar clinical characteristics and routine pathological findings. Hence prognosis did not differ with identical pathological stages and curative resections. Whether multiple primary DLBCLs are associated with distant metastases than a single case requires further investigation and analysis. Prognostic factors include the use stage at diagnosis, the perforation presence, tumour resectability, histological subtype, and multimodal treatment. Lymphoma perforations have a higher tumour stage and poorer prognosis. Unfortunately, our patient sustained acute critical conditions with gradually worsening hemodynamics, congestive heart failure, complicated hospital bacterial infection, massive pleural effusion with acute respiratory failure, and hypovolemic shock-related acute kidney failure. The patient expired four months after surgery.

Conclusion

The multiple primary DLBCLs of the jejunum with pleural and disseminated nodal involvement presenting initially as pleural effusion and mimicking intestinal obstruction with JJ intussusception in elderly men is unusual. The preoperative variable imaging tests are nonspecific. Hence, the diagnosis is usually confirmed by histopathology and IHC investigation after obtaining the surgical specimen.

Ethical approval

This study was approved by the Institutional Review Board of the Tri-Service General Hospital (TSGH), National Defense Medical Center. The reference number for their IRB approval is TSGHIRB: C202215109.

Consent of patient

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

J.-L.C.: drafting manuscript review, corresponding author, data interpretation, evaluation, information acquisition, and final approval; K.-T.L.: responsible for operating pathological tissue/specimen processing, information acquisition and final approval, concept and design, critical review, and final approval. Y.-C.C.: responsible for operating pathological tissue sections, special chemical staining and immunohistochemical staining, information acquisition, critical review, and final approval. Y.-C.L.: responsible for information acquisition and final approval, concept and design, critical review, and final approval.

Conflicts of interest disclosure

The authors have no conflicts of interest to declare.

Research registration unique identifying number (UIN)

This paper is a case report; there was no registration. The datasets in this article are available in the Department of pathology and Laboratory Medicine database, Junn-Liang Chang, upon request, from the corresponding author.

Provenance and peer review

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