



## Case report

## Primary appendiceal diffuse large B-cell lymphoma initially presenting as acute appendicitis: A case report

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## ABSTRACT

**Introduction:** Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL), accounting for approximately 25% of all NHL cases. Primary appendiceal lymphomas (PAL) presenting as acute appendicitis are very rare, occurring in only 0.015% of all cases of gastrointestinal lymphoma.

**Case presentation:** A 57-year-old man who was initially presented as acute appendicitis and subsequently underwent interval laparoscopic appendectomy. Pathological examination revealed diffuse large B cell lymphoma with cut end involvement. Whole-body positron emission tomography (PET) scan revealed enlarged right palatine tonsil and raised a suspicion of lymphoma involvement in two right cervical lymph nodes (level II and III); biopsy, however, showed that the lymph nodes were benign, with non-specific cellular changes. Bone marrow biopsy of the iliac crest also did not show lymphoma involvement. Subsequently, a diagnosis of primary appendiceal diffuse large B cell lymphoma (Ann Arbor Stage II) was established. After six courses of definite chemotherapy with cyclophosphamide, doxorubicin HCl, vincristine, and rituximab (R-CHOP), PET/CT showed complete remission of the prior FDG-avid malignancy of appendiceal DLBCL. The patient continued to be stable with no recurrence for fifteen months of regular outpatient department follow-ups.

**Conclusions:** PAL is rare, and it clinically manifests the signs and symptoms of acute appendicitis. Specific characteristics of lymphoma in CT scans may lead to a more confirmative diagnosis. PET/CT is important for staging the lymphoma. Patients with PAL should be managed with surgical resection followed by R-CHOP-21 for 6 cycles regardless of whether they have localized disease or disseminated disease.

## 1. Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common histologic subtype of non-Hodgkin lymphoma (NHL), accounting for approximately 25% of all NHL cases [1]. The gastrointestinal tract is the most common site for extranodal involvement of NHL [2]. However, primary appendiceal lymphomas (PALs) presenting as acute appendicitis are very rare, occurring in only 0.015% of all gastrointestinal lymphoma cases [3]. Six cycles of R-CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone plus rituximab), with an interval of 21 days between 2 cycles, has been the standard chemotherapy regimen used for the treatment of most cases of DLBCL [4]. Herein, we present a

case that was initially presented as acute appendicitis but was pathologically proven as appendiceal DLBCL with the cut end involved. This case was reported in line with the SCARE 2020 criteria [5].

## 2. Case presentation

The patient was a 57-year-old man who was a hepatitis B virus (HBV) carrier, with a history of essential hypertension, mild tricuspid regurgitation, fatty liver, reflux esophagitis with gastric ulcer grade A, lumbar spondylosis with stenotic pain status post caudal neuroplasty, and epidurolysis. The patient denied drug history, family history, and psychosocial history.

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The patient complained of progressive right lower quadrant abdominal pain for 4 days. Abdominal computed tomography (CT) revealed an enlarged appendix with dirty surrounding fat infiltrations (Fig. 1). The patient was subsequently admitted under the impression of acute appendicitis. Owing to the high surgical risk of appendectomy because of marked regional inflammation and as the patient's symptoms had lasted for more than 3 days, he was treated with antibiotics, and interval laparoscopic appendectomy was scheduled 1 month later. A thick appendix wall with severe and dense adhesion between the appendix, omentum, terminal ileum, and cecum was noted during the appendectomy. The patient stood the operation well and could tolerate soft diet and self-ambulation on postoperative day one.

However, pathological examination of the appendix revealed a DLBCL composed of large-sized atypical lymphoid cells arranged in sheets. The tumor cells had some basophilic cytoplasm and vesicular nuclei with prominent nucleoli. The lymphoma involved the mucosa, submucosa, and muscularis propria of the appendix (Fig. 2). Necrosis was focally noted. The cut end of the appendix was also a part of the lymphoma.

A whole-body positron emission tomography (PET) scan revealed an enlarged right palatine tonsil, and lymphoma involvement in two right cervical lymph nodes was suspected (level II and III; Fig. 3a) Ultrasonography of the neck and fine needle aspiration demonstrated benign nonspecific cellular changes, with the presence of a few mixed lymphoid cells. Bone marrow biopsy of the iliac crest showed no lymphoma involvement. Immunohistochemically, no evidence of lymphoma involvement was observed in this bone marrow biopsy based on CD3, CD10, CD20, and BCL6 staining.

A diagnosis of primary appendiceal diffuse large B-cell lymphoma, Ann Arbor Stage II, was established. Multidisciplinary approaches with surgeons, oncologists, and radiotherapist were conducted owing to the cut end of the appendix being involved in the lymphoma. Due to non-inferiority of conservative treatment modality, reoperation with radical right hemicolectomy conferred no survival benefit, and share

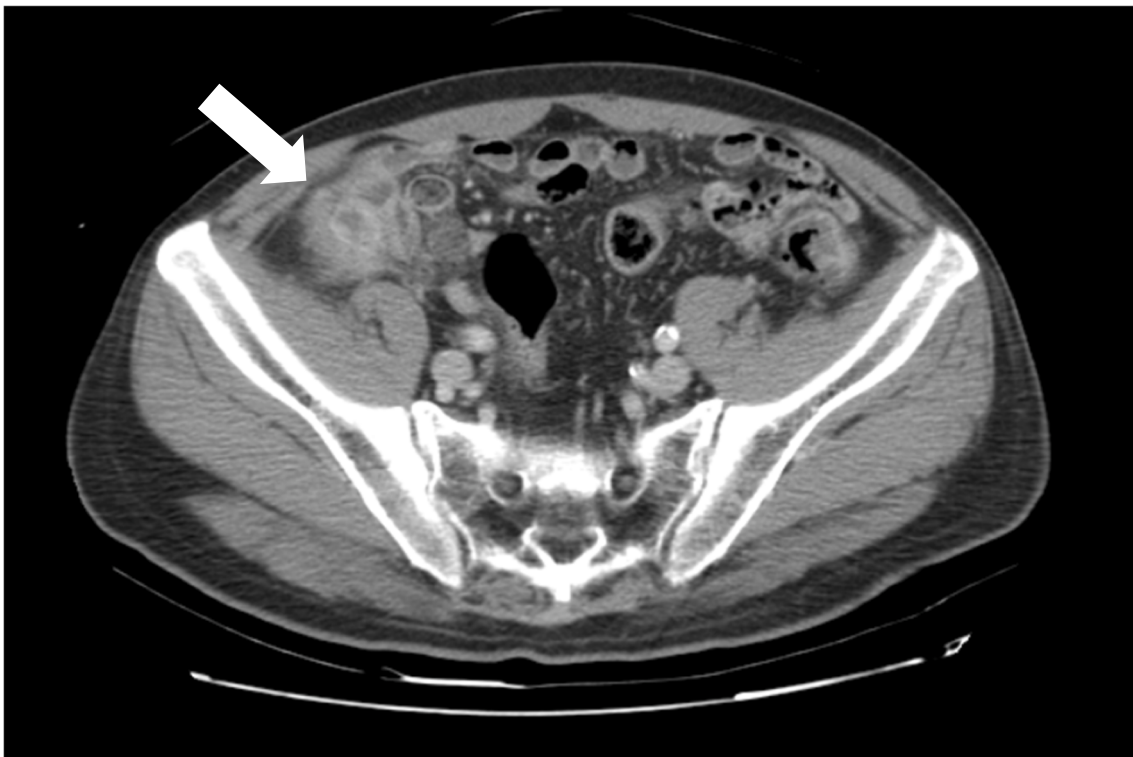
decision making family meeting, the patient accepted definite chemotherapy. The AASLD 2018 guidelines recommend anti-HBV prophylaxis for patients with HBsAg (+), anti-HBc (+), and those receiving anti-CD20 antibody therapy (e.g., rituximab). In addition, the patient's HBV viral load was high (2,480,000). Thus, he was started on oral Vemlidy 25 mg per day for treatment of his HBV infection.

The first course of definite chemotherapy with cyclophosphamide, doxorubicin HCl, vincristine, and rituximab (R-CHOP) was administered approximately 1 month after diagnosis. The patient tolerated all six courses of chemotherapy (with an interval of 21 days between 2 cycles) well. Side effects, including neutropenia and alopecia, resolved after chemotherapy. Follow-up CT scans performed after 1 month and 7 months of the last chemotherapy showed no sign of recurrence of the lymphoma or suspicious liver or lung metastasis lesion. PET/CT scan performed after 2 months of the last chemotherapy cycle showed complete remission of prior FDG-avid malignancy of appendiceal DLBCL, right tonsil, and cervical lymph nodes; however, prominent sigmoid colon physiological activity was noted (Fig. 3b). Subsequent colonoscopy was normal, except for the presence of mild internal hemorrhoids. The patient continued to be stable with no recurrence for fifteen months of regular outpatient department follow-ups.

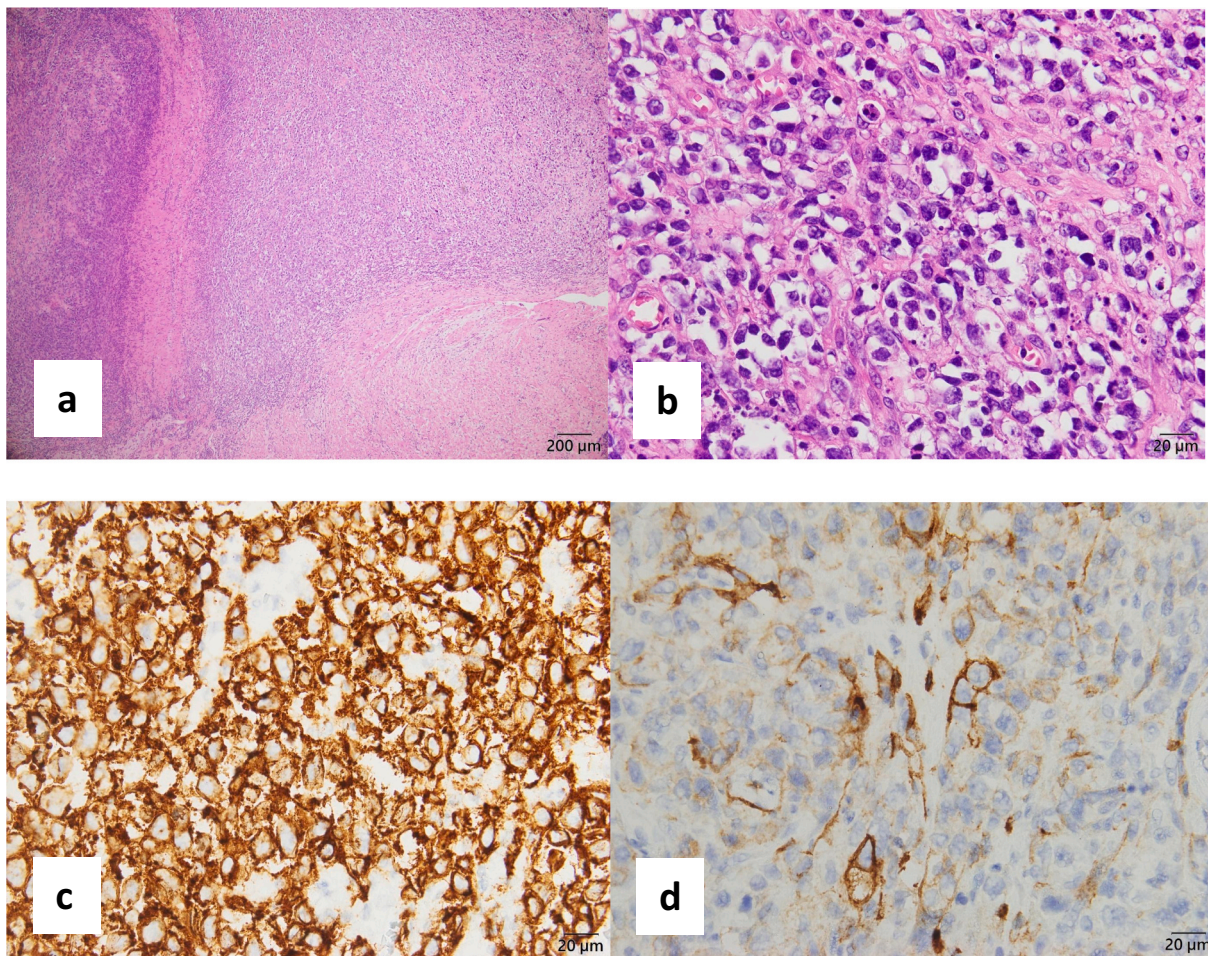
### 3. Discussion

PALs presenting as acute appendicitis are very rare, accounting for approximately 0.015% of all gastrointestinal lymphoma cases [3]. In this report, we described a case with primary DLBCL at the appendix, which initially presented as acute appendicitis. Interval laparoscopic appendectomy was performed under the impression of acute appendicitis, but the formal pathologic report revealed cut end invasion. Follow-up PET performed after six courses of R-CHOP-21 revealed complete remission.

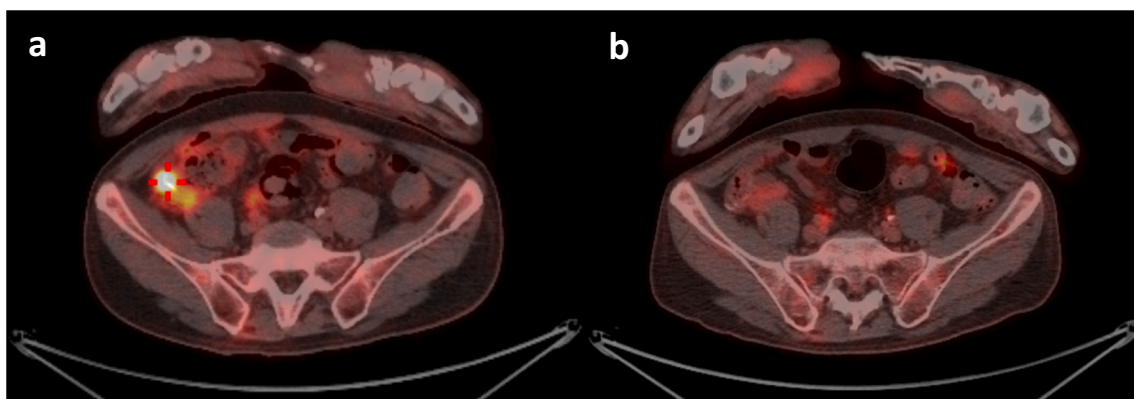
Early detection and differential diagnosis of acute appendicitis from the appendiceal tumor through preoperative imaging are important for



**Fig. 1.** Axial view of abdominal and pelvic CT scan with contrast shows enlarged appendix with dirty surrounding fat infiltrations. The appendix measured 16 mm in diameter, with a density of approximately 100 HU (arrow).



**Fig. 2.** Photomicrograph shows (a) lymphoma cells arranged in a diffuse pattern (arrow) in the appendiceal wall (H&E, original magnification 40×); (b) large-sized lymphoma cells with vesicular nuclei, distinct nucleoli, and scanty cytoplasm (H&E, original magnification 400×); (c) CD20 expression in lymphoma cells (Immunohistochemical stain, original magnification 400×); and (d) CD10 expression in lymphoma cells (Immunohistochemical stain, original magnification 400×). Diffuse large B-cell lymphoma (DLBCL) was impressed by germinal center immunophenotype by Hans algorithm.



**Fig. 3.** PET/CT scan (a) at admission revealed focal bowel wall thickening with stitches and increased FDG uptake in the right lower abdomen, compatible with recent surgery. Both postoperative inflammatory processes and residual lymphoma could not be excluded. Pathological examination showed that the cut end of the appendix was involved by the lymphoma; and (b) 2 months after six courses of R-CHOP showed complete remission of prior FDG-avid malignancy of appendiceal DLBCL.

determining the surgical approach and treatment plans [6]. The specificity for lymphoma is increased in the settings of abdominal lymphadenopathy or aneurysmal dilatation of the appendiceal lumen [7]. Birnbaum et al. suggested that an inflamed appendix without a neoplasm usually would not exceed 15 mm in diameter on a CT scan,

and any enlargement beyond this size should be viewed with suspicion [8]. A retrospective review by Brassil et al. suggested that diffuse mural thickening and enlargement of the appendix with preservation of the vermiform shape could be observed in CT scan of a appendiceal lymphoma, whilst, adhesive bowel disease and contiguous spread from local

nodal disease should be differentiated [9].

In a retrospective analysis of 116 patients with PAL, Ayub et al. reported that the mean age at diagnosis of the patients is 48 years, and DLBCL was the most common histologic subtype (34.5%). The mean overall survival (OS) for the whole cohort was 185 months, with a 5-year survival rate of 67%. No statistically significant difference in OS was observed in terms of gender, race, and histologic subtypes. Right hemicolectomy conferred no survival benefit over appendectomy and/or partial colectomy. In multivariate analysis, increasing age at diagnosis was significantly associated with an increased risk of death, whereas gender, race, tumor histology, disease stage, and nature of resection were not significantly associated with OS [10].

The optimal management of primary gastrointestinal NHL has been determined mostly from retrospective and prospective nonrandomized studies [11]. According to the largest of these studies by Kim et al., patients with PAL should be managed with surgical resection, followed by R-CHOP-21 for 6 cycles, irrespective of whether they have localized disease (Lugano Stage I/II) or disseminated disease (Lugano Stage IV). Patients who underwent surgery showed better OS than patients who did not (5-year OS rate 77% versus 57%,  $P < 0.001$ ). However, this beneficial effect of surgery was statistically significant in patients with B-cell lymphomas ( $P < 0.001$ ), but not in those with T-cell lymphomas ( $P = 0.460$ ). Comparison of survival based on the anatomic site of involvement showed that ileocecal regions had a higher 5-year rate of OS (72%) than the other sites did, owing to the fact that the ileocecal region was involved in a higher proportion of patients with DLBCL who underwent surgery [4].

It remains controversial between the benefit of radical surgical resection and non-invasive treatment for patients with gastrointestinal DLBCL [12]. Surgery was once the standard procedure for primary gastrointestinal DLBCL for the benefits of removing primary lesions, availability of availability of precise histological classification, staging, and avoiding complications in adjuvant chemotherapy and radiotherapy [13]. However, studies had reported a non-inferiority of conservative treatment modalities as first-line therapy in recent years. A retrospective study reported by Selçukbiricik et al. demonstrated a non-inferiority of OS (86.5% vs. 94.0%,  $p = 0.8$ ) and disease-free survival (DFS) (82.1% vs. 85.7%,  $p = 0.18$ ) between conservative treatment and surgery in early-stage primary gastric lymphomas (Lugano I/II or IIE) [14]. A multivariate analysis reported by Zheng et al. confirmed that the conservative treatment modality was unrelated to DFS (HR = 1.036,  $p = 0.618$ ) in primary gastrointestinal lymphomas [15]. Moreover, radical right hemicolectomy conferred no survival benefit over appendectomy and/or partial colectomy [10]. In our case, owing to the non-inferiority of conservative treatment modality, reducing complication risks of reoperation, patient's personal issue, and multidisciplinary approaches, we conducted laparoscopic appendectomy and definite chemotherapy with R-CHOP for 6 cycles with complete remission. Further large multicenter studies are needed to determine the optimal management of primary appendiceal lymphoma.

#### 4. Conclusion

PAL is rare, and it clinically manifests the signs and symptoms of acute appendicitis. Although it might be difficult to differentiate between appendiceal lymphoma and acute appendicitis on a CT scan, specific characteristics of lymphoma in CT scans may lead to a more confirmative diagnosis. Patients with PAL should be managed with surgical resection followed by R-CHOP-21 for 6 cycles regardless of whether they have localized disease or disseminated disease.

#### Abbreviations

AASLD	American Association for the Study of Liver Diseases
CT	computed tomography
DFS	disease-free survival

DLBCL	diffuse large B-cell lymphoma
FDG	fluorodeoxyglucose
HBV	hepatitis B virus
HR	hazard ratio
HU	Hounsfield unit
NHL	non-Hodgkin lymphoma
OS	overall survival
PAL	primary appendiceal lymphomas
PET	positron emission tomography
PET-CT	positron emission tomography-computed tomography

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#### Ethics approval and consent to participate

Not applicable.

#### Consent for publication

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

#### Author contributions

Kai-Yuan Liu conducted a literature search, drafted the manuscript, and prepared Figs. 1-3.

Sheng-Mao Wu and Kai-Yuan Liu performed the operation.

Wei-Yu Chen analysis and interpretation of pathology.

Chia-Lun Chang, Sheng-Mao Wu, and Kai-Yuan Liu managed the treatment for the patient.

All authors reviewed the manuscript.

#### Registration of research studies

This study is not a first man study.

#### Guarantor

Kai-Yuan Liu.

#### Provenance and peer review

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#### Availability of data and materials

The data that support the findings of this study are available on reasonable request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

#### Declaration of competing interest

The authors declare that they have no conflicts of interest.

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