

Case Report

Intestinal non-Hodgkin lymphoma with peritoneal lymphomatosis mimicking acute appendicitis

María Guadalupe Sánchez-Villegas^{1,2,*}, Daniel Zúñiga-Mejía^{1,2}, Elio Germán Recinos-Carrera³, Gerardo Gabriel Montero-Flores^{1,4}, Alejandra Nuñez-Venzor^{1,2}

¹Faculty of Medicine, National Autonomous University of Mexico (UNAM), Escolar 411A, Copilco Universidad, Coyoacán, 04360 Mexico City, Mexico

²Department of General and Endoscopic Surgery, Dr. Manuel Gea González General Hospital, Calzada de Tlalpan 4800, Belisario Domínguez Section XVI, Tlalpan, 14080 Mexico City, Mexico

³Department of Pathological Anatomy, Dr. Manuel Gea González General Hospital, Calzada de Tlalpan 4800, Belisario Domínguez Section XVI, Tlalpan, 14080 Mexico City, Mexico

⁴Department of Diagnostic and Therapeutic Imaging, Dr. Manuel Gea González General Hospital, Calzada de Tlalpan 4800, Belisario Domínguez Section XVI, Tlalpan, 14080 Mexico City, Mexico

*Corresponding author. Faculty of Medicine, National Autonomous University of Mexico (UNAM), Escolar 411A, Copilco Universidad, Coyoacán, 04360 Mexico City, Mexico. E-mail: maria.schz.villegas@comunidad.unam.mx; maria.schz98@gmail.com

Abstract

The gastrointestinal tract is the most frequent extranodal site of non-Hodgkin lymphoma (NHL), accounting for up to 40% of cases. However, appendiceal lymphoma is exceptionally rare, with peritoneal involvement being even rarer. Appendiceal lymphoma often mimics acute appendicitis (AA), although it is an uncommon initial manifestation of intestinal NHL, complicating diagnosis. We report a 29-year-old male with human immunodeficiency virus (HIV) who presented with AA. An open appendectomy was planned; however, intraoperative findings—including cecal induration, ascites, peritoneal thickening, and macronodular lesions on the peritoneum and intestines—led to abandonment of the procedure. Postoperative evaluation excluded peritoneal tuberculosis (PTB), while computed tomography (CT) suggested peritoneal carcinomatosis (PC). Histopathological analysis of a parietal peritoneum specimen provided the definitive diagnosis of NHL. Appendiceal NHL should be considered in HIV-positive patients with AA. Routine histopathological evaluation and surgical intervention are essential for accurate diagnosis and effective management.

Keywords: non-Hodgkin lymphoma; intestinal lymphoma; peritoneal lymphomatosis; acute appendicitis; human immunodeficiency virus

Introduction

Primary gastrointestinal lymphoma (PGIL) is rare, accounting for 1–4% of all gastrointestinal tumors. In advanced stages, it can disseminate, obscuring its origin and mimicking the more frequent secondary gastrointestinal involvement. The gastrointestinal tract is the most frequent extranodal site, representing up to 40% of cases, predominantly due to NHL. The stomach (47%), small intestine (27%), and colon (17%) are the most commonly affected sites [1]. Appendiceal lymphoma, first described by Kundra in 1893, is exceptionally rare, comprising only 1.7% of appendiceal neoplasms [2, 3]. PGIL symptoms are nonspecific, with abdominal pain being the most common presentation across all sites [4]. Appendiceal involvement typically mimics AA, although it is an uncommon initial manifestation of intestinal NHL, with peritoneal involvement being even rarer [5].

Case presentation

A 29-year-old male with a 7-year history of HIV, on Biktarvy for 3 years, presented with a 2-week history of periumbilical pain, nausea, vomiting, and later, right iliac fossa pain and diarrhea. Physical examination revealed abdominal distension, reduced peristalsis, and tenderness at McBurney's point.

Laboratory results showed white blood cell count $8.1 \times 10^3/\mu\text{L}$, neutrophils $5.04 \times 10^3/\mu\text{L}$, lymphocytes $2.11 \times 10^3/\mu\text{L}$, hemoglobin 14.1 g/dL, platelets $508 \times 10^3/\mu\text{L}$. Blood chemistry indicated elevated blood urea nitrogen 32.7 mg/dL, urea 70 mg/dL, alanine aminotransferase 64 IU/L, aspartate aminotransferase 68 IU/L, lactate dehydrogenase 291 IU/L, and C-reactive protein 11.97 mg/dL. The CD4 T-cell count was 223 cells/ μL , with an undetectable HIV viral load. Coagulation tests and serum electrolytes were normal.

Received: January 16, 2025. Accepted: March 1, 2025

Published by Oxford University Press and JSCR Publishing Ltd. © The Author(s) 2025.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

For commercial re-use, please contact journals.permissions@oup.com

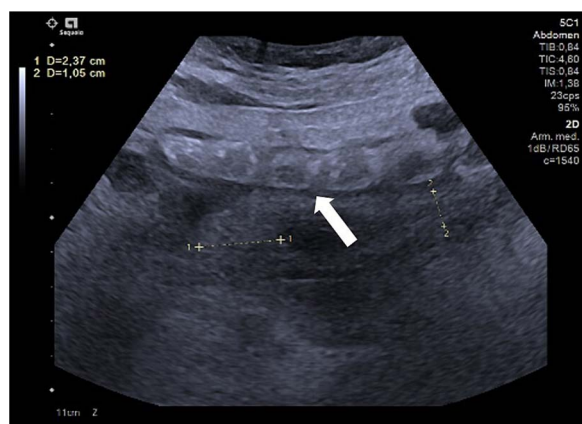


Figure 1. Ultrasound of the right iliac fossa showing the cecal appendix (arrow), measuring 1.1 cm in diameter with a wall thickness of 0.34 cm. It demonstrated increased vascularity and non-collapsibility with compression.



Figure 2. Contrast-enhanced CT in the venous phase: Axial view (A) and coronal reconstruction (B) demonstrated nodular thickening of the peritoneum with vascular enhancement, peritoneal implants measuring up to 6 mm (arrow), and plaque-like implants along the splenic margin (head arrow).

An abdominal ultrasound suggested AA (Fig. 1), prompting an open appendectomy. Intraoperative findings included cecal induration with distorted anatomy, thickened parietal peritoneum, 100 mL of ascitic fluid, and macronodular lesions on the peritoneum and intestines. Consequently, the appendectomy was not performed, and only a peritoneum biopsy and ascitic fluid sample were obtained for analysis.

Postoperatively, suspected PTB was evaluated. Diagnostic tests, including sputum smear microscopy and GeneXpert MTB/RIF, peritoneal fluid culture and microscopy, and auramine-rhodamine stool staining, were negative. Thoracoabdominal CT (Figs 2 and 3) revealed generalized PC, plaque-like involvement at the hepatic flexure of the colon, and inflammatory lymph nodes. Histopathology provided the definitive diagnosis of NHL (Figs 4 and 5). Following an uneventful postoperative recovery, the patient was discharged after one week and referred to a tertiary care center, where chemotherapy was initiated, leading to significant improvement.

Discussion

Most gastrointestinal NHL originate from B cells, with diffuse large B-cell lymphoma (DLBCL) being the most common subtype overall and specifically in the appendix, where it is followed in frequency by Burkitt lymphoma [1, 5].

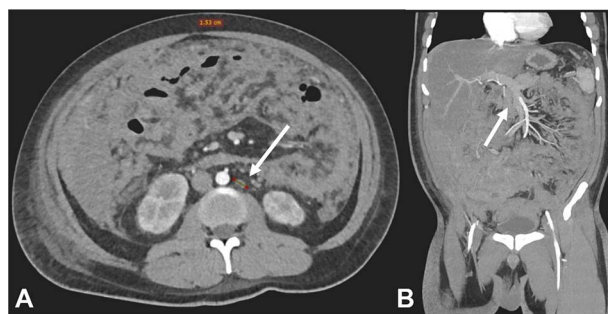


Figure 3. Contrast-enhanced CT in the arterial phase: Axial view (A) and coronal reconstruction (B) demonstrated mesenteric lymphadenopathy measuring up to 1.53 cm (white arrows).



Figure 4. Representative sections of two tissue samples from the parietal peritoneum. The smaller fragment (A) measures $2.0 \times 1.0 \times 0.3$ cm, has an irregular oval shape, and exhibits a soft consistency. The larger fragment (B) measures $3.5 \times 2.0 \times 0.3$ cm, has an irregular laminar shape, and is similarly soft.

HIV-positive patients have a significantly higher risk of NHL, which often presents at advanced stages with extranodal involvement. HIV-associated lymphomagenesis occurs through two mechanisms: 1) Uncontrolled proliferation of Epstein-Barr virus-infected B cells due to impaired T-cell control, driving Epstein-Barr-positive NHL subtypes; and 2) Chronic B-cell activation from antigenic stimulation by HIV or other infections, exacerbated by bacterial translocation from gut CD4+ T-cell depletion. This activation promotes class-switch recombination, somatic hypermutation and mutations [6].

Lymphomatous infiltration of the appendix causes diffuse wall thickening, increasing its diameter to 2.5–4.0 cm. On ultrasound, it appears hypoechoic, while CT shows homogeneous attenuation and poor enhancement. The appendix retains its vermiform shape and may show aneurysmal dilation. Abdominal lymphadenopathy improves diagnostic specificity and, combined with intestinal involvement, suggests secondary appendiceal involvement. However, definitive diagnosis of appendiceal NHL requires excisional biopsy [7, 8].

The prevalence of AA is higher in HIV-positive patients (0.6–3.6%) than in the general population (0.1%). In this group, additional causes of AA to consider include immune reconstitution inflammatory syndrome following antiretroviral therapy initiation, opportunistic infections (e.g. Kaposi's sarcoma, *Streptococcus*

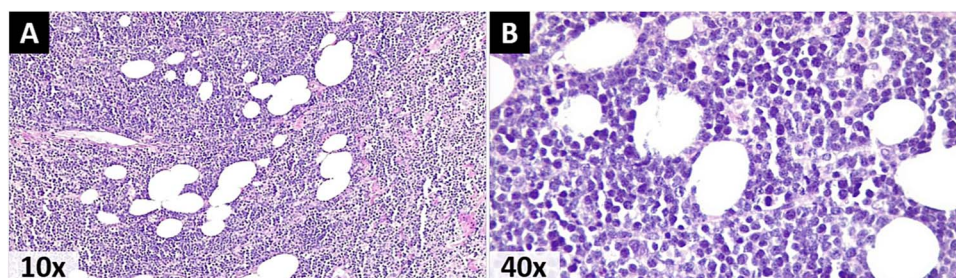


Figure 5. Photomicrographs stained with Hematoxylin and eosin. A) A malignant lymphoproliferative neoplasm infiltrating the omental adipose tissue, morphologically consistent with NHL. B) Small cells with scant eosinophilic cytoplasm, pleomorphic nuclei with dispersed granular chromatin, prominent nucleoli, and atypical mitoses.

pneumoniae, *Mycobacterium* spp., *Salmonella*, cytomegalovirus, cryptosporidiosis, histoplasmosis, and amebiasis), and potential direct HIV effects on the appendix [9].

Extrapulmonary tuberculosis (EPTB) is also more common in HIV-positive individuals, with the abdomen being the sixth most frequent site and PTB comprising 4.9% of all EPTB cases. Diagnosing PTB is challenging due to nonspecific symptoms, insidious onset, and diagnostic limitations. It should be suspected in cases of exudative ascites with lymphocyte predominance, a serum-ascitic albumin gradient <1.1 g/dL, and adenosine deaminase >30 U/L. Smear and culture of ascitic fluid have low sensitivity ($<5\%$ and 35% , respectively), while peritoneal biopsy smear and culture are more sensitive ($50\text{--}63\%$ and 70% , respectively). Histopathological and/or microbiological analysis of a laparoscopic peritoneal biopsy is the gold standard [10, 11].

Peritoneal lymphomatosis (PL) is a rare manifestation of lymphoma, attributed to the absence of lymphoid tissue in the peritoneum. Proposed dissemination pathways include the gastroduodenal ligament, transverse mesocolon, and visceral peritoneal surfaces. Between 2001–2023, 46 cases have been reported, predominantly involving high-grade lymphomas, particularly DLBCL and Burkitt lymphoma. PL is often misdiagnosed as PC, it also has overlapping imaging findings with mesothelioma, pseudomyxoma, sarcomatosis, and PTB [12]. O'Neill identified distinctive CT features of PL: large nodules (>5 cm in 75% , $p=0.004$), splenomegaly ($p=0.002$), and more frequent lymphadenopathy ($p<0.0001$), with 76% showing >10 affected lymph nodes ($p=0.01$). Mesenteric masses were more common in PL (41%) than in PC (2%), with 78% exceeding 10 cm. In this case, lymphadenopathy was the sole feature suggestive of PL, whereas peritoneal thickening resembled PC. Although fine nodularity is uncommon in PC, when present, it is often ill-defined and may coalesce into plaques, as seen in this patient's CT findings [13].

The Lugano classification is the standard for NHL staging and is performed using positron emission tomography/CT, preferred for its high sensitivity to extranodal involvement [14]. Intestinal NHL treatment often relies on studies primarily focused on gastric lymphoma. Chemotherapy is the cornerstone for aggressive and widespread intestinal NHL, as in this case, while surgery is reserved for refractory cases, localized disease, and complications (bleeding, perforation, occlusion). Surgery combined with chemotherapy may improve overall and cancer-specific survival; however, patient stratification based on surgical timing and indications is necessary for definitive conclusions [15].

Conclusions

Although NHL of the appendix is rare, surgeons should include it in the differential diagnosis of AA, particularly in high-risk patients such as those with HIV. Urgent surgery may be required to manage complications. This case underscores the importance of routine histopathological examination of appendectomy specimens and highlights surgery's critical role in achieving a definitive diagnosis.

Conflict of interest statement

The authors declare no conflicts of interest.

Funding

National Autonomous University of Mexico (UNAM).

References

1. Olszewska-Szopa M, Wróbel T. Gastrointestinal non-Hodgkin lymphomas. *Adv Clin Exp Med* 2019;**28**:1119–24. <https://doi.org/10.17219/acem/94068>.
2. Gustafsson BI, Siddique L, Chan A, et al. Uncommon cancers of the small intestine, appendix and colon: an analysis of SEER 1973–2004, and current diagnosis and therapy. *Int J Oncol* 2008;**33**: 1121–31. https://doi.org/10.3892/ijo_00000101.
3. Henley A, Slack BM. Lymphosarcoma of the appendix. *Br Med J* 1954;**1**:378. <https://doi.org/10.1136/bmj.1.4858.378>.
4. Ge Z, Liu Z, Hu X. Anatomic distribution, clinical features, and survival data of 87 cases primary gastrointestinal lymphoma. *World J Surg Oncol* 2016;**14**:85. <https://doi.org/10.1186/s12957-016-0821-9>.
5. Ayub A, Santana-Rodríguez N, Raad W, et al. Primary appendiceal lymphoma: clinical characteristics and outcomes of 116 patients. *J Surg Res* 2017;**207**:174–80. <https://doi.org/10.1016/j.jss.2016.08.079>.
6. Epeldegui M, Hussain SK. The role of microbial translocation and immune activation in AIDS-associated non-Hodgkin lymphoma pathogenesis: what have we learned? *Crit Rev Immunol* 2020;**40**: 41–51. <https://doi.org/10.1615/CritRevImmunol.2020033319>.
7. Fenwick AKC, Hartery A. Appendicitis and beyond: a pictorial review of various appendiceal abnormalities. *Emerg Radiol* 2021;**28**:651–64. <https://doi.org/10.1007/s10140-021-01908-3>.
8. Pickhardt PJ, Levy AD, Rohrmann CA Jr, et al. Non-Hodgkin's lymphoma of the appendix: clinical and CT findings with

- pathologic correlation. *AJR Am J Roentgenol* 2002;**178**:1123–7. <https://doi.org/10.2214/ajr.178.5.1781123>.
9. Mahmood A, Raza SH, Elshaikh E, et al. Acute appendicitis in people living with HIV: what does the emergency surgeon needs to know? *SAGE Open Med* 2021;**9**:2050312120982461. <https://doi.org/10.1177/2050312120982461>.
 10. Koff A, Azar MM. Diagnosing peritoneal tuberculosis. *BMJ Case Rep* 2020;**13**:e233131. <https://doi.org/10.1136/bcr-2019-233131>.
 11. Jha DK, Pathiyil MM, Sharma V. Evidence-based approach to diagnosis and management of abdominal tuberculosis. *Indian J Gastroenterol* 2023;**42**:17–31. <https://doi.org/10.1007/s12664-023-01343-x>.
 12. Fujimi A, Nagamachi Y, Yamauchi N, et al. High-grade B-cell lymphoma, not otherwise specified, presenting as primary peritoneal lymphomatosis and successfully treated with dose-adjusted EPOCH-R. *J Clin Exp Hematop* 2024;**64**:37–44. <https://doi.org/10.3960/jslrt.23044>.
 13. O'Neill AC, Shinagare AB, Rosenthal MH, et al. Differences in CT features of peritoneal carcinomatosis, sarcomatosis, and lymphomatosis: retrospective analysis of 122 cases at a tertiary cancer institution. *Clin Radiol* 2014;**69**:1219–27. <https://doi.org/10.1016/j.crad.2014.06.019>.
 14. Tamayo P, Martín A, Díaz L, et al. ¹⁸F-FDG PET/CT in the clinical management of patients with lymphoma. ¹⁸F-FDG PET/TC en el manejo clínico de los linfomas. *Rev Esp Med Nucl Imagen Mol* 2017;**36**:312–21. <https://doi.org/10.1016/j.rem.2017.03.004>.
 15. Zhang C, Zhang X, Liu Z, et al. The impact of surgery on long-term survival of patients with primary intestinal non-Hodgkin lymphomas based on SEER database. *Sci Rep* 2021;**11**:23047. <https://doi.org/10.1038/s41598-021-02597-1>.