Case Report

Double-Expressor Appendiceal Burkitt’s Lymphoma: A Case Report and Literature Review

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Background. Appendiceal lymphoma is a very rare entity accounting for 0.015% of all gastrointestinal lymphoma cases. Acute appendicitis is the most common presentation of primary appendix neoplasms. Burkitt’s lymphoma presenting as an acute appendicitis is a rare entity with around 21% of the cases presenting as a lower iliac fossa mass. Case Presentation. A 23-year-old male was admitted to the surgical ward as a case of acute appendicitis with localized tenderness in the right iliac fossa, positive rebound tenderness, a positive Rovsing’s sign, and ultrasound findings of suspected complicated appendicitis. Appendectomy was performed. Histopathological examination of the appendectomy specimen revealed a double-expressor non-Hodgkin diffuse large cell lymphoma with Burkitt’s-like morphology. He was sent for chemotherapy treatment. Conclusion. Only 34 cases of Burkitt’s lymphoma have been reported to present as acute appendicitis. Histological examination following appendectomy for an apparent appendicitis is essential. Furthermore, complete blood count and a computed tomography scan aid the diagnosis of lymphoma. Double-expressor lymphoma has been shown to have poor outcomes. Therefore, prompt and aggressive treatment is vital.

1. Introduction

Neoplasms of the appendix are rare and account for only 0.5 to 1 percent of intestinal neoplasms [1] and found in ~0.5–1.0% of appendectomy specimens at pathologic evaluation [2]. Appendiceal lymphomas are exceedingly rare and constitute around 0.015% of all gastrointestinal lymphoma cases [2].

Burkitt’s lymphoma (BL) is a highly aggressive B-cell non-Hodgkin lymphoma characterized by the translocation and deregulation of the Myc gene on chromosome 8. A case series of 116 patients with appendiceal lymphomas showed that BL was the second most prevalent pathology, diagnosed in 25.9% of patients [2].

This rapidly growing tumor can cause symptoms due to mass effect or direct involvement of the bowel [3] which may manifest as bowel obstruction, intussusception, or appendicitis [4].

Acute appendicitis is the most common presentation of primary appendix neoplasms [5]. Therefore, histological examination following appendectomy for an apparent appendicitis is essential and can provide the diagnosis of BL, which leads to the specific disease management. Herein, we present a 23-year-old male patient who presented with acute appendicitis and was found to have BL.

2. Case Presentation

A 23-year-old male presented to our center complaining of right lower quadrant (RLQ) abdominal pain of 12-hour duration.

The pain started in the periumbilical region and then became more localized to the right iliac fossa where the pain was colicky in nature and was increasing in severity. Moreover, the pain was not related to food or movement.
Furthermore, the patient had nausea and vomiting. However, the patient denied any change in bowel habits or any history of dysuria or change of urine color.

On physical examination, the patient had normal vital signs. The abdomen was normal in shape with a normal inverted umbilicus. There were no visible scars or dilated veins. Moreover, the abdomen was soft with localized tenderness in the right iliac fossa and positive rebound tenderness. Rovsing’s sign was also positive. However, there were no features of generalized peritonitis and no masses or organomegaly.

The patient had a sore throat with enlarged cervical lymph nodes 1 week ago and was managed as acute tonsillitis.

Abdominal ultrasound revealed complicated appendicitis.

Urinalysis was normal and laboratory investigations were as follows: hemoglobin level was 16.25 gm/dl (N: 13.5 to 17.5 gm/dl for men); RBC count was 5.663 mCL (N: 4.6–6.2 mCL); WBC was 14.07 × 10³ (N: 4–11 × 10³ uL); neutrophils were 70.4% (N: 45–65%); platelets count was 99.39 × 10⁹ L (N: 150–400 × 10⁹ L); lymphocyte was 3.76% (N: 25–45%); monocyte was 19.3% (N: 0–6%); basophil was 6.51% (N: 0–1%).

The patient was found to have positive Epstein-Barr virus (EBV) IgG antibodies but negative EBV IgM antibodies. Cytomegalovirus antibodies (CMV-IgG and CMV-IgM) were also negative.

We performed an appendectomy through a McBurney’s abdominal incision and found a perforated huge appendiceal mass with mild to moderate fluid (Figure 1); the base of the appendix was normal. Free abdominal fluid was not aspirated. The remainder of the intra-abdominal organs appeared unremarkable.

Postoperatively, the patient was sent to the surgical ward and was kept NPO with IV fluids and IV antibiotics. The patient was afebrile and had stable vital signs. Hospital stay was three days with no postoperative complications.

Whole-body CT scan postoperatively showed a soft tissue lesion in the left axilla consistent with lymph node involvement (Figure 2). CT scan also showed liver enlargement (about 20 cm) but no focal lesions. However, there was no mesenteric lymphadenopathy.

Histopathological examination of the appendectomy specimen revealed a non-Hodgkin diffuse large cell lymphoma with Burkitt’s-like morphology. Specifically, the hematoxylin and eosin slide demonstrated sheets of highly neoplastic lymphoblasts with high nucleus-to-cytoplasmic (N:C) ratio, hyperchromasia, and apoptotic bodies giving focally starry sky appearance. Zones of necrosis and brisk mitosis were also identified (Figures 3(a)–3(c)).

Immunohistochemistry testing demonstrated the cells being positive for CD20, CD79a, CD10, CD3, Bcl-2, Bcl-6, C-Myc (>40%), and Ki-67 (expressed in >95% of lymphoma cells) and negative for CD30 and CD43.

Genetic testing and FISH were not done unfortunately because they are unavailable at our hospital.

The patient was diagnosed with double-expressor lymphoma according to the immunohistochemistry testing (co-expression of Myc and Bcl2 proteins).

Histology for specimens taken from the bone marrow and cerebrospinal fluid (CSF) showed no evidence of tissue involvement with lymphoma.

The patient thereafter was started on chemotherapy with four cycles of R-IVAC (rituximab, ifosfamide, etoposide, cytarabine), mesna, neupogen, cytarabine, methotrexate, and folic acid. His chemotherapy treatment was complicated with mild anemia, mild thrombocytopenia, nausea, and vomiting.
A PET scan done 7 months later showed no evidence of active lymphoma. The patient is currently alive and has been clear from lymphoma for 2 years.

3. Discussion

Acute appendicitis (AA) is traditionally a clinical diagnosis, but the diagnosis is further supported by laboratory and radiological investigations, such as ultrasound and CT scans [6]. Burkitt’s lymphoma is further subdivided into three subtypes (endemic, sporadic, and immunodeficiency-associated) which vary in epidemiology, clinical presentation, and risk factors [7]. Sporadic subtype is associated with Epstein-Barr virus (EBV) with the most common site of involvement being the abdomen and commonly affecting the bowel [7]. Our patient had a positive EBV IgG and appendiceal tumor making the sporadic subtype of Burkitt’s lymphoma more likely.

A diagnosis of Burkitt’s lymphoma is dependent on a combination of histologic (diffuse lymphoid infiltration with scattered macrophages), immunophenotypic (CD20, CD10, Bcl6 positive, and Ki-67 near 100%), and genetic features (c-Myc translocation) [8]. All of these features were identified in the present case. Although the most common finding on flow

![Image](image-url)
| Publication year | Sex | Age | Ethnicity | Presentation | WBC (count/mm³) | Lymph node involvement | Surgical procedure | Chemo-therapy | Follow-up |
|------------------|-----|-----|-----------|--------------|-----------------|-----------------------|-------------------|--------------|-----------|
| 2022             | M   | 23  | NA        | Right lower quadrant (RLQ) pain | 14070 | Left axillary | Appendectomy | Yes | 24 months in remission |
| 2021 [23]        | M   | 18  | Not available | Pelvic pain | 17400 | Not available (NA) | Appendectomy | Yes | 30 months in remission |
| 2021 [24]        | M   | 15  | NA        | RLQ pain | NA | Para-aortic | Appendectomy | Yes | NA |
| 2020 [25]        | M   | 22  | NA        | RLQ pain | 15500 | Para-aortic | Appendectomy | Yes | 7 months in remission |
| 2020 [9]         | F   | 6   | NA        | Right iliac fossa (RIF) pain | 44600 | No | Cecectomy | Yes | NA |
| 2019 [26]        | F   | 40  | NA        | RIF pain | 12400 | NA | Appendectomy | Yes | NA |
| 2018 [27]        | F   | 13  | NA        | Diffuse abdominal pain | 15100 | NA | Appendectomy and salpingo-oophorectomy | Yes | NA |
| 2018 [28]        | M   | 36  | NA        | RLQ pain | 13200 | NA | Appendectomy | Yes | NA |
| 2017 [9]         | M   | 16  | NA        | RLQ pain | NA | NA | Appendectomy | NA | NA |
| 2017 [29]        | M   | 20  | Middle-Eastern | Diffuse abdominal pain and left flank pain | NA | No | Appendectomy | Yes | NA |
| 2016 [30]        | M   | 53  | NA        | RLQ pain | NA | Peri-ileal and pericaecal | Right hemi-colectomy | NA | After 2 months, a significant reduction in tumor masses |
| 2015 [32]        | M   | 17  | NA        | RLQ pain | 7300 | Mesentric | Laparoscopic exploration without appendectomy | Yes | NA |
| 2015 [33]        | F   | 16  | NA        | NA | NA | No | Right hemi-colectomy and end-lateral ileotransversostomy | Yes | NA |
| 2014 [34]        | M   | 10  | NA        | Fatigue and RLQ pain | 12800 | No | Appendectomy | Yes | 14 months in remission |
| 2014 [34]        | M   | 23  | NA        | Abdominal pain, vomiting, and diarrhea | 11800 | No | Appendectomy | Yes | 17 months in remission |
| 2014 [34]        | F   | 24  | NA        | RLQ pain | NA | No | Appendectomy | Yes | 18 months in remission |
| 2014 [4]         | F   | 13  | NA        | RIF pain | NA | Ileal | Appendectomy | Yes | 96 months in remission |
| 2014 [4]         | F   | 18  | NA        | Cecal fistula | NA | Ileocecal | Ileocecal resection and end-to-end anastomosis of the ileum and ascending colon | Yes | 104 months in remission |
| 2013 [35]        | M   | 4   | NA        | Abdominal pain | 12700 | Perirectal and mesenteric | Incision and drainage of abscess | Yes | 24 months in remission |
| 2012 [36]        | M   | Caucasian | Periumbilical pain | 11500 | No | Appendectomy | Yes | 12 months in remission |
| 2010 [37]        | M   | 10  | NA        | Periumbilical pain | 15800 | No | Appendectomy | Yes | Recurrence after 7 months + died after 8 months |
| 2010 [38]        | M   | Caucasian | RIF pain | 15100 | No | Right hemi-colectomy | Yes | NA |
| 2010 [5]         | M   | 49  | NA        | Gross haematuria and RLQ pain | 10800 | Mesenteric | Right hemi-colectomy | Yes | 1 month in remission |
| 2006 [9]         | M   | 14  | NA        | RLQ pain | NA | No | Appendectomy | NA | NA |
| 2006 [39]        | M   | Caucasian | RLQ pain | NA | NA | No | Appendectomy | Yes | NA |
cytometry is an expression of IgM immunoglobulin on the surface of biopsied tissue, mature B-cell markers such as CD19, CD20, CD22, CD79a, and CD10 can be found. However, CD5, CD23, CD34, and tdt are usually negative [9].

Patients with Burkitt’s lymphoma who have an abdominal mass may present with nausea, vomiting, loss of appetite, gastrointestinal bleeding, signs and symptoms of acute abdomen, intestinal perforation, or renal failure [9]. Although preoperative CT scans can be used in confirming the presence of appendicitis with high sensitivity [6], they are not great at identifying if the cause is neoplastic [10]. A cohort study was published in 2020 which concluded that even if CT scans cannot identify neoplastic causes, they cannot exclude them either [10]. On the other hand, if the tumor has lymph node involvement, distant metastasis, or features that suggest an underlying malignancy, a preoperative CT scan could give us some hints on the underlying etiology [11].

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Our patient has positive Myc and Bcl2 making the diagnosis of double-expression diffuse large B-cell lymphoma most likely.

Double-expression lymphoma has worse outcomes than non-double-expression lymphoma [14]. Double-expression lymphoma is standardly treated by R-CHOP chemotherapy which includes rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone.

Even though there are several induction regimens for diffuse large B-cell lymphoma, patients who received R-HyperCVAD/MA (rituximab, cyclophosphamide, doxorubicin, vincristine, cytarabine, dexamethasone/methotrexate) and DA EPOCH-R (rituximab, cyclophosphamide, methotrexate/ifosfamide, doxorubicin, vincristine, etoposide, cytarabine) had higher rates of complete remission compared to R-CHOP [15].

In 2018, a retrospective study by Ichiro Kawashima and Yoshihiro Inamoto revealed that poor outcomes were noticed after allogeneic transplantation for double-expressor lymphoma [16].

The prognosis of lymphoma is dependent on many factors, such as the primary site of the lymphoma [17]. It has been shown that the 5-year survival rate of lymphomas in the ileocecal region was found to be 64.3% which is higher than that in large intestine (48.8%) and small intestine (32.5%) [17]. Primary central nervous system lymphoma on the other hand showed a low 5-year survival rate of 18% [18]. That being said, appendicular lymphomas have a good prognosis as it was shown that low-grade tumors including lymphomas have a 5-year survival rate of 67%–97% [19].

Another factor that plays a vital role in the prognosis of lymphoma is the histological type [20]. It was found that the 5-year survival rate of double-expressor lymphomas is 33%, which is 5–13 times higher than that of non-double-expressor ones [20]. Similar to double-hit lymphomas, triple-hit lymphomas have worse outcomes than normal ones [21].

Different systems of staging have been used to stage Burkitt’s lymphoma, and we would like to emphasize on Murphy’s staging system which has emphasis on extranodal disease which also distinguishes CNS disease and bone marrow disease [22].

Including this case, 34 cases of Burkitt’s lymphoma have been reported in the literature to present as an acute appendicitis (see Table 1).[5].

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### Table 1: Continued.

| Publication year | Sex | Age | Ethnicity | Presentation | WBC (count/mm³) | Lymph node involvement | Surgical procedure | Chemotherapy | Follow-up |
|------------------|-----|-----|-----------|--------------|-----------------|-----------------------|-------------------|--------------|----------|
| 2002 [9] [40]    | 12 M | European | RLQ pain | NA | NA | Right hemi-colectomy | NA | NA | NA |
| 1996 [9]         | 22 M | NA | RLQ pain | NA | NA | No | Cecrectomy | NA | NA | NA |
| 1993 [41]        | 17 M | NA | RLQ pain | NA | NA | No | Appendectomy | Yes | 5.5 months in remission |
| 1990 [42]        | 3 F | Caucasian | RLQ pain | 17100 | No | Appendectomy | Yes | 2 months in remission |
| 1984 [43]        | 22 M | Malay | Right sided abdominal pain | 15800 | Serosal | Appendectomy | Yes | |
| 1983 [44]        | 22 M | NA | RLQ pain | 18200 | No | Appendectomy | NA | NA | |
| 1980 [45]        | 8 M | Caucasian | Diffuse abdominal pain | 10300 | No | Appendectomy | Yes | 36 months in remission |
| 1980 [45]        | 10 M | White | Lower abdominal pain | 19800 | Mesenteric | Appendectomy | Yes | NA | |
A cohort study by Alexander H. Mimery revealed that most of the patients with appendiceal lymphoma were predominantly males accounting for 66.7% of the cases and the average age of onset was around 20 years. A palpable right iliac fossa mass was only identified in around 21% of the cases. However, an appendectomy was done in 65% of the cases (22 out of 34 cases), while 8 of the cases ended up in right hemicolectomy.

4. Conclusion
Burkitt’s lymphoma, although rare, may present as an acute appendicitis. Complete blood count and a computed tomography scan aid the diagnosis of lymphoma. Moreover, immunohistochemistry testing helps in detecting double/triple-hit Burkitt’s lymphoma which has worse prognosis.

Only 34 cases of Burkitt’s lymphoma have been reported to present as an acute appendicitis.

Ethical Approval
Informed consent was signed for publication.

Conflicts of Interest
The authors declare no conflicts of interest.

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