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CLINICAL CASE

Solitary splenic neoplasm as an unusual presentation in an adolescent with sporadic Burkitt lymphoma

Neoplasia esplénica solitaria como presentación inusual en una adolescente con linfoma de Burkitt esporádico

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What do we know about the subject matter of this study?

Burkitt lymphoma is a malignant mature B-cell neoplasm common in pediatric patients. Its main onset symptoms are abdominal pain, fever, and weight loss and its treatment is based on polychemotherapy according to institutional protocols.

What does this study contribute to what is already known?

In our patient, in addition to the known symptoms described above, a well-demarcated splenic tumor was present, which was an approachable site for biopsy and confirmation of the diagnosis. This presentation in the spleen has not been reported frequently since it usually presents as splenomegaly. Treatment with chemotherapy was successful as remission of the splenic tumor and resolution of intestinal involvement were achieved.

Abstract

Burkitt lymphoma is a non-Hodgkin B-cell lymphoma with a high prevalence in the pediatric population. Abdominal manifestations are well known in sporadic Burkitt lymphoma and vary from nonspecific symptoms to intestinal obstruction due to intussusception; however, mass-like splenic involvement has been scarcely described. **Objective:** To present a case of a patient with a splenic mass whose histopathological analysis revealed Burkitt lymphoma. **Clinical Case:** A 13-year-old female patient presented with abdominal pain, progressive weight loss, and fever. Imaging studies showed a splenic mass, intestinal thickening, and ileal intussusception. Histopathological analysis of spleen biopsy revealed Burkitt lymphoma. After the first cycle of chemotherapy (BFM95-NHL protocol), abdominal symptoms resolved; no other signs suggestive of intussusception were observed, as well as a significant reduction of the splenic mass was observed. **Conclusions:** Burkitt lymphoma in pediatric patients can present as a well-defined splenic tumor, causing no splenomegaly. In addition, its management does not require surgery since it can be resolved with chemotherapy.

Keywords:
Splenic Neoplasm;
Intussusception;
Burkitt Lymphoma;
Adolescent

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Introduction

Burkitt lymphoma (BL) is a type of high-grade mature B-cell non-Hodgkin lymphoma (NHL) that manifests aggressively due to its high rate of tumor replication. It is associated with Epstein-Barr virus (EBV) and human immunodeficiency virus (HIV), in addition to a genetic association given the presence of a chromosome translocation, the most frequent being t(8;14)(q24:q32), which activates the *MYC* oncogene[1]. According to the geographic distribution of the cases presented, there is an endemic variant, a sporadic variant, and a third variant related to HIV infection, each with different clinical presentation[1,2].

The sporadic variant, the one presented outside the endemic areas of Africa, presents variable incidences according to geographic location. In developed countries such as the United States, there are 10 cases of NHL per million inhabitants under 20 years of age, with BL being the most frequent, accounting for 40% of cases[3]. In South America, specifically in Brazil, an average of 2.97 cases of BL per million inhabitants under 19 years of age is reported[4].

The endemic variant presents with mandibular or facial tumors, while the sporadic variant has greater abdominal involvement, with the small intestine being the most affected, specifically the ileal region[1,5]. Symptoms range from non-specific abdominal pain and alterations of the circadian rhythm of the bowel evacuatory function to intussusception in different areas of the intestine[5-7].

Splenic masses are uncommon in pediatrics. In this stage of life, most of them are benign, being malignant neoplasms less frequent; among these is the BL[8]. Splenic involvement in this disease is rarely reported, especially in pediatric patients. The confirmatory study for lymphoma is generally based on the study of pathological lymph nodes; however, in the case of splenic involvement, a biopsy of the splenic lymph nodes can also be considered and thus obtain a more representative sample.

The objective of this article is to present the case of an unusual presentation of BL, which manifested with a solitary and delimited splenic mass, to be considered in the differential diagnosis of splenic tumors.

Clinical Case

A 13-year-old female patient, born in Cajamarca (highlands of Peru) and coming from Lima, with no relevant pathological or surgical history.

She consulted the emergency department due to a 1-month history of diffuse and intermittent abdominal pain, which subsided with oral analgesics, associated with weight loss. One week before admission, the patient presented intermittent fever, nausea and vomiting after food intake, and a progressive increase in the intensity of abdominal pain.

On admission, abdominal physical examination revealed no bowel sounds; superficial palpation revealed increasing pain in the left hypochondrium, where the spleen was palpable 3 cm below the left costal ridge; and on deep palpation, the pain intensified in the mesogastrium. Laboratory tests showed anemia with hemoglobin 10.1 g/dL (NV: 12-16); neutrophil count 7.85 x 103/uL (NV: 1.8-8), platelets 371 x 103/uL (NV: 150-350), lactate dehydrogenase (LDH) 4242 U/L (NV: 240-435), and erythrocyte sedimentation rate 35 mm/h (NV: 0-20). Serology for hepatitis B and C, HIV, syphilis, and Koch's bacillus (KB) in sputum and stool was negative.

Given the suspicion of acute surgical abdomen, an abdominal CT scan was performed, showing two areas with intussusception, one at the ileo-ileal level and the other at mesenteric-ileal level (Figure 1), and a spleen of usual size for age, but with the presence of a solid mass of 34x41x43 mm in size, with soft tissue density, in addition to a hypodense mass of 30x42x77 mm in size, with probable lymph node mass in the splenic hilum (Figure 1).

With the result of the CT scan, laboratory tests were extended, showing B2 microglobulin 2.79 mg/L (NV: 0.8-2.2) and positive EBV viral load (227 copies/ml). Tumor markers such as carcinoembryonic antigen and alpha-fetoprotein, as well as IgM TORCH serology (Toxoplasma, Rubella, Cytomegalovirus, Herpes Viruses) were negative; immunoglobulins remained in adequate ranges (Table 1).

An ultrasound-guided percutaneous needle biopsy of the splenic mass was performed. The result of the histopathological analysis revealed lymphoid proliferation of medium-sized, monotonous, round nuclei, clumped chromatin cells intercalated with histiocytes and tingible bodies ("starry sky" appearance). Immunohistochemical markers (BCL6+, CD10+, BCL2-, TdT-, CD30-, LMP1 (EBV)-, CD21-, Ki close to 100%, c-MYC+, MUM1-, CD5-, CD3-) were analyzed, which were consistent with a final diagnosis of BL (Figure 2).

The complementary tests, bone marrow biopsy and cerebrospinal fluid (CSF) flow cytometry, showed negative results for marrow and central nervous system (CNS) infiltration. However, CSF cytospin analysis showed positive results for the presence of lymphoid malignant neoplasm which, according to Murphy's classification, was at clinical stage IV.

Before the start of systemic therapy, the patient presented unfavorable intussusception evolution, so exploratory laparotomy was performed. During the procedure, ileo-ileal invagination was found 70 cm

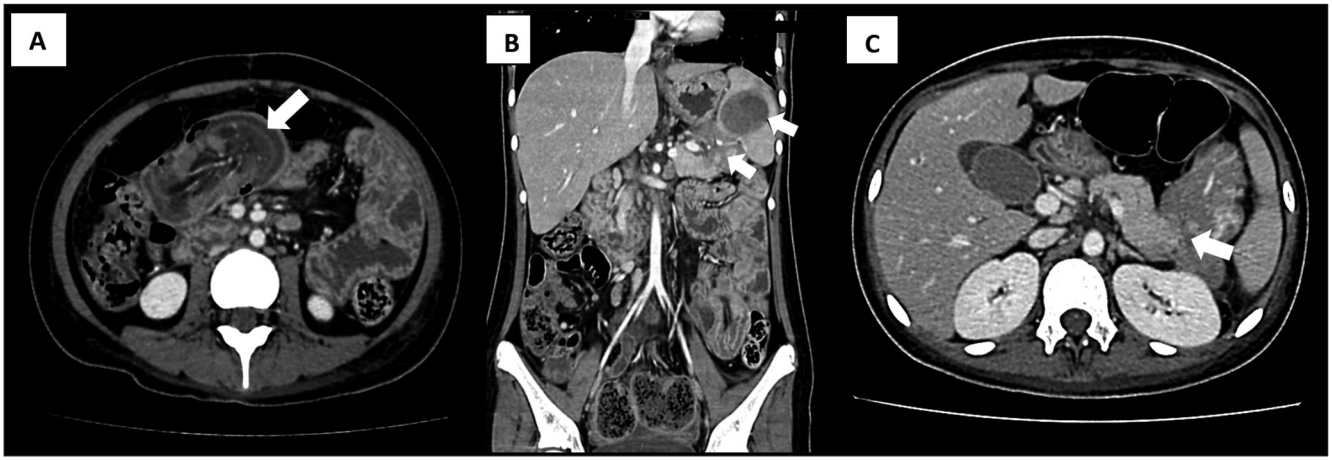

Figure 1. Contrast abdominal computed tomography. **A.** Transverse section, showing intussusception and parietal thickening of intestinal loops predominantly on the left flank. **B.** In coronal section, heterogeneous splenic parenchyma is seen with the presence of a solid mass with a soft tissue density of 34 x 41 x 43 mm. In addition, a hypodense mass, probable lymph node conglomerate at the level of the splenic hilum, 30 x 42 x 77 mm. **C.** In transversal section, the lymph node conglomerate in the splenic hilum that surrounds the splenic artery and veins appears to infiltrate the tail of the pancreas. Source: Carestream Vue Pacs - Imaging (INSNSB)

from the ligament of Treitz, with an invaginated area of 20 cm, in addition to multiple areas of wall thickening of thin loops, which in the context of the patient were attributed to infiltration by the lymphoma diagnosed through the spleen tumor biopsy, therefore, disinvagination was performed. After surgery, total parenteral nutrition support was started and antibiotic coverage was extended to meropenem, vancomycin, and caspofungin due to persistent fever and elevated inflammatory parameters.

With clinical improvement, the patient started chemotherapy according to the institutional protocol based on the NHL-BFM-95 scheme for the R4 risk group due to the detection of malignant neoplasm by CSF cytomorphology. Ultrasounds were performed to rule out the appearance of new foci of intussusception. After completing the first cycle of chemotherapy, no new foci of intussusception were evidenced by ultrasound; consequently, the patient was already tolerating oral intake, therefore, total parenteral nutrition was suspended. Studies were performed to rule out CNS infections due to the appearance of post-chemotherapy headaches, showing negative viral loads. In addition, the flow cytometry test was repeated with negative results while the cytospin showed a positive result for lymphoid neoplasia.

A positron emission tomography-computed tomography (PET-CT) scan was performed after her first treatment cycle, which showed the disappearance of intussusception foci and the absence of hypermetabolic foci in intestinal walls, in the splenic lesion and at the CNS level. At 2 years of follow-up, the patient is asymptomatic, with a negative PET-CT scan for lymphoproliferative disease.

Table 1. Results of laboratory test

	Values
Hemoglobin	10,1 g/dL
Leucocytes	11,380x103/uL
Neutrophils	69%
Lymphocytes	23%
Monocytes	7%
Eosinophils	1%
Platelets	371,000 x 103/uL
HIV	Negative
Total HBcAb	2.4 (Negative: > 1)
Australia antigen	0.468 (Negative: < 1)
IgA	95 mg/dL (NV: 58-358)
IgM	38 mg/dL (NV: 35-239)
IgG	624 mg/dL (NV: 759-1549)
IgE	355.6 mg/dL (NV: 0-199)
EBV-VL	227 copies/ml (RT-PCR), log10: 2.36
EBV-VL (maximum value)	177580 copies/ml (RT-PCR), log10: 5.25
ESR	35 mm/h (NV: 0-20)
LDH	4242 U/L (NV: 240-435)
AFP	1.75ng/mL (NV: <12)
CEA	0.52ng/mL (NV: <3.4)
Beta-2 microglobulin	2.79mg/L (NV: 0.8-2.2)
Uric acid	2.4mg/dL (NV: 2.2-6.4)
Albumin	2,45g/dL (NV: 3.8-5.4)
Amylase	57U/L (NV: 28-100)
HVC	0.058 (Negative: < 1)

Source: SIS-GalenPlus – Laboratory (INSNSB). HIV: Human Immunodeficiency Virus, HBcAb: Hepatitis B core antibodies, Ig: Immunoglobulin, EBV: Epstein Barr Virus – Viral Load, ESR: Erythrocyte sedimentation rate, LDH: lactate dehydrogenase, AFP: Alpha-feto-protein, CEA: Carcinoembryonic antigen, RT-PCR: Real time polymerase chain reaction, HVC: Hepatitis C virus, NV: normal values.

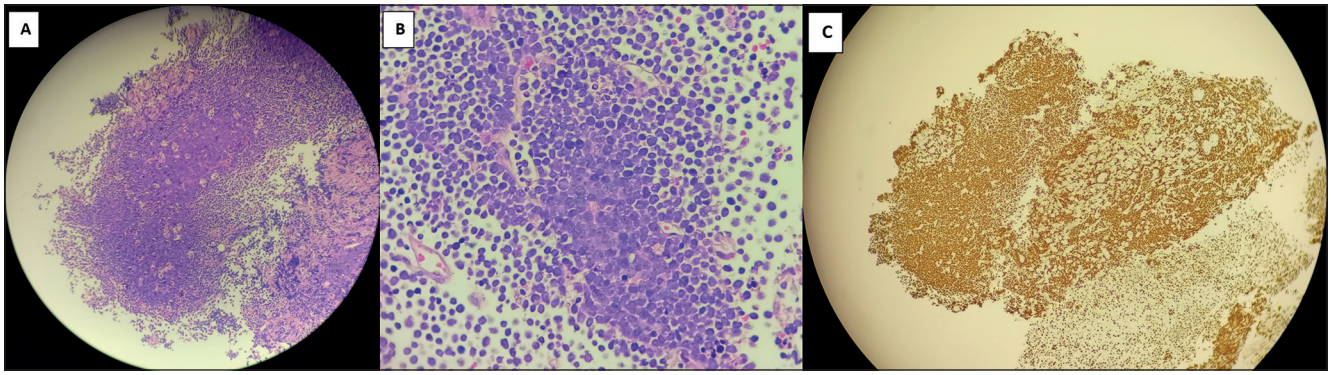

Figure 2. Splenic mass biopsy. **A.** At lower magnification, notable cell proliferation is observed with a "starry sky" appearance. **B.** At higher magnification, monomorphic neoplastic cells of lymphoid lineage with the presence of atypical lymphocytes of intermediate or medium size with little cytoplasm, hyperchromatic nucleus, some present 1 to 3 nucleoli with a diffuse pattern. **C.** The image shows cell proliferation index (Ki) close to 100%. The rest of the markers were CD20+, BCL6+, CD10+, BCL2-, TdT-, CD30-, LMP1 (EBV)-, cMYC+, MUM1-, CD5-, CD3-. Source: Anatomical Pathology (INSNSB).

Discussion

The presentation of BL as a solitary splenic tumor is rarely reported, although it is one of the most frequent types of lymphoma in the pediatric stage of life. Intestinal involvement is the most frequent, presenting as a wall or nodular thickening and, consequently, causing intestinal intussusception[5-7].

Our case corresponds to a 13-year-old adolescent girl, who presented with abdominal symptoms, initially nonspecific, but progressing until she suddenly decompensated during hospitalization due to intussusception. The patient had no exposure to malaria-endemic areas. Although living in these areas is considered a risk factor for the development of lymphoma, the association is not fully established[9].

The presentation symptoms related to intussusception are variable; including abdominal pain (95% of cases), nausea and vomiting (28%), altered bowel rhythm (11%), gastrointestinal bleeding (13%), weight loss (7%), and abdominal mass (13%)[6]. Our patient had all the symptoms except for gastrointestinal bleeding. At the intestinal level, there is the greatest variety of presentations, including circumferential thickening of the wall, aneurysmal dilatation, or intraluminal nodules[5].

Regarding the diagnosis, when acute surgical abdomen was suspected, an ultrasound was performed which showed images suggestive of intussusception and splenic mass which were better detailed in the abdominal CT scan with contrast. The findings of a solid mass of soft tissue density in the spleen, signs of ileo-ileal intussusception, and heterogeneous wall nodular thickening were found in this same image.

A solitary splenic tumor can make us suspect pathologies such as splenic infarction, splenic abscess, and benign or malignant neoplasia[10,11]. In addition to the intestinal alterations described, the case was oriented towards a malignant neoplasm, so it was decided to perform a percutaneous biopsy of the splenic mass. Splenic lesions are generally indolent and detected by imaging. Kim et al.[12] presented an algorithm for the study of these lesions, whether cystic or solid, and the latter as single and multiple. The differential diagnosis of a solitary solid tumor as in our case, may include vascular lesions such as hemangiomas, hamartomas, or angiosarcomas and lymphoid lesions such as lymphomas. The benign ones tend to be asymptomatic, while the malignant ones present some associated symptoms, as in our case it was abdominal pain, nausea, and vomiting due to intestinal involvement.

At the splenic level, it is reported that BL can present as a mass or splenomegaly. The size of the spleen is not a predictor of lymphomatous infiltration; in the case of our patient, the splenic size was normal, however, it was compromised, therefore, the performance of a PET-CT scan was crucial to determine the metabolic activity that the spleen may have when there is suspicion of lymphomatous infiltration, considering it pathological according to the Deauville 5-point scale qualitatively or quantitatively according to the standardized uptake value (SUV)[5,13,14].

Davinson et al.[13] published a case report of 20 patients who, despite the large abdominal involvement, did not present splenic compromise, and postulated that the scarce splenic involvement is a possible characteristic of BL. Our patient presented marked intestinal and splenic involvement simultaneously, which is unusual for the presentation of BL.

In another study, Biko et al.[14], published a series of images of pediatric patients with a confirmed diagnosis of BL also concluding the infrequency of splenic involvement and less frequently as a single mass.

In our case, the patient presented plasma circulating EBV DNA; at admission, she presented 227 copies/ml and the viral load increased progressively with the evolution of the disease reaching 177.580 copies/ml, suggesting a relationship between the level of circulating EBV DNA, and the stage of progression of the neoplasm. This relationship was also documented by Machado et al.[15], who collected and analyzed by real-time PCR peripheral blood samples from 30 pediatric patients diagnosed with B-cell NHL of which 28 had BL and showed a direct relationship between the decrease in the number of copies and the progression of treatment in those patients with EBV viral DNA detected at the beginning of the disease. This highlights the importance of requesting an EBV detection test when lymphoid neoplasia is suspected.

Pannone et al.[16] evaluated CD20, CD79a, CD10, CD3, CD5, BCL-6, BCL-2, Ki67, and LMP-1 markers by immunohistochemistry in 48 patients with BL, 41 of them were pediatric. Of these, all expressed CD20+, 10 patients presented Ki67 with 100% expression, 34 with expression higher than 95%, 32 presented BCL-6, 32 presented BCL-2, and 17 presented LMP-1. In our case, immunohistochemical analysis of the splenic tumor biopsy revealed a Ki67 marker expression level close to 100%, with CD20 and CD79a for B cells, and CD10+, BCL-6 markers for germinal center positive. The c-MYC was positive, being a characteristic marker of BL.

Lymphoma treatment in our institution is based on the NHL-BFM-95 scheme protocol. Our patient was included in the R4 risk group due to CNS involvement detected by cytomorphology, in addition to the LDH value > 1.000 U/L[16,17]. After completing the first cycle of chemotherapy, abdominal symptoms resolved and the spleen tumor had no hypermetabolic uptake on PET-CT scan suggesting resolution of the neoplasm.

This case shows us that spleen lesions can go unnoticed and many times detected only by imaging. The symptoms that brought the patient to the hospital were due to intestinal involvement. However, this case shows us that the spleen can also be affected by BL and present intussusceptions simultaneously.

Conclusions

The abdominal involvement of BL can encompass a wide range of abdominal symptoms, from nonspecific pain to intussusception. It should be considered that the involvement may not only be intestinal but also the spleen may be simultaneously affected in this lymphoma.

BL in pediatric patients can present as a well-demarcated splenic tumor, without generating splenomegaly. Furthermore, it is an approachable site for biopsy and its management does not require surgery since it can be resolved with chemotherapy. It should be considered as a differential diagnosis in case any single splenic tumor is present as in our case.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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