Title

Gallstones, Abdominal Pain, and a Lipase of 1304 U/L: Isolated Gastrointestinal Burkitt's Lymphoma Presenting as Pancreatitis

Journal

Proceedings of UCLA Health, 23(1)

Authors

Cook, Erin Atkinson
Lazarus, Michael E.

Publication Date

2019-05-15

CLINICAL VIGNETTE

Gallstones, Abdominal Pain, and a Lipase of 1304 U/L: Isolated Gastrointestinal Burkitt's Lymphoma Presenting as Pancreatitis

Erin Atkinson Cook, MD and Michael E. Lazarus, MD

Introduction

Burkitt's Lymphoma, a highly aggressive B-cell neoplasm, is rare, compromising less then 1% of all non-Hodgkin's lymphomas in the United States. If diagnosed promptly, survival rates can be as high as 90% depending on the population. Misdiagnosis can lead to a delay in treatment without timely therapy the malignancy can be fatal.

Case Description

A 51-year-old Armenian male smoker with no known past medical history was seen in the emergency department (ED) with a 12-hour history of worsening acute right upper abdominal pain that radiated to both shoulders. He reported intermittent right upper quadrant abdominal pain for the past 2 months aggravated by food. Esophagogastroduodenoscopy (EGD) two months prior showed a gastric ulcer. He was given omeprazole and antacids which improved his pain. Abdominal ultrasound in the ED showed gallbladder wall thickening, extensive sludge formation, and pericholecystic fluid, "compatible with acute cholecystitis". Physical exam of his abdomen was significant for a positive Murphy's sign. His labs were notable for a lipase of 1304U/L and hemoglobin of 10.7g/dl. The initial basic metabolic panel, hepatic function panel, and remaining complete blood count were all within normal limits. He was diagnosed with acute cholecystitis and gallstone pancreatitis and admitted to the general surgery team where he was started on IV antibiotics and bowel rest. By the second day of hospitalization, there was no improvement of symptoms. A computed tomography (CT) scan of abdomen/ pelvis was ordered out of concern for necrotizing pancreatitis. The CT scan showed a severely thickened and irregular stomach (see Figure 1). Gastroenterology was consulted for upper endoscopic evaluation and biopsy; the patient was transferred to the general medicine service. Further history included an 11kg weight loss over 2 months, a one-week history of melena, and early satiety. He denied fever, chills, or night sweats. The EGD revealed irregular, nodular, friable, and ulcerated gastric mucosal surface with loss of normal vascularity. The involvement extended from the base of the cardia and the fundus throughout the body of the stomach wall into the proximal antrum. His gastric biopsy was consistent with Burkitt's Lymphoma. Further evaluation showed he was EBV and HIV negative and that his disease was limited to the stomach and pancreas with 10% involvement of his bone marrow. He was started on emergent chemotherapy consisting of cyclophosphamide, vincristine, doxorubicin (CODOX), high-dose methotrexate, ifosfamide, mesna, cytarabine, and etoposide (M/IVAC) and responded very well. Follow up CT scan after his second cycle showed marked improvement of his disease (see Figure 2).

Discussion

Burkitt's lymphoma (BL) is an extremely aggressive B cell non-Hodgkin's lymphoma and comprises less than one percent of non-Hodgkin's lymphomas in adults. Translocation of the c-myc oncogene on chromosome 8 to chromosome 14 is the classic genetic mutation found [t(8;14)][1] and occurs in 80% of cases. The translocation can also occur between the myc oncogene on chromosome 8 and two other immunoglobulin genes, t (2;8) and t(8;22). There are three subtypes of BL including endemic, sporadic, and immunodeficiency-associated that differ in their epidemiology, case presentation, and genetic makeup. However, they are histochemically identical. BL is diagnosed by pathology showing a "starry-sky" pattern of histiocytes and tumor cells, immunochemistry markers, and demonstration of the c-myc oncogene.[2] Gene expression profiling may be utilized in the future in diagnosing BL.[3]

The endemic form is the most common subtype found mainly in equatorial Africa and is associated with the Epstein-Barr virus. The sporadic form, which is what this patient has, is more common in the United States and Western Europe, albeit still rare with roughly 1200 patients diagnosed each year.[4] It is usually not associated with the Epstein-Barr virus. Both the endemic and sporadic form of BL are more common in children and men and are responsible for 30-50% of pediatric cancer in equatorial Africa and 30% of pediatric lymphomas in the United States. BL only comprises less than one percent of non-Hodgkins lymphoma in adults and is typically seen in male patients less than 35 years old.[5] Europe has a similar incidence of BL of 2.2 cases per million persons per year.[6] The immunodeficiency-associated subtype is typically associated with HIV compared with other immunodeficient states. The incidence of this subtype has not changed despite improvements in antiretroviral therapy.

The endemic form of Burkitt's lymphoma has a well-known presentation of a rapidly growing jaw or facial tumor and can be found in extra-nodal sites. Immunodeficiency-related BL

usually involves the bone marrow, central nervous system, and lymph nodes. The sporadic form of BL, as seen in our patient, presents with abdominal symptoms such as bowel obstruction, ascites, or abdominal bleeding and can mimic an acute abdomen. Other presenting symptoms include tumor lysis or B symptoms. At the time of presentation, bone marrow involvement is seen in 30% of cases and disease in the central nervous system is seen in 15% of cases.[1] Interestingly there is also a leukemic presentation of this disease known as Burkitt Leukemia.[7]

The highly aggressive nature of the tumor requires prompt diagnosis and initiation of therapy. Distinguishing BL from diffuse large B cell lymphoma is vital given differences in treatment strategies between the two malignancies.[8] Traditional chemotherapy for diffuse large B cell lymphoma such as R-CHOP is not as effective.[9] There have been no randomized controlled trials of adults with BL and thus there are different treatment approaches available. The addition of rituximab to these regimens has improved survival.[10] The most commonly used approach involves multiple rounds of intensive short-duration combination chemotherapy accompanied by central nervous system prophylaxis and rituximab. This regimen, known as the Magrath regimen, includes CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate, ifosfamide, cytarabine, etoposide) and has a 67-92% 2-year survival.[11-14] Fewer studies have been done on older patients but analysis from various studies show inferior 2-year survival outcomes on patients greater than 40 years. Some experts suggest using dose-adjusted EPOC plus rituximab in older adults while others feel short intensive chemotherapy like the Magrath regimen remain the standard of care.[15] Given the serious complications associated with BL treatment an individual approach may be needed depending on the patient's age and comorbidities. Tumor lysis syndrome is a serious complication of therapy.

This patient's clinical presentation was classic for cholecystitis and pancreatitis. It was fortuitous that a CT scan was performed to further evaluate for necrotizing pancreatitis: additional delay in diagnosis and initiation of treatment would have likely resulted in the patient's death. It is important to diagnose this malignancy accurately and quickly given its highly aggressive nature. While abdominal symptoms are a common presenting complaint with BL it is rare for the disease to mimic pancreatitis not only by history but with laboratory values as well. BL should be considered in the differential diagnosis of all patients with abdominal pain. A careful review of systems (i.e. melena, early satiety, and weight loss) even in the most obvious of diagnoses such as cholecystitis and pancreatitis can help differentiate these common medical conditions from a more serious mimicking disease.

In conclusion, our epidemiologic picture of a typical BL patient may not be accurate. This patient does not fit the classic description of a young male less then 35 years of age. This description is probably outdated. The 2009 National Cancer Institute Surveillance, Epidemiology and End Results (SEER) database shows that patients older then 40 years account for roughly 59% of all adult Burkitt lymphoma cases in the United States.[15,16] This reinforces the need for more clinical trials of patients older then 40 with BL to further evaluate the efficacy and safety of treatment.

Figures

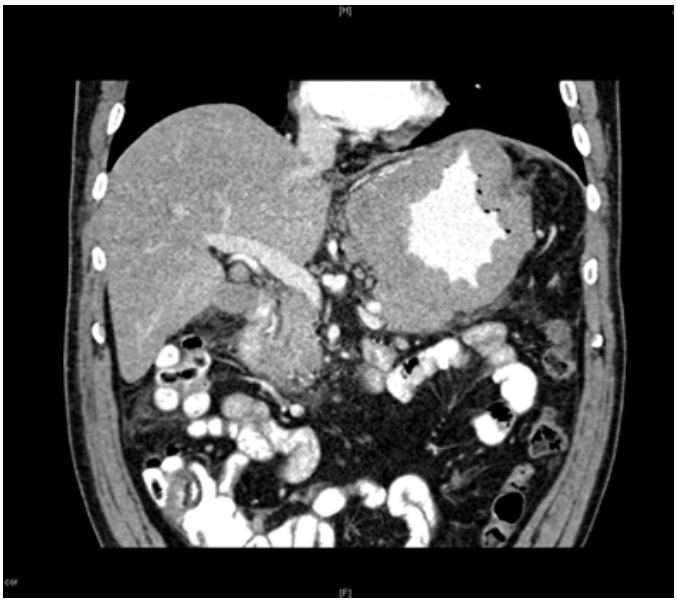

Figure 1: CT Abdomen/Pelvis with contrast showing thickened and irregular stomach.

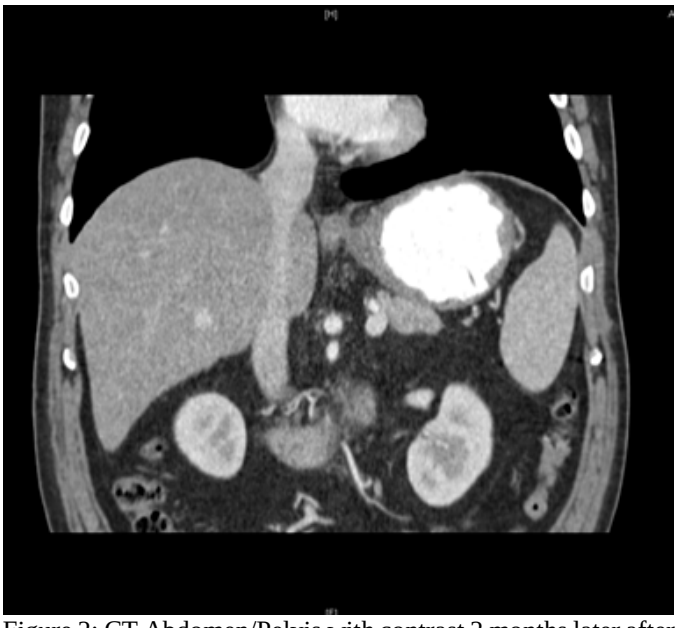

Figure 2: CT Abdomen/Pelvis with contrast 2 months later after initiation of therapy with CODOX-M/IVAC.

REFERENCES

1. **Blum KA, Lozanski G, Byrd JC**. Adult Burkitt leukemia and lymphoma. *Blood*. 2004 Nov 15;104(10):3009-20. Epub 2004 Jul 20. Review. PubMed PMID: 15265787.

2. **Ziegler JL**. Burkitt's lymphoma. *N Engl J Med*. 1981 Sep 24;305(13):735-45. Review. PubMed PMID: 7022215.
3. **Dave SS, Fu K, Wright GW, Lam LT, Kluin P, Boerma EJ, Greiner TC, Weisenburger DD, Rosenwald A, Ott G, Müller-Hermelink HK, Gascoyne RD, Delabie J, Rimsza LM, Braziel RM, Grogan TM, Campo E, Jaffe ES, Dave BJ, Sanger W, Bast M, Vose JM, Armitage JO, Connors JM, Smeland EB, Kvaloy S, Holte H, Fisher RI, Miller TP, Montserrat E, Wilson WH, Bahl M, Zhao H, Yang L, Powell J, Simon R, Chan WC, Staudt LM; Lymphoma/Leukemia Molecular Profiling Project**. Molecular diagnosis of Burkitt's lymphoma. *N Engl J Med*. 2006 Jun 8;354(23):2431-42. PubMed PMID: 16760443.
4. **Perkins AS, Friedberg JW**. Burkitt lymphoma in adults. *Hematology Am Soc Hematol Educ Program*. 2008:341-8. doi: 10.1182/asheducation-2008.1.341. Review. PubMed PMID: 19074108.
5. **Morton LM, Wang SS, Devesa SS, Hartge P, Weisenburger DD, Linet MS**. Lymphoma incidence patterns by WHO subtype in the United States, 1992-2001. *Blood*. 2006 Jan 1;107(1):265-76. Epub 2005 Sep 8. PubMed PMID: 16150940; PubMed Central PMCID: PMC1895348.
6. **Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, Marcos-Gragera R, Maynadié M, Simonetti A, Lutz JM, Berrino F; HAEMACARE Working Group**. Incidence of hematologic malignancies in Europe by morphologic subtype: results of the HAEMACARE project. *Blood*. 2010 Nov 11;116(19): 3724-34. doi: 10.1182/blood-2010-05-282632. Epub 2010 Jul 27. Erratum in: *Blood*. 2011 Mar 24;117(12):3477. PubMed PMID: 20664057.
7. **Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES**. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016 May 19;127(20):2375-90. doi: 10.1182/blood-2016-01-643569. Epub 2016 Mar 15. Review. PubMed PMID: 26980727; PubMed Central PMCID: PMC4874220.
8. **Bellan C, Stefano L, Giulia de F, Rogena EA, Lorenzo L**. Burkitt lymphoma versus diffuse large B-cell lymphoma: a practical approach. *Hematol Oncol*. 2010 Jun;28(2):53-6. doi: 10.1002/hon.916. Review. PubMed PMID: 19844983.
9. **Aldoss IT, Weisenburger DD, Fu K, Chan WC, Vose JM, Bierman PJ, Bociek RG, Armitage JO**. Adult Burkitt lymphoma: advances in diagnosis and treatment. *Oncology (Williston Park)*. 2008 Nov 30;22(13):1508-17. Review. PubMed PMID: 19133605.
10. **Kenkre VP, Stock W**. Burkitt lymphoma/leukemia: improving prognosis. *Clin Lymphoma Myeloma*. 2009;9 Suppl 3:S231-8. doi: 10.3816/CLM.2009.s.017. Review. PubMed PMID: 19778846.
11. **Magrath I, Adde M, Shad A, Venzon D, Seibel N, Gootenberg J, Neely J, Arndt C, Nieder M, Jaffe E, Wittes RA, Horak ID**. Adults and children with small non-cleaved-cell lymphoma have a similar excellent outcome when treated with the same chemotherapy regimen. *J Clin Oncol*. 1996 Mar;14(3):925-34. PubMed PMID:8622041.
12. **Mead GM, Sydes MR, Walewski J, Grigg A, Hatton CS, Pescosta N, Guarnaccia C, Lewis MS, McKendrick J, Stenning SP, Wright D; UKLG LY06 collaborators**. An international evaluation of CODOX-M and CODOX-M alternating with IVAC in adult Burkitt's lymphoma: results of United Kingdom Lymphoma Group LY06 study. *Ann Oncol*. 2002 Aug;13(8):1264-74. Erratum in: Ann Oncol. 2002 Dec;13(12):1961. Norbert, P [corrected to Pescosta, N]. PubMed PMID: 12181251.
13. **Mead GM, Barrans SL, Qian W, Walewski J, Radford JA, Wolf M, Clawson SM, Stenning SP, Yule CL, Jack AS; UK National Cancer Research Institute Lymphoma Clinical Studies Group; Australasian Leukaemia and Lymphoma Group**. A prospective clinicopathologic study of dose-modified CODOX-M/IVAC in patients with sporadic Burkitt lymphoma defined using cytogenetic and immunophenotypic criteria (MRC/NCRI LY10 trial). *Blood*. 2008 Sep 15;112(6):2248-60. doi: 10.1182/blood-2008-03-145128. Epub 2008 Jul 8. PubMed PMID: 18612102; PubMed Central PMCID: PMC2532802.
14. **Lacasce A, Howard O, Lib S, Fisher D, Weng A, Neuberg D, Shipp M**. Modified magrath regimens for adults with Burkitt and Burkitt-like lymphomas: preserved efficacy with decreased toxicity. *Leuk Lymphoma*. 2004 Apr;45(4):761-7. PubMed PMID: 15160953.
15. **Kelly JL, Toothaker SR, Ciminello L, Hoelzer D, Holte H, LaCasce AS, Mead G, Thomas D, Van Imhoff GW, Kahl BS, Cheson BD, Magrath IT, Fisher RI, Friedberg JW**. Outcomes of patients with Burkitt lymphoma older than age 40 treated with intensive chemotherapeutic regimens. *Clin Lymphoma Myeloma*. 2009 Aug;9(4):307-10. doi: 10.3816/CLM.2009.n.060. PubMed PMID: 19717381; PubMed Central PMCID: PMC2909640.
16. **Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W, Ruhl J, Howlader N, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Cronin K, Chen HS, Feuer EJ, Stinchcomb DG, Edwards BK (eds)**. SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.

Submitted April 1, 2019