A Case Report of an Aggressive Mantle Cell Lymphoma Masquerading as a Chronic Lymphocytic Leukemia With Catastrophic Treatment Complications

Ranjit R. Nair MD
Lehigh Valley Health Network, Ranjit_R.Nair@lvhn.org

Nicholas Lamparella DO
Lehigh Valley Health Network, Nicholas.Lamparella@lvhn.org

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A Case Report of an Aggressive Mantle Cell Lymphoma Masquerading as a Chronic Lymphocytic Leukemia With Catastrophic Treatment Complications

Ranjit Nair, MD, Shereen Gheith, MD, PhD, Nicholas Lamparella, DO

Lehigh Valley Health Network, Allentown, Pennsylvania

Case Presentation:

Mantle cell Lymphoma (MCL) and chronic lymphocytic leukemia (CLL) account for majority of Small B-cell neoplasms (SBCNs) that express CD5 without CD10. We present a patient case with aggressive MCL presenting with leukocytosis and splenomegaly mimicking CLL initially on immunophenotypic features.

A 55-year-old presented with abdominal pain, drenching night sweats, early satiety, anorexia and significant weight loss for 8-month duration. On exam she had generalized lymphadenopathy and massive splenomegaly. Complete blood cell count showed pancytopenia with normal blood chemistry and LDH 778 U/L (Table1). Differential count showed predominant lymphocytosis. Peripheral smear showed increased lymphocytes, condensed nuclear chromatin, smudge cells and occasional left shifted neutrophils. CT imaging showed diffuse lymphadenopathy and splenomegaly measuring 24 x 17 cm (Figure 1). Flow cytometry showed a large monoclonal B-cell population kappa light chain restriction, dim CD19, CD20, CD5, and variable expression of CD23. This population demonstrated moderate to bright CD38 and negative for CD10 and CD11c (Figure 2). The findings were most compatible with a diagnosis of chronic lymphocytic leukemia. FISH panel was pending at this point.

Table 1

Labs	At Presentation	4 Hours Post Rituximab
Hemoglobin	9.4 g/ dL	6.2 g/ dL
WBC	44, 000 / µL	24, 000 / µL
Platelet Count	106,000 / µL	74,000 / µL
Serum Potassium	4.4 mEq/L	7.1 mEq/L
Serum Uric Acid	2.2 mg/L	6.8 mg/L
LDH	777 U/L	8750 U/L
Lactate	-	>30 mmol/L
PT	1.1	2.8
PTT	14	28.8
D-Dimer	-	12.2 µg/mL
Fibrinogen	-	296 mg/dL
Haptoglobin	-	<7mg/dL
AST	44 U/L	1326 U/L
ALT	38 U/L	200 U/L
T. bilirubin	1.2 mg/dL	8.2 mg/dL
Serum Cortisol	-	122 µg/dL

Due to B-symptoms and ongoing pain, decision was made to initiate FCR chemotherapy (Fludarabine, Cyclophosphamide, Rituximab). A bone marrow was done and rituximab treatment was initiated a day later. Thirty minutes post-initiation of Rituximab, patient developed rigors, chills and nausea. She became hypotensive, hypoglycemic and developed respiratory failure requiring intubation and vasopressor support. Her clinical features and work up (Table 1) were consistent with Cytokine Release Syndrome (CRS) and she was started on steroids.

She was treated with antibiotics, aggressive fluid resuscitation, bicarbonate infusion and emergently initiated on hemodialysis. Echocardiogram showed dilated right ventricle with decreased Ejection fraction and CT scan showed findings concerning for splenic infarction.

By this time the peripheral blood FISH panel resulted with t(11;14) consistent with MCL. Bone marrow biopsy resulted as very aggressive MCL with associated TP53 deletion and Ki-67 proliferation index 60% (Figure 3). Though her clinical status improved, she developed decreased vision in both eyes. On day 30, she developed intractable abdominal pain and severe thrombocytopenia. Urgent CT scan demonstrated splenic rupture and hemoperitoneum (Figure 4). She was made comfort care and died shortly after.

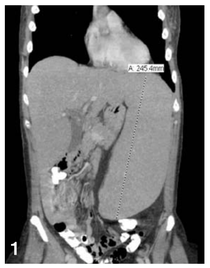

Figure 1: CT scan image showing massive splenomegaly.

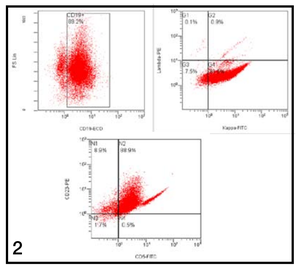

Figure 2: Flow cytometry showing a large monoclonal B-cell population Kappa light chain restriction, dim CD19, CD20, CD5, and variable expression of CD23.

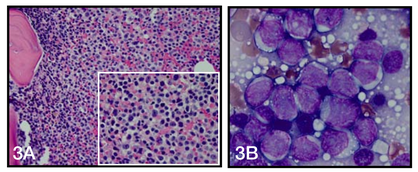

Figure 3A: Bone marrow core biopsy (40x magnification) (insert in white box 100x magnification) showing sheets of large transformed lymphocytes with occasional nucleoli prominent nucleoli.

Figure 3B: Bone marrow aspirate (100x magnification) showing large lymphoid cells with slightly folded nuclei and vasicular chromatin.

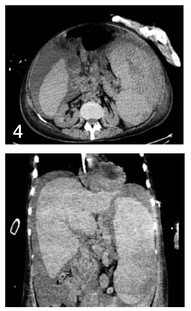

Figure 4: CT scan image showing splenic rupture.

Discussion:

MCL is an aggressive non-Hodgkins lymphoma with poorer prognosis of all other lymphomas. Though not curable outside of transplant, frequent remissions (60%-90%) can be obtained albeit short lasting (1-2 years).[1] MCL is often misdiagnosed as CLL. Flow cytometric immunophenotyping often helps differentiate CLL from MCL, and a characteristic CLL phenotype is considered essentially diagnostic.[2] There is significantly higher expression of CD23 in CLL. MCL typically is negative for CD23, but 25 % cases can be dim positive.[3,4] CLL on the other hand can occasionally be CD23 negative. Thus NHL often can be less obvious and confounds the diagnosis if a leukemic phase occurs at presentation. MCL is more specifically identified by the presence of the translocation t(11;14)(q13;q32), but cyclin D1-negative variants do exist. FISH assay is by far the most sensitive and specific technique for t(11:14) identification.[5] This should be considered in newly diagnosed CLL patients with atypical features especially B grade symptoms at initial presentation, massive splenomegaly, immunopenotypic feature showing moderate bright CD20 and bright surface light chain expression. Given the importance of stem cell transplants for MCL patients, it is important to recognize this, as fludarabine therapy can impair successful collection of stem cells.[6] Bone marrow biopsy though not required for diagnosis for CLL, but should be considered in atypical presentations, discordance in the immunophenotypic markers, presence of cytopenias and preferably prior to treatment initiation.

Rituximab induced CRS or splenic rupture is very rarely reported in literature. There is emerging evidence which implicates IL-6 as a central mediator in CRS. Toclilizumab (IL-6 blocker) is used as first line immunosuppressive therapy in clinical trials.[7] Ophthalmic side effect of rituximab is reported including transient ocular edema, transient visual changes and severe loss of visual acuity; however these are very rare. The risk of reaction may correlate with the aggressiveness and burden of the disease. Hence we should consider aggressive hydration, pre-treatment with steroids, antihistamines and holding or dose reduction of rituximab with first cycle. Post-marketing surveillance database on rituximab indicates a mortality of 0.04–0.07% associated with the drug, however due to it increasing use, there should be high index of suspicion for these side effects as they are life threatening.

References:

1 Ghielmini M, Zucca E. How I treat mantle cell lymphoma. Blood 2009;114(8):1469-1476.

2 Ho, Albert K., et al. “Small B-cell neoplasms with typical mantle cell lymphoma immunophenotypes often include chronic lymphocytic leukemias.” *American Journal of Clinical Pathology* 131.1 (2009): 27-32.

3 Klapper W. Histopathology of mantle cell lymphoma. *Semin Hematol*.2011;48(3):148-154.2. Kraus TS, Sillings CN, Saxe DF, et al.

4 The role of CD11c expressionin the diagnosis of mantle cell lymphoma. *Am J Clin Pathol*. 2010;134(2):271-277.

5 Li J-Y, Gaillard F, Moreau A, et al. Detection of Translocation t(11;14)(q13;q32) in Mantle Cell Lymphoma by Fluorescence in Situ Hybridization. *The American Journal of Pathology.* 1999;154(5):1449-1452.

6 D. Laszlo, P. Galieni, D. Raspadori. Fludarabine containing-regimens may adversely affect peripheral blood stem cell collection in low-grade non Hodgkin lymphoma patient. *Leuk Lymph*, 37(1–2) (2000), pp. 157–161

7 Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood.* 2014;124(2):188-195. doi:10.1182/blood-2014-05-552729.

8 Rituxan® (rituximab) [package insert]. South San Francisco, CA: Genentech, Inc. and Cambridge, MA: Biogen Idec Inc., February 2006.