Case Report

T-Lymphoblastic lymphoma presenting with obstructive jaundice and pleural effusion; role of flow cytometry on pleural fluid: A case report

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A B S T R A C T

T-cell lymphoblastic lymphoma often presents as a large mediastinal mass in the anterior mediastinum with shortness of breath as chief complaint. We, put forward a case of T-LBL, presenting with obstructive jaundice and, later developing pleural effusion. Diagnosis was clinched by Flow Cytometry (FCM) performed on the pleural fluid, which revealed, neoplastic lymphoid cells; suggesting T-cell Lymphoproliferative disorder. Bone marrow examination and immunohistochemistry revealed CD3+, TDT+, CD10+, CD34- and CD20-blasts. Thus, diagnosis of T-ALL/LBL was rendered. Clinicians should be mindful that T-ALL/LBL can uniquely present with obstructive jaundice, proffering serious diagnostic dilemma. FCM should be attempted on any available body fluids/effusions, in appropriate clinical settings, as it can contribute substantially, in making a rapid diagnosis and, initiating early therapy.

Key Messages: 1. Leukemia/lymphoma should be considered, when the initial work-up for obstructive jaundice, is inconclusive; 2. FCM can be performed on any fluid/effusion sample for hematolymphoid neoplasm and can aid in making a rapid diagnosis.

1. Introduction

T-Lymphoblastic leukemia/lymphoma (T-ALL/LBL) is precursor T-cell neoplasm, typically involving bone marrow and blood (T-acute lymphoblastic leukemia/T-ALL), or primarily involving thymus (mediastinum), or nodal/extra-nodal sites (T-acute lymphoblastic lymphoma/T-LBL). T-LBL often presents with rapidly growing large mediastinal mass and, sometimes pleural effusion and respiratory emergency. Presentations like obstructive/cholestatic jaundice, have been rarely reported in literature. Our manuscript foregrounds two highlights: firstly, that T-ALL/LBL can present with, unusual manifestation like obstructive jaundice. Thus, leukemia/lymphoma should be considered, when the initial work-up for obstructive jaundice, is inconclusive. Secondly, in T-ALL/LBL with unusual presentation, immunophenotyping by flowcytometry (FCM) on any representative specimen and not only blood and bone marrow, can play a pivotal role in appropriate clinical settings.

2. Case Report

23-years-old male, presented with epigastric pain, low-grade fever and jaundice for 1 month, along with hepatosplenomegaly and no peripheral lymphadenopathy. Complete blood count (CBC) showed hemoglobin of 10.8g/dl, total leucocyte count (TLC) of 2.8x10⁹/L, normal platelet and differential leucocyte count (DLC). Liver function test (LFT) was deranged, suggesting obstructive jaundice and, confirmed by ultrasonography (USG) with biliary dilatation. Diagnostic paracentesis was attempted, which revealed lymphoid cells by FCM; suggesting T-cell Lymphoproliferative disorder. Bone marrow examination and immunohistochemistry revealed CD3+, TDT+, CD10+, CD34- and CD20-blasts. Thus, diagnosis of T-ALL/LBL was rendered.
jaundice (total bilirubin of 42 mg/dL, direct bilirubin of 25 mg/dL, alanine transaminase of 38 U/L, aspartate transaminase of 72 U/L, alkaline phosphatase of 514 U/L). Coagulation screening was normal; and viral serology was negative. Magnetic resonance cholangiopancreatography (MRCP) revealed hepatosplenomegaly, with enlarged confluent retroperitoneal, mesenteric and iliac lymph nodes (LNs); large confluent soft tissue at porta hepatitis, encasing common bile duct (CBD) and biliary confluence. He underwent percutaneous transhepatic biliary drainage (PTBD), after which bilirubin levels declined gradually. CT-guided biopsy and fine needle aspiration (FNA) from abdominal LNs were performed and he was discharged.

Patient returned after two weeks, with complain of increasing breathlessness. His biopsy was non representative, while FNA reported presence of small to medium sized, monomorphic atypical cells, suggestive of a neoplastic pathology. CT-abdomen and CT-thorax were performed. CT-abdomen findings were like MRCP. CT-thorax showed mediastinal and axillary lymphadenopathy, moderate bilateral pleural effusion, basal lung consolidation and collapse of bilateral lungs.

Pleural fluid was drained which had a TLC of 2x10^9/L, DLC: polymorphs 10lymphocytes90 and, cytologically monomorphic lymphoid cells, with high nucleo-cytoplasmic ratio, round nuclei, fine chromatin, indistinct nucleoli and, scant cytoplasm (Figure 1). Considering a possibility of lymphoproliferative disorder, flow cytometric immunophenotyping performed on pleural fluid, revealed a population of abnormal T-cells, expressing CD45, CD3, CD4, CD5 (dim) and CD7 (normal), as compared to normal T cells (Figure 2); and negative for CD8, CD56 and CD25. Thus, FCM on pleural fluid suggested T-cell Lymphoproliferative disorder, with aberrant T cell antigen expression. Review of the peripheral blood smear at this point of time, revealed occasional atypical lymphoid cells, morphologically resembling blasts.

Bone marrow examination with immunohistochemistry done, showed hypercellular marrow with 80% blasts, which were positive for CD3, TDT, CD10; and negative for CD4, CD20. Ki- 67 proliferation index was ~70%. A diagnosis of T-cell lymphoblastic lymphoma secondarily infiltrating bone marrow was thus, rendered.

Chemotherapy was planned, but before it could be initiated, he developed increasing dyspnoea and dizziness, with eventual drop in BP and SPO2. Resuscitation measures were tried, but he succumbed to his illness.

3. Discussion

T-ALL involves bone marrow in almost all cases, while T-LBL mostly presents as mediastinal mass, with/without involvement of LNs and other extra-nodal sites: like skin, liver, spleen, CNS and testes. With no treatment intervention, patients show high mortality rate, due to complications like respiratory emergency, owing to the rapidly growing mediastinal mass and pleural effusion; and complications associated with leukostasis, among which intracranial bleeding and respiratory failure, account for the majority of early deaths,1 potentiating the importance of early diagnosis and treatment of lymphoblastic leukemia/lymphoma, as chemotherapy, eliminating leukemic cells from bone marrow; and therapies ameliorating other clinical manifestations, have dramatically improved the survival rates for ALL.2 Jaundice caused by hematopoietic neoplasms (HLN) is not infrequent, though rarely, the initial presentation and, has been rarely reported in the literature, as presenting feature of leukemia/lymphoma.

To the best of our knowledge, only two reports of T-ALL/LBL, manifesting as jaundice, have been reported.2,3 Table 1 highlights features of these two cases, and those of ours. Jaundice has also been reported in B-ALL/LBL, more than T-ALL/LBL;4-8 and in acute myeloid leukemia.9,10 The cause of obstructive jaundice, in a case of leukemia/lymphoma, can be either due to, obstruction of hepato-biliary tract (extra-/intra-hepatic),10 or due to leukemic infiltration of hepatic sinusoids.5 Jaundice in leukemia/lymphoma, may present with/without hyperleukocytosis. Presentation without hyperleukocytosis and/or, blasts/ atypical cells in peripheral blood, as in our case, make the clinical diagnosis even more difficult.2

FCM is clearly indicated in the diagnosis of HLN.11 Nevertheless, its diagnosis, is frequently based upon cytomorphology of specimens, like FNAs. FCM is an integral part of work up in leukemia/lymphoma, but is usually done on blood and bone marrow samples. FCM performed on samples, like FNAs, effusions,12 BAL fluid,13 and other cavity fluids, has been demonstrated, not only to increase the sensitivity of HLN detection but also, help in diagnostic sub-classification of lymphoma, in these specimens.14-16 Thus, in appropriate clinical settings like, in our patient with poor general condition, no accessible LNs and, no atypical cells in the peripheral blood, we must attempt FCM on available body fluids/effusions. Differential diagnoses of jaundice are wide, posing diagnostic dilemma as seen in our case. Thus, clinicians should be sagacious, to consider the T-/B-cell leukemia/lymphoma, in the differentials of obstructive jaundice, to forestall undue delay, in the diagnosis and management.

4. Conclusion

Jaundice as presenting feature of T-ALL/LBL, has been rarely reported in the literature. FCM is an integral part of work up in leukemia/lymphoma, which is usually done on blood and bone marrow samples. In a patient with poor general condition, no accessible LNs and no atypical cells in blood smear, we attempted to perform FCM on pleural
Fig. 1: Pleural fluid cytology: showing monomorphic atypical lymphoid cells (Pap, Oil immersion); B. Flow cytometric immunophenotyping on pleural fluid: R1 population (red) represent blasts and R2 population (green) represent normal T cells. Blasts have dim expression of CD45, CD3, CD4, CD5; normal expression of CD7 and no expression of CD8 as compared to normal T cells.

Fig. 2: Bone marrow aspirate smears: showing blasts (Leishman, 200X & Oil immersion); B. Bone marrow biopsy: showing infiltration by blasts (H&E, 400X); C-F. On immunohistochemistry, these blasts are positive for CD3 (2C), TdT (2E) and CD10 (2F), negative for CD20 (2D)
Table 1: Summary of case reports of T-ALL/LBL presenting as obstructive jaundice.

| Authors          | Age/Sex | Symptoms/signs                                                                 | CBC/PBS                                                                                       | LFT (at presentation)                                                                 | Radiological findings                                                                                       | Bone marrow | Outcome                                  | Notes                                                                                      |
|------------------|---------|------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|-------------|----------------|-------------------------------------------------------------------------------------------|
| Patel et al.     | 42yr/Male | Loss of weight and appetite, nausea, jaundice, pale stools, dark urine; hepatomegaly without peripheral lymphadenopathy. | No significant abnormality;                                                                 | AST (U/L): 107 ALT (U/L): 130 Alk. Phosphatase (U/L): 894 Bilirubin (mg/dL): 7.9 Direct: 6.1 Coagulation profile: Normal | Massive hepatomegaly with coarse echotexture, with contracted gall bladder and, normal sized common bile duct. Huge anterior mediastinal mass. | 85% blasts. | responded to chemotherapy | Mediastinal mass and liver biopsy: CD1a, CD3, CD4, CD5, CD8 and CD43+ atypical lymphoid cells. |
| Ford et al. 2019 | 7yr/Male | History of recentonset motor ics and jaundice; hepatosplenomegaly and peripheral lymphadenopathy. | Only mild leukocytosis and thrombocytopenia; no significant abnormality. | AST (U/L): 1693 ALT (U/L): 1295 Bilirubin (mg/dL): 9.3 Direct: 6.8 Coagulation profile: Normal | Diffuse gallbladder wall thickening, surrounding lymphadenopathy with hepatomegaly. | Showed blasts. | responded to chemotherapy | Liver biopsy was also performed; it revealed atypical lymphocytes |
| Present case     | 23yr/Male | Epigastric pain, fever and jaundice; hepatosplenomegaly without peripheral lymphadenopathy. | Anemia and leucopenia (at presentation). Anemia, leukocytosis and presence of blasts (later) | AST (U/L): 72 ALT (U/L): 38 Alk. Phosphatase (U/L): 514 Bilirubin (mg/dL): 42 Direct: 25 Coagulation profile: Normal | Hepatosplenomegaly, with abdominal lymphadenopathy, confluent soft tissue at porta hepatis, encasing common bile duct and biliary confluence. (at presentation) Bilateral pleural effusion, lung collapse and consolidation, with mediastinal and axillary lymphadenopathy. (later) | Showed CD3, TdT and CD10+ blasts (80%). | Patient developed respiratory distress; and succumbed to his illness | Flow cytometry of pleural fluid helped to clinch the diagnosis. |
fluid, which suggested T-cell Lymphoproliferative disorder. Bone marrow examination eventually, rendered the final diagnosis.

Leukemia/lymphoma should be considered in the differential diagnosis, when initial workup for jaundice is inconclusive. FCM performed on any fluid sample, in appropriate clinical settings, is extremely helpful, in making a rapid diagnosis and, initiating early specific therapy.

5. Abbreviations

T-ALL/LBL: T-Lymphoblastic leukemia/lymphoma; FCM: Flow Cytometry; MRCP: Magnetic resonance cholangiopancreatography; T-ALL: T-acute lymphoblastic Leukemia; T-LBL: T acute lymphoblastic lymphoma; CBC: complete blood count; DLC: differential leucocyte count; LFT: liver function test; LN: lymph node; PTBD: percutaneous transhepatic biliary drainage; FNA: fine needle aspiration; CT: computed tomography; HLN: hemato-lymphoid neoplasms.

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7. Conflict of Interest

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References

1. Porcu P, Cripe LD, Ng EW. Hyperleukocytotic leukemias and leukostasis: a review of pathophysiology, clinical presentation and management. Leuk Lymphoma. 2000;39(1-2):1–18.

2. Ford J, Rainey S, Hanson K. Acute lymphoblastic leukemia presenting as cholestatic jaundice in a 7-year-old boy. SAGE Open Med Case Rep. 2019;7:2050313X19875318.

3. Patel KJ, Latif SU, Calaca WMD. An unusual presentation of precursor T cell lymphoblastic leukemia/lymphoma with cholestatic jaundice: case report. J Hematol Oncol. 2009;2:2663564–2663564.

4. Chang LS, Yu HR, Chen YC. Acute lymphoblastic leukemia presented as severe jaundice and hyperferritinemia: a case report. J Pediatr Hematol Oncol. 2011;33(3):117–9.

5. Siddique MN, Popalzai M, Aoun N. Precursor B-cell acute lymphoblastic leukemia presenting as obstructive jaundice: a case report. J Med Case Rep. 2011;5.

6. Oladiran O, Nwosu I. Obstructive Jaundice due to Pancreatic Involvement as an Initial Presentation of Adult Acute Lymphoblastic Leukemia. Case Rep Hematol. 2018;p. 9175360.

7. Melendez-Rosado J, Bartel MJ, Jiang L. Cell Acute Lymphocytic Leukemia Presenting as a Bile Duct Stricture Diagnosed With Cholangioscopy. ACG Case Rep J. 2016;17:3(4):e107.

8. Senadhia V, Emuron D, Gupta R. Acute hepatitis A induction of precursor B-cell acute lymphoblastic leukemia: a causal relationship? J Pediatr Hematol Oncol. 2010;3(3):505–9.

9. Sun K, Reynolds RJ, Sheu TG. Acute myeloid leukemia presenting as acute liver failure case report and literature review. Examenmedicalscience. 2009;13:960.

10. Lee JY, Lee WS, Jung MK. Acute myeloid Leukaemia presenting as obstructive jaundice caused by granulocytic sarcoma. Gut Liver. 2007;1(2):182–5.

11. Davis BH, Holden JT, Bene MC. Bethesda International Consensus recommendations on the flow cytometric immunophenotyping of hematolymphoid neoplasia: medical indications. Cytometry B Clin Cytom. 2006;72(1):5–13.

12. Rangan A, Handoo A, Sinha S. Ascitic fluid cytology and flow cytometry in the primary diagnosis of lymphoma - a case report. Indian J Hematol Blood Transfus. 2010;26(1):15–8.

13. Song JY, Filie AC, Venzon D. Flow cytometry increases the sensitivity of detection of leukemia and lymphoma cells in bronchoalveolar lavage specimens. Cytometry B Clin Cytom. 2012;82(5):305–12.

14. Medda B, Buss DH, Woodruff RD. Diagnosis and subclassification of primary and recurrent lymphoma. The usefulness and limitations of combined fine-needle aspiration cytomorphology and flow cytometry. Am J Clin Pathol. 2000;113(5):688–99.

15. Dong H, Harris NL, Preffer FL. Fine-needle aspiration biopsy in the diagnosis and classification of primary and recurrent lymphoma: A retrospective analysis of the utility of cytomorphology and flow cytometry. Mod Pathol. 2001;14(5):472–81.

16. Dahmoush LHY, Barnes E, Stetler-Stevenson M. Adult T-cell leukemia/lymphoma - A cytopathologic, immunocytochemical, and flow cytometric study. Cancer Cytopathology. 2002;96(2):110–6.

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