Chest Heart Journal
Vol. 42, No. 1, January 2018

CASE REPORT

Unilateral Pleural Effusion: An Uncommon Initial Presentation of Acute Lymphoblastic Leukaemia

Nirmal Kanti Sarkar[1], Md. Mofazzal Haider Siddique[2], Sarmin Sultana[4], Sanjoy Kumar Kar[1], Mahmud Masum Attar[1]

Abstract

Hematologic malignancies like acute and chronic leukemia rarely present with or develop pleural effusion during the clinical course of disease. We report a patient with acute lymphoblastic leukemia (ALL), who presented with right sided pleural effusion. There was no symptom related to leukemia at the time of presentation. Radiologically there was moderate right-sided pleural effusion which was exudative, plenty RBC and predominant cell was lymphocytes (80%). Subsequent haemogram, bone marrow aspiration study and flow cytometry analysis confirmed the diagnosis of T-cell lymphoblastic leukaemia (Pro-T variant). Induction chemotherapy was started but the patient developed severe neutropenic sepsis and expired 10 days after starting chemotherapy.

Key words: *Pleural effusion, acute lymphoblastic leukemia (ALL)*

[Chest Heart Journal 2018; 42(1) : 59-62]

DOI: http://dx.doi.org/10.33316/chab.j.v42i1.2019579

Introduction

Leukemias are diseases in which abnormal proliferation of haematopoietic cells cause progressively increasing infiltration of the bone marrow, although in certain forms the lymphatic tissues are particularly affected. Acute lymphoblastic leukemia (ALL) involve lymphoid cell line and have an aggressive course.[1]In day-to-day clinical practice, clinicians dealing with pleural effusions discover diverse underlying aetiology. Though it is not an uncommon presentation of different malignancies, unilateral pleural effusion as an initial manifestation of acute lymphoblastic leukemia (ALL) is a rare occurrence. The most common mode of presentation of ALL is anaemia, haemorrhage, infective lesion of mouth, pharynx and respiratory tract, fever, prostration and malaise.[1]Rarely a pleural effusion lead to discovery of an underlying haematological malignancy like ALL.[2]In an area of high tuberculosis burden, a patient presenting with fever and pleural effusion may mislead clinician regarding diagnosis especially where other features of haematological malignancy is absent.

Case study

A 30-year-old man presented with the complaints of cough for two and a half months, low grade fever and gradual weight loss for the same duration, heaviness of right chest and abdominal distension for two weeks. Cough was mostly dry with occasional sputum production, fever was low-grade, and intermittent which subsided with

1. Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka-1212, Bangladesh.
2. Resident, Pulmonology, National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka-1212, Bangladesh.
3. Resident, Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka, Bangladesh.

Corresponding to: Dr. Nirmal Kanti Sarkar, FCPS, MD, FCCP, Junior Consultant, Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Mohakhali, Dhaka-1212, Bangladesh. Phone: +8801711461925, E-mail: nirmalsarker@gmail.com

Submission on: 5 January 2018 **Accepted for Publication:** 29 January 2018

Available at http.//www.chabjournal.org

taking antipyretics. There was loss of 12 kg weight in preceding months. Two weeks before hospitalization, he felt heaviness in right chest with increasing cough and abdominal distension. There was no history of hemoptysis, bleeding diathesis, skin rash, and history of tuberculosis or contact with active TB patient. There was no significant past medical history. He was a shopkeeper from semi-urban area, married with no history of exposure and use of illicit drug.

On examination, he was apathetic and moderately anaemic, body weight 58 kg, axillary temperature 100^0 F. There was generalized lymphadenopathy involving bilateral cervical, axillary and left epitrochlear region. Nodes were variable sizes, firm in consistency, mobile, non-tender, without any discharging sinus and the largest one 5 cmX3cm in right axillae. There was no bony tenderness. Respiratory system examination revealed diminished breath sound and vocal fremitus with stony dull percussion note over right lower chest, features consistent with right sided pleural effusion. There was mild ascites, enlarged liver with 4.5 cm from right costal margin and mild splenomegaly. Diagnostic tests were performed.

Chest X-ray P/A view showed right sided moderate pleural effusion (Fig-1). Sputum AFB and GeneXpert were negative. Haemogram revealed Hg 7.8 gm/dl (12.5-17.5 gm/dl), ESR 33 mm/1^{st} hr, total leukocyte count 13390/cmm (4000-11000/cmm), with 47% atypical cells and platelet count 70000/cmm (150000-450000/cmm). Peripheral blood film showed many atypical cells in WBC series and reduced platelet count, features suggestive of acute leukemia. Diagnostic pleural fluid aspiration and bone marrow aspiration was planned.

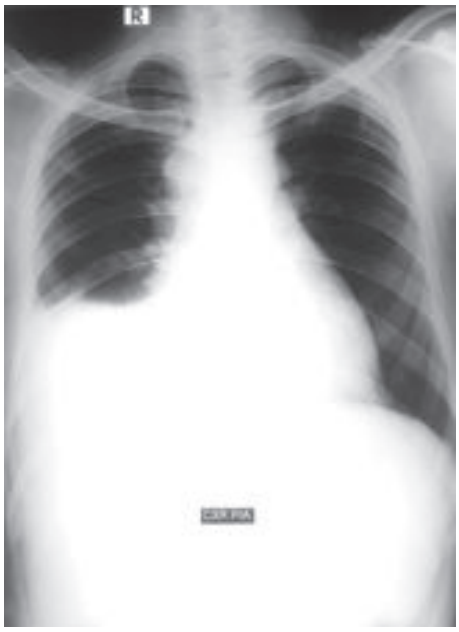
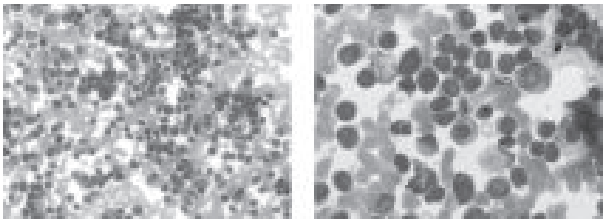


Fig.-1: *Right sided pleural effusion*

About 1200 ml haemorrhaegic pleural fluid was aspirated from right pleural cavity. There was plenty RBC/hpf, total count 200/cmm with 80% lymphocyte, protein 3.9 gm/L, sugar 5-8 mmol/L, ADA 23.9 U/L (0-24 U/L), malignant cell was absent. Bone marrow aspiration revealed features consistent with acute lymphoblastic leukaemia (Fig-2). A clinical diagnosis of ALL with haemorrhagic pleural effusion was made. Haemato-oncologist's opinion was sought and the patient was referred to Haematology department of a multidisciplinary teaching hospital.



A **B**

Fig.-2 (a, b): *Bone marrow aspiration cytology. Arrow indicates blast cell (Leishman stain 400x and 1000x).*

Flow-cytometry of bone marrow was done. On immunophenotyping, it was seen that CD45 slightly dim blastoid population expresses CD7 (strong), CD33 (dim partial) and cCD3. These blastoids were negative for surface CD3, CD5, CD2 and all B-lymphoid and other myeloid markers. Feature was consistent with diagnosis of T-cell lymphoblastic leukaemia (Pro-T variant).

Induction chemotherapy was started with doxorubicin, vincristine, L-asperginase, methotrexate and cytarabin. As there was re-accumulation of pleural effusion and worsening dyspnoea, tube thoracostomy was done after consulting thoracic surgical team. But his condition was deteriorating with persistent high grade fever, with severe neutropenia and

thrombocytopenia and the patient died 10 days after starting chemotherapy due to severe neutropenic sepsis.

Discussion:

Nearly all hematological malignancies can present with or may develop pleural effusion during the clinical course of disease. Among the most common disorders, are

Hodgkin and non-Hodgkin lymphomas, with a frequency of 20 to 30%, especially if mediastinal involvement is present. Acute and chronic leukemia are rarely accompanied by pleural involvement.[3]

Pleural infiltration with malignant cells in acute leukemia is rarely diagnosed during life. It is a common finding at autopsy.[4]Currently, due to increased patient

survival, such cases are being reported. However after an extensive internet search, a very few casereports of malignant pleural effusion that have ledto the diagnosis of ALL are available. Further, due to the rarity of such cases, the underlying etiology of these leukemic effusions is poorly understood.[5]

Leukemic infiltration of lungs may occur as a part of systemic relapse or rarely as an isolated pulmonary leukemic infiltration. Possible pathogenic mechanisms suggested include extramedullary proliferation of a quiescent leukemic clone of cells with subsequent metastasis to bone marrow or alternatively, a subclinical marrow relapse undetected by standard methods with consequent seeding to extramedullary sites.[4]

In leukemic patients, the possibility of other causes responsible for presence of pleural effusion such as bacterial or viral infections, other disseminated solid tumors or complications of chemotherapy should be excluded.Immunocytological examination of cells obtained from pleural effusion, flow cytometry, as well as polymerase chain reaction applied to cytology specimens can contribute to the differential diagnosis. The obtained findings sometimes need to be confirmed by pleuroscopyor thoracoscopicsurgical biopsy.[6-8]

Faiz et al. published the largest series of 111 cases of pleural thoracocentesis in leukemicpatients. In this series, 69 cases were acute myeloid leukemia (AML), 7 were acute lymphoblastic leukemia and 15 were of myelodysplastic syndromes. Major causes attributable to such effusions included associated bacterial or viral infections (47%) and underlying malignancy (36%)[9] Other possible causes may be secondary malignancies, associated autoimmune diseases and treatment toxicities due to chemotherapy, radiation or bone marrow transplant. Desatinib, a tyrosine kinase inhibitor has been found to be linked with exudative pleural effusion.[10]

The prognostic significance of the presence of a pleural effusion at diagnosis with ALL is not easy to determine. Some authors argue that it does not affect the rate of remission or survival. Others report a worse prognosis.[3]Thepleural effusion in patients with ALL usually disappear after induction of chemotherapy. This results in direct improvement of symptoms. However recurrence of pleural exudates is almost inevitable if patients do not achieve remissions. They may present with massive fluid accumulation and respiratory failure. In such case pleurodesis is a treatment option.[11]

Conclusion:

The diagnosis of unilateral pleural effusion as a consequence of haematological malignancy especially acute lymphoblastic leukaemia is always difficult and challenging. Sometimes such pleural effusion may be the first clinical manifestation of an underlying undiagnosed haematological malignancy. Thorough clinical examination and appropriate investigation leads to prompt diagnosis and treatment of theprimary disease.

Conflict of interest: There is no conflict of interest to declare.

Reference:

1. Firkin F, Chesterman C, Penington D, Rush B (editors). de Gruchy's Clinical Haematology in Medical Practice. 5th ed. Oxford: Blackwell Science; 1989.
2. Brunning RD, Matutes E, Harris NL, et al. Acutemyeloid leukaemia: introduction. In:

Jaffe ES, HarrisNL, Stein H, et al (editors). Pathology and genetics of tumours of haematopoietic and lymphoid tissues. 3rded. Lyon, France: IARC Press; 2001. P.77-80.

3. Alexandrakis MG, Passam FH, Kyriakou DS, Bouros D. Pleural effusions in hematologic malignancies. *Chest* 2004; 125: 1546-55.
4. Dix DB, Anderson RA, McFadden DE, Wadsworth LD.Pleural relapse during haematopoietic remission inchildhood acute lymphoblastic leukaemia. *J PediatrHematolOncol.* 1997; 19(5):470-2.
5. Chabbra S, Kalra R, Malik S, et al. Unilateral malignant pleural effusion as an initial manifestation of acute lymphoblastic leukemia: a case report. *Middle East Journal of Cancer* 2015; 6(1): 61-4.
6. Aasebo U, Norum J, Sager G, et al. Intrapleurally instilled mitoxantrone in metastatic pleural effusions: a phase II study. *J Chemother*1997; 9:106-11.
7. Light RW. Malignant pleural effusions. In Light RW, ed. Pleural diseases. Philadelphia PA: Lea &Febiger, 1990; 97-116.
8. Horn KD, Penchansky L. Chylous pleural effusions simulating leukemia infiltrate with thoracoabdominal disease and surgery in infants. *Am J Clinical Pathol*1999; 111: 99-104.
9. Faiz SA, Bashoura L, Lei X, et al. Pleural effusions in patients with acute leukemia and myelodysplastic syndrome. *J Leukemia & Lymphoma* 2013; 54(2): 329-35.
10. Brixey AG, Light RW. Pleural effusions due todesatinib. *CurrOpinPulm Med*. 2010; 16(4): 351-6.
11. BronnerGM, Baas P, Beijnen JH. Pleurodesis inmalignant pleural effusion [Article in Dutch]. *NedTijdschrGeneeskd.* 1997; 141(38):1810-4.