

# Hyperleukocytosis Associated Pulmonary Leukostasis in Acute Leukaemia

H Singh\*, BNS Prasad\*\*, Jagdish\*\*\*, A Batra+

## Abstract

Leukostasis is a fatal complication in granulocytic leukaemia. Brain and lung are most commonly involved organs in leukostasis. In the lung, the clinical presentation simulates infections and haemorrhagic complications of acute leukaemia. Being a medical emergency, early recognition of leukostasis and initiation of therapy prevents mortality. ©

## INTRODUCTION

About 5-13% of adult patients with acute myeloid leukaemia present quite differently. They have hyperleukocytosis (i.e. white blood cell counts  $>1,00,000/\text{mm}^3$ ).<sup>1,2</sup> These patients of hyperleukocytosis present with symptoms primarily due to leukostasis – a clinicopathological syndrome caused by sludging of circulating leukaemic blasts in tissue microvasculature.<sup>3</sup> Leukostasis can affect any organ but symptoms usually arise from involvement of lungs, heart, brain and testes. Clinical presentation in the lung may simulate infection, embolisation and acute respiratory failure.

## CASE REPORT

15 years boy presented with complaints of increasing pallor, easy fatigability and generalized weakness for duration of one month. There was no history of fever, bleeding tendencies, chest pain, sore throat, urinary or bowel trouble. There was no history of altered sensorium/ behavior or any focal neurological deficit. He also complained of gradually increasing breathlessness for past one week, which restricted his routine works. He denied any drug intake.

On general physical examination, patient was anaemic and there was no evidence of jaundice, rash, purpuric spots or lymphadenopathy. Bony tenderness was present. Respiratory system examination revealed increased respiratory rate of 30 per minute and on auscultation had bilateral basal crackles. On abdominal examination, firm hepato-splenomegaly was present. Cardiovascular and nervous system examination was

essentially normal.

Laboratory evaluation revealed normal biochemical parameters especially renal and liver function tests. Complete haemogram showed: Hb - 2gm%; TLC 1,20,000/cmm with 90% blast; and platelets – 60,000/cmm. Bone marrow aspiration showed acute promyelocytic leukaemia (M3). Chest X-ray was normal (Fig. 1). Electrocardiogram was normal. Microbiological evaluation of blood, urine and sputum (bacterial and fungal) was negative. His arterial blood gas analysis showed PaO<sub>2</sub> of 80% with oxygen saturation of 60%. CT scan was done (Figs. 2, 3 and 4) which showed ground glass opacities with areas of consolidation in both lung fields predominantly in the right lung. A diagnosis of hyperleukocytosis with pulmonary leukostasis was made. The patient was given chemotherapy with cytosine arabinoside and doxorubicin. The patient responded to therapy especially respiratory symptoms along with blood counts. The patient was also started



Fig. 1 : Chest X-ray PA view

\*Associate Professor; \*\*Senior Resident; \*\*\*Professor; +Resident; Department of Medicine, Pt. B.D. Sharma, Post Graduate Institute of Medical Sciences, Rohtak-124001 (Haryana) India. Received : 23.1.2006; Accepted : 10.4.2006

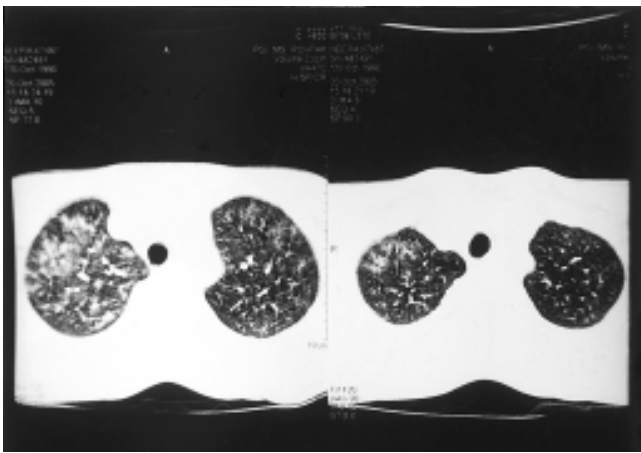


Fig. 2 : CT scan chest showing upper section

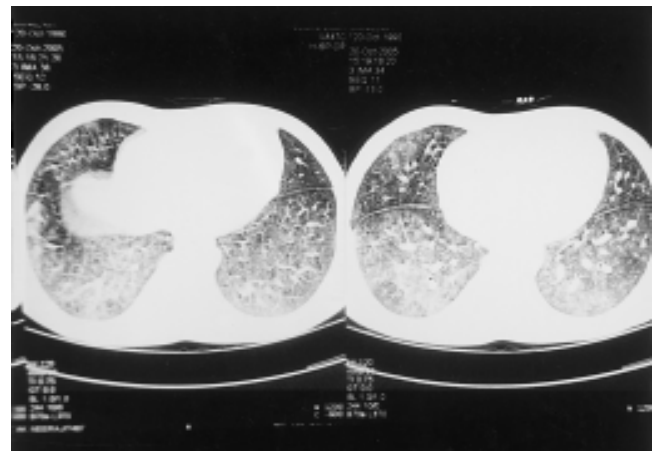


Fig. 4 : CT scan showing lower section

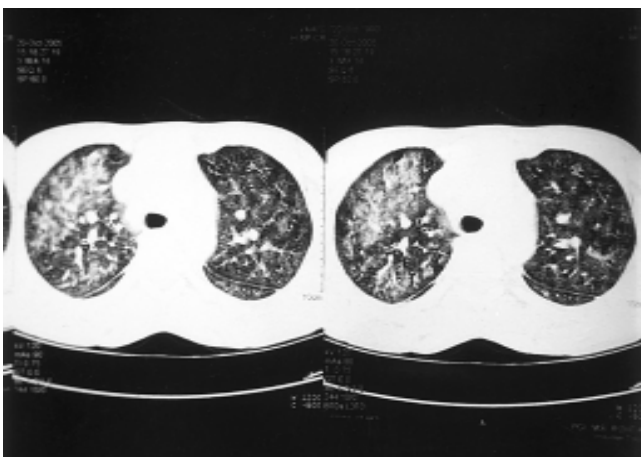


Fig. 3 : CT scan chest showing middle section

on all-trans retinoic acid. He was discharged in stable condition, but lost the follow up since then.

## DISCUSSION

Pulmonary disease in leukaemia is frequent and often lethal. Lung involvement in leukaemia is primarily due to a) leukostasis of vessels and b) true leukaemic infiltration of interstitium and alveoli.<sup>1,2</sup> Clinically, leukostasis in leukaemia should be suspected in patients with unexplained fever and cardiopulmonary or cerebral dysfunction. Pulmonary leukostasis was found in about 40% of autopsy series.<sup>4</sup> Maile *et al*<sup>5</sup> noted parenchymal opacities on 90% of chest radiographs obtained shortly before death in adults patients with leukaemia. These radiologic opacities on autopsy were attributed to infections, haemorrhage, leukaemic infiltrations and edema. In addition, drug induced pulmonary infiltrates and leukoagglutinin transfusion reactions were also reported.<sup>4</sup> In spite of above data, pulmonary leukostasis in leukaemia has been mentioned only incidentally as a cause of abnormalities on chest radiography. Radiographic features of lung disease in leukaemia are often nonspecific and may remain invisible per se.<sup>4</sup> The distribution of infiltrates on chest radiograph has

been mentioned as a rough indicator of the cause of opacities. Local infiltrations are frequently reported in bacterial infections; diffuse infiltrations are reported more often in opportunistic infections, haemorrhages and pulmonary oedema. When no abnormalities are visible on chest radiograph of dyspneic leukaemic patients, leukostasis should be considered as other alternate diagnosis besides pulmonary embolisation.<sup>4</sup> A scintigraphic study will not differentiate between these conditions, because perfusion defects can be expected in both. Arterial blood gas samples should be interpreted cautiously, as spuriously low arterial oxygen tension (pseudohypoxaemia) can result from rapid consumption of plasma oxygen by the markedly increased number of white blood cells.<sup>1</sup>

The risk factors for leukostasis are acute leukaemia, younger age (most common in infants), certain types of leukaemia like acute promyelocytic (microgranular variants), acute myelomonocytic, acute monocytic leukaemia and T cell type of ALL. Cytogenetic abnormalities – 11q23 translocations and presence of Philadelphia chromosome are also associated with leukostasis.<sup>2</sup>

The Pathogenesis of leukostasis is determined by: - 1) Sluggish flow with stasis, 2) Aggregation of leukaemic cells, 3) Formation of microthrombi, 4) Release of toxic granules, 5) Endothelial damage, 6) Oxygen consumption by leukocytes, 7) Tissue invasion.<sup>6</sup>

Leukostasis is usually associated with counts of >1,00,000 but acute monocytic leukaemia may present with leukostasis with counts of 50,000/cmm. 5-13% of patients of AML and 10-30% of patients of ALL will manifest with hyperleukocytosis.<sup>1</sup> Earlier leukostasis was thought to be due presence of critical leukocrit (fractional leukocyte volume) and increased viscosity. Now, there is increased evidence that, interaction of endothelium and blast cell leading to aggregation of blast cells in microcirculation. It is due to difference in expression of adhesion molecules in lymphoblast and myeloblast cell surfaces. The adhesion molecules

expressed on the leukaemic blast cells and their hemotactic response to the cytokines in the vascular microenvironment is more important than cell number.<sup>7</sup>

Leukocytoreduction is the mainstay of management of leukostasis. This can be achieved either by chemotherapy or leukapheresis. Chemotherapy can precipitate lung injury due to acute lysis of circulating blasts occurs within hours of initiation of treatment, this phenomenon is called leukaemic cell lysis pneumopathy.<sup>8</sup> Leukapheresis can reduce 20-50% of blast cell count in a single session. It removes the circulating blasts with recruiting the marginated cells into intravascular space. The role of cranial irradiation is controversial.<sup>1</sup>

In the present case, the patient had a count of more than 1 lac with breathlessness. The chest x-ray was normal. Initially it was thought to be due to infection but the microbiological evaluation was negative which made us to think of alternate diagnosis, like leukostasis or pulmonary embolisation. CT chest was helpful. Review in the literature led us to make a diagnosis of hyperleukocytosis with pulmonary leukostasis.

## REFERENCES

1. Majhail NS, Lichtin AE. Acute leukemia with a very high leukocyte count: confronting a medical emergency. *Cleveland Clin J Med* 2004;71:633-7.
2. Porcu P, Cripe LD *et al.* Hyperleukocytic leukemias and leukostasis: a review of pathophysiology, clinical presentation, and management. *Leuk Lymphoma* 2000;39:1-18.
3. Van Buchem MA, te Velde J, Willemze R, Spaander PJ. Leucostasis, an underestimated cause of death in leukaemia. *Blut* 1988;56:39-44.
4. Mark A, Van Buchem, Wondergem JH, Schultze LJ, te Velde J, Kluin PM, Bode PJ, *et al.* Pulmonary leukostasis: Radiologic - Pathologic study. *Radiology* 1987;165:739-41.
5. Maile CW, Moore AV, Ulreich S, Putman CE. Chest radiographic-pathologic correlation in adult leukemia patients. *Invest Radiol* 1983;18:495-9.
6. Litchman MA, Heal J, Rowe JM. Hyperleukocytic leukaemia. Rheological and clinical features and management. *Ballier's Clinical Haematology* 1987;1:725-46.
7. Stucki A, Rivier AS, Gikic M, Monai N, Schapira M, Spertini O. Endothelial cell activation by myeloblasts: molecular mechanisms of leukostasis and leukemic cell dissemination. *Blood* 2001;97:2121-9.
8. Gucalp R, Dutcher J. Oncological emergencies. In: Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL, editors. *Harrison's Principles of Internal Medicine*. McGraw Hill, New York, 16<sup>th</sup> edn. 575-83.

### Announcement

#### **Indian Society of Electrocardiology Aligarh Arrhythmia Course - 2006 (AAC-2006)**

**Indian Society of Electrocardiology is organizing 3rd Mid Term Conference - AAC - 2006 at Hotel Gayatri Palace, Aligarh on 2<sup>nd</sup> and 3<sup>rd</sup> September 2006.**

For further details please contact : **Dr KK Varshney**, Organising Secretary, AAC 2006, KK Hospital and Heart Centre, Ramghat Road, Aligarh (UP) 202001.

Ph : 0571-2741062, 3090757 Telefax : 0571-2741061

Mobile : 09358258116 Email : vardhneykk5@yahoo.com

**Dr. SB Gupta**, Hon. Secretary ISE, Head, Department of Medicine and Cardiology, Central Railway Headquarters Hospital, Byculla. Mumbai 400 027.

Ph : 022-23717246 (Hosp) 022-22624556 022-22651044 (Fax)

Cell : 09821364565/09821638617 E-mail : sbgupta@vsnl.net

Visit the website : [www.iseindia.org](http://www.iseindia.org)

### Announcement

**APICON KRISHNA, The 2<sup>nd</sup> AP State API Annual Conference, 19th and 20th August 2006 at Vijayawada.**

For further details contact : **Dr. Meher N Prasad**, Organizing Secretary, APICON KRISHNA 2nd AP State API Annual Conference, Vijayawada - 520 010