The Clinical& Radiological Respiratory Features in Acute Leukemia At Presentation: A Descriptive Study of 118 Iraqi Adult Patients .

Adil Siwan Al-Aqabi* , Azher Sebieh AL Zubaidy* ,Khudyer Abaas aLKhalisi **

ABSTRACT:

BACKGROUND:

Acute leukemia is a hematological malignancy characterized by an uncontrolled proliferation of hemopietic primitive cells. Presenting features of acute leukemia include fever, anemia, pallor; hepatosplenomegaly &lymphadenopathy, bleeding tendency, bone pain&gum hypertrophy. Intrathoracic manifestations of acute leukemia include infection, mediastinal widening , hemorrhage, infiltration, embolism, edema, pericarditis ´ respiratory distress syndrome. **OBJECTIVE:**

To describe the clinical &radiological respiratory features of acute leukemia at presentation, before starting chemotherapy.

PATIENTS AND METHODS:

Patients with acute leukemia of age ranged from 15-75 years were incorporated in this study, patients were excluded from the study if they had previous malignancy, lung disease, or if received cytotoxic treatment. Every patient had a detailed history of pulmonary symptoms & chest examination, chest x-ray examination, sputum samples & pleural aspirates for relevant patients.

RESULTS:

Of 118 patients with actue leukemia at presentation, 60% of patients were males& 40% were females. Respiratory symptoms including cough, dyspnea&chest pain were found in27.7% of patients (cough 24.4%, dyspnea 2.5%, chest pain 0.8%). Respiratory signs including crepitations, decreased air entry & bronchial breathing were found in 12.5% of patients (crepitation 3.3%, decreased air entry in 6.7%, bronchial breathing in 2.5%). Chest X-ray abnormalities were found in 14.3% of patients, these include mediastinal widening in 5.9% of patients. Pleural effusion in 4.2% & parenchymal infiltrates in 4.2% of patients

CONCLUSION:

The chest findings in patient with actue leukemia at presentation were not uncommon. mediastinal widening was the commonest, pleural effusion&parenchymal infiltrates were less common findings. *KEY WORDS*: acute leukemia, chest x ray

INTRODUCTION:

Acute leukemias are defined pathologically as malignancies of immature hemopietic cells ⁽¹⁾. Common clinical presentations of acute leukemia include anemia, infection &bleeding ⁽²⁾. Acute leukemia is classified into ALL &AML based on morphological, cytogenetic &molecular studies⁽³⁾ Acute leukemia may infiltrate into extramedullary tissues such as lungs, nervous system & cardiovascular system including

pericarditis⁽⁴⁾.

Leukemic infiltrates in the chest was often found at necropsy ,but nowdays newer radiological

*Consultant Hematologist /Baghdad Teaching Hospital/Medical City.

** Consultant Hematologist& Assistant professor/Baghdad Medical College. imaging such as spiral CT scan &MRI with or without contrast can diagnose these infiltrates if not recognized by plain chest radiology, they may present as numerous milliary nodules scattered in both lung fields,most frequently the leukemic infiltrates are peribronchial,

 $perivas cular, pleural \& intra alveolar^{(5)}.$

The radiographic appearance of pulmonary leukemic infiltrates has been described as a diffuse reticular pattern, although pulmonary nodules and focal homogeneous opacities were also reported⁽⁶⁾. Respiratory infections are usually viral or bacterial at pretreatment period,but after chemotherapy there is increase in fungal &opportunistic infections, many of infections were unrecognized &offending organism was seldom isolated;Moreover,the differentiation between

leukemic infiltrates, infection & haemorhage was impossible radiologically but newer radiological imaging can make the distinction ⁽⁷⁾. Clinically the physical findings are usually scant and recognition of pulmonary involvement depend upon the demonstration of abnormalities on chest imaging, radiologically the most frequent abnormality is enlargement of hillar lymph nodes&mediastinal adenopathy which occure mostly with Tcell ALL (8). Massive thymic enlargement can cause dyspnea especially when associated with pleural effusion, pleural effusion is due to small sub pleural infarcts, leukemic deposits ,pleural lymphocytic obstruction or infection⁽⁹⁾.Respiratory viruses are widespread in the community & easily transmitted to patients with a hematological malignancy⁽¹⁰⁾. focal pulmonary infiltrates were usually caused by ordinary bacterial infections while diffuse pulmonary infiltrates were commonly caused by opportunestic organisms or by a variety of noninfectious disorders such as hemorrhage, pulmonary edema, or leukemic infiltrates, clinically defined respiratory events are frequent and occur early in the course of acute leukemia, half are of infectious origin and all are of a major prognostic significance ⁽¹¹⁾

PATIENTS & METHODS:

during the interval between December1998 &july2000 ,118 patients whose age range 15-75 years old, admitted to Baghdad teaching hospital with diagnosis of acute leukemia based on clinical peripheral blood and bone marrow examination were incorporated in this study ,patients were excluded from the study only if they had previous hematological malignancy such as chronic myeloid leukemia, lymphoma or myelodysplastic syndrome, previous history of lung disease such as chronic bronchitis, emphysema, asthma or tuberculosis or previously received cytotoxic treatment . Every patient had adetailed history of pulmonary (cough, symptoms sputum production, dyspnea, chest pain , tachypnea and haemoptysis;past medical history of tuberculosis, pneumonia or other respiratory diseases; smooking habit; detailed chest examination, chest x rays ; sputum samples were collected from patients with productive cough &sent for investigations; pleural aspiration was done, if feasible &sent for investigations.

RESULTS:

Of 118 adult Iraqi acute leukemia patients admitted to Baghdad teaching hospital ,60% of patients were males&40% were females as shown in table (1). The distribution of subtypes of AML with their relative incidence is shown in table

(2).main respiratory features were shown in table (3), symptoms including cough (whether dry or productive of sputum),dyspnea&chest pain were found in27.7% of patients(cough 24.4% ,dyspnea 2.5%, chest pain 0.8%) .Respiratory signs including crepitations ,decreased air entry&bronchial breathing were found in 12.5% of patients(crepitation 3.3%, decreased air entry in 6.7%, bronchial breathing in 2.5%). .Abnormal chest x -rays were shown in table (4),chest X-ray abnormalities were found in 14.3% of patients ,these include mediastinal widening due to lymphadenopathy in 5.9% of patients .Pleural effusion in 4.2% of patients & parenchymal infiltrates in 4.2% of patients .

DISCUSSION:

The clinical and radiological chest findings of 118 patients with acute leukemia at presentation were studied . In this study, AML was more common than ALL in adult (58.5% versus34.8%), this also stated by many studies ^(12,13).

Respiratory symptoms were found in 27.7% of patients (9.7% of ALL,41.8% of AML) ,in previous study ⁽¹⁴⁾ the respiratory symptoms were reported in 30% of patients. Cough was the commonest symptom which found in 17.7% of patients(7.3% of ALL,26% of AML)with or without other symptoms. Productive cough was found in 6.7% Of patients(11.5% of AML),the colour of sputum range from white to yellow –

green; except one sample which was positive for strept.pneumoniae growth,all other samples were negative for bacteria or AFB.Shortness of breath was found in 2.5% of patients (4.2% of ALL, 2.9% of AML) & always accompanied by abnormal parencymal infiltrate on chest x ray, either focal or diffuse; chest pain increased by cough & respiration was found in one patient (1.4 % of AML), patient subsequently showed pleural effusion on chest x ray. Respiratory signs were found in 12.5% of patients(9.6% of ALL,15% of AML);unilateral or bilateral coarse crepitations were found in 3.3% of patients(2.4% of ALL, 4.3% of AML); decreased air entry was found in 6.7% of patients (4.8% of ALL ,8.7% of AML)either due to effusion or due to consolidation ;bronchial breathing was found in 2.5% of patients(2.4% of ALL ,2.9% of AML)&subsequently CXR showed lobar or patchy consolidations. Abnormal CXR were found in 14.4% of patients (14.6% of ALL ,15.9% of AML)in previous studies^(14,15), abnormal CXR were found in22% of ALL patients&in16% of AML patients respectively . Mediastinal widening due to lymphadenopathy was found in 5.9 of patients (9.7% of ALL ,4.3% of AML); this appear as

widening of mediastinum with smooth lobulated margins. Burns et al (16)reported mediastinal mass in 3% of ALL. The appearances of an anterior mediastinal mass on chest radiographs are

nonspecific, and the differential diagnosis is wide. Differentiation between benign lesions and

malignant lesions may not be possible. Pleural effusion was found in 4.2% of patients(2.4% of ALL, 5.6% of AML),in previous studies^(17,18) pleural effusion was found in 6% &8% of ALL patients; pleural aspirate was feasible in a patient with M3 ,deep venous thrombosis & effusion which was acellular ,haemorhagic&exudative, although there is a case report of pulmonary thromboembolism at the onset of M3, our patient was neither dyspneic nor tachypneic, he died soon afterward. The second patient had parapnumonic

effusion(positive sputum culture); the third patient had both pleural effusion& mediastinal mass; the fourth patient had pleurisy with effusion but she passed soon after admission as did the fifth patient. Parenchymal infiltrates were found in 4.2% of patients(2.4% of ALL, 5.6% of AML),Burns reported parenchyma infiltrates by CXR in 6% of ALL patients at presentation. Two patients had diffuse pattern simulating bronchopneumonia; the third patient had diffuse milliary nodular foci in both lung fields; the fourth patient had homogenous middle lobe opacity with mediastinal mass; the fifth patient had non homogenous opacity of upper&middele zones.Transbronchial lung biopsies are generally considered to be unsafe in patients with decreased platelet count because of bleeding risk⁽¹⁹⁾

 Table 1:The age &sex distribution &main types of acute leukemia
 AUL acute undifferentiated leuk.,AMLL

 acute mixed lineage leuk.

| | ALL | AML | AUL | AMLL |
|----------------------|----------------|----------------|--------------|------------|
| NO. | 41 | 69 | 7 | 1 |
| % | 34.8 | 58.5 | 5.9 | 0.8 |
| M:F ratio NO. | 1.5:1 25/16 | 1.5:1 42/27 | 1:1.3 3/4 | 1:0 1/0 |
| Age range (years) | 13-49 | 11-75 | 18-60 | |
| Mean± SD | 23.2±8.6 | 33.7±16.8 | 36.5±15.6 | 18±0 |

 Table 2: The distribution of subtypes of AML

| | M0 | M1 | M2 | M3 | M4 | M5 | M6 | M7 |
|---------------------|------------|------------|--------------|---------------|--------------|--------------|------------|------------|
| No. | 2 | 9 | 17 | 13 | 15 | 11 | 1 | 1 |
| % | 2.9 | 13.3 | 24.6 | 18.8 | 21.7 | 15.9 | 1.4 | 1.4 |
| M:F ratio No. | 2:0 2/0 | 8:1 8/1 | 1:1.1 8/9 | 3.3:1 10/3 | 1.1:1 8/7 | 1:1.2 5/6 | 0:1 0/1 | 1:0 1/0 |

| feature | AL | ALL | AML | M0 | M1 | M2 | M3 | M4 | M5 | M7 |
|-------------------|--------|-------|--------|-------|--------|--------|--------|--------|-------|-------|
| 1000000 | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) |
| symptoms | 33 | 4 | 29 | | | | | | | |
| | (27.7) | (9.7) | (41.8) | | | | | | | |
| 1-Dry cough | 21 | 3 | 18 | 2 | 5 | 6 | 2 | 2 | 3 | 1 |
| | (17.7) | (7.3) | (26) | (100) | (33.3) | (39.8) | (15.2) | (13.3) | (18) | (100) |
| 2Productive-cough | 8 | | 8 | | 1 | 2 | 1 | 3 | 1 | |
| | (6.7) | | (11.5) | | (11.1) | (11.6) | (7.6) | (19.9) | (9) | |
| 3-Shortness of | 3 | 1 | 2 | | | 1 | 1 | | | |
| breath | (2.5) | (2.4) | (2.9) | | | (5.8) | (7.6) | | | |
| 4-Chest pain | 1 | | 1 | | 1 | | | | | |
| | (0.8) | | (1.4) | | (11.1) | | | | | |
| Signs | 15 | 4 | 11 | | | | | | | |
| | (12.5) | (9.6) | (15) | | | | | | | |
| 1-Crepitation | 4 | 1 | 3 | | | 1 | 1 | 1 | | |
| | (3.3) | (2.4) | (4.3) | | | (5.8) | (7.6) | (96.6) | | |
| 2-Decreased air | 8 | 2 | 6 | | 2 | 1 | 1 | 1 | 1 | |
| entry | (6.7) | (4.8) | (8.7) | | (22.2) | (5.8) | (7.6) | (6.6) | (9) | |
| 3-Bronchial | 3 | 1 | 2 | | | 1 | | 1 | | |
| breathing | (2.5) | (2.4) | (2.9) | | | (5.8) | | (6.6) | | |

Table 3: Respiratory clinical features in acute leukemia patients

Table 4: Abnormal chest radiographic features in acute leukemia patients

| feature | AL | ALL | AML | M1 | M2 | M3 | M4 | M5 |
|-----------------------------|--------|--------|--------|--------|--------|-------|--------|-------|
| | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) | no(%) |
| Mediastinal mass | 7 | 4 | 3 | | | | 1 | 2 |
| | (5.9) | (9.7) | (4.3) | | | | (6.6) | (18) |
| Pleural effusion | 5 | 1 | 4 | 2 | | 1 | 1 | |
| | (4.2) | (2.4) | (5.6) | (22.2) | | (7.6) | (6.6) | |
| Parenchymal infiltrate | 5 | 1 | 4 | | 2 | | 2 | |
| | (4.2) | (2.4) | (5.6) | | (11.7) | | (13.3) | |
| Total no.(%)of abnormal CXR | 17 | 6 | 11 | | | | | |
| | (14.3) | (14.5) | (15.5) | | | | | |

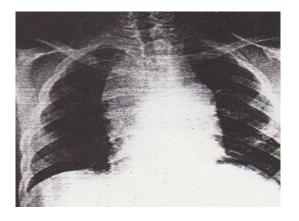


Figure 1: Mediastinal mass due to lymphadenopathy

CONCLUSION:

The clinical&radiological chest findings in patient with AL at presentation were not uncommon. Mediastinal adenopathy was the commonest feature ;pleural effusion&parenchymal infiltrates were less common findings.

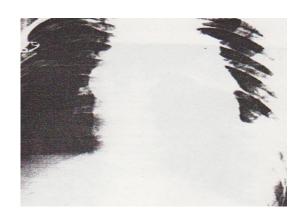


Figure 2: Mediastinal mass with left pleural effusion

REFERENCES:

- Catovsky D,:Acute leukemia In: Hoffbrand V,Lewis M,Tuddenham E(eds.) Postgraduate hematology 4th ed. Black-Well 1999;373.
- Apelbaum F :The acute leukemia In :Goldman L, Ausiello E(eds) Cecil text book of medicine 23th ed. Philadelphia, WB- Saunders 2007;194.
- **3.** moor J, Rosse W : Acute Leukemia. In: Thomas E , Charles C (eds) Cecil Essentials of Medicine 6^{th} ed. Philadelphia, WB Saunders. 2004;444.
- 4. Sptswood S:Acute monoblastic leukemia presenting with pericardial effusion &tamponade. Pediatric radio 1994;24:495.
- Wetzler M ,Bloom F: Acute &chronic myeloid leukemia In : Fauci et al (eds).Harrison's principles of internal medicine ,16th ed . McGraw –Hill 2005:631-41.
- 6. Laura E : Pulmonary Leukemic Infiltrates& High-Resolution CT Findings in 10 Patients. AJR 2000;174:517-21.
- Reid P,Innes A :Secondary tumours of the lung In:Colledge N, Walker B, Ralston S (eds.) Davidsons principle&practice of medicine.21 ed. Churchil- Livingstone 2010;703.
- **8.** Hoelzer D,Arnold R :Charachteristics of outcome &risk factors in adult T lineage ALL.Blood 1999;94:2926.
- **9.** Hoelzer D,Gokbuget N:Adult acute lymphoblasic leukemia In :Hoffbrand V,Catovsky D,Tuddenham E(eds.) Postgraduate hematology 5th ed. Black-Well 2005;527.

- **10.** Englund J:Diagnosis & epidemiology of community acquired respiratory viral infections in the immune-compromised host.Biol Blood Marrow Transplant.2001;7:25-45.
- **11.** Chaoui D : Incidence and prognostic value of respiratory events in acute leukemia. Leukemia 2004; 18:670–675.
- **12.** YAKO A:The clinical&haematological presenting features of acute leukemia in correlation with FAB classification .A thesis submitted to Iraqi Scientific Council of Medicine,1998;27.
- **13.** Armitage J ,Longo D :Malignancy of lymphoid cells in: Fauci et al (eds.)Harrison's principles of internal medicine 16th ed McGraw-Hill 2005;641-52.
- **14.** Ali K:Chest X-rays in leukemic Iraqi patients. .A thesis submitted to Iraqi Scientific Council of Radiology,1998;18.
- **15.** Hamidi C:Mode of clinical presentation&outcome of management of AML.A thesis submitted to Iraqi Scientific Council of Medicine,1991;22.
- **16.** Burns et al:Analysis of presenting features of adult AL.Cancer 1998 ;2460-2469.
- **17.** Dalham Y:Clinical features &treatment of ALL.A thesis submitted to Iraqi Scientific Council of Medicine,1995;29.
- **18.** Armstong A:Progostic factors in childhood ALL.Ir J Med Sci 1990;15912:40-43.
- Steven M:Treatment of infection in immunocompromised host In :Ernest B,Marshall A(eds.) William hematology 6th ed. Mcgraw-Hill 2001; 220.

THE IRAQI POSTGRADUATE MEDICAL JOURNAL