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ACUTE LYMPHOCYTIC LEUKEMIA, CASE REPORT

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Abstract

Patients with acute lymphoblastic leukemia (ALL) may present with fever without any other evidence of infection.

This study aims at the importance of conducting counts blood cells (CBC) for each patient who has continuous fever without evidence of the location of the infection in order to exclude the possibility of acute lymphocytic leukemia.

In these patients, all persistent fever must be assumed to be (ALL) until proven otherwise. As in many cases of blood cancer the diagnosis was delayed because of the unusual clinical presentation. Blood test was normal at present (white blood cells: 5.3, Lymphocyte Auto 0.04%), but the persistent fever followed by weight loss and neutropenia in repeated CBC test (white blood cells: 3.8, Lymphocyte Auto 0.00%) guided the diagnosis of ALL. The blood study and bone marrow confirmed the diagnoses.

This study was conducted on a patient who visited the health center several times with a headache, high temperature, weight loss and symptoms of upper respiratory tract infection, before he was diagnosed with acute lymphocytic leukemia and transferred to the hospital for follow-up treatment.

Keyword: Acute lymphocytic leukemia, Fever, Neutropenia, Bone Marrow Biopsy.

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الملخص :

المرضى الذين يعانون من سرطان الدم الليمفاوي الحاد قد يصابون بالحمى دون أي دليل أخر على مصدر الحرارة ، لذلك عند هؤلاء المرضى يجب اعتبار ارتفاع الحرارة المستمر هو سرطان الدم الليمفاوي الحاد حتى يثبت عكس ذلك . كما هو الحال في الكثير من سرطانات الدم فقد تأخر تشخيص المرض بسبب التظاهرات السرسرية الغير اعتيادية .

تهدف هذه الدراسة الى أهمية اجراء تحليل تعداد كريات الدم عند كل مريض لديه حرارة مستمرة دون وجود دليل على مكان العدوى او الاصابة و ذلك لاستبعاد امكانية وجود سرطان الدم الليمفاوي الحاد .

تمت الدراسة على مريض راجع المركز الصحي عدة مرات بشكوى صداع مع ارتفاع درجة الحرارة و اعراض اصابة الجهاز التنفسي العلوي و نقصان الوزن، قبل أن يتم التأكد بإصابته بسرطان الدم الليمفاوي الحاد و تحويله للمستشفى لمتابعة العلاج.

في البداية لقد كان تحليل الدم طبيعيا، لكن ارتفاع الحرارة المستمر و المصاحب لفقدان الوزن ثم قلة الكريات المتعادلة في التحاليل اللاحقة و المتكررة وجهت لتشخيص سرطان الدم الليمفاوي الحاد ، ثم أثبت التشخيص عن طريق خزعة نقي العظم و الدراسة الشكلية لكريات الدم البيضاء .

الكلمات المفتاحية : سرطان الدم الليمفاوي الحاد، ارتفاع درجة الحرارة،قلة الكريات المتعادلة،خزعة نقي العظم .

1. Introduction

I. Epidemiology and etiology:

Acute lymphocytic leukemia (ALL) is a type of cancer of the blood and bone marrow — characterized by the proliferation and accumulation of lymphoid progenitor cells in the blood, bone marrow, and other tissues.

Leukemia may affect red blood cells, white blood cells, and platelets.

Approximately 60% of cases are diagnosed in patients' ≤20 years old, with a median age at diagnosis of 14 years.

Acute lymphoblastic leukemia represents 20% of adult leukemia (Balletic et al., 2019).

II. Symptoms may include: (Arber et al., 2018)

- Bleeding from the gums, nose.
- Bone pain

- Fever
- Frequent infections
- Lumps (swollen lymph nodes)
- Pale skin
- Weakness, fatigue or a general decrease in energy.

III. Tests and procedures used to diagnose acute lymphocytic leukemia include:

Patients with ALL may present with a variety of hematologic derangements ranging from pancytopenia to hyper leukocytosis. In addition to a history and physical, the initial workup should include: (Gerds and Sekeres, 2020)

- Complete blood count with differential.
- A chemistry panel (including uric acid, creatinine, blood urea nitrogen, potassium, phosphate, calcium, bilirubin, and hepatic transaminases).
- Fibrinogen and tests of coagulation as a screen for disseminated intravascular coagulation.
- A careful screen for evidence of active infection.
- A bone marrow biopsy and aspirate are routinely performed even in T-cell ALL to determine the extent of marrow involvement.
- Imaging tests.

IV. Subtypes of Acute Lymphocytic Leukemia (ALL): (Rochester, 2016)

World Health Organization (WHO) system, divides ALL into several groups:

- B-cell ALL : with certain genetic abnormalities (gene or chromosome changes)
- T-cell ALL: Early T-cell precursor lymphoblastic leukemia
- Mixed lineage acute leukemia: A small number of acute leukemia have both lymphocytic and myeloid features

V. Risk factors: Factors that may increase the risk of acute lymphocytic leukemia include: (Arber et al., 2018)

- Previous cancer treatment.
- Exposure to radiation
- Genetic disorders.

- Having a brother or sister with ALL.

VI. Treatment: (Richard and Larson, 2019; Tim et al., 2017)).

Educate and motivate patient to promote engagement with therapy.

Support: Blood/platelet transfusion, IV fluids,

Infections: These are dangerous, due to neutropenia caused by the disease and

Treatment: give immediate IV antibiotics. (Tim et al., 2017)

In general, treatment for acute lymphocytic leukemia falls into separate phases:

- Induction therapy: to kill most of the leukemia cells
- Consolidation therapy: Aimed at destroying any remaining leukemia in the body.
- Maintenance therapy: Prevents leukemia cells from re-growing. (Richard and Larson, 2019).

Treatment includes: (Richard and Larson, 2019).

- Chemotherapy, which uses drugs to kill cancer cells.
- Targeted therapy. Targeted drugs attack specific abnormalities present in cancer cells (like Philadelphia chromosome)
- Radiation therapy. Radiation therapy uses high-powered beams, such as X-rays or protons, to kill cancer cells.
- Bone marrow transplant. To re-establish healthy bone marrow by replacing leukemic bone marrow with leukemia-free marrow from a healthy person.

VII. Prognostic factors for ALL: (Rochester, 2016)

As leukemia treatment has improved over the years, research has focused on why some people have a better chance for cure than others. Different factors that affect a person's prognosis (outlook) are called prognostic factors.

i. Age: Among adults, younger patients tend to have a better prognosis than older patients.

i. Initial white blood cell (WBC) count: People with a lower WBC count when they are first diagnosed tend to have a better prognosis.

ii. Gene or chromosome abnormalities: Whether the leukemia cells have certain changes in

their genes or chromosomes can affect prognosis. For example, patients tend to have a poorer outcome if the leukemia cells have The Philadelphia.

iii. Response to chemotherapy: Patients who go into a complete remission (no visible leukemia in the bone marrow – see below) within 4 to 5 weeks of starting treatment tend to have a better prognosis than those for whom this takes longer.

iv. Status of ALL during and after treatment

How well leukemia responds to treatment affects the patient's long-term chance for recovery.

Remission

- A remission (complete remission) is usually defined as having no evidence of leukemia after treatment, even when using very sensitive lab tests, such as polymerase chain reaction (PCR).
- Minimal residual disease (MRD) is a term used after treatment when leukemia cells can't be found in the bone marrow using standard lab tests, but they can still be detected with more sensitive tests (such PCR).

Patients with MRD after treatment are more likely to have the leukemia relapse (come back after treatment) and overall have a poorer outlook than those who achieve a complete remission.

2. Case presentation

A 41-year-old Egyptian man consulted for left side frontal headache and mild fever, headache increase when laying forward, medical history of HTN, no family history for blood disorder. Physical exam was normal except frontal and maxillary sinuses tender.

His Peripheral blood film was normal (Figure 1), also Chemistry panel were normal. Patient has been given Augmentin, after sinusitis diagnosed. Patient come back after one week with, cough produced white sputum, mild fever, general fatigue. Chest auscultation: diffuse wheezes, prolonged expiratory phase accompanied with crackles. Chest X-ray show increased Broncho vascular marking (figure 2). Patient treated as bronchitis.

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Lab view	15/11/2018
General Hematology	
WBC	5.3
RBC	H 6.0
Hgb	17.0
Htc	48.6
MCV	L 81.3
MCH	28.4
MCHC	H 35.0
RDW-CV	12.2
Platelet	253
MPV	
Absolute Neutrophil count Auto #(ANC)	9.2
Lymphocyte Auto #	10.5
Monocyte Auto #	2.05
Eosinophil Auto #	2.62
Basophil Auto #	0.41
Neutrophil Auto %	0.21
Lymphocyte Auto %	0.04
Monocyte Auto %	38.4
Eosinophil Auto %	49.2
Basophil Auto %	7.7
Figure 1 : first visit laboratory test ; normal	

Figure 2 : Chest x ray show increased Broncho vascular marking

XR Chest

Chest x-ray PA view

- Normal cardiothoracic ratio, prominent aortic knuckle.
- Slightly increased bronchovascular markings
- No focal lung masses or consolidation
- No mediastinal shift.
- Both costophrenic angles appear clear

XR Chest

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Result type: XR Chest
Result date: 16 11, 2018 16:47 AST

Chest X- Ray report

One-week later patient presented with persistent night fever, sweating, significant lose weight (5 Kg, last month). Urgent CBC test shows low white blood cells (Figure 3),

- Red Cells: mild normochromic normocytic anemia
- Leukocytes: mild leukopenia with marked neutropenia and many circulating blasts (60 %)
- Platelets: mild thrombocytopenia.
- Patient referred to the hospital and admitted as neutropenic fever.
- In the hospital, Bone marrow biopsy: suggestive B-ALL
- Fish test: abnormal hybridization pattern, multiple rearrangements in 60-65 % the cells analyzed.
- Fish BCR-ABL translocation: negative
- Scan whole body FDG PET CT:
- Increase bone marrow uptake compatible with the diagnosis of ALL.
- No lymphadenopathy or hepatosplenomegaly
- Confirmed diagnosis was (B- Lymphoblastic leukemia).

Treatment started with TAZOCIN for septic fever, then shift to UKALL 14 protocol phase I and Phase II.

After 5 months of well-tolerated treatment with UKALL 14 protocol discharge patient and follow up to continue chemotherapy treatment. Lab test at the discharge (Figure 4)

Lab view	19/11/2018
General Hematology	
WBC	L 3.8
RBC	L 3.9
Hgb	L 11.1
Htc	L 32.7
MCV	84.1
MCH	28.5
MCHC	33.9
RDW-CV	H 14.8
Platelet	*L 69
MPV	
Absolute Neutrophil count Auto	10.4
Lymphocyte Auto #	
Monocyte Auto #	*C 0.2
Eosinophil Auto #	1.7
Basophil Auto #	H 1.8
Neutrophil Auto %	0.0
Lymphocyte Auto %	L 0.09
Monocyte Auto %	6.1
Eosinophil Auto %	44.5
Basophil Auto %	46.7
Figure 3 : Second visit Neutropenia	

Lab view	11/04/2019
General Hematology	
WBC	L 3.10
RBC	L 2.7
Hgb	L 9.1
Htc	L 26.6
MCV	98.6
MCH	H 33.6
MCHC	34.0
RDW-CV	H 24,8
Platelet	*L 49
MPV	
Absolute Neutrophil count Auto #(ANC)	L 7.2
Lymphocyte Auto #	
Monocyte Auto #	L 1.1
Eosinophil Auto #	1.7
Basophil Auto #	0.2
Neutrophil Auto %	0.0
Lymphocyte Auto %	L 0.00
Monocyte Auto %	35.3
Eosinophil Auto %	56.5
Basophil Auto %	6.9

Figure 4: Laboratory test at the discharge

3. Differential diagnosis (Richard and Larson, 2019).

The presenting signs and symptoms of ALL/LBL are often nonspecific and morphology alone is not diagnostic, so it is important to consider a wide range of malignant and nonmalignant conditions in the differential diagnosis.

A. Malignant disorder

- Burkitt lymphoma
- Other acute leukemia: Acute myeloid leukemia (AML), Acute undifferentiated leukemia (AUL), Mixed phenotype acute leukemia (MPAL)
- Chronic myeloid leukemia (CML)
- Aplastic anemia
- Small round blue cell tumors

B. Nonmalignant disorder

- Immune thrombocytopenia (ITP)
- All Infectious disease

4. Discussion

In our patient, as in many cases of blood cancer the diagnosis was delayed because of the unusual clinical presentation. Blood test was normal at present, but the persistent fever followed by weight loss and neutropenia in repeated CBC test guided the diagnosis of ALL. The blood study and bone marrow were fixed the diagnoses.

5. Conclusion

This case confirms that Acute lymphocytic leukemia may presented as symptoms of bronchitis, any case of persistent fever must have CBC test to ruled out ALL diagnosis.

There are a set of challenges and difficulties that we faced in this study, which were that the fever continued for more than two weeks despite antibiotic treatment in addition to weight loss without any explanation for that. Also, laboratory analyzes did not guide us to the diagnosis until two weeks after the beginning of the disease.

The most important question that we did not find an explanation for, why was the blood analysis normal and suddenly the blood changes started to appear clearly.

6. Abbreviation

ALL: Acute lymphocytic leukemia

AML: Acute myeloid leukemia

AULL: Acute undifferentiated leukemia

CBC: Peripheral blood film

CML: Chronic myeloid leukemia

CT: Computed tomography

ITP: Immune thrombocytopenia

MRD: Minimal residual disease

MPAL: Mixed phenotype acute leukemia

PCR: polymerase chain reaction

WBC: white blood cell

7. Clinical trials

Clinical trials are experiments to test new cancer treatments and new ways of using existing treatments. While clinical trials give chance to try the latest cancer treatment, treatment benefits and risks may be uncertain (Richard and Larson, 2019).

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