



## Subleukemic Leukemia with Pancytopenia – A Case Study

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### ABSTRACT

Subleukemic leukemia involves abnormal white blood cells in the blood while the overall white blood cell count remains within normal levels. Common symptoms include fever, fatigue, bleeding tendencies, and bone pain, with fever and fatigue being the most common initial signs. Leukemia, a disease affecting blood cell formation, exhibits different manifestations based on where cell growth is disrupted. Current treatment strategies for acute leukemia focus on immediate support, infection prevention, and elimination. Chemotherapy is frequently used to reduce abnormal blood cell counts or encourage the growth of healthy cells. Pancytopenia is not a standalone condition but refers to the simultaneous presence of anemia, leukopenia, and thrombocytopenia, resulting from various disease origins. Examining bone marrow through aspiration and biopsy is crucial for identifying the root cause.

**KEYWORDS:** Subleukemic leukemia, leukemia, chemotherapy, pancytopenia.

### INTRODUCTION

Subleukemic leukemia is identified by the existence of unusual or abnormal white blood cells in the bloodstream, with the overall white blood cell count falling within the normal range. Factors that increase the chances of developing this uncommon form of leukemia encompass exposure to ionizing radiation, certain medications such as chloramphenicol, nitrogen mustard, and genetic conditions like Down syndrome, Fanconi Anemia, Ataxia Telangiectasia, Bloom Syndrome, and Li-Fraumeni Syndrome. Subleukemic leukemia is identified by a normal total white blood cell count in the blood but with a few abnormal or unusual cells seen in a blood smear. Common clinical signs include fever, overall fatigue, bleeding tendencies, and bone pain. Fever and fatigue stood out as the most common initial symptoms. Pale skin and enlarged liver and spleen were frequently noticed during physical examinations. Some individuals also displayed swollen lymph nodes<sup>1</sup>.

Leukemia, a form of cancer impacting blood cell formation, manifests distinct conditions depending on the specific stage where cell growth stops. This classification includes myeloproliferative disorders, affecting diverse blood cell types, and lymphoproliferative disorders, originating from lymphoid cells like T and B lymphocytes, along with plasma cells<sup>2</sup>. Subleukemic leukemia is identified when the overall count of white blood cells in the bloodstream is either normal or low, yet there are enough abnormal cells present to confirm the diagnosis of leukemia. Acute leukemias typically have a brief clinical duration and are distinguished by the prevalence of mostly immature cells in the blood or bone marrow<sup>2</sup>.

The treatment plan for mild leukemia involves a 21-day cytosine arabinoside regimen. It's recommended to combine it with corticosteroids to prevent side effects like depression, fatigue, and loss of appetite caused by cytarabine. Immediate supportive care using medications is crucial to halt and avoid infections. Chemotherapy is often employed to decrease abnormal blood cells and encourage the development of healthy cell lines<sup>1</sup>.

Current treatment strategies for individuals with acute leukemia involve swift initiation of supportive care and interventions targeting infection prevention and eradication. Chemotherapy is commonly introduced to reduce abnormal blood cell counts or encourage the growth of healthy cell populations. Advanced therapies might eventually involve the utilization of colony-stimulating factors (CSF) that regulate the development and maturation of blood-forming cells, such as granulocytes and monocyte macrophages. Laboratory studies demonstrate that exposing immature myeloid leukemic cells to granulocyte CSF prompts the maturation of blast cell clusters. Once these cells undergo differentiation, their continued growth is hindered as the differentiated cells lose their ability to multiply<sup>2</sup>.

### CASE PRESENTATION

A 63-year-old female patient was admitted in the hospital with the complaints of fever with chills, hemoptysis, cold, breathlessness and loose stools for past on day. The patient had a past medical history of type 2 diabetes mellitus and hypertension was diagnosed three months back along with acute leukemia one month back. On examination the patient was conscious, oriented and febrile. On admission the vital signs showed an increase in temperature

(102.2°F), blood pressure (150/70 mmHg), Pulse rate (144 beats/min), and respiratory rate (32 breaths/min). Patient was under treatment with anti-hypertensives and oral hypoglycemic agents.

Peripheral smear study showed red blood cells with mild anisocytosis, poikilocytosis and normocytic normochromic cells with few microcytes, target cells and occasional tear drop cells and many nucleated RBCs seen. Leukocytes were markedly reduced, Differential count showed Neutrophils (10%), Lymphocytes (15%). No immature cells were seen in smear. Platelet count was markedly reduced. Impression showed the patient was having pancytopenia. CT-chest plain report shows a patchy ground glass opacities noted in superior basal segment of upper lobe of right lung. Urine culture and sensitivity test showed a commensal growth in culture and blood culture report shows that the culture was sterile after 48 hours of aerobic incubation. Complete blood count report shows a decrease in red blood cell count (2.76 million/cmm), hemoglobin (7.2g/dl), packed cell volume (22.4%), mean cell volume (79cu. microns), mean cell hemoglobin (26pg), potassium (3mmol/l) and platelet count (0.18 lakh/cmm).

550ml of whole human blood transfusion was done on day 1, day 2, day 3, day 4 and day 11th. The patient was given with IV antibiotics, IV antifibrinolytics, IV colony stimulating agents, oral anti-hypertensives, oral hypoglycemic agents, IV corticosteroids was given for first two days. And nebulizers were given to the patient along with electrolyte supplement. During the time patient had complaints of fever, bleeding gums, cough with expectoration, hemoptysis and hematuria. After sixteen days of treatment patient was discharged with beta lactam antibiotics, antifibrinolytics, anti-hypertensives and insulin and was advised to review after seven days.

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## DISCUSSION

A case study involving a horse was conducted, detailing both myeloproliferative and lymphoproliferative types of the illness. The report outlines a horse affected by subleukemic acute myelomonocytic leukemia, where a secondary systemic fungal infection was linked to the leukemia, indicating a significant weakening of the immune system. Additionally, during examination after death, intravascular accumulation of white blood cells was a prominent discovery in all tissues studied. Treating leukemia in horses is rarely attempted due to high costs, the absence of established treatment guidelines, and a poor prognosis for complete recovery.

Efforts to treat myelomonocytic leukemia in horses involved a 21-day cytosine arabinoside regimen, which did not influence the disease's progression. While cytarabine is commonly used in non-lymphoid leukemias in humans due to its differentiation abilities at lower doses, its application in horses, alongside corticosteroids, aims to alleviate potential side effects like depression, fatigue, and reduced appetite. In the case discussed, treatment was considered due to the horse's overall good health upon presentation. The objective was to reduce the number of abnormal cells in circulation and bone marrow.

However, despite starting low-dose cytarabine therapy alongside oral prednisolone, the horse only survived the initial day of treatment. Future approaches for treating leukemia in horses might encompass bone marrow transplants or the use of CSF to facilitate the maturation of normal cells. Understanding the disease process and persistent efforts towards treatment are crucial for advancing the management of leukemia in horses and other species<sup>2</sup>.

Pancytopenia isn't a distinct disease but rather a set of findings indicating the simultaneous presence of anemia, leukopenia, and thrombocytopenia, stemming from various disease processes. The assessment of bone marrow through aspiration and biopsy is crucial for determining the underlying cause. This condition can arise due to the bone marrow's reaction against destructive agents or the replacement of normal bone marrow elements by abnormal or malignant tissues. In numerous cases, it's due to the unexplained suppression of the bone marrow's usual production and differentiation of apparently normal blood-forming elements. Several mechanisms underlie these conditions, such as ineffective blood cell production with marrow cell death, the formation of faulty cells rapidly removed from circulation, antibody-mediated sequestration and destruction of cells, and the entrapment of normal cells in an overactive reticuloendothelial system.

Examining peripheral blood smears provides valuable information on the cause, like identifying macro ovalocytes and hypersegmented neutrophils in megaloblastic anemia, occasional blast cells in subleukemic leukemia, absence of abnormal or immature cells in aplastic anemia, leucoerythroblastic features in myelofibrosis, pelgeroid neutrophils in myelodysplastic syndrome (MDS), and nucleated red blood cells with abnormal cells in metastatic malignancies. Accurate diagnosis greatly improves when a comprehensive clinical history, physical examination, complete blood counts, and evaluation of peripheral smears are combined. Confirmatory diagnosis often requires a bone marrow study (aspiration/biopsy).

Collaboration between the hematopathologist and the treating clinician before an invasive procedure like bone marrow aspiration or biopsy is crucial for the overall management of these patients. Such discussions guide further actions, aiding in identifying the root cause of pancytopenia and directing targeted investigations and therapy. This approach saves time, avoids unnecessary tests, reduces hospital stays, and facilitates prompt treatment<sup>3</sup>.

Hematopoietic neoplasms causing pancytopenia often include acute leukemias as a common category. The clinical presentation varies, typically reflecting the patient's underlying pancytopenia caused by the replacement of bone marrow by lymphoblasts. Common symptoms upon presentation include fatigue, easy bruising, susceptibility to infections, enlarged lymph nodes, liver, and spleen, as well as bone pain. Peripheral blood examinations frequently reveal B-lymphoblasts, with leukocyte counts ranging from decreased to normal or significantly increased. Diagnosis is usually confirmed through bone marrow analysis, revealing sheets of B lymphoblasts. Additional characterization is aided by flow cytometry, cytogenetic studies, and bone marrow aspirate and biopsy findings. In a study, 0.9% of cases were identified as subleukemic leukemia, primarily differentiated based on the patient's profile<sup>4</sup>.

A research investigated 104 cases of pancytopenia, examining aspects such as age, gender-based occurrence, initial symptoms, peripheral blood analysis, bone marrow aspiration findings, and the various causes behind pancytopenia. These observations were compared with existing literature. The study

found a 3.85% occurrence of subleukemic leukemia, contrasting with the 5% reported by Khunger JM et al. Kumar R et al. indicated a 12% prevalence of aleukemic leukemia. Pancytopenia emerged as a common characteristic in this research, aligning with similar findings reported by Kumar R et al. and Khunger JM et al<sup>5</sup>.

Another study analysed all instances of pancytopenia observed in two hematology centers over a span of six years. Patients undergoing myelotoxic chemotherapy or displaying leukemic cells in peripheral smears were not included. The study encompassed a total of 166 cases, where the primary causes identified were: aplastic anemia in 49 cases, megaloblastic anemia in 37 cases, aleukemic leukemia or lymphoma in 30 cases, and hypersplenism in 19 cases<sup>6</sup>.

A study focusing on granulocytic sarcoma in the parotid gland of a child with acute myeloid leukemia (AML) found that the progression of myeloid sarcoma carries a similar prognosis to the underlying leukemia. Specifically, individuals with AML linked to genetic abnormality and concurrent myeloid sarcoma tend to achieve complete remission at a low rate, resulting in poor overall survival. For patients with chronic myeloproliferative disorders (CMPD) and myelodysplastic disorders (MDS), myeloid sarcoma often signifies a blastic transformation that is frequently associated with a short lifespan<sup>7</sup>.

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