

A 5-year-old boy is brought to the emergency department for increasing fatigue. He was well until 2 weeks ago when he had an upper respiratory infection from which he has not recovered. He has had poor appetite and lost 1 kg (2.2 lb) over the last 3 weeks. His past medical history is unremarkable. His temperature is 39.4° C (103° F), blood pressure is 100/70 mm Hg, pulse is 134/min, and respirations are 18/min. Height and weight are at the 80th percentile. The oropharynx is clear. His conjunctivae and skin are pale, and petechiae are present on the extremities. Rubbery, nontender lymph nodes are palpable in the cervical, axillary, and inguinal regions. Lungs are clear to auscultation. Hepatosplenomegaly is present. Laboratory results are as follows:

Hemoglobin	7.8 g/dL
Hematocrit	24%
Platelets	30,000/ μ L
Leukocytes	34,000/ μ L
Lymphocytes	65%
Atypical lymphocytes	6%
Lymphoblasts	26%

Chest x-ray shows a widened mediastinum. Which of the following is the best method of confirming the diagnosis?

- ☐ A. Bone marrow biopsy
- ☐ B. Computed tomography scan of the chest
- ☐ C. Lymph node biopsy
- ☐ D. Magnetic resonance imaging of the abdomen
- ☐ E. Peripheral blood smear
- ☐ F. Serology for Epstein-Barr virus
- ☐ G. Serum uric acid

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Explanation:

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Acute Lymphoblastic Leukemia	
Epidemiology	<ul style="list-style-type: none">• Most common childhood cancer• Peak age: 2-5 years• Male > female
Clinical features	<ul style="list-style-type: none">• Nonspecific systemic symptoms• Bone pain• Lymphadenopathy• Hepatosplenomegaly• Pallor (from anemia)• Petechiae (from thrombocytopenia)
Diagnosis	<ul style="list-style-type: none">• Bone marrow biopsy with >25% lymphoblasts
Treatment	<ul style="list-style-type: none">• Multi-drug chemotherapy

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Based on clinical presentation and cancer epidemiology, this patient most likely has acute lymphoblastic leukemia (ALL). ALL is the **most common cancer in children**. The peak incidence occurs at **age 2-5 years**. Boys are at increased risk of developing ALL. Patients with Down syndrome are also at increased risk. On physical examination, pallor and petechiae may be present due to bone marrow infiltration resulting in anemia and thrombocytopenia, respectively. Half of patients with ALL may have leukocytes <10,000/ μ L but >20% have leukocytes >50,000/ μ L. Lymphadenopathy and hepatosplenomegaly can result from extramedullary leukemic spread. The chest x-ray finding in this patient suggests lymphadenopathy in the mediastinum. **Bone marrow biopsy** is required to confirm the type of leukemia. The presence of >25% lymphoblasts is diagnostic of ALL.

(Choices B and D) Imaging is performed when there is concern for metastatic spread beyond the blood and bone marrow. However, biopsy is the only method of determining the underlying malignancy.

(Choice C) Because leukemia can be diagnosed by evaluation of the blood and bone

and thrombocytopenia, respectively. Half of patients with ALL may have leukocytes $<10,000/\mu\text{L}$ but $>20\%$ have leukocytes $>50,000/\mu\text{L}$. Lymphadenopathy and hepatosplenomegaly can result from extramedullary leukemic spread. The chest x-ray finding in this patient suggests lymphadenopathy in the mediastinum. **Bone marrow biopsy** is required to confirm the type of leukemia. The presence of $>25\%$ lymphoblasts is diagnostic of ALL.

(Choices B and D) Imaging is performed when there is concern for metastatic spread beyond the blood and bone marrow. However, biopsy is the only method of determining the underlying malignancy.

(Choice C) Because leukemia can be diagnosed by evaluation of the blood and bone marrow, lymph node biopsy is usually unnecessary. If lymphoma is suspected or bone marrow biopsy is equivocal for leukemia, lymph node biopsy should be performed.

(Choice E) Peripheral blood smear is an excellent, quick, and noninvasive initial step to assess cytopenias. Abnormal findings, such as blasts on peripheral smear, may support the diagnosis of leukemia, but bone marrow biopsy is still required for confirmation.

(Choice F) Fever, hepatosplenomegaly, and atypical lymphocytosis can be seen in infectious mononucleosis caused by Epstein-Barr virus (EBV). Hemolytic anemia and thrombocytopenia can also be seen in EBV infection. However, the lymphadenopathy associated with nonmalignant illnesses is typically mobile and tender. Also, atypical lymphocytosis is nonspecific and can be seen in many conditions. The absence of pharyngitis and the presence of significant leukocytosis with lymphoblasts suggest leukemia rather than EBV infection.

(Choice G) Tumor lysis syndrome is an oncologic emergency that results from tumor cell breakdown and the release of dangerous amounts of potassium, phosphate, and uric acid into the circulation. This can occur spontaneously in patients with massive lymphoma or leukemia burden or more commonly after initiation of chemotherapy. Measurement of electrolytes is extremely important but does not identify the underlying malignancy.

Educational objective:

Acute lymphoblastic leukemia is the most common leukemia in children. The presence of $>25\%$ lymphoblasts on bone marrow biopsy confirms the diagnosis.

References:

1. [Acute lymphoblastic leukaemia.](#)