Diffuse Pulmonary Alveolar Hemorrhage in Acute Promyelocytic Leukemia

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A 60-year-old male with acute promyelocytic leukemia demonstrated bilateral diffuse airspace consolidation on chest X-ray. An autopsy on the next day revealed pure pulmonary alveolar hemorrhage without leukemic infiltration or inflammation. Disseminated intravascular coagulation was confirmed microscopically. In severe hemorrhagic diathesis and leukopenia, it is impossible to distinguish pulmonary hemorrhage from pneumonia by X-ray alone. Broncoalveolar lavage may be the only possible diagnostic approach.

Key words: acute promyelocytic leukemia, disseminated intravascular coagulation, pulmonary hemorrhage

Case Report

A 60-year-old man was admitted to the hospital with dizziness and tarry stool of a half day's duration. He had no cough or sputa. On admission, his blood pressure was 72/54 mmHg, temperature 38.1°C and respiratory rate 30/min. Chest auscultation revealed no rales. Heart sound was normal. Remarkable purpura was noticed on his extremities and trunk.

Laboratory tests were as follows: WBC 1,100/μl with 40% promyelocytes, 2% myelocytes, 4% metamyelocytes, 6% band-form neutrophils, 34% segment cells, 14% lymphocytes, RBC 252 × 10^6/μl, hematocrit 25.1%, hemoglobin 8.2 g/dl, platelet 22,000/μl, LDH 480 IU/l, erythrocyte sedimentation rate 20 mm/h, fibrinogen 239 mg/dl, and antithrombin III 64%. Initial arterial blood gas levels were: pH 7.335, PaCO₂ 23.3 mmHg, and PaO₂ 64.5 mmHg. Bone marrow aspiration specimen showed 86.5% atypical promyelocytes with a total cell count of 256,500/μl. The diagnosis was acute promyelocytic leukemia [French, American, and British (FAB) classification: M3].

Hypotension was treated with blood products and dopamine. Chemotherapy with daunomycin, cytosine arabinoside, vincristine and prednisolone was carried out on the second day. Heparin infusion and platelet transfusions were used with these drugs. Cimetidine was administered for gastrointestinal bleeding. Fever persisted despite intravenous cefoxitin and fosfomycin. Chest roentgenogram on the third hospital day demonstrated bilateral infiltrate (Fig. 1). The patient died on...
the fourth day in the hospital. An autopsy revealed massive bilateral pulmonary alveolar hemorrhage without leukemic infiltration or inflammation (Fig. 2). Disseminated intravascular coagulation (DIC) was confirmed microscopically. Subarachnoidal hemorrhage in the brain proved fatal.

Discussion

Acute promyelocytic leukemia (APL) is characterized by frequent massive hemorrhage. The bleeding tendency is ascribed to DIC. The bleeding sites include skin, gingiva, cerebrum, upper gastrointestinal tract, urinary tract and thorax (1). In spite of aggressive chemotherapy and control of DIC, fatal hemorrhage is the most common cause of early deaths. More than forty percent of early death patients die of cerebral hemorrhage (2). The factors associated with increased incidence of early fatal hemorrhage are aging, fever, and low hemoglobin, platelet and fibrinogen levels, and also elevated WBC, absolute blast plus promyelocyte counts, and elevated LDH levels (3).

Leukemic involvement of organs other than bone marrow is not constant. Frequent sites are liver, spleen and lymph nodes (4). Pulmonary parenchyma is not a common site of infiltration. Leukopenia is present in 59 percent of APL patients (1), and fever, often without documented infection, is reported in 50–80 percent of patients at the diagnosis (5). We could not find any inflammatory lesions in the lung. A chest roentgenogram (Fig. 1) on the day preceding autopsy revealed diffuse air-space consolidation on both lungs except for the left lower field. Poor margined lesions and airbronchogram represent air-space diseases, therefore pure leukemic infiltrate was thought to be less likely in differential diagnosis. In severe hemorrhagic diathesis and leukopenia, it is impossible to distinguish pulmonary hemorrhage from pneumonia by X-ray alone. And one most consider a marrow suppressive effect of anti-neoplastic agents. In these situations, open lung biopsy is contraindicated. We did not perform a bronchoscopic study because of the critical state of the patient; however, bronchoalveolar lavage may be the only possible diagnostic approach (6).

References