

Malignant Pleural Effusion in Acute Myeloid Leukemia with Hepatitis B Virus Infection

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ABSTRAK

Efusi pleura dapat merupakan presentasi pertama dari keganasan hematologi. Di antara gangguan yang paling umum adalah limfoma hodgkin dan limfoma non-hodgkin, dengan frekuensi 20 sampai 30%, terutama jika terdapat keterlibatan mediastinum. Leukemia akut dan kronis jarang disertai dengan keterlibatan pleura. Kami melaporkan wanita 46 tahun dengan sesak nafas yang progresif. Pemeriksaan fisik ditemukan dengan efusi pleura kiri masif. Hitung darah lengkap menunjukkan anemia, trombositopenia, dan hitung leukosit normal. Tes serologi virus menunjukkan HBsAg dan antiHBc total positif. Foto torak menunjukkan efusi pleura kiri. Pemeriksaan sitologi cairan pleura didapatkan mieloblast. Aspirasi sumsum tulang, biopsi sumsum tulang dan analisis flowcytometry sesuai dengan leukemia myeloid akut tanpa maturasi (AML M0- klasifikasi FAB).

Kata kunci: leukemia myeloid akut, efusi pleura, infeksi.

ABSTRACT

Pleural effusions can be the first presentation of a hematologic malignancy. The most common disorders with pleural effusion are Hodgkin and non-Hodgkin lymphoma with a frequency of 20 to 30%, especially if mediastinal involvement. Acute and chronic leukemia are rarely accompanied by pleural involvement. We describe a 46-year-old female with history of progressive dyspnoea. Physical examination was revealed massive left pleural effusion. Complete blood count revealed anemia, trombositopenia and normal leucocyte count. Viral serology test shown positive of HBsAg and total antiHBc. Chest X-ray revealed left pleural effusion. Pleural fluid cytology was myeloblast consistent with acute myeloid leukemia (AML). Bone marrow aspiration smear, bone marrow biopsy smear, and flow cytometry analysis were consistent with acute myeloid leukemia without maturation (AML M0-FAB classification).

Key words: Acute myeloid leukemia, pleural effusion, infection.

INTRODUCTION

Nearly all hematologic malignancies can present with pleural effusions. The most common disorders with plural effusin are Hodgkin and non-Hodgkin lymphomas, with a frequency of 20 to 30%, especially if there

is mediastinal involvement. Acute and chronic leukemias, myelodysplastic syndromes, are rarely accompanied by pleural involvement. Furthermore, 10 to 30% of patients receiving bone marrow transplantation develop pleural effusions. In cases of hematologic pleural

effusions, should be carefully sought the drug toxicity, underlying infectious, secondary malignant or rarely autoimmune causes. In most cases, the pleural fluid responds to treatment for the primary disease and if there are clinical worsening may necessitate pleurodesis.^{1,2}

CASE ILLUSTRATION

A 46-year-old female was admitted to hospital with history of progressive dyspnea for two weeks. The onset of these symptoms were insidious, gradually progressive. There was history of fever, cough, weakness and loss of appetite. Previously patient was hospitalized at district hospital for 3 days.

Physical examination of patient revealed tachypnoea and tachycardia. The conjunctival palpebrae were pale. There were echimosis on the hand, enlarged of right inguinal lymph nodes. There were no sternal tenderness and gum hypertrophy. Chest examination showed severe left side pleural effusion.

Complete blood count revealed haemoglobin: 6,60 g/dL, leukocyte : 4300/mm³, platelets : 10.000/mm³, hematocrit : 21,5%. The differential count were eosinophils 0% / basophils 0% / band neutrophils 0% / segmented neutrophils 41% / lymphocytes 43% / Monocytes 2%. Peripheral blood smear were erythroblast, myelocyte and atypical mononuclear cells.

The biochemical analysis were glucose 149 mg/dL, urea 23 mg/dl, creatinine 0,88 mg/dl, lactate dehydrogenase 221 U/L, uric acid 4,20 mg/dL, total protein 6,9 gr/dL, albumin 2,8 gr/dL, AST 48 U/L. The viral serology were HBsAg positive, total anti HBc positive. The prothrombine time (PPT) were 14,5" (control 13") and activated partial thromboplastin time (aPTT) was 31,4" (control 29,3").

The anteroposterior and lateral chest X-ray were consistent with severe left side pleural effusion. Abdomen ultrasonography showed no hepatosplenomegaly.

Bone marrow aspiration revealed 30% myeloblasts, no maturation (M0-FAB classification) (**Figure 1**). Bone marrow biopsy revealed >50% myeloblasts (**Figure 2**). Pleural fluid cytology contained myeloblast. (**Figure 3**). Flow cytometry analysis was consistent

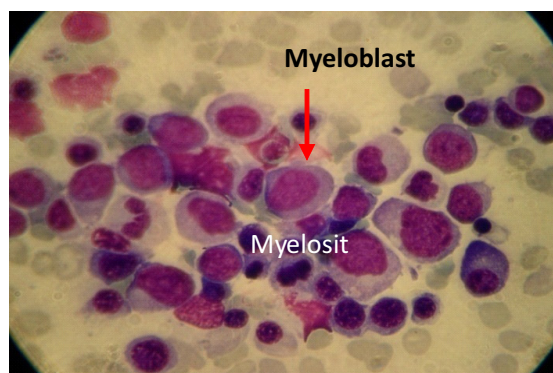


Figure 1. Bone marrow aspiration smear demonstrating myeloblast (HE, 400x)

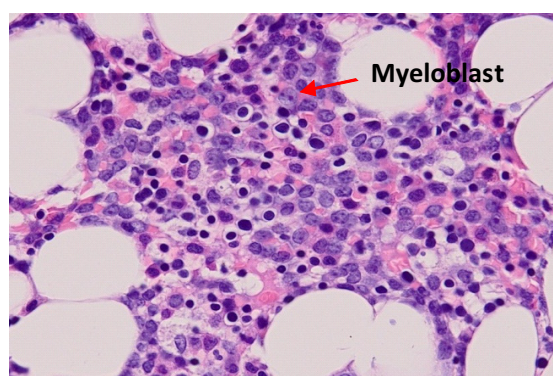


Figure 2. Bone marrow biopsy smear demonstrating myeloblast (HE, 400x)

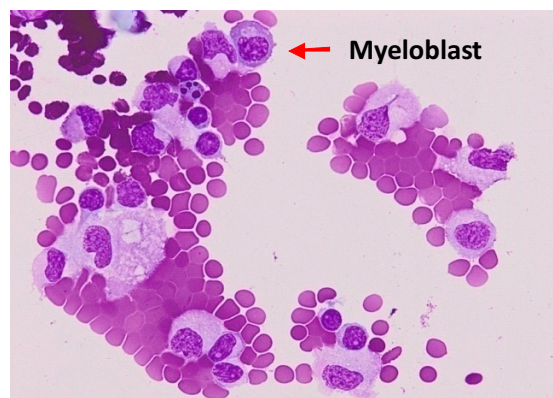


Figure 3. Pleural fluid cytology showing myeloblast (cystopin, 400x)

with acute myeloid leukemia (positive of CD34, cyMPO and CD7). Pleural fluid culture showed *Staphylococcus aureus* (MSSA/Methicillin-sensitive *Staphylococcus aureus*).

The patient underwent therapeutic thoracentesis (1000 mL) with platelet transfusions prophylaxis. Packed red cell (PRC) transfusion

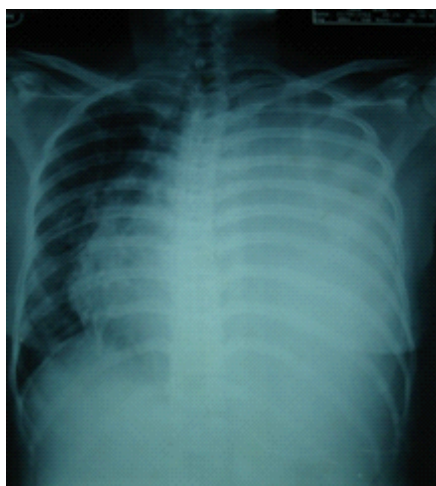


Figure 4. Anteroposterior chest X-ray showed masive left sided pleural effusion



Figure 5. Anteroposterior chest X-ray four weeks after therapy showed reduction of pleural effusion

was given after bone marrow aspiration and biopsy procedure. Broad spectrum antibiotic (ceftriaxone 2 gr iv daily) was given for community acquired pneumonia.

After four weeks therapy with thoracentesis and ceftriaxon, there were clinical improvement. The anteroposterior and lateral of chest X-ray showed reduction of pleural pleural effusion (**Figure 4, Figure 5**).

She was planned treatment with 3+7 AML protocol (100 mg/m² cytarabin for 7 days and 45 mg/m² daunorubicin for 3 days). Prophylactic antiviral therapy using lamivudine 100 mg p.o qd for reduction of hepatitis B virus reactivation following cytotoxic chemotherapy. She refused chemotherapy because of economical reason and dischrge home with supportive care.

DISCUSSION

The manifestation of pleural effusion can be as a hematological malignancy or complication. The possible pathogenesis are extramedullary proliferation of occult leukemic clone or a subclinical marrow relapse to extramedullary sites.¹ The other causes of pleural effusion were infections,disseminated of solid tumor, or complications of treatment.²

The most common disorders are Hodgkin and non-Hodgkin lymphomas, with a frequency of 20 to 30%, especially mediastinal involvement. Acute and chronic leukemias are rarely

accompanied by pleural involvement.¹ Acute myeloid leukemia with pleural effusion is a very rare condition.²⁻⁵

The pleural infiltration of acute leukemias is rarely diagnosed during life, it is a common finding at autopsy. The presence of leukemic infiltrates in other tissues in patients with acute leukemias were found at autopsy in 10 of 15 patients who died of an unrelated cause, during complete bone marrow remission.¹ Besides direct infiltration of leukemic cells in the pleura, pleural effusion can be secondarily caused by drug toxicity, underlying infections, secondary malignant or rarely autoimmune causes in hematologic malignancies.⁶

The presence of a pleural effusion in a patient with a hematologic malignancy always presents a diagnostic challenge. The effusion is very small and thoracentesis is typically considered. If fever is present, thoracentesis is usually performed to exclude infection and parapneumonic effusion or empyema. Performing a thoracentesis has a high risk for some patients with hematologic malignancies because of coagulation abnormalities and multiple medical comorbidities. The main indication of thoracentesis was to detect an infection, relieve dyspnea and cancer restaging.^{7,8}

The pleural effusion in patients with acute leukemia usually disappears after induction chemotherapy. However, recurrence of pleural

exudates is almost inevitable if patients do not achieve remission; they may present with respiratory failure due to massive fluid accumulation. In this circumstance, treatment or palliation of pleural disease by intrapleural chemotherapy or chemical sclerosis is impeded.¹

Reactivation of HBV replication with increase in serum HBV DNA and ALT levels has been reported in 20% to 50% of hepatitis B carriers undergoing immunosuppressive or cancer chemotherapy. In most instances, the hepatitis flares are asymptomatic, but icteric flares, and even hepatic decompensation and death have been observed. Clinical studies including two controlled trials showed that prophylactic therapy with lamivudine can reduce the rate of HBV reactivation.^{9,10}

HBsAg and antiHBc testing should be performed in persons who have high risk of HBV infection, prior to initiation of chemotherapy. Prophylactic antiviral therapy should be administered to hepatitis B carriers (regardless of baseline serum HBV DNA levels) before and during chemotherapy, and maintenance treatment for 6 months.¹⁰⁻¹²

CONCLUSION

Pleural effusion can be a presentation of hematology malignancy or a complication. Pleural fluid should analysis for culture and cytology in suspected patient with hematology malignancy.

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