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CASE PRESENTATION OF 55-YEAR-OLD MAN WITH ACUTE MYELOID LEUKEMIA AND COVID 19

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ABSTRACT

Background: Acute myeloid leukemia (AML) is a malignancy from hematopoietic cells, characterized by clonal proliferation of abnormal blast cells in the bone marrow and failure of average cell production. Coronavirus disease-19 (COVID-19) is a respiratory infectious disease caused by the SARS-CoV-2 virus. COVID-19 infection in AML patients will affect laboratory examinations to support the diagnosis of COVID-19 and the patient's prognosis. **Case presentation:** A 55-year- old man went to the hospital for chemotherapy and was diagnosed of acute myelomonocytic leukemia. He noted gingival bleeding. The results of the routine haematological examination showed pancytopenia and the patient requires blood transfusion before chemotherapy. On the third day of treatment, he was experiencing fever, continued with cough and shortness of breath. Physical examination showed pulse rate 100x/minutes, respiratory rate 26x/minutes, temperature 39.8˚C, crackles of the lungs. RT-PCR examination from the nasopharyngeal swab showed a positive SARS-CoV-2. During the treatment, the laboratory tests showed pancytopenia, increased of D-Dimer, C-reactive protein, ferritin and procalcitonin. After the 42nd day of treatment, the patient had clinical improvement, and the fifth evaluation swab showed a negative RT-PCR result. **Conclusion:** AML patients have a higher risk of infection, especially COVID-19 infection. Correct laboratory examinations and treatment will promote a better prognosis. It is necessary to educate leukemic patients to always take precautions against infection, especially the prevention of COVID-19.
Keyword : *AML COVID-19, SARS-CoV-2*

BACKGROUND

Acute myeloid leukemia (AML) also known as acute myelogenous leukemia is a hematologic malignant disease characterized by abnormal differentiation and proliferation of systemic hematopoietic stem cells and malignant transformation causing suppression and replacement of marrow components of normal bone. This disease can cause pancytopenia condition and characterized by clonal expansion of blast cells in the peripheral blood, and bone marrow, so that resulting in ineffective erythropoiesis and bone marrow failure [1]. Symptoms and signs of AML often occur are anemia, thrombocytopenia, skin infections, anorexia, and weight loss. Fever may occur early in the disease with mild splenomegaly. The diagnosis is based on WHO criteria if blast/myeloblast cells are found in the bone marrow more than 20% [2].

Leukemia is the most common malignant disorder, ranked as the fifteenth most cancer diagnosis and eleventh in mortality. Prevalence in developing countries is higher than in developed countries, and more common in males. In United States the incidence of leukemia in men and women in 2018 is 6.1 and 4.3 per 100,000 population[3].

Acute myelomonocytic leukemia, also was known as AML M4 is acute leukemia that describe by the proliferation of both neutrophil and monocyte precursors[4]. This leukemia can affect all age groups, often in the elderly. Acute myelomonocytic leukemia patients are accompanied by anemia, fatigue, thrombopenia, and leukocytosis. Patients with myelomonocytic leukemia usually have gingival hyperplasia with gingival bleeding. Muramidase (lysozyme) are usually elevated in serum and urine because of the monocytic proliferation. The leukocyte count is usually increased with predominant of monocytic cells. Immunological studies show positivity with CD13, CD33, CD11b, and CD14[5].

In December 2019, there was pneumonia cases in Wuhan, China, of unknown cause with clinical presentations of viral pneumonia. The disease was named coronavirus disease 2019 (COVID-19) caused by new type of coronavirus namely Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-Cov-2)[6,7]. Symptoms of COVID-19 infection can be in mild, moderate, severe or critical symptoms. The main clinical symptoms are fever (temperature 38˚C), and

respiratory symptoms like cough or sore throat, and difficulty breathing. In addition, patients with COVID-19 can feel fatigue, myalgia, gastrointestinal symptoms such as diarrhea. Some of the patients develop shortness of breath within one week. In severe cases, patient can worsen progressively, they can have acute respiratory distress syndrome (ARDS), septic shock, and bleeding or coagulation dysfunction within a few days. In some patients, symptoms appear mild, not even accompanied by fever[8,9].

The main routine laboratory tests for COVID-19 patients include complete blood count (CBC), coagulation and fibrinolysis cascades (PT, PPTK, and D-dimers), and inflammation marker like ESR, CRP, ferritin, and procalcitonin. In AML patient the laboratory test finding may interfere with the diagnosis of COVID-19[10].

CASE PRESENTATION

A 55-year-old man came Dr. Kariadi Hospital Semarang on 5th January2021 for chemotherapy. Three months before hospital admission the patient was diagnosed with acute myelomonocytic leukemia. The patient came with complaints of gingival bleeding. On the third day of chemotherapy, the patient had a fever. The chemotherapy was then postponed. The patient had blood transfusions and improved general condition. However, on the tenth day, the patient had a cough, shortness of breath, weak and the nutritional intake was reduced.

General condition was weak, heart rate 100 x/minute, respiratory rate 26x/minute, and temperature 39,8^{o}C. Anemic palpebral conjunctiva. There were no retractions and no enlarged lymph nodes in thorax examination. The basic sound of breathing was vesicular, with crackles and no wheezing. The examination of the extremities appeared pale and cyanotic and warm. Acute myelomonocytic leukemia was established through bone marrow aspiration (fig.1) and immunophenotyping (fig.2). The results of bone marrow showed: mild hypercellular, decreased erythropoiesis and granulopoiesis activity with a myeloid: erythroid ratio of 0.68: 1 and an increase in monocytic activity of 43% with 27% of monoblast, concordance with acute myelomonocytic leukemia. Cytochemical staining with Sudan Black B showed disperse granulation. The results of immunophenotyping of bone marrow found cell populations in the blast area expressing CD33 (+) DIM, CD34 (+) DIM, HLA-DR (+), CD36 (+) DIM, and CD13 (+). (fig. 2)

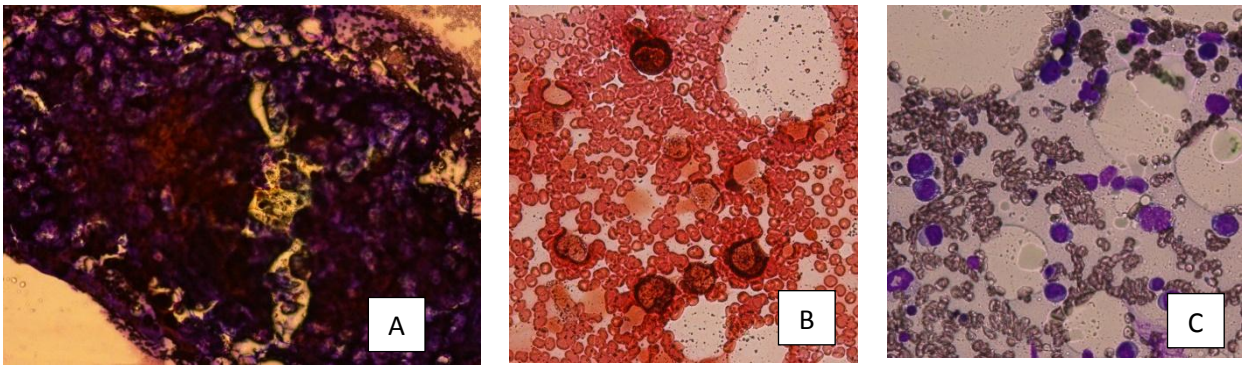

Fig.1 Bone marrow aspiration. A. mild hypercellular of bone marrow fragment. B. disperse granulation of Sudan Black B. C. Distribution of bone marrow aspirated cells with May Grunwald Giemsa staining

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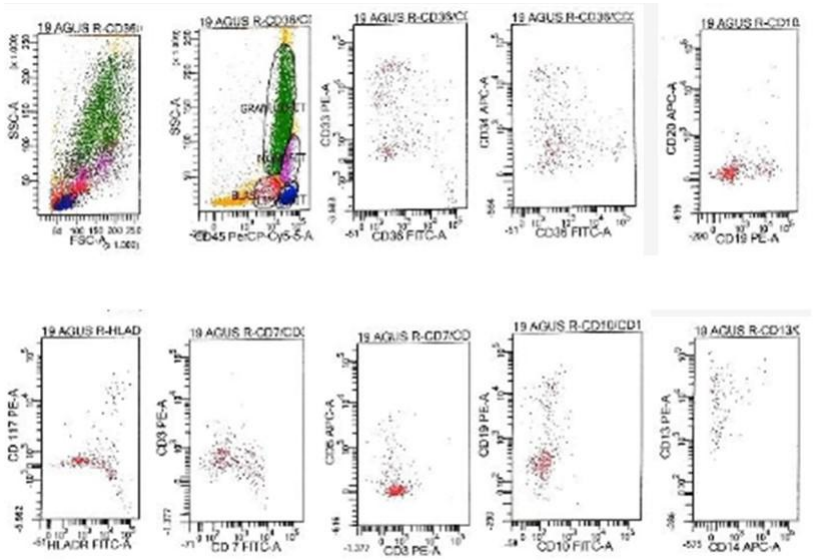

Fig.2 The result of immunophenotyping from bone marrow aspirate

Table 1. Laboratory data for the patient

Test	15/1	18/1	20/1	25/1	28/1	31/1	4/2	7/2	9/2	15/2
Hb gr/dL (13.2-17.3)	8.6	8.4	9	10.6	9.2	10.7	10.8	9.3	8.5	10.4
HCT % (32-62)	23.9	23.1	25.6	31	27.3	32.2	31.4	25.6	28	29.4
RBC 10^6 cell/µL (4.4-5.9)	2.53	2.45	2.80	3.55	3.08	3.57	3.63	3.05	2.75	3.56
MCH pg (27-32)	34	34.3	32.1	29.9	29.9	30	29.8	30.5	30.9	29.2
MCV fl (76-96)	94.5	94.3	91.4	87.3	88.6	90.2	86.5	83.9	82.2	82.6
MCHC g/dL (29-36)	36	36.4	35.2	34.2	33.7	33.2	34.4	36.3	37.6	35.4
WBC 10^3 cell/µL (3.8-10.6)	0.4	0.5	0.6	0.5	1.2	3.4	5.7	2.7	3.2	1.4
Eosinophil % (1-3)	0		0							
Basophil % (0-1)	0		0							
Neutrophil band % (2-5)	0		0							
Neutrophil segment % (50-70)	15		15							
Lymphocyte % (20-40)	33		25							
Monocyte % (1-6)	11		1							
NLR	0.45		0.6							
Platelets 10^3 cell/µL (150-400)	37	25	38	47	36	54	47	64	116	75
INR					1.32					
PTT second (11.0-14.5)		20.0		16.0	13.5	14.7			14.7	
PTTK second (24.0-36.0)		36.6		32.3	39.4	33.8			58.4	
D-Dimer ng/mL (<500)		10420		7050	4270	3960			1120	
Fibrinogen mg/dL (200-400)		336		240	232	302			346. 8	
CRP mg/dL (0-0.3)		10.57								
Procalcitonin ng/mL (<0.5)				5.47						
Ferritin ng/dL (30-350)		8989								
RT PCR	+			+		+		+		-

Reverse transcription PCR of nasopharyngeal swab was positive on 15th January, and the patient was moved to the isolation ward. The results of RT-PCR were still positive until day 42. D-dimer, C-reactive protein, and ferritin increased in day three after positive RT-PCR. Procalcitonin increased on day 5. Blood gas analysis on found oxygen saturation 91% with NRM, pH 7.493, pCO2 26.9, and HCO3 20.2 concluded respiratory alkalosis. Laboratory tests found pancytopenia, increase of PT, PPTK, D-Dimer, CRP, AST, ALT, and procalcitonin (Table 1). After 42 days of treatment, he was allowed to discharge from the hospital for outpatient treatment.

DISCUSSION

Our patient with underlying leukemia was pancytopenia at the time of presentation. This finding was consistent with a study from Iran, that showed acute myeloid leukemia could manifest as pancytopenia, especially in adults[11]. Acute myelomonocytic leukemia accounts for 5-10% of AML cases. It occurs in all age groups, but is more common in older individuals, and the median patient age is 50 years. Patients typically present with anemia, thrombocytopenia, fever, and fatigue[4].

From bone marrow aspiration, we found an increase in monocytic activity of 43% with 27% of monoblast. This was in concordance with acute myelomonocytic leukemia by WHO criteria, that characterized by an increased proportion of leukemia monocytic cells in the bone marrow less than 80% of total non-erythroid cells. The characteristic of monoblasts are large cells with abundant cytoplasm with moderate to intensely basophilic and may show pseudopod formation. The monoblasts usually have spherical nuclei with finely lacy chromatin and one or more large prominent nucleoli. The peripheral blood usually shows an increase in monocytes, which are often more mature cells than those in the bone marrow. Therefore, the monocytic component may be more apparent in the peripheral blood than in the bone marrow[4].

Immunophenotyping of bone marrow in our patient found expressing CD33 (+) DIM, CD34 (+) DIM, HLA-DR (+), CD36 (+) DIM and CD13 (+). This is in concordance with acute myelomonocytic leukemia, which generally shows several populations of blasts that are variably expressing the myeloid antigens CD13, CD33, CD65, and CD15[4].

This patient suddenly had a fever on the third day. From blood smear, we found that the absolute neutrophil count was low, and fever was usually present in acute myelomonocytic leukemia. Febrile neutropenia is a complication in leukemic patients caused by low of neutrophil and they have greater risk of infection. In the COVID-19 pandemic, patients with a hematologic disorder like acute myeloid leukemia had a higher risk of getting infection of SARS-Cov-2. The symptom like fever can be distinguished with COVID-19 symptoms. In several days after getting a fever, the patients had a cough, shortness of breath, weak and the nutritional intake was reduced, and then the result of RT-PCR had positive SARS-Cov-2 infection. He et al, (2020) found in 128 hospitalized patients with hematological cancers, 13 (10%) of whom developed COVID-19. Most of them (39%) had acute myeloid leukemia (AML), acute lymphoblastic leukemia/ALL (20%), non-Hodgkin lymphoma/ NHL (14%), plasma cell myeloma/PCM (14.8%) and myelodysplastic syndrome/MDS (6.3%)[12].

According to research by Mardani et al, laboratory parameters that can support the diagnosis of COVID-19 are neutrophil count, WBC count, CRP, LDH, AST, ALT, albumin, and urea. Patient with positive RT-PCR had a significantly higher neutrophil count, lower WBC count, higher CRP, higher AST and ALT, lower albumin, and higher urea[13]. In our case, the patient came for a chemotherapy session and the hematological parameters found pancytopenia with neutropenia. After positive RT-PCR SARS Cov-2, there were no significant change in hematological parameters, but we found that increase of some laboratory parameters like CRP, D-dimer, and procalcitonin. The presence of inflammation in our patient was indicated by elevated levels of C-reactive protein (CRP). The increase in CRP at the onset of the disease is related to the lung parenchymal lesions and disease severity[14]. Sharifpour et al, reported higher CRP levels in patients with a poor prognosis[15].

In several cases have been reported by Ghandili et al (2020) found that four patients of 12 patients (33%) were asymptomatic at COVID-19 diagnosis, but all patients became symptomatic after several days. Ten patients (83%) were admitted to the intensive care unit (ICU). Eleven patients (92%) developed pneumonia[16]. In our case, the patients develop a fever after several days of chemotherapy treatment, which is the most common symptom in COVID-19 patients. The other clinical presentations are fatigue, dry cough, dyspnea.

Tabriz et al, report one case misinterpretation of hematologic presentation of COVID-19 as acute myeloid leukemia in a 39-year-old woman. The patient had persistent leukopenia with suspicious immature and blastoid cells. Like most viruses that can influence hematopoiesis and the immune system, SARS Cov-2 may enhance release of immature blood cells from bone marrow by inflammatory mechanisms[17]. Clinical feature of AML can overlap with COVID-19. Patient with AML had signs ineffective of erythropoiesis and bone marrow failure, including anorexia and bleeding. Patient can also have recurrent infections. Disseminated intravascular coagulation is also common in patient with AML. In our patient there were increase of PT, PTTK and D-dimer. Unlike the healthy population, patients with immunocompromised are at higher risk of fatal infections, like patients with AML. Acute myeloid leukemia infected with COVID-19 had a challenge in diagnosis and treatment. Similarity in symptoms can confuse the diagnosis[18].

A survey from hematologists in Brazil. 60.6% of AML patients, COVID-19 was diagnosed when the patient had active AML, while in 39.3% AML was in remission. The diagnosis was done because patients had symptomatic of COVID-19, but one patient diagnosis was done when investigation for febrile neutropenia. There were 54.4% deaths attributed to COVID-19 and they did not identify any other factor associated with death. From this survey more than 50% of patients who survived COVID-19 had a delay in their treatment like in our patient[19].

CONCLUSION

A 55-year-old man came Dr. Kariadi Hospital Semarang on January 2021 and will do the second chemotherapy for acute myelomonocytic leukemia. The patient came with complaints of gingival bleeding. Because of his condition, he must have a transfusion before chemotherapy. However, during therapy, the patient is infected with COVID-19. Acute myeloid leukemia infected with COVID-19 had a challenge in diagnosis and treatment. Laboratory parameters for supporting the diagnosis COVID-19 patients can affect the condition of AML, like complete blood count and coagulation cannot be used as a support for the diagnosis of COVID-19 in AML patients compared with healthy people.

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