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Clinical Significance of D-dimer,SF and LDH Levels in Patients with Acute Leukemic

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Abstract: Objective: This study aimed to investigate the clinical significance of plasma D-dimer,serum ferritin (SF) and lactate dehydrogenase(LDH) levels to determine the useful laboratory markers for diagnosing acute leukemia. Methods: We compared laboratory data such as D-dimer,SF and LDH levels in AML non-APL, APL and ALL group with that in normal control group, and we also compared D-dimer,SF and LDH levels among AL patients before the first cycle of chemotherapy (newly diagnosed group), complete remission after chemotherapy (CR group), and relapse after complete remission in 1 year (recurrent group).Results: 1.The D-dimer,SF and LDH levels in AML non APL group, APL group and ALL group are significantly higher than that in normal control group($P<0.05$). LDH and SF levels in AML non-APL group, APLgroup and ALL group were compared, the difference was no statistical significance($P>0.05$). D-dimer level in APL group was significantly higher than that in AML non-APL group and ALL group($P<0.05$).2. D-dimer, LDH and SF levels in CR group were significantly lower than that in newly diagnosed group and recurrent group ($P <0.05$). There was no statistical differences between recurrent group and newly diagnosed group, and there was no statistical differences between normal control group and CR group in D-dimer, LDH and SF levels ($P>0.05$).Conclusion: Detection of plasma D-dimer is particularly valuable in clinical diagnosis of APL. D-dimer, LDH and SF can be used as indicators in diagnosis and curative effect evaluation and prognosis judge for patients with AL.

Keywords: Acute leukemia; D-dimer; Serum ferritin; Lactate dehydrogenase

1. Introduction

At present, the incidence of acute leukemia (AL) ranks among the top 10 in malignant tumors. With the popularization of the diagnostic criteria of MICM (morphology , immunology , cytogenetics and molecular biology) proposed by WHO, the clinical diagnosis, curative effect evaluation and judgment of prognosis in AL have achieved significant progress. however, the morphological and cytochemical staining features of bone marrow (BM) aspiration are still the basic means in AL diagnosis. Due to the high cost of diagnostic tests, some patients choose simple morphological examination of BM on account of their family's financial status. Thus, It is difficult to accurate diagnosis for some patients whose features of morphology and cytochemical staining are atypical. Therefore, the clinical diagnosis, curative effect evaluation and judgment of prognosis in AL were affected. There are some studies on useful laboratory markers for the diagnosis, curative effect evaluation and prognostic prediction of malignant tumors. However, useful laboratory markers for the diagnosis of AML remain unknown. Investigating the effect of AL on laboratory data may be helpful for the diagnosis of AL in clinical practice. In this article we observed the D–dimer plasma, ferritin (SF) and lactate dehydrogenase (LDH) serum levels in patients with acute leukemia (AL). The aim of this study was to investigate the clinical significance of D-dimer, SF, and LDH detection in diagnosis and curative effect evaluation and prognosis judge for patients with AL.

2. Patients and Methods

2.1. Patients

We analyzed data from 96 AL patients between 2015 and 2017 at the Affiliated Hospital of Engineering University of Hebei and Affiliated Zhongshan Hospital of Dalian University. These patients exhibited different types of AL. All patients were diagnosed with the criteria based

on the 2008 WHO classification,1 and they had no previous history of liver, kidney and heart diseases, diabetes, and other malignancies. There were 56 males and 40 females, with a median age of 39. (range 8-79). 52 of the AL patients were acute myleoid leukemia non- acute promyelocytic leukemia, (group of AML non-APL), 31 males and 21 females, with a median age of 41.0 (range 14-79); 15 of the AL patients were APL (APL group), 9 males and 6 females, with a median age of 37.0 (range 20-73); 29 of the AL patients were acute lymphoblastic leukemia, (ALL group), 16 males and 13 females, with a median age of 35.0 (range 8-75). 85 cases of AL patients treated with chemotherapy achieved complete remission (CR group), 35 Patients with AL induced by chemotherapeutic agents relapsed in 1 year after CR (recurrent group). In the same period, 60 healthy subjects were treated as the control group, 35 males and 25 females, with a median age of 39.0 (range 18-70). There was no statistically significant differences with respect to age and gender between groups, and data between the groups were comparable.

2.2. Collection of data

We analyzed laboratory data at the first diagnosis, which included D–dimer, ferritin (SF) and lactate dehydrogenase (LDH) levels. D-dimer was detected by immunoturbidimetry using the Sysmex CA7000 automatic blood coagulation analyzer ,with a reference range of 0-0.55μg/ml. LDH was determined by the enzyme reaction rate method using Hitachi 7180 automatic biochemical analyzer, with a reference range of 15-220 U/L. SF was detected by electrochemiluminescence assay using Siemens XP automatic chemiluminescence analyzer, with a reference range of 21-274 ng/ml. The d-dimer, LDH and SF levels of the AL patients (AML non-APL, APL and ALL group) were compared with the control group before the first cycle of chemotherapy, and we also compared the d-dimer, LDH and SF levels among AL patients before the first cycle of chemotherapy(newly diagnosed group), complete remission after chemotherapy(CR group), relapse after complete remission in a year(recurrent group).

2.3. Statistical analysis

The SPSS16.0 software package was used for the statistical tests. The difference of measurement data was compared with t test and one-way ANOVA and LSD were used for evaluating the relationship among the groups.

3. Results

3.1. D-dimer,SF and LDH levels were compared among AML non-APL, APL ,ALL and control group.

The D-dimer, SF and LDH levels in AML non-APL group, APL group and ALL group were significantly higher than that in normal control group(P<0.05). LDH and SF levels in AML non-APL group, APLgroup and ALL group were compared, the difference was no statistical significance(P>0.05). D-dimer level in APL group was significantly higher than AML non-APL group and ALL group(P<0.05). (Table 1)

Table 1. Comparison of the laboratory markers among AML non-APL, APL, ALL and control groups $(\bar{x}\pm s)$

group	n	D-dimer（μg/ml)	SF（ng/ml）	LDH（U/L）
non-APL AML	52	10.81±3.78*	484.95±23.89*	496.37±195.06*
APL	15	16.24±3.56*#Δ	502.29±39.96*	512.59±209.31*
ALL	29	9.64±5.96*	497.56±37.64*	507.20±199.28*
control	60	0.25±0.11	99.27±40.12	125.15±76.27

Note: compared with control group, *P<0.05; Compared with AML non-APL group, # P<0.05; Compared with ALL groups, Δ P < 0.05

3.2. D-dimer,SF and LDH levels were compared among newly diagnosed group, CR group, recurrent group and control group.

D-dimer, LDH and SF levels in CR group were significantly lower than that in newly diagnosed group and recurrent group (P <0.05). There was no statistical differences between recurrent group and newly diagnosed group, and there was no statistical differences between control group and CR group in D-dimer, LDH and SF levels (P>0.05). (Table 2)

Table 2. Comparison of the laboratory markers among newly diagnosed, recurrent, CR and control groups $(\bar{x}\pm s)$

group	n	D-dimer（μg/ml)	SF（ng/ml）	LDH（U/L）
newly diagnosed group	96	11.62±4.98*#	491.47±31.25*#	502.17±201.31*#
recurrent group	35	10.69±5.21*	495.71±36.14*	510.21±226.37*
CR group	85	0.28±0.22Δ	102.32±48.36Δ	132.78±79.65Δ
Control group	60	0.25±0.11	99.27±40.12	125.15±76.27

Note: compared with CR group, *P<0.05; Compared with the recurrence group, #P>0.05; Compared with control group, Δ P > 0.05

4. Discussion

AL is a kind of hematopoietic malignancies characterized by a marked expansion of hematopoietic stem cells, with infection, anemia and hemorrhage as the main clinical manifestations. In recent years, there is a trend toward a greater incidence of AL in China. The occurrence and development of AL is a complex process with multiple factors, which is closely related to immune dysfunction.2 AL poses a serious threat to the nation's public health in China. However, the treatment is still difficult. According to the diagnostic criteria proposed by WHO, diagnosis of AL requires the combination of morphology, immunology, cytogenetics, molecular biology, and clinical symptoms and signs. Multi-means combined application is of great significance in diagnosis and curative effect evaluation and prognosis judge for patients with AL.3

In this study, we investigated laboratory data such as D-dimer, LDH and SF and determined the useful laboratory markers for AL diagnosis.

D-dimer is a specific product of cross-linked fibrin degradation, which is an important and direct indicator of the activation of coagulation and fibrinolytic system. D-Dimer is a prothrombotic biomarker and Determination of D-dimer is a sensitive method for endogenous fibrinolysis. Thus, it is used to screen for deep vein thrombosis and diagnose early diffuse intravascular coagulation (DIC), and It is also used for the detection of thrombogenic diseases such as acute myocardial infarction and cerebral thrombosis; D-dimer is also an ideal test index to observe the therapeutic effect of thrombolysis.4-5 Leukemia cells in AL patients release a large number of strong coagulant which can activate the exogenous coagulation system. the change of the blood coagulation function enhance the tumor cell activity. Thus, it make the tumor cell proliferate, infiltrate and metastasize easily in local area. This study found that D-dimer level in M3 group is significantly higher than that in AML non-APL group and ALL group(P<0.05). The reason may be that in APL, abnormal promyelocytes release more coagulant than other leukemia cells, Moreover, the proportion of abnormal promyelocytes in bone marrow and peripheral blood is always higher than that of leukemia cells in other types. Thus, more coagulants are released, resulting in more serious hyperfibrinolysis. Detection of plasma D-dimer is particularly valuable in clinical diagnosis of APL.6-10

Lactate dehydrogenase (LDH) is a glycolytic enzyme, which is abundant in red blood cells, and mainly in myocardium, skeletal muscle and kidney of human. Elevated LDH levels have frequently been observed in animal and human malignancies. in addition, there appears to be a strong correlation between disease activity and tumor mass. Disorder of cell metabolism in tumor and pathological conditions result in injury of cell, which lead to release of a large number of LDH into the blood; regulated disorders by leukemia gene, metabolism of leukemic cell becomes hyperactive. Thus, excessive synthesis and release of LDH result in increasing levels of serum LDH. The level of serum LDH can reflect the invasive degree of tumor cells and be correlated with disease progression and prognosis in AL patients. The frequent performance of LDH levels can indicate the trends in disease development.11-12

There is the highest concentration of SF in mononuclear macrophages in the bone marrow and spleen, which is one of the main forms of iron storage. The level of SF has diagnostic value for iron deficiency anemia.13-14 The malignant proliferation of leukemia cells in AL patients leads to the increase in ferritin synthesis; The destruction of blood cells result in the release of ferritin into the blood, and excessive ferritin cannot be eliminated in time. Thus, SF increases.15-17

This study found The D-dimer, SF and LDH levels in AML non-APL group, APL group and ALL group are significantly higher than that in normal control group(P<0.05). LDH and SF levels in AML non-APL group, APLgroup and ALL group were compared, the difference was no statistical significance(P>0.05). D-dimer level in M3 group is significantly higher than that in AML non-APL group and ALL group(P<0.05); D-dimer, LDH and SF levels in CR group were significantly lower than that in newly diagnosed group and recurrent group (P <0.05). There was no statistical differences between recurrent group and newly diagnosed group, and there was no statistical differences between normal control group and CR group in D-dimer, LDH and SF levels (P>0.05).

To sum up, Detection of plasma D-dimer is particularly valuable in clinical diagnosis of APL. D-dimer, LDH and SF can be used as indicators in diagnosis and curative effect evaluation and prognosis judge for patients with AL.

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