RESEARCH ARTICLE

Elevated Serum Ferritin Levels in Patients with Hematologic Malignancies

Xue-Zhong Zhang*, Ai-Ling Su, Ming-Qiu Hu, Xiu-Qun Zhang, Yan-Li Xu

Abstract

Purpose: To retrospectively analyze variability and clinical significance of serum ferritin levels in Chinese patients with hematologic malignancies. Materials and Methods: Serum ferritin were measured by radioimmunoassay, using a kit produced by the Beijing Institute of Atomic Energy. Patients with hematologic malignancies, and treated in the Department of Hematology in Nanjing First Hospital and fulfilled study criteria were recruited. Results: Of 473 patients with hematologic malignancies, 262 patients were diagnosed with acute leukemia, 131 with lymphoma and 80 with multiple myeloma. Serum ferritin levels of newly diagnosed and recurrent patients were significantly higher than those entering complete remission stage or in the control group (p<0.001). Conclusions: Serum ferritin lever in patients with hematologic malignancies at early stage and recurrent stage are significantly increased, so that detection and surveillance of changes of serum ferritin could be helpful in assessing conditions and prognosis of this patient cohort.

Keywords: Hematologic malignancies - serum ferritin

Asian Pac J Cancer Prev, **15 (15)**, 6099-6101

Introduction

Iron is one of the necessary elements in human vital activities, which is involved in the expression of multiple cyclins and apoptosis-related genes, playing an important role in the process of growth and differentiation of tumor cells. The lack of iron may lead to various physiological dysfunction, whereas the overdose of may also do harm to human body at the same time, and even add risks to tumorigenesis (Dreyfus, 2008). Iron chelator could affect iron content extra-and intracellular. This activity is associated with anti-proliferation, cytotoxic effect, and inducing cell apoptosis that has attracted more attention from researchers. To evaluate the value of iron chelator in clinical practice of hematologic malignancies, it is necessary to analyze serum ferritin levels of patients with hematologic malignancies, providing clinical evidence for using iron-deprivation to treat hematological tumor.

We retrospectively analyzed serum ferritin level in patients with hematologic malignancies under the help of RIA center of our hospital between January 1st, 1998 to January 1st, 2014.The results were reported as follows.

Materials and Methods

Clinical Data

The 473 patients with hematologic malignancies were all recruited from inpatients of our hospital between January 1st, 1998 to January 1st, 2004, including patients untreated, with complete re-mission or with recurrence. Among them, 262 patients were diagnosed with acute leukemic, 131 patients with malignant lymphomas, 80 patients with multiple myeloma. Two hundred ninety were male, and 251 female; age: 14-91 years, median age: 44±28 years. Less than six unit of erythrocyte suspension were injected to patients. In remission group, only testing results from patients whose remission period longer than three months were adopted. The control group contains healthy people from the Medical Examination Center of our hospital.

Testing method: The content of serum ferritin were measured with radioimmunoassay, using the serum ferritin radioimmunological analysis kit produced by Beijing institute of atomic energy, procedure of manipulation and quality control following the introduction of kits.

Statistical analysis: testing results were expressed by mean±standard deviation, and t examination was used to test comparison between groups.

Results

The variation of serum ferritin in patients with acute leukemic

In Table 2, level of serum ferritin of patients with acute leukemia in newly diagnosed group and recurrent group were significantly higher than those in the remission group, difference between groups was statistically significant (p<0.001); but not between patients newly diagnosed and recurrent (p>0.05). Patients in remission group had higher ferritin level than that in control group, but not with statistically significant difference (p>0.05).

*Department of Hematology, Nanjing First Hospital, Nanjing Medical University, Nanjing, China *For correspondence: xuezhongzhang19681968@126.com*

Table 1. Number of Patients with Hematologic Malignancies

Group	AL			ML			MM		
	Newly diagnosed	Remission	Recurrence	Newly	Remission	Recurrence	Newly diagnosed	Remission	Recurrence diagnosed
Patients	86	108	68	54	40	37	32	18	30

*Abbreviations: AL= acute leukemia, ML= malignant lymphomas, MM= multiple myeloma

Table 2. Comparison of Serum Ferritin Among Patients with Acute Leukemia (x±s)

Group	Number of patients	Serum ferritin (ug/L)
Newly diagnosed	86	782.9±268.8
Remission	108	234.3±146.6
Recurrent	68	812.5±245.2
Control group	50	102.3± 57.6

Table 3. Comparison of Serum Ferritin Among Patients with Malignant Lymphomas (x±s)

Group	Number of patients	Serum ferritin (ug/L)
Newlydiagnosed	54	622.7±297.8
Remission	40	242.9±169.3
Recurrent	37	681.4±248.1
Control group	50	102.3± 57.6

The variation of serum ferritin in patients with malignant lymphomas.

In Table 3, level of serum ferritin of patients with malignant lymphomas in newly diagnosed patients and recurrent patients were significantly higher than those in the remission group, difference between groups was statistically significant ($p<0.05$); but not between newly diagnosed and recurrent patients ($p>0.05$). Level of ferritin in remission group was higher than that in control group, but there was no statistically significant difference ($p>0.05$).

The variation of serum ferritin in patients with multiple myeloma

In Table 4, level of serum ferritin of patients with multiple myeloma in newly diagnosed and recurrent patients were significantly higher than those in the remission group, difference between groups was statistically significant ($p<0.05$); but not between newly diagnosed and recurrent group ($p>0.05$). Level of ferritin in remission group was higher than that in control group, but there was no statistically significant difference ($p>0.05$).

A comparison of the level of serum ferritin among newly diagnosed patients with hematologic malignancies.

In Table 5, level of serum ferritin of patients with newly diagnosed hematologic malignancies was significantly higher than that in control group ($p<0.01$). Level of serum ferritin for patients with acute leukemia was slightly higher than that of patients with malignant lymphomas and multiple myeloma, but there was no statistically significant difference ($p>0.05$).

Discussion

Hematologic malignancies are a common disease in Asian Pacific areas (Feng et al., 2013; Jiang et al., 2013; Karami et al., 2013; Khodabandehloo et al., 2013; Kooshyar et al., 2013; Li et al., 2013; Liu et al., 2013; Ozbas-Gerceker et al., 2013; Qin et al., 2013; Shan et al., 2013). As our present study confirmed, the level of serum ferritin of patients with hematologic malignancies was significantly increased. In many hospital, serum ferritin is routinely monitored as a tumor marker. The goal of this retrospective study is to provide clinical evidence for measuring serum ferritin to guide the treatment and even helpful to develop a new way for the treatment of hematologic malignancies. In this field, iron chelator has been demonstrated to affect the iron content intra-or extracellular, and could be applied to the treatment of iron overload disease (Fukushima et al., 2011). It was reported that a Japanese patient with acute refractory leukemia who received multiple blood transfusions, was given appropriate symptomatic therapy with iron chelator, the patient unexpectedly achieved complete remission (Fukushima et al., 2011). Thus, in recent years, researchers focus on effects of iron chelator, eg., anti-proliferation, cytotoxic effect, and inducing cell apoptosis, and suppose that iron-deprivation could control the proliferation of various tumor cells and induce apoptosis.

Table 4. Comparison of Serum Ferritin Among Patients with Multiple Myeloma (x±s)

Group	Number of patients	Serum ferritin (ug/L)
Newly diagnosed	32	697.2±278.6
Remission	18	233.7±179.4
Recurrent	30	712.5±317.3
Control group	50	102.3± 57.6

Table 5. Comparison of Serum Ferritin Among Patients with Newly Diagnosed Patients with Hematologic Malignancies (x±s)

Diagnosis	Number of patients	Serum ferritin (ug/L)
AL	86	782.9± 268.8
ML	54	622.7± 297.8
MM	32	697.2±278.6
Control group	50	102.3± 57.6

In this study, the level of serum ferritin in untreated patient group and remission group were significantly higher than that of control group. The level of serum ferritin in patients who achieved complete remission after chemotherapy decreased significantly, but slightly higher than that of normal control. The reason may be attributed to the fact that few residual tumor cells exists when complete remission was achieved, indicating a positive correlation between serum ferritin and tumor burden. Experiment suggested that iron overload may boost the growth of leukemia cell, inhibit apoptosis (Chen et al., 2005). Acute leukemia is one of the malignant cloning disease of hemopoietic stem cell, the significantly increased level of serum ferritin among patients newly

diagnosed, or on remission stage, or refractory to treatment may indicate that leukemia cell could affect iron matebolism. It is hypothesized that down-regulation of serum ferritin could be associated with the growth of leukemia cell. Our research suggested that the level of serum ferritin of patients with malignant lymphomas and multiple myeloma significantly increased, but lower than that of the patients with acute leukemia, the reason is still not clear.

In conclusion, serum ferritin lever in patients with hematologic malignancies at early stage and recurrent stage are significantly increased, the detection and surveillance of changes of serum ferritin could be helpful for assessing conditions and prognosis of this patient cohort.

References

Chen CC, Yang CF, Yang MH, et al (2005). Pretreatment prognostic factors and treatment outcome in elderly patients with de novo acute myeloid leukemia. *Ann Oncol*, **16**, 1366-73.

Dreyfus F (2008). The deleterious effects of iron overload in patients with myelodysplastic syndromes. *Blood Rev*, **22**, 29-34.

Feng DQ, Huang B, Li J, et al (2013). Selective miRNA expression profile in chronic myeloid leukemia K562 cell-derived exosomes. *Asian Pac J Cancer Prev*, **14**, 7501-8.

Fukushima T, Kawabata H, Nakamura T, et al (2011). Iron chelation therapy with deferasirox induced complete remission in a patient with chemotherapy-resistant acute monocytic leukemia. *Anticancer Res*, **31**, 1741-44.

Jiang Y, Hou J, Zhang Q, et al (2013). The MTHFR C677T polymorphism and risk of acute lymphoblastic leukemia: an updated meta-analysis based on 37 case-control studies. *Asian Pac J Cancer Prev*, **14**, 6357-62.

Karami H, Baradaran B, Esfahani A, et al (2013). siRNA-mediated silencing of survivin inhibits proliferation and enhances etoposide chemosensitivity in acute myeloid leukemia cells. *Asian Pac J Cancer Prev*, **14**, 7719-24.

Khodabandehloo M, Hosseini W, Rahmani MR, et al (2013). No detection of xenotropic murine leukemia virus-related viruses in prostate cancer in Sanandaj, west of Iran. *Asian Pac J Cancer Prev*, **14**, 6929-33.

Kooshyar MM, Ayatollahi H, Keramati MR, et al (2013). Lack of KRAS gene mutations in chronic myeloid leukemia in Iran. *Asian Pac J Cancer Prev*, **14**, 6653-6.

Li XH, Huang ML, Wang SM, et al (2013). Selective inhibition of bicyclic tetrapeptide histone deacetylase inhibitor on HDAC4 and K562 leukemia cell. *Asian Pac J Cancer Prev*, **14**, 7095-100.

Liu J, Xu CY, Cai SZ, et al (2013). Senescence effects of Angelica sinensis polysaccharides on human acute myelogenous leukemia stem and progenitor cells. *Asian Pac J Cancer Prev*, **14**, 6549-56.

Ozbas-Gerceker F, Bozman N, Kok S, Pehlivan M, et al (2013). Association of an LMP2 polymorphism with acute myeloid leukemia and multiple myeloma. *Asian Pac J Cancer Prev*, **14**, 6399-402.

Qin LL, Wang QR, Wang Q, et al (2013). T-SPOT.TB for detection of tuberculosis infection among hematological malignancy patients and hematopoietic stem cell transplant recipients. *Asian Pac J Cancer Prev*, **14**, 7415-9.

Shan WL, Ma XL (2013). How to establish acute myeloid leukemia xenograft models using immunodeficient mice.