Case of Covid-19 in patients with T-large granular leukemia

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Introduction and Aim

SARS-CoV-2 is a new coronavirus, which first appeared at the end of 2019, and associated with a high level of mortality in elderly patients and patients with comorbidity, including oncological diseases, among which death rate reaches 15% (Yang X. et al, 2020; Guan W.J. et al, 2020). The last data show that among patients with cancer, the infection rate is higher, than in the general cohort (0.79% vs 0.37%) (Jing Yu. et al). At this moment, only a few clinical cases and one study with inclusion of patients with hematological pathology and COVID-19 have been published. All clinical cases of COVID-19 in hematological patients described subjects under 65 with lymphoproliferative diseases and favorable outcome (Liang W. et al, 2020; Jin X.H. et l, 2020; Zhang X. et al, 2020). The study of 25 hematological patients and COVID-19 also mentioned that most of them had lymphoproliferative neoplasms and the one-month survival was equaled 60% (Malard F. et al, 2020). In a few studies with COVID-19 patients the high level of ferritin was found as one of the markers of an unfavorable prognosis (Thirumalaisamy P. et al., 2020). The mean ferritin level in the non-surviving COVID-19 patients was 1297.6 ng/ml, while was 614.0 ng/ml in the cohort with the favorable outcome (Mehta P., 2020). Currently, there are none publications with the analysis of the impact of hyperferritinemia on survival prognosis of patients with COVID-19 and hematological diseases.

The aim: demonstration of the clinical case of the T-large granular leukemia (T-LGL) patient with COVID-19 and hyperferritinemia.

Case Report

The patient L., 67 year old. In the peripheral blood analysis dated 12/17/17 leukocytes 6.4 G/l, erythrocytes 2.15 T/l, hemoglobin 7.4 g/dl, platelets 384 G/l, ESR 22 mm/h, eosinophils 5%, bound neutrophils 6%, segmented neutrophils 20%, lymphocytes 64%, monocytes 5 %. The morphological examination of the peripheral blood cells revealed an increased number of the large granular lymphocytes. Clonal mature lymphocytes (CD3+, TCRab+, CD42-, CD5dim, CD81+, CD161+, CD27-, CD28-, CD45R0-) was found at flow cytometry and T-large granular leukemia was diagnosed. The patient was transfusion-dependent. On December 2017, his ferritin level was 396 ng/ml, the transferrin saturation was 73.7%. In January 2018, cyclosporine 200 mg/day was prescribed for 4 months, the response was not achieved and on 05/25/18 cyclosporine was changed to cyclophosphamide 100 mg/day. In peripheral blood test dated 10/19/2018 leukocytes 3,1 G/l, erythrocyte 2,5 T/l, hemoglobin 6.8 g/dl, platelets 320 G/l, ESR 24 mm/h eosinophils 3%, basophils 2%, bound neutrophils 5%, segmented neutrophils 59%, lymphocytes 21%, monocytes 9%. Due to the long period of the transfusion dependency, 10/14/18 ferritin concentration was assessed and highly increased level of 4168 ng/ml was detected. Chelation with deferoxamine at a dose of 37.5 mg/kg was started. After 6 chelations, the hemoglobin level reached 9.8 g/dl by 12/26/18 and cyclophosphamide therapy was stopped. After 15 chelations (by 02/12/19) the hemoglobin and ferritin level was 14.4 g/l and 2410 ng/ml, respectively. 26 chelations were performed by March, 2020. On March 10, 2020, the patient was consulted by hematologist. The complete remission of T-LGL was confirmed, complaints were absent and ferritin level was 1807 ng/ml. 18/03/20 patients felt general weakness, the temperature was 37.5° C and infrequent dry cough was appeared. On 23/03/20 temperature was 39.0° C. On 24/03/20 lung auscultation: breath was rigid, rales were absent. On Chest X-ray, infiltrative or other changes of the lung were not detected. On March 27, 2020, the nasopharyngeal lavage material was examined by PCR for the SARS-CoV-2 virus RNA and a positive result was obtained. The patient received azithromycin 500 mg/day per os, hydroxychloroquine 200 mg/2 times/day, acetaminophen 500 mg/day. On 03/31/20 at the bacteriological analysis of sputum, S. aureus 1.2×10^5 CFU/ml and S. pneumoniae 3×10^8 CFU/ml was found. The blood C-reactive protein was 13.94 mg/l. On the chest X-ray dated 03/31/20: the pulmonary fields are focally infiltrated on the right. It was verified the lower lobe pneumonia on the right. Ceftriaxone 2.0 i.v./ day was initiated. On 04/07/2020 the chest radiography was repeated: bilateral lower lobe pneumonia. On the background of antibacterial therapy, the next control radiography was performed on 13/04/20: focal-infiltrated changes were not detected. On 15/04/20 PCR was performed for detection of SARS-CoV-2 RNA and was positive. The PCR analysis dated 04/22/20 and 04/27/20 - the result for SARS-CoV-2 RNA was negative. The level of ferritin from 04/29/20 was 1852 ng / ml.

Discussion

Hyperferritinemia in the patient was found before T-LGL remission with depression of its level during chelation with dipheroxamine. During the period of SARS-CoV-2 infection, with the subsequent occurrence of bacterial complications, only a slight increase of ferritin was detected from 1807 ng / ml (03/10/2020) to 1852 ng / ml (04/29/2020).

A high level of ferritin in patients with hematological neoplasms is caused not only by transfusions of erythrocytes but also, in the case of ineffective erythropoiesis, by reduction of hepcidin synthesis. The low hepcidin level followed by overexpression of the iron carrier protein DMT-1 leads to release of iron from enterocytes into blood and then from blood into macrophages. Hyperexpression of DMT-1 causes a high concentration of iron both in blood serum and in the macrophages, where ferritic protein synthesis occurs (Brierley C.K. et al., 2017; Lyle L. et al, 2018;). Therefore, usually, at the moment of diagnosis COVID-19, patients with hematological pathology have a high ferritin level. Thus, the use of ferritin, as an additional marker for assessing the intensity of the synthesis of the pro-inflammatory cytokine, if not to take into account other inflammation markers, in some hematological patients is probably limited, given its often high base level. On the other hand, elevated synthesis of pro-inflammatory cytokines associated with the increased ferritin level. So, we can find an increase of ferritin levels during the period of infection in patients with an elevated concentration of this marker before COVID-19. According to the study of hemodialysis patients, the ferritic level before SARS-CoV-2 infection corresponded to 584 ng / ml, and after - 1446 ng / ml (Bataille S. et al, 2020).

Conclusions

Thus, the use of ferritin as an additional marker for assessing the inflammatory intensity due to COVID-19 in hematological patients could be limited at the beginning of the infection, if not to take into account other inflammation markers, given its often high base level in some of these patients.

Key words

Ferritin, SARS-CoV-2, T-large granular leukemia