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CASE REPORT

Two Cases of False Elevation of MCHC

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SUMMARY

Background: **Mean corpuscular hemoglobin concentration (MCHC) is one of the parameters detected by blood cell analyzers, often used together with mean corpuscular volume (MCV) and mean corpuscular hemoglobin content (MCH) as diagnostic indicators for anemia classification. It has important clinical value in early detection of the cause of anemia and the underlying etiology of anemia. Therefore, the accuracy of MCHC results is of great significance for the diagnosis and treatment of diseases.**
Methods: **We reported two cases of false elevation of MCHC. Considering the possibility of cold agglutination and lipid blood interference detection, we used 37℃ water bath and plasma exchange to correct for interference on the sample.**
Results: **After correcting the interference, MCHC returned to normal, consistent with the patient's disease status. Therefore, the two cases of abnormal elevation of MCHC are considered to be pseudo elevation caused by interference.**
Conclusions: **For specimens with abnormally elevated MCHC levels, experimenters should first analyze possible interfering factors and choose effective methods to correct different interferences, providing accurate testing reports for doctors and patients.**
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KEYWORDS

MCHC, cold agglutination, lipid blood, 37℃ water bath, plasma exchange

INTRODUCTION

MCHC is one of the important parameters in blood routine examination, which is calculated based on the results of red blood cells (RBC), hemoglobin (HGB), and hematocrit (HCT). MCHC is the ratio of HGB to HCT, which is a stable indicator with minimal variation. Research has shown that the detection of MCHC has important clinical value in the differential diagnosis of iron deficiency anemia (IDA) and megaloblastic anemia (MA) [1,2]. We report two cases of false elevation of MCHC caused by interference of cold agglutination specimen and lipid blood specimen in the blood routine analysis process. The specific situation is as follows:

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CASE PRESENTATION

Case 1

Male, 34 years old. On November 6, 2023, the patient sought medical attention in the emergency room due to upper abdominal pain accompanied by nausea and vomiting.

Admission examination: white blood cell count 18.59 x 10^9/L; HGB 213 g/L; MCHC 452 g/L. The clinical doctor contacted us and had doubts about the results of HGB and MCHC. So, we retested the original blood sample and found that the results were close to the original ones. At the same time, reviewing the patient's case, it was found that the serum triglycerides were as high as 7.02 mmol/L (reference value: 0.56 - 1.7 mmol/L). CT scan showed pancreatic enlargement with peripheral exudation, indicating pancreatitis. We speculated that the patient's pancreatitis led to a decrease in lipid breakdown and caused hyperlipidemia. However, hyperlipidemia has a higher lipid content in the blood. When using a blood analyzer to measure hemoglobin (HGB), the transmittance decreases and the absorbance increases, leading to a false increase in the results of HGB. Pseudo elevation of HGB leads to pseudo elevation of MCHC. So, we centrifuged the blood routine samples and found that the plasma layer was milky white lipid plasma, confirming our hypothesis. We quantitatively removed blood lipid plasma from the sample and replaced it with an equal amount of physiological saline. Then the sample was retested, and the results of HGB and MCHC significantly decreased (Table 1). Therefore, this sample is a false elevation of MCHC caused by lipid blood.

Case 2

Female, 6 years old. On December 31, 2023, hospitalized for 4 days due to fever and cough. Admission examination shows: white blood cell count 5.49 x 10^9/L, MCHC 350 g/L, positive for Mycoplasma pneumoniae DNA and influenza B virus RNA. Azithromycin 0.22 g/qd combined with oseltamivir granules 45 mg/bid for anti-infection treatment. On January 6, 2024, blood routine examination showed that MCHC was as high as 455 g/L, which was significantly higher than before. Due to the fact that MCHC is a relatively stable indicator, laboratory personnel raised doubts about the results for unusual short-term increases. When checking the test results of the instrument, it was found that the instrument indicated the presence of "RBC aggregation?" in the sample. Therefore, the blood sample was examined and a large number of fine sand-like particles were found to adhere to the wall of the test tube, indicating the presence of condensation in the sample. Upon reviewing the patient's medical records, the concentration of Mycoplasma pneumoniae IgM increased to 101.72 AU/mL. The laboratory personnel suspect that the specimen was exhibiting cold agglutination phenomenon. In order to verify the presence of cold agglutinin, RBC cold agglutination experiments were performed on the patient's blood samples, and the results showed cold agglutinin positive (title of 1:128). Therefore, we treated the sample with a 37°C water bath for 30 minutes, and then retested the sample. The MCHC result decreased to 343 g/L, returning to the normal level shown in Table 2. Therefore, the phenomenon of cold agglutination in the patient's sample caused RBC aggregation, and abnormal RBC count caused a false increase in MCHC.

DISCUSSION

Blood routine testing is one of the three major routine tests and plays an important role in disease screening, diagnosis, treatment monitoring, and prognosis assessment. Mean corpuscular hemoglobin concentration (MCHC), as an important parameter of red blood cells, is often used in clinical practice to distinguish between anemia types and differential diagnosis of hereditary spherocytosis [3]. MCHC is the ratio of HGB to HCT, which is a stable indicator with little variation. If there is a significant fluctuation, it indicates the existence of detection errors and may indicate abnormalities in the sample state. It is necessary to check the specimen for the presence of lipid blood, RBC cold agglutination, and other conditions. The correction method usually involves plasma exchange and 30 minutes water bath at 37°C before testing.

Lipid blood is one of the common influencing factors that interfere with blood routine analysis and detection, affecting the detection of RBC parameters [4]. The principle of HGB determination is to add a hemolytic agent to diluted blood, dissolve RBC, and release HGB. HGB combines with relevant components in the hemolytic agent to form HGB derivatives, which enter the HGB testing system for colorimetry [5]. The change in absorbance is directly proportional to the HGB content in the liquid. The lipid blood sample appears milky white due to its high content of chylomicrons, causing turbidity interference in the plasma. When conducting HGB colorimetric measurement, it will reduce the transmittance and increase the absorbance, leading to a false increase in the HGB measurement results and a false increase in MCHC. After replacing the blood lipid plasma with physiological saline, the HGB of the sample in Case 1 significantly decreased, and the related MCH and MCHC calculation parameters returned to normal.

Cold agglutination refers to the phenomenon of red blood cells clumping in a cold environment caused by autoantibodies (cold agglutinin) [6]. Cold agglutination reaction generally occurs below 31°C, with the strongest at 0 - 4°C, and the most obvious is red blood cell agglutination. There are reports that cold agglutinin may appear in the serum of patients infected with Mycoplasma pneumoniae [7]. When the level of cold agglutinin in the patient's blood increases, it will affect the results of blood cell analysis to varying degrees. After being infected with Mycoplasma pneumoniae, the patient in Case 2 began to produce immunoglobulin IgM type

Table 1. Case 1 of RBC parameters before and after plasma exchange.

Test items	Results (before plasma exchange)	Results (after plasma exchange)	Reference value	Unit
RBC	5.7	5.32	4.30 - 5.80	10^{12}/L
HGB	213↑	162	130.0 - 175.0	g/L
HCT	0.470	0.436	0.400 - 0.500	
MCV	82.5	81.8	82.0 - 100	fl
MCH	37.3↑	30.4	27.0 - 34.0	pg
MCHC	452↑	371	316.0 - 354.0	g/L

Table 2. Case 2 of RBC parameters before and after 37℃ water bath.

Test items	Results (before 37℃ water bath)	Results (after 37℃ water bath)	Reference value	Unit
RBC	3.36	4.91	4.30 - 5.80	10^{12}/L
HGB	137	137	130.0 - 175.0	g/L
HCT	0.301	0.399	0.400 - 0.500	
MCV	89.6	81.3	82.0 - 100	fl
MCH	40.8↑	27.9	27.0 - 34.0	pg
MCHC	455↑	343	316.0 - 354.0	g/L

cold agglutinin. Due to the similarity between Mycoplasma pneumoniae antigen and the antigen on the red blood cell membrane, cold agglutinin caused red blood cell aggregation. The RBC clusters formed by the aggregation of multiple RBCs cause an increase in pulse size when passing through the counting hole, leading to a false increase in MCV and a decrease in RBC count, resulting in a decrease in HCT [8]. However, HGB detection is a colorimetric method, which is not affected by agglutination. MCHC = HGB/HCT. HGB remains unchanged and HCT falsely decreases, leading to a false increase in MCHC results. We treated the sample in Case 2 with a 37℃ water bath for 30 minutes, which is based on the principle that the phenomenon of RBC aggregation caused by cold agglutinin is reversible. When the temperature returns to 37℃, the antigen-antibody complex gradually dissociates, and the aggregated red blood cells depolymerize accordingly. After being treated with a 37℃ water bath, the samples showed a significant increase in RBC and HCT, and the related MCH and MCHC calculation parameters regressed to normal. In summary, this article emphasizes that when laboratory staff discover abnormal elevation of MCHC, the possibility of interference from lipid blood and RBC cold agglutination should be considered. Corresponding corrective measures should be taken to provide timely and accurate reporting results for clinical doctors, so that patients can receive accurate diagnosis and precise treatment.

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Declaration of Interest:
All authors declare that they have no competing interests.

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