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CASE REPORT

A Case of Pseudoreduction of IgA

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SUMMARY

Background: **Immunoglobulin A (IgA) is an important biomarker for clinical evaluation of immune system function and multiple myeloma. The hook effect may lead to a false decrease in IgA test results, especially at extremely high IgA concentrations, which may mask the true disease state and result in misdiagnosis or missed diagnosis.**
Methods: **We report a case of false decrease in IgA due to the hook effect.**
Results: **The detection values of IgA (6.89 g/L), IgM (0.33 g/L), and IgG (2.72 g/L) in the patient were significantly different from the serum globulin level (52.5 g/L). After dilution, the true value of IgA was retested to be 37.25 g/L. The original value of IgA was falsely reduced due to the hook effect.**
Conclusions: **When the IgA test results contradict the serum globulin levels, attention should be paid to the hook effect. Laboratory personnel should obtain the true level of IgA through sample dilution retesting to avoid misdiagnosis and missed diagnosis of multiple myeloma.**
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KEYWORDS

IgA, hook effect, multiple myeloma

INTRODUCTION

IgA is an important immunoglobulin secreted by plasma cells, and its abnormal elevation is common in diseases such as IgA type multiple myeloma. At present, clinical laboratories mainly use immunoturbidimetry to detect IgA concentration. However, the linear range of this method is limited, and when the concentration of IgA in the sample is too high, an imbalance in the ratio of antigen to antibody may lead to a hook effect, resulting in a false decrease in the detection results [1]. This article reports a case of false decrease in IgA caused by hook effect, and explores its mechanism and coping strategies in combination with literature.

CASE PRESENTATION

The patient was a 77-year-old female. She was admitted for treatment on April 7, 2025 due to rectal mucosal prolapse for over a month. Laboratory tests show (Table

Table 1. The results of the patient's serum biochemistry.

Test items	Results	Reference value
ALT	7.7	7 - 40 U/L
AST	14.4	13 - 35 U/L
Total protein	83.2	65 - 85 g/L
Albumin	30.7	40 - 55 g/L
Globulin	52.5↑	20 - 40 g/L
IgG	2.72	7 - 16 g/L
IgG (after 5-fold dilution)	2.80	7 - 16 g/L
IgA	6.89	0.7 - 5 g/L
IgA (after 5-fold dilution)	37.25↑↑	0.7 - 5 g/L
IgM	0.33	0.4 - 2.8 g/L
IgM (after 5-fold dilution)	0.30	0.4 - 2.8 g/L

Table 2. The Results of serum immunofixation electrophoresis and urinary/ serum free light chain.

Test items	Results	Reference value
Type IgG M protein	negative	negative
Type IgA M protein	positive (+)	negative
Type IgM M protein	negative	negative
Type κ light chain	negative	negative
Type λ light chain	positive (+)	negative
Serum M protein	36.2 g/L (+)	negative
Serum free κ light chain	0.71 g/L	1.7 - 3.7 g/L
Serum free λ light chain	10.5 g/L ↑	0.9 - 2.1 g/L
Urinary free κ light chain	9.4 mg/L	≤ 7.1 mg/L
Urinary free λ light chain	309 mg/L ↑↑	≤ 3.9 mg/L

1) that the level of serum globulin (52.5 g/L) has significantly increased. Immunoglobulin IgA (6.89 g/L) slightly increased, while IgG (2.72 g/L) and IgM (0.33 g/L) decreased compared to the normal range. Globulins are produced by the human liver, including IgM, IgA, IgG, C3, C4, etc. IgG, IgA, IgM and other immunoglobulins are the main components of serum globulin [2]. The patient's liver function was normal and there were no related diseases such as immunodeficiency. The results of mild elevation of IgA and decrease of IgM and IgG are inconsistent with the significant increase in serum globulin levels. The total mass of the three (9.94 g/L) only accounts for 18.93% of serum globulin (52.5 g/L), which is much lower than the normal proportion.

So, the laboratory personnel checked the quality control on that day, and all were under control. At the same time, the instrument was running well, the reagents were normal, and the specimen had no abnormalities such as clots, hemolysis, lipid blood, jaundice, etc. The staff suspected the presence of detection interference. To verify the results, the sample was diluted 1:5 and retested. The IgM and IgG values were consistent with the original values, while the IgA value increased to 37.25 g/L, which was extremely high. After calculation, the total mass of IgG, IgA, and IgM accounted for 76.76% of the total globulin, which returned to normal levels. Therefore, we believed that the initial result of IgA in this patient was a pseudo decrease caused by the hook effect. So we suggest that clinical doctors further perform serum immunofixation electrophoresis, urine light chain, and other tests on patients. The test results showed a significant increase in urinary lambda light chain and positive IgA-lambda monoclonal immunoglobulin (Table 2). Based on clinical manifestations and imaging results, the patient was ultimately diagnosed with IgA type multiple myeloma.

DISCUSSION

IgA multiple myeloma is a hematological malignancy characterized by abnormal secretion of monoclonal IgA antibodies by plasma cells [3]. Accurate and error free IgA laboratory test results are crucial for the diagnosis and differential diagnosis of IgA type multiple myeloma.

IgA is often detected using immunoturbidimetry. The principle is to use sheep anti human IgA antibodies and IgA in the test blood sample for antigen antibody reaction and calculate the concentration of IgA by detecting the change in absorbance after the reaction is completed. Many studies have reported the interference of the hook effect on immune detection results [4-7]. The hook effect refers to the phenomenon in immune reactions where the ratio of antigen and antibody concentrations is not appropriate, resulting in low or even false negative test results [1,8]. In this case, the actual concentration of IgA in the patient was extremely high, far exceeding the linear upper limit of the detection system and the ability of the antibody to bind to the antigen. The antigen and antibody could not form large grid-like aggregates and could not form particles to produce turbidity, resulting in a hook effect and making the detection result much lower than the actual value. The diagnosis of multiple myeloma relies on the detection of monoclonal immunoglobulin, but the hook effect may normalize IgA values and mask disease characteristics. Therefore, when there is a contradiction between IgA levels and serum globulin levels, laboratory personnel should actively investigate the hook effect, verify the results through dilution retesting or changing the detection method, and recommend further clinical examinations such as immunofixation electrophoresis and bone marrow puncture.

This case suggests that the hook effect in IgA testing may lead to a false decrease and interfere with the diagnosis of multiple myeloma. Laboratory personnel need to master the identification methods of such interference, timely dilute and retest, and combine with other detection methods to provide accurate basis for clinical practice and avoid misdiagnosis and missed diagnosis of multiple myeloma.

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

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