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A Proposed Solution to the Interference of IgG Kappa-Type M Protein on LDL-C Detection

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Abstract: *Objective:* To explore the interference of monoclonal immunoglobulin (M protein) on the detection of serum LDL-C in patients with multiple myeloma, improve the understanding of this matter, determine and establish the correct method, and provide more accurate clinical results through this case. *Methods:* A case was selected for analysis by the direct method. *Results:* The interference of IgG kappa-type M protein on LDL-C detection could not be completely eliminated by the enzymatic method. *Conclusion:* IgG-type type M protein affects the detection of LDL-C by the enzymatic method; thus, light reagents can be used with the direct method for detection.

Keywords: M protein; Interference; Biochemical detection

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1. Introduction

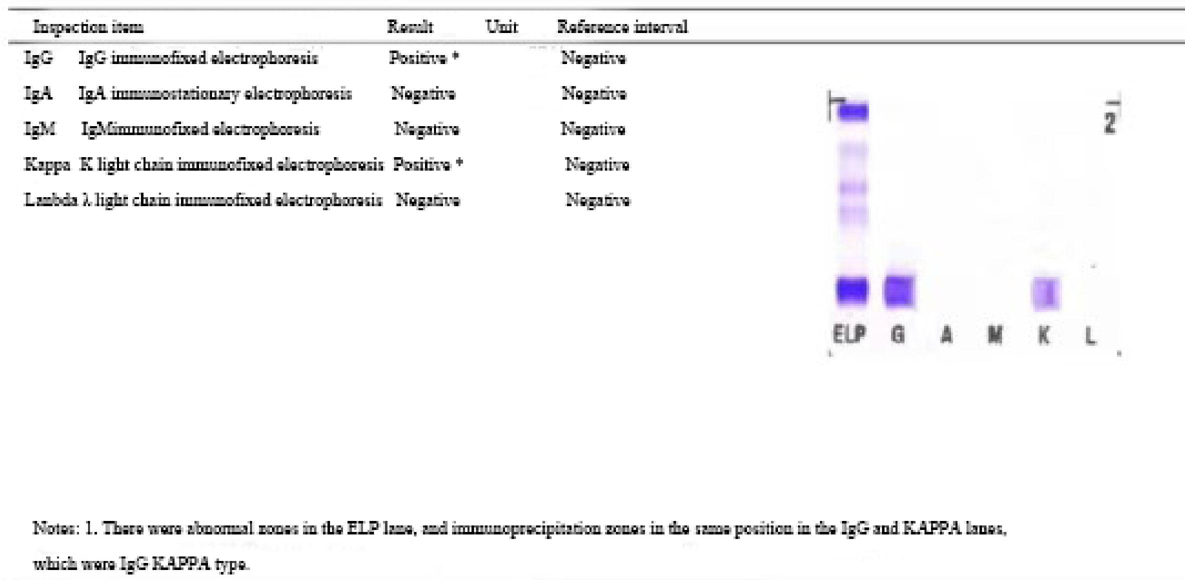
Monoclonal immunoglobulin (M protein) is an immunoglobulin molecule or its fragment with the same amino acid sequence and protein structure produced by the proliferation of monoclonal B lymphocytes or plasma cells [1]. It is commonly seen in multiple myeloma, macroglobulinemia, *etc*., all of which start with M; therefore, it is called "M protein." M protein can be IgG, IgM, IgA, IgE, or IgD, or any of the kappa (κ) or lambda (λ) light chains. In recent years, there have been many reports on the interference of IgM-type M protein on biochemical detection indicators, but there are only a few reports on the interference of IgG-type M protein on low-density lipoprotein (LDL) detection. Therefore, a case of IgG-type M protein interfering with the detection of LDL via the direct method and a solution that can eliminate the interference is reported in this paper.

2. Materials and methods

2.1. Information

A 74-year-old male patient presented with lower back pain without any obvious inducement or radiation. The pain was dull and tolerable and was not aggravated by postural changes. He was not on any oral analgesics. He was admitted to Xushui District People's Hospital. His lower back pain improved after lumbar vertebrae surgery on May 27. On postoperative day one, the lower back pain recurred with the same nature as before; however, the pain was disregarded. On June 30, he visited Xushui District People's Hospital again, and a magnetic resonance imaging (MRI) was done over his lumbar spine; his MRI examination was similar with the original film, showing lumbar degeneration, hyperosteoplasia, and intervertebral disc deformation and contact. No further treatment was given. On July 4, during his third visit to Xushui District People's Hospital, he complaint of shortness of breath after exercise 4 days ago,

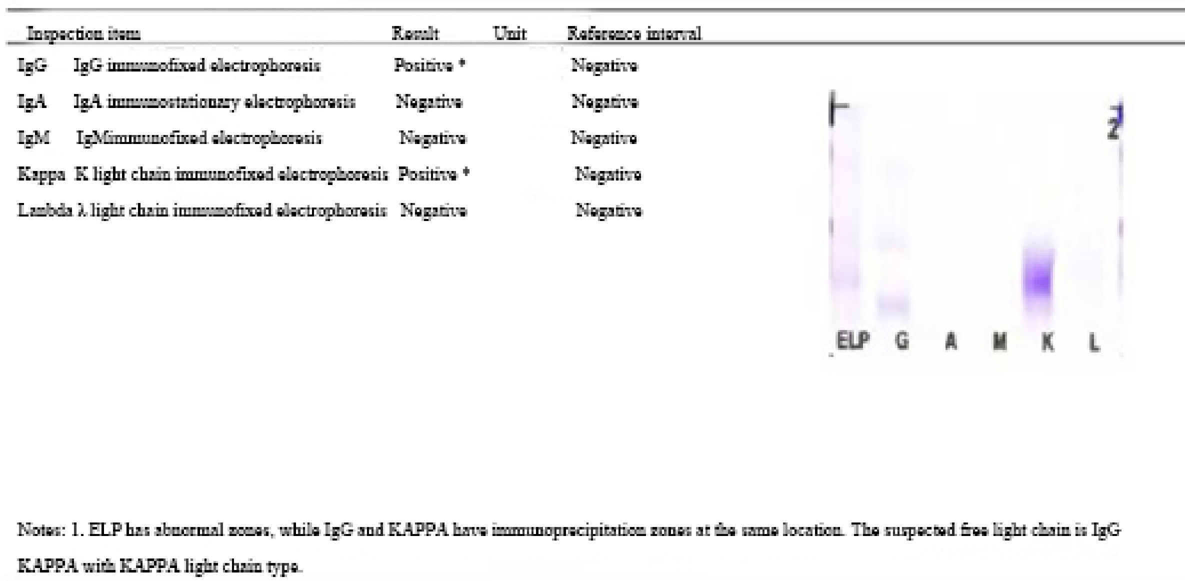
which was relieved with rest. It was accompanied by fatigue, loss of appetite, and loss of weight that developed one month ago. Otherwise, he did not experience any discomfort over his anterior chest. He was admitted for further investigations. His blood investigations were as follows: (routine blood examination) red blood cell (RBC) 2.09×10^{12}/L; hemoglobin (HGB) 72 g/L; (renal function) blood urea nitrogen (BUN) 14.26 mmol/L, creatinine (CR) 154 μmol/L, uric acid (UA) 606 μmol/L; immunoglobulin G (IgG) 72.6 g/L; (liver function) total protein (TP) 109 g/L, globulin (GLB) 81 g/L. Serum and urine immunofixation electrophoresis showed IgGκ type. In consideration of his clinical manifestations and investigation results, the patient was diagnosed with multiple myeloma (**Figures 1** and **2**).



Inspection item		Result	Unit	Reference interval
IgG	IgG immunofixed electrophoresis	Positive *		Negative
IgA	IgA immunostationary electrophoresis	Negative		Negative
IgM	IgMimmunofixed electrophoresis	Negative		Negative
Kappa	K light chain immunofixed electrophoresis	Positive *		Negative
Lambda	λ light chain immunofixed electrophoresis	Negative		Negative

Notes: 1. There were abnormal zones in the ELP lane, and immunoprecipitation zones in the same position in the IgG and KAPPA lanes, which were IgG KAPPA type.

Figure 1. Serum immunofixation electrophoresis result



Inspection item		Result	Unit	Reference interval
IgG	IgG immunofixed electrophoresis	Positive *		Negative
IgA	IgA immunostationary electrophoresis	Negative		Negative
IgM	IgMimmunofixed electrophoresis	Negative		Negative
Kappa	K light chain immunofixed electrophoresis	Positive *		Negative
Lambda	λ light chain immunofixed electrophoresis	Negative		Negative

Notes: 1. ELP has abnormal zones, while IgG and KAPPA have immunoprecipitation zones at the same location. The suspected free light chain is IgG KAPPA with KAPPA light chain type.

Figure 2. Urine immunofixation electrophoresis result

2.2. Instruments and reagents

Beckman Coulter's AU5821 automatic biochemical analyzer and LDL-C original supporting reagents were used to detect LDL-C.

2.3. Methods

The direct method was used. The protective agent in Reagent 1 protected LDL from participating in the enzymatic reaction, while the addition of Reagent 2 released the protective agent from the LDL and inhibited hydroperoxide ester through sodium azide. LDL was quantitatively determined by an enzymatic chromogenic system (CHOPAP system).

3. Discovery of interference

3.1. Negative value for very-low-density lipoprotein (VLDL)

The results showed a negative value for VLDL (**Figure 3**).

Standard coding	Project name	Result		Unit	Reference interval
1 TCH	★ Total cholesterol	2.64	↓	mmol/L	3.00-5.18
2 TG	★ Triglyceride	0.70		mmol/L	<1.70
3 HDL	★ HDL cholesterol	1.25		mmol/L	1.04-1.55
4 LDL	★ Low density lipoprotein cholesterol	2.03		mmol/L	1.89-3.37
5 VLDL	Very low density lipoprotein cholesterol	-0.64	↓	mmol/L	0.00-0.76
6 APO-A1	Apolipoprotein A1	0.80	↓	g/L	1.00-1.60
7 APO-B100	Apolipoprotein B100	0.34	↓	g/L	0.60-1.20
8 A1/B100	A1/B100	2.35			0.90-2.67

Figure 3. Results showing negative very-low-density lipoprotein (VLDL)

3.2. Serum quality control

The serum appeared clear and bright without any visible clots, blood, *etc*. (**Figure 4**).

Figure 4. Serum after the test

3.3. Response curves

The response curves are shown in **Figures 5**, **6**, and **7**.

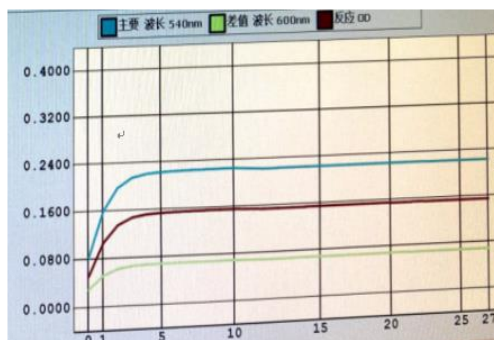


Figure 5. Normal response curve (total cholesterol). Blue: main wavelength; green: difference wavelength; red: reaction.

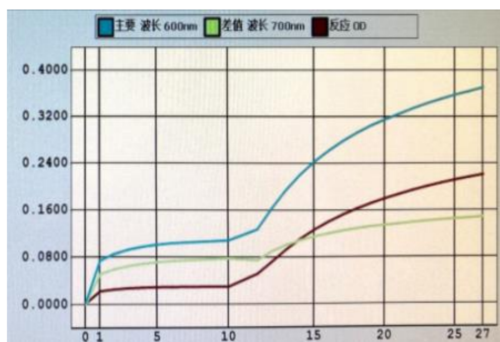


Figure 6. Normal response curve (high-density lipoprotein cholesterol). Blue: main wavelength; green: difference wavelength; red: reaction.

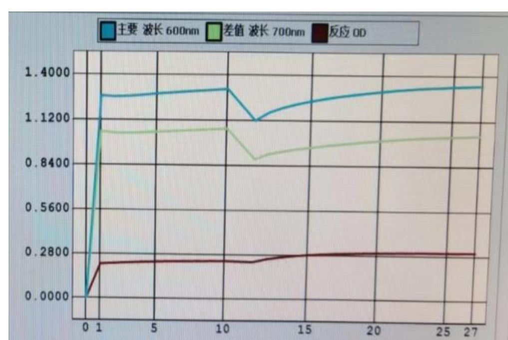


Figure 7. Abnormal response curve (low-density lipoprotein cholesterol). Blue: main wavelength; green: difference wavelength; red: reaction.

3.4. Reasons for interference

The response curves for total cholesterol (CHOL) and high-density lipoprotein cholesterol (HDL-C) were both normal, but the response curve for LDL-C was abnormal. As shown in **Figure 7**, at the 0–1 point, the increase in M protein causes hyperviscosity syndrome, and its specific binding with certain substances in the body (forming giant enzymes) can interfere with the experiment, thus affecting the detection results. After adding the sample, the absorbance increased abnormally, thus displaying an abnormal curve.

3.5. Solution

After changing the reagent, the curve became normal, as shown in **Figure 8**.

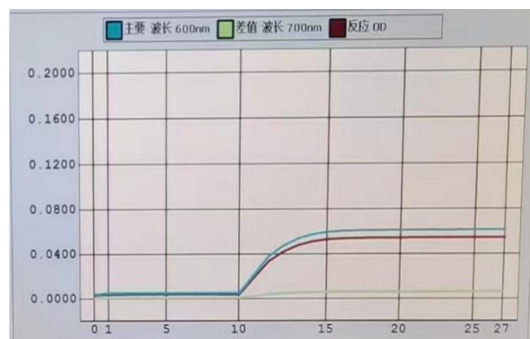


Figure 8. Response curve after changing reagent. Blue: main wavelength; green: difference wavelength; red: reaction.

According to Friedewald formula, when serum TG < 4.52 mmol/L, LDL-C = TC – HDL-C – TG/2.2. After calculation, LDL = 1.03, which was close to the detection result as shown in **Figure 3**.

4. Discussion

In clinical biochemical tests, hemolysis and lipemia are the most common influencing and interference factors [2] . In recent years, the interference of M protein on biochemical indicators has been reported from time to time, such as the interference of IgM protein on serum prealbumin detected by immune transmission turbidimetry [3] and IgG-κM protein in multiple myeloma patients on the analysis of bilirubin detected by the enzymatic method [4]. The present study found that IgG κM protein interferes with LDL-C and showed that using another reagent to detect LDL-C can solve the interference of IgG-type M protein on LDL-C. With the increasing number of case reports, the interference of M protein on many biochemical indicators is recognized. At the same time, reagent manufacturers have also begun to pay attention to this issue and taken corresponding measures, such as using reagent blanks to replace water blanks and dual wavelength and rate analysis methods to replace one-point end-point or two-point end-point methods; adjusting the pH value and ionic strength of the reagents to prevent protein precipitation; and adding surfactants to the reagents to promote protein dissolution [5,6]. However, as of now, there is no reagent that can eliminate the interference of M protein on all detection indicators. Therefore, there is still a need to investigate the interference of M protein on biochemical detection indicators and find a solution for it in order to provide more accurate test results in clinical practice settings.

Disclosure statement

The author declares no conflict of interest.

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