

## CASE REPORT

# A Case of Pseudoelevation of Serum HCG Caused by Rheumatoid Factor

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### SUMMARY

**Background:** Serum human chorionic gonadotropin (HCG) is a glycoprotein hormone secreted by the trophoblast cells of the placenta. HCG levels are helpful in confirming and monitoring pregnancy, as well as in the diagnosis and monitoring of trophoblastic tumors. Therefore, the accuracy of HCG detection results is of great significance for the diagnosis and differential diagnosis of pregnancy and germ cell tumors.

**Methods:** We report a case of pseudo elevation of serum HCG in a patient with rheumatoid arthritis. The possibility of abnormal increase in HCG concentration caused by rheumatoid factor (RF) was evaluated using polyethylene glycol (PEG) precipitation method and different detection platforms.

**Results:** Samples pretreated with polyethylene glycol and samples using another detection platform showed a significant decrease in serum HCG concentration and a negative reaction. Therefore, the patient's HCG result showed an abnormal increase, which is considered a false increase caused by RF interference.

**Conclusions:** When serum HCG levels are abnormally elevated in patients with rheumatoid arthritis but there is no evidence of pregnancy or clinical symptoms related to trophoblastic tumors, staff should consider the possibility of RF interference in HCG detection, take corresponding corrective measures, and communicate with clinical doctors in a timely manner.

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#### KEYWORDS

rheumatoid factor, interference, polyethylene glycol

#### INTRODUCTION

HCG is a glycoprotein synthesized by the trophoblast tissue. It helps to detect normal pregnancy early and is used for diagnosing diseases such as ectopic pregnancy, molar pregnancy, choriocarcinoma, etc. [1]. Serum rheumatoid factor is often elevated in patients with rheumatoid arthritis (RA) and is one of the diagnostic criteria for RA [2]. We found one patient with rheumatoid arthritis who had no clinical evidence related to pregnancy or choriocarcinoma, but had false elevation of serum HCG due to interference from rheumatoid factors. The specific situation is as follows:

**Table 1. The results of serum tumor markers, biochemistry, and autoantibodies.**

Test items	Results	Reference value
Carbohydrate antigen 125 (CA125)	13.59	≤ 35.00 U/mL
Carbohydrate antigen 15-3 (CA15-3)	6.5	≤ 31.30 U/mL
Alpha fetoprotein (AFP)	2.94	≤ 13.4 ng/mL
Carcino-embryonic antigen (CEA)	1.22	≤ 5.00 ng/mL
Human chorionic gonadotropin (HCG)	105.51	≤ 5.00 IU/mL
Rheumatoid Factor (RF)	276.3	≤ 14 IU/mL
Anti-Streptolysin O (ASO)	185	≤ 200 IU/mL
Anti-cyclic citrullinated peptide (anti-CCP)	870	≤ 5 U/mL
Follicle stimulating hormone (FSH)	2.9	3.03 - 8.08 mIU/mL
Luteinizing hormone (LH)	1.43	1.8 - 11.78 mIU/mL
Prolactin (PRL)	112.71	108.8 - 557.10 mIU/mL
Urine HCG	negative	negative

**Table 2. The results of HCG and RF before and after PEG pretreatment.**

	No pretreatment	PEG pretreatment	Reference ranges
HCG	105.51	< 1.20 (negative)	0 - 5 IU/mL
RF	276.3	12.3	0 - 14 IU/mL

**Table 3. The results of HCG in different detection platforms.**

	Abbott No pretreatment	Abbott PEG pretreatment	Roche No pretreatment
HCG (U/mL)	105.51	< 1.20 (negative)	< 0.20 (negative)
Reference ranges	≤ 5.00 U/mL		0.20 - 5.00 U/mL

## CASE PRESENTATION

The female patient is 48 years old. She was admitted on July 12, 2024, due to rheumatoid arthritis. Admission auxiliary examination included: Serum tumor markers (Abbott detection system), biochemical and autoantibodies are shown in Table 1: HCG (105.51 IU/mL), anti-cyclic citrullinated peptide (870 U/mL) and RF (276.3 IU/mL) are significantly elevated, while other markers are within the normal range. The patient's routine electrocardiogram, cardiac ultrasound, abdominal ultrasound, urinary tract ultrasound, chest CT and other examinations showed no significant abnormalities. The patient's HCG significantly increased, and additional urine HCG and reproductive hormone tests showed negative results (Table 1). At the same time, a transvaginal ultrasound examination of the uterus and adnexa was performed, and no evidence of pregnancy or germ cell tumors was found.

Due to the contradiction between serum HCG positive

and urine HCG negative results, and the absence of any evidence of pregnancy or germ cell tumors, the clinical doctor contacted our laboratory. After receiving this feedback, the staff first checked the indoor quality control and found that the indoor quality control for that day was completely under control, ruling out the possibility of testing errors caused by instruments and reagents. The staff also retested the sample, and the result was 110.62 IU/mL, which is consistent with the previous result. Analysis of the patient's case and related examinations revealed a long-term increase in rheumatoid factor levels. Considering the possibility of RF interference in detection, we pretreated the patient's serum with polyethylene glycol and retested RF and HCG. The serum RF level significantly decreased to 12.3 U/mL, while the serum HCG level decreased to < 1.20 U/mL, which is negative and consistent with the urine HCG results (Table 2). At the same time, the samples were sent to the Roche detection platform for testing, and we found that the serum HCG level was also significantly

decreased, dropping to  $< 0.20$  U/mL, consistent with PEG pretreatment (Table 3).

After discussion with clinical doctors, it was found that the abnormal increase in HCG levels in the patient was not consistent with clinical symptoms. After PEG pretreatment, HCG levels returned to the normal range. We ultimately determined that the abnormal increase in HCG in the patient was due to false elevation caused by rheumatoid factor interference.

## DISCUSSION

Serum HCG plays an important role in the diagnosis, treatment, and follow-up of pregnancy and germ cell tumor diseases, but its measurement can be interfered by factors such as biotin, streptomycin, and heterophile antibody, leading to clinical misdiagnosis and mistreatment, and causing patients to undergo unnecessary examinations and treatments [3,4]. In this case, the HCG results of the patient were significantly inconsistent with the urine HCG and uterine adnexal ultrasound results, and it is suspected that this result is a false elevation.

Analyzing the medical history, the patient is a middle-aged and elderly female rheumatoid arthritis patient, with a 20 fold increase in serum RF, reaching 276.3 IU/mL. There are studies showing that polyethylene glycol can eliminate the interference of RF on immune detection [5]. We first pretreated the patient's serum with PEG precipitation, and the serum RF significantly decreased to the normal range. With the decrease of RF, the serum HCG level also significantly decreased, showing a negative result, which is consistent with clinical diagnosis. The significant decrease in RF in serum samples after PEG precipitation is consistent with the negative results of HCG in patient serum, indicating that RF is the cause of the pseudo increase in HCG. RF mainly exists in RA patients and is an autoantibody with affinity for the Fc portion of IgG structure [6]. Research on the interference of commercial reagent immunoassay shows that RF positive serum has strong reactivity to mouse IgG reagents, affecting HCG determination [7]. The Abbott testing platform in our laboratory uses mouse monoclonal antibodies. At the same time, we sent the specimens to the Roche testing platform of an external hospital for retesting of HCG, and the result was  $< 0.2$  U/mL (negative). Why did the Roche detection system not experience interference? We have reviewed the reagent manual and found that unlike the Abbott detection platform, the Roche detection platform uses electrochemiluminescence. At the same time, Roche's detection reagent adopts anti-interference technology, which clearly indicates that RF concentration  $\leq 1,200$  IU/mL will not interfere with the detection. However, Abbott's reagent did not evaluate the interference of RF on the detection. Therefore, this case is a false increase in serum HCG measurement caused by high concentration RF interference. We can use comparative

tests with different instruments and reagents, as well as polyethylene glycol precipitation tests, to correct interference. Polyethylene glycol is a better choice due to its low price, easy availability, and simple and effective method.

In summary, this case emphasizes that the laboratory should be aware of and suspect the presence of interfering factors as the cause of inconsistent laboratory results and clinical symptoms. They should take necessary anti-interference measures to avoid misleading diagnosis and unnecessary treatment.

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## Declaration of Interest:

All authors declare that they have no competing interests.

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