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Phantom Human Chorionic Gonadotropin in an End Stage Renal Disease Case

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Authors' contributions

This work was carried out in collaboration between all authors. Author BKT designed the study, wrote the first draft of the manuscript. Authors HT and GA managed the clinical follow up of the case, Authors BKT, HT and GA managed the literature searches. All authors read and approved the final manuscript.

Case Study

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ABSTRACT

Aims: Gestation is very difficult in women with end stage renal disease (ESRD). In addition, human chorionic gonadotropin (HCG) may be increased in Non-pregnant women with ESRD. Therefore, elevated HCG levels in ESRD patients may cause diagnostic confusion. Here we present a case with suspicious HCG elevation who desire of pregnancy and without gonadal deficiency. We also discussed the possible reasons of this HCG elevation.
Presentation of Case: A twenty-two year old young woman with ESRD for seven years has been followed up outpatient clinics of our institution. She was receiving hemodialysis treatment for last three years after renal transplant rejection. In gynecological examination, obstetric ultrasound scan revealed no embryonic yolk sac or other radiological images of pregnancy. The case evaluated according to the algorithm of HCG elevation. Advanced clinical differential diagnosis and laboratory analyzes were performed. A diagnosis of HCG elevation due to heterophile antibodies made, which has not been previously described in the literature in ESRD patients.
Discussion and Conclusion: Heterophile antibodies should be kept in mind in

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evaluation of HCG increase in reproductive women with ESRD patients with transplantation history.

Keywords: Human chorionic gonadotropin; end stage renal disease; pregnancy; heterophile antibodies.

1. INTRODUCTION

Human chorionic gonadotropin (HCG) is a glycoprotein hormone consisted with two subunits; alpha and beta. HCG has two main functions in the human body. First, the support of progesterone synthesis in the beginning of the pregnancy, and second, constitution and durability of the vascular support of placenta during pregnancy [1]. HCG is also a useful biomarker for different clinical conditions such as; normal and ectopic pregnancies, gestational trophoblastic diseases and non-gestational malignancies [2]. Small amounts of HCG secreted from the pituitary in men and non-pregnant women [3]. It's production in the human body reach larger amounts from syncytiotrophoblastic cells after fertilization during endometrial implantation. Assessment of serum HCG concentration before diagnostic and therapeutic interventions is advised for all women in childbearing age [2].

Gestation is very difficult in women with end stage renal disease (ESRD). Studies on women with ESRD in reproductive age revealed that the incidence of pregnancy was 1-7% in this population [4]. In addition, HCG may be increased in non-pregnant women with ESRD [5-7]. Two possible explanations for that are the increase in pituitary HCG secretion due to gonadal deficiency and the reduction of renal clearance of HCG [8]. Therefore, elevated HCG levels in ESRD patients may cause diagnostic confusion. Major changes should be applied when a hemodialysis (HD) patient become pregnant. It is very important to make these treatment modifications as soon as possible after diagnosis of pregnancy in sake of fetal-maternal health [9,10]. On the other hand elevated HCG levels without pregnancy may delay or alter some treatments or interventions (such as cadaveric renal transplantation, treatment of catheter infection). Thus, it is critically important to detect the reason of HCG elevation in ESRD patients.

Here we present a case with suspicious HCG elevation who desire of pregnancy and without gonadal deficiency. We also discussed the possible reasons of this HCG elevation.

2. PRESENTATION OF CASE

A Twenty-two year old young woman with ESRD for seven years has been followed up outpatient clinics of our institution. Renal replacement treatment initiated with peritoneal dialysis and 2 years later a renal transplantation performed. Renal transplant rejection occurred two years after transplantation. She has been on HD treatment for three years since then. She has a history of desire of pregnancy. Her menstruations were irregular. She had experienced elevation in HCG four times; however, radiological evidences of pregnancy were missing each time resulting a depression in her mood.

The patient admitted to our clinic for suspected pregnancy. Routine laboratory assays were as follows: Hemoglobin:12.7g/dL, Hematocrit:38.2%, Leukocyte count:$4.55x10^9$cell/L, Platelet:239K/µL (BC-6800 Auto Hematology Analyzer, Shenzhen Mindray Bio-Medical Electronics, China), Serum glucose:70 mg/dL, Blood urea nitrogen:35mg/dL, Serum

creatinine:6.11mg/dL, Potassium: 4.9mmol/L (Architect c 8000, Abbot Laboratories, USA). The HCG level was 21.15mIU/mL (reference range:<5mIU/mL). The patient's hormone levels were as follows:Follicle Stimulating hormone:5.9mIU/ml, Luteinizing hormone:30.29mIU/ml, Estradiol:86.49pg/mL Progesterone:4.15ng/ml (Cobas e 601, Roche Diagnostics, Germany). Repeat HCG test 2 days later advised for detecting doubling of HCG. HCG 2 days later was 24.67mIU/mL. Meantime obstetric ultrasound scan revealed no embryonic yolk sac or other radiological images of pregnancy. The HCG kit used in our laboratory was measured intact HCG, in addition to beta subunit. Urinary HCG could not be evaluated since the patient was anuric. Repeat HCG assessed in the same sample with the same method to avoid analytical errors and a 23.26mIU/mL level of HCG was found. HCG was reduced to 19.75mIU/mL in the repeat test after 1:1 dilution of the sample with a solution that not contains HCG. Heterophile antibody blocking tubes used to determine HCG interferences with heterophile antibodies (Scantibodies Laboratory Inc, Santee, CA) and the final HCG was 1.27mIU/mL with this method.

3. DISCUSSION

False negative and false positive results of HCG are common though intensive efforts for decades to minimize these errors. These errors may cause unnecessary treatment or delay of necessary interventions [11-13]. HCG is a routine simple test which all of the results have the same importance for clinicians. However, in the side of clinical chemistry, HCG has 15 different variants in serum and urine [2]. Different isoforms of HCG increase in each condition that HCG elevation considered relevantly. But commercial HCG kits define some of these isoforms and different incomparable test results occur with each system [14,15]. False negative and false positive results may occur with heterophile antibodies which may affect all immunoassays [16,17]. Because the clearance of HCG reduces in ESRD patients, cause of elevated HCG may become more complex [8]. Furthermore, pituitary HCG secretion increases due to gonadal dysfunction in ESRD patients [5].

There are some procedures in patients with irrelevant HCG increase [2]. These include (a) Urinary HCG assessment; heterophile antibodies are weighted 150kD, therefore, they are unable to pass thorough urine. Thus, urinary HCG measurement should be the first step test when HCG elevation due to heterophile antibodies suspected. Normal urinary and elevated serum HCG suggests circulating heterophile antibodies [13]. (b) HCG doubling test; which is frequently used in the diagnosis of ectopic pregnancy, abortus, and misdiagnosis. HCG test repeat after 48 hours of the first assay. HCG should be at least twice of the first test in normal pregnancy [1], (c) Dilution of the sample; HCG should be repeated in the samples after serial dilution with a serum that not contain HCG. Heterophile antibodies are suspected if the decline in HCG concentration is not compatible with the dilution factor [18]. (d) Investigation of interference with heterophile antibodies; heterophile antibody blocking tubes block heterophile antibodies. Lower levels of HCG in repeated test by these tubes indicate the interference by heterophile antibodies [17] and (e) Repeat of the test with a different system; which is an alternative method if assay interference is suspected. HCG test repeat in another laboratory using different measurement system. Difficulties of this option are possibility of interference in a different system, difficulties of proper transport of the samples, unavailability of a different measurement system [17]. We followed up these suggestions in observing the reason of HCG elevation in the present case. Main reasons of the clinical suspect were a history of HCG elevation without pregnancy and no signs of gonadal insufficiency. We could not make urine tests since the patient was anuric. There were no radiological evidences of pregnancy. Repeat HCG test showed no doubling in serum HCG levels. Dilution of the serum not revealed a linear reduction in HCG levels.

Therefore, we suspect of heterophile antibodies and HCG was found in normal range after repeating test in Heterophile antibody blocking tubes. In lights of these findings, we think that the elevation of HCG in the present case was due to interference with heterophile antibodies. This hypothesis has been supported by lack of HCG doubling two days after first test, transplantation and rejection history, and lack of radiological evidences of pregnancy. Heterophile antibodies bind to assay antibodies and results of high analyte levels although no analyte present in the sample. Heterophile antibodies occur in response to animal antibodies, diagnostic or therapeutic human antibodies or autoantibodies of human itself. Renal transplantation in the present case may lead to the development of heterophile antibodies. To our knowledge, there is no data about HCG elevation due to heterophile antibodies in ESRD patients in the literature.

4. CONCLUSION

Heterophile antibodies should be taken into account in ESRD patients with HCG elevation especially received renal transplantation.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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