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False Positive Test or Phantom hCG: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Authors OE and YI wrote the draft of the manuscript. Authors ZD and OBT managed the literature searches. Author YI designed the figures, managed literature searches and contributed to the correction of the draft. Authors OE and YI provided the case, the figures and supervised the work. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

A 45-year-old female patient,gravida3,para3 was admitted to the emergency room because of pelvic pain and irregular menstruation. An human chorionic gonadotropin level ordered as part of the routine test was 210 IU/L. A pelvic ultrasound was negative for intrauterine pregnancy and the lower right lateral uterine tube measuring 1,5×2 cm. The patient was admitted to the gynecology clinic and following β -hCG levels remained between 250-300IU/L. She received methotrexate (MTX) 50 mg/m2 for a presumed ectopic pregnancy. Surgical management a diagnostic laparoscopy, which was negative for tubal and ovarian pregnancy. A diagnosis of chronic pelvic pain and with high β -hCG levels (where systemic methotrexate and laparascopic management is fail) was made and an abdominal hysterectomy was thus planned. Total abdominal hysterectomy with bilateral salpingooophorectomy was done. The patient was plateau in serum human chorionic gonadotropin after operation.

Keywords: Increased β-hCG levels; emergency room; suspected pregnancy; phantom hCG.

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1. INTRODUCTION

Human Chorionic Gonadotropin (hCG) is a glycoprotein made of α (92 amino acid alpha-subunit) and β (145 amino acid beta-subunit) subunits that are noncovalently linked. Most hCG is secreted into circulation by trophoblastic cells as an intact dimer, free α and β subunits can also be found in the serum and urine. Several isoforms of hCG exist in the circulation; some are synthesized by cells and others are degradation products [1]. Human chorionic gonadotropin is alpha-subunit which is identical to that for Luteinizing Hormone (LH), follicle-stimulating hormone (FSH), and Thyroid-Stimulating Hormone (TSH) [2]. Human chorionic gonadotropin is produced in pregnancy, in gestational trophoblastic diseases, gestational trophoblastic neoplasms, ovarian germ cell tumors and in men with testicular germ cell malignancies [3]. Human chorionic gonadotropin is detected in rare cases that do not fit into any of these categories. We present a case of treatment-resistant with persistent high-level human chorionic gonadotropin.

2. CASE REPORT

A 45-year-old female patient, gravida 3, para 3 was admitted to the emergency room because of pelvic pain and irregular menstruation. She was treated with NSAIDs up to now. Pelvic pain worsened for the last two month. Her last normal menstrual period was six weeks prior to admission. Her past medical history was normal. Physical examination was normal, but her cervical movements in pelvic examination was found painful. Laboratory data revealed WBC count as 9900/mm^3, hemoglobin as 12.3 gr/dL, hematocrit as 36.6, and platelets as 201.000 /uL. Serum β-hCG level was elevated (β-hCG; 210 IU/L). A urinary pregnancy test was positive. Chemistry results, urine analysis and hormonally profile (TSH, fT3, fT4, Progesterone, FSH and LH) were normal. All biochemical tests were performed using Abbott Laboratories Archietect C16000 analyzer (Abbott Laboratories). Ultrasound showed that ectopic pregnancy, and revealed a well-encapsulated bulging mass over the lower right lateral uterine tube measuring 1,5×2 cm. The gross appearance revealed cystic and solid areas. Patients were consulted Obstetrics and Gynecology. In following serial serum β-hCG levels, it see a rise within the days (Day 1: 230, day 2: 220, day 3: 260 IU/L) after hospitalization. A single dose intramuscular injection of MTX (50 mg/m2) without citrovorum rescue was used with unruptured ectopic pregnancies. Patient had a increase in serum β-hCG between days 4 and 7 after treatment (Day 4: 255, day 7: 269, day 8: 287 and day 9: 295 IU/L). Additional doses of MTX were given but hCG level did not decline. Second, intramuscular injection of MTX was used, but patient's serum β-hCG levels continued to rise. Patient underwent either is not needed laparascopy for a persistent rise in β-hCG levels despite the treatment. The uterus, left fallopian tube and the left ovary was normal in size, but a bulging mass was seen, measuring 2 cm in diameter arising from the right ovary. The right fallopian tube and ovarian mass were removed. Postoperative day 1: 171, day 2: 180, day 3: 186, day 4: 226 IU/L. Histopathology revealed corpus luteum. At second laparatomy an slightly enlarged uterus and bilateral ovaries were found of normal apperance. Abdominal organs were normal in appearance. Total abdominal hysterectomy with bilateral salpingooophorectomy was done. Patient had decreased in serum β-hCG after second operation (Postoperative day 1: 223, day 6: 174, day 8:187 IU/L). β-hCG level was followed after surgery. The comprehensive specimens was normal. Histopathological examination of specimen did not reveal choriocarcinoma, hydatidiform mole or placental site trophoblastic tumor. The patient was discharged on the fifth postoperative day after an uneventful recovery. After her discharge, follow-up continued on an outpatient basis until the β-hCG level was 190 IU/L on day 15. Differential diagnosis of trophoblastic.and nontrophoblastic neoplasms should be done in phantom hCG. Whole-body scanning should be done in nontrophoblastic neoplasms. We sought to determine whether consultation with a medical oncologist is associated with nontrophoblastic neoplasm, but whole-body CT scanning were normal. Serum levels of Alpha-Fetoprotein (AFP), Carcinoembryonic Antigen (CEA), cancer antigen 125 (CA 125), cancer antigen 19-9(CA 19-9) and cancer antigen 15-3 (CA 15-3) were normal. The evidence of medical oncology to nontrophoblastic neoplasm did not find. Clinical control of medical oncology was suggested in six months later. Repeat screening six months later in patient by medical oncology but did not find evidence of neoplasm. However serum β-hCG levels still high (β-hCG; 189 IU/L) (Fig. 1).

Patient extensively exposed to animals or certain animal byproducts when false positive test or "Phantom hCG" was considered (farmer).

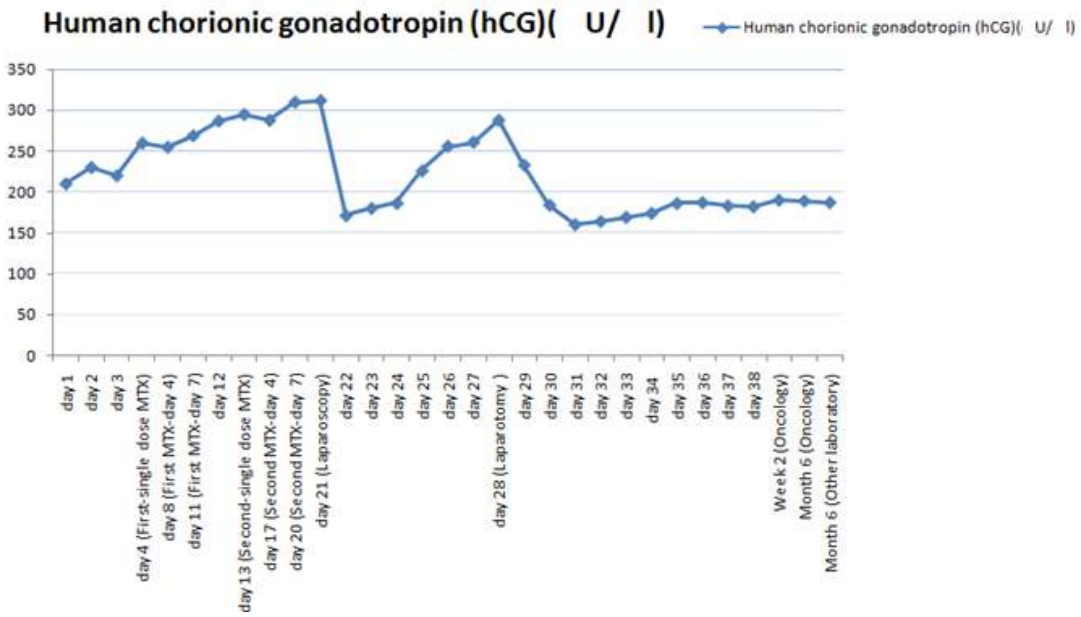

Fig. 1. Serial serum hCG measurement

3. DISCUSSION

A recent phenomenon of the “False-positive” or “Phantom hCG” has been noted in both laboratory and clinical medicine. These false-positive results have led to confusion and unwarranted treatment for suspected diagnoses of abnormal pregnancy and gestational trophoblastic disease. There are three main methods for identifying false positive hCG; a) Send the serum to two laboratories using different commercial assays, b) Request a serial dilution of the serum, c) Determine hCG in the urine [4]. We performed all three methods in this case. The False-positive hCG is a consequence of interference of heterophil antibodies. Anti-animal immunoglobulin antibodies; the capture and tracer antigens used for hCG testing may be from various animals. Humans extensively exposed to animals or certain animal by products can develop human antibodies against animal antibodies. Humans with recent exposure to mononucleosis and IgA deficiency syndrome also often have heterophilic antibodies [5,6]. This is case, the most likely differential diagnosis of an hCG value that does not match the clinical scenario, as presented in the prior pituitary hCG, quiescent gestational trophoblastic diseases, placental site trophoblastic tumor, and nontrophoblastic neoplasms. The problem of “Phantom hCG” was identified in the early 1970s. [7]. Literature reports show that false-positive hCG tests are due to human heterophilic antibodies interfering [8-11]. False positive hCG test results are at risk for recurrent false positive hCG assay results. CA-125 and thyroid antibodies should be studied in false positive hCG test results. CA-125 and thyroid antibodies results should be normally [12]. A false positive hCG result has also been reported in a patient with *E.Coli* septicemia due to an *anti-E.Coli* antibody with human anti-mouse antibodies activity [13] Serum TSH, sT3, sT4, and CA-125 concentrations should be normal. Normal finding on a routine urinalysis in asymptomatic patient. The clinician to appropriately diagnose these patients and prevent potentially harmful treatments. If the Phantom hCG is suspected or identified, the test should be repeated by employing a different assay. A False-positive hCG test can be identified by sending the serum to two laboratories using different commercial assays, which vary greatly or are negative in one or both alternative tests. Laboratories, need to also take responsibility in avoiding false results that occur. They need to consider legal responsibilities and the possibility of being sued for false-positive hCG results. An unknown, possibly very large number of women are misdiagnosed with ectopic pregnancies because of false positive hCG results. False-negative diagnosis is less likely to ocur but its clinical implications are potentially much more serious. Also an unknown, possibly very large number of women have been erroneously diagnosed with cancer throughout the World, and not recognized

as having false positive hCG by a reference laboratory.

4. CONCLUSION

Pelvic pain, irregular menstrual cycles and high levels β-hCG in patients presenting with emergency department, ectopic pregnancy should be kept in mind. If is not found the cause of high levels of hCG, must be consulted with Obstetrics and Gynecology. Phantom HCG should be considered when any etiological factor to cause beta HCG rising did not found.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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