

**Case Report****Molar Pregnancy with False Negative urine  $\beta$ -HCG: Hook effect in molar pregnancy**Anuradha Salvi<sup>1</sup>, Premlata Mital<sup>2</sup>, Usha Shekhawat<sup>3</sup>, Alka Batar<sup>4</sup>, Priyanka Makkar<sup>5</sup>, Pradeep KumarSoni<sup>6</sup><sup>1</sup>Senior Resident, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India<sup>2</sup>Senior Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India<sup>3</sup>Senior Professor, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India<sup>4</sup>PG Student, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India<sup>5</sup>PG Student, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India<sup>6</sup>PG Student, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India**ARTICLE INFO:****ABSTRACT****Article history:**

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Urine pregnancy test is widely used in emergency department as the first screening test for patients of reproductive age presenting with gynaecological problem in order to rule out pregnancy. Conditions such as complete molar pregnancy which produces large amount of serum beta Human chorionic gonadotrophin ( $\beta$  hCG), may cause a false negative result due to oversaturation of the assay system known as the "Hook Effect". We report a case where the exclusion of pregnancy by urine test lead to initial misdiagnosis of molar pregnancy. The patient demonstrated clinical features of hydatidiform mole, despite multiple negative urine pregnancy tests. These false- negative qualitative human chorionic gonadotropin assays were likely caused by the "high – dose Hook Effect". Gynaecologists need to be reminded of the possibility of false negative result with this commonly used test.

**1. Introduction**

Gestational trophoblastic disease encompasses a spectrum of tumors, including complete and partial hydatidiform mole (molar pregnancy) and locally invasive or disseminated choriocarcinoma[1]. Complete hydatidiform mole produces characteristic clinical features, including Amenorrhea, vaginal bleeding and uterine size beyond expected gestational age[1]. Many other clinical features of molar pregnancy including hyperemesis gravidarum, hyperthyroidism and theca lutein ovarian cysts are believed to be induced by markedly elevated serum human chorionic gonadotropin ( $\beta$ -hCG) levels produced by the trophoblastic tissue[1]. Thus in addition to a complete physical and pelvic examination, complete blood count (CBC), blood chemistry and pelvic ultrasound a hallmark of diagnosing hydatidiform mole is a positive  $\beta$ -hCG assay pregnancy test. Interestingly sandwich chromatographic immunoassays such as qualitative  $\beta$ -hCG assays may produce false-negative results in the presence of excessively high antigen concentrations in a phenomenon known as the "high-dose hook effect." We report a case of molar pregnancy presenting as amenorrhea, abdominal pain and vaginal spotting with multiple false negative urine pregnancy tests.

**2. Case report**

A 22 year old Gravida 0 Para 0 female presented in the Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur on 24 April 2014 with three months of amenorrhea, fifteen days of abdominal pain, vaginal spotting & nausea, vomiting off & on. The abdominal pain was described as cramping in the mid-epigastric and pelvic regions. There was no history of fever, diarrhea, and urinary tract infection. She was sexually active without contraceptive use and described a history of regular periods since menarche. Two weeks prior she was seen at a private hospital at periphery where she had a negative urine pregnancy test and a pelvic examination that revealed tenderness. At that time she was treated with antibiotics and analgesics but her symptoms continued.

On examination she was pale & cachexic, uncomfortable with pain. She was afebrile. Her pulse was 96/min, respiratory rate was 22/min, Blood Pressure 110/70 mm of Hg .Physical examination revealed diffusely tender abdomen but soft without rebound tenderness. Uterus was enlarged to 20 weeks size and tender. Pelvic examination revealed soft cervix with closed external os with slight vaginal bleeding, a 20-week sized uterus with cervical motion and adenexal tenderness.

\*Corresponding author: Anuradha Salvi, Senior Resident, Department of Obstetrics and Gynaecology, S.M.S. Medical College, Jaipur (Rajasthan) India.; Tel.: 09462678724; E-mail: [dranuradhasalvi@gmail.com](mailto:dranuradhasalvi@gmail.com)

Laboratory qualitative urine  $\beta$ -hCG assays were negative. Molar pregnancy was suspected clinically and pelvic ultrasound, blood chemistries, serum beta – hCG levels and ABO Rh grouping and cross matching were advised. Intravenous antibiotics, analgesics were started. Initial complete blood count showed hemoglobin of 5.0 g/dL with rest normal parameters. Her coagulation and basic metabolic panels were within normal limits. Ultrasound showed enlarged uterus with a 180×85 mm complex mass with mixed echogenic area within the endometrium with multiple hypoechoic cystic area noted in it with increased vascularity suspicious for molar pregnancy. Hence a clinical diagnosis of H. mole made. Blood transfusion started & dilatation and evacuation was planned in the morning. Sample for serum  $\beta$  hCG levels was sent and her qualitative urine  $\beta$  hCG test repeated which was again negative. But unfortunately patient started bleeding in night so emergency dilatation & curettage was done in OT. On dilatation typical vesicles of hydatidiform mole started protruding through cervical os. Products were saved & sent for histopathology. She was transfused 3 units of blood for correction of anemia. Patient absconded in the evening after evacuation and lost to follow up.

### 3. Discussion

The Hydatidiform mole commonly known as Molar pregnancy is a non-malignant tumor that arises from anomalous growth of trophoblastic tissue in early pregnancy after an embryo has failed to develop[1]. Clinical decision-making regarding women of childbearing age with amenorrhea, abdominal pain and vaginal bleeding is often dictated by pregnancy testing specifically qualitative urine hCG assays[2]. Current urine and serum pregnancy test use antibodies directed against beta hCG for immunological identification. Most of them are chromatographic sandwich immunoassays in which two antibodies directed against different parts of beta chain are used and the resultant “sandwich” they form around the antigen is detected and interpreted as “positive”. When the  $\beta$ hCG is present it is immobilized by a capture antibody and labeled by tracer antibody resulting in an immobilized antibody hCG tracer sandwich. Most of the antibodies to site  $\beta$ 1 and another to the C-terminus of the  $\beta$  subunit ( $\beta$ -CTP) or to the  $\alpha$ -subunit. When HCG levels are high both the capture and the tracer antibodies saturate and the signal response is decreased thus overwhelms the assay system and blocks the formation of “sandwiches” between the two sites[3,4,5]. This is known as the “Hook effect” or “Prozone Phenomenon” and can be observed in immunometric sandwich assays[2]. Despite the high sensitivity and specificity of the assay our patient had repeated negative urine pregnancy tests. A false negative  $\beta$  hCG may delay the diagnosis.

In some reports the diagnosis of molar pregnancy was already suspected prior to the false-negative test because of ultrasound evidence or a previous positive pregnancy test[5-8]. A retrospective analysis has suggested that the positive predictive value of transvaginal ultrasound for molar pregnancy is 100%[9].

However often this procedure is delayed or not considered when a pregnancy test is negative as was likely the case when our patient was initially seen at an outside facility. Since her screening pregnancy test was negative, an ultrasound was never performed, making the correct diagnosis delayed & difficult.

### 4. Conclusion

Molar pregnancy is an uncommon yet serious condition that may cause significant pain, hyperemesis, pre-eclampsia, hyperthyroidism and possibly metastatic disease. Qualitative  $\beta$ -hCG assays may be falsely negative due to the “high-dose hook effect” if serum levels are extremely elevated. When suspicion exists for molar pregnancy, sonographic evaluation and quantitative  $\beta$ -hCG levels are necessary in the work-up. Although modern assay methods have much improved reliability, gynaecologist should be aware of the potential for false negative urinary and serum  $\beta$ -hCG results to the “high dose Hook effect”, especially in the setting of H. mole to avoid delay in patient care.

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