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CASE REPORT

FALSE LOW BETA-HCG IN A COMPLETE HYDATIDIFORM MOLAR PREGNANCY: A CASE OF HOOK EFFECT

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ABSTRACT

Introduction: *Hydatidiform molar pregnancy presents as a proliferative disorder of trophoblastic cells. Complete hydatidiform molar pregnancy presents typically with abnormally high levels of beta human chorionic gonadotropin (β-hCG). The high level of β-hCG is taken as a marker in its diagnosis and follows up. However, many a times very high levels of β-hCG may be associated with falsely low or negative β-hCG levels because of "Hook effect". The hook effect occurs with extremely high levels of β-hCG, saturating detection antibodies, leading to falsely low laboratory results. If unrecognized, this can lead to misdiagnosis and a delayed therapy or mismanagement of care that may have a negative treatment outcome. Here, we report a case of Hook effect presented to Emergency Department of a tertiary care center, National Medical College Teaching Hospital, Birgunj, Nepal.*

Keywords: *β-hCG, False Low hCG, Hook Effect, Molar Pregnancy*

INTRODUCTION

Hydatidiform molar pregnancy presents as a proliferative disorder of trophoblastic cells. Complete hydatidiform molar pregnancy presents typically with abnormally high levels of beta human chorionic gonadotropin (β-hCG).[1] Low serum β-hCG test results may be misreported in cases of extremely high levels of β-hCG due to the "hook effect," where falsely low or negative results occur from oversaturation of the signaling antibodies employed to detect β-hCG by the testing method and analyzer. Excessive beta-hCG production may produce a false negative result due to prozone phenomenon—also known as the 'hook effect'. Herein we have put forward a case where the hook effect was noted in a patient with a complete hydatidiform mole.

CASE SUMMARY

A 25 year old primi gravida, presented to the emergency department of National Medical College Teaching Hospital, Birgunj complaining of abdominal pain, persistent nausea and vomiting for two weeks, and a twenty-pound weight loss. The patient reported a positive home pregnancy test 14 weeks prior to presentation, but had not presented for obstetric care. She thought she had miscarried four weeks prior, with passage of a profuse amount of "jelly-like" substance, which had persisted.

On examination of the patient, general condition was stable with pulse 88/minute and a blood pressure of 130/90 mm of Hg. The cardiac examination was normal and the chest was clear on physical examination. She had a large, non-tender abdominal mass corresponding to 16 weeks of gestation. On consultation with the Obstetrician, pelvic examination revealed a closed cervical os with blood mixed discharge and 15 weeks sized uterus.

The laboratory investigation was immediately requested

and the Ultrasonography abdomen and pelvis was suggested. A complete blood count, blood chemistries, pelvic ultrasound and quantitative serum β-hCG were performed. Ultrasound revealed an enlarged uterus filled with echogenic material. Serum β-hCG was found to be 987 mIU/mL. The patient was transferred to Gynecology and Obstetrics Department with findings concerning but not final diagnosis for a complete molar pregnancy.

Ultrasound findings were re-confirmed and serum β-hCG was requested for repeat analysis, revealing a value of only 877 mIU/mL again. The patient was found to be thrombocytopenic with a platelet value of 99,000 per cumm, anemic with a hemoglobin value of 7.2 gm%, and PT INR of 2.01. Maintaining the body fluid volume, the patient was taken to the operating room for suction evacuation of uterine contents. Pathology was very much consistent with a complete hydatidiform mole. Sample for thyroid function test was also sent that gave a picture of primary hyperthyroidism with a TSH of < 0.001 (0.34 – 5.6 uIU/mL) and free T4 of 3.97 (0.61 – 1.12 pg/mL).

The hospital laboratory was contacted for discussion regarding the discordant β-hCG reports with the provisional diagnosis as complete molar pregnancy. We performed the repeat analysis with serial dilutions of the original β-hCG sample. Dilutions were performed to 1:1000 and the β-hCG result was recalculated to be over 600,000 mIU/mL. This was consistent with the diagnosis made.

On postoperative day 1, the β-hCG was again estimated with the level falling to 290,000 mIU/mL. This again fell down to lower level of 45,000 mIU/mL on 5th post operative day. The patient's presentation of hyper emesis was resolved following the evacuation and hematological parameters were towards the normal line.

The patient's β-hCG continued to fall, but subsequently plateaued between 456 and 489 mIU/mL after approximately ten weeks, requiring ten cycles of weekly methotrexate therapy. She has now achieved a negative β-hCG value, and has shown no evidence of recurrence or metastasis.

DISCUSSION

β-hCG is commonly used as a marker for gestational trophoblastic disease. A very high total β-hCG levels highly suggests a diagnosis of complete hydatidiform mole.[1] But a very high β-hCG concentrations in the blood can give false low test results, as the sensitivity of most β-hCG tests is set to the pregnancy range of 27,300 to 233,000 at 8 to 11 weeks gestational age.[2] The laboratory test result error i.e, false low β-hCG can occur with β-hCG levels higher than 500,000.[2] And the complete molar pregnancy can present with an extremely high β-hCG levels, reaching as high as 3,000,000.[3]

Falsely low test result in analyzers for serum β-hCG may occur with hydatidiform moles—by a phenomenon called the 'high dose hook effect.' Hook effect was first described by Miles in 1975.[4] When β-hCG is present in the serum sample, it is immobilized by a capture antibody, and labeled by a tracer antibody, resulting in an immobilized antibody-hCG-tracer sandwich in a immunoassay principle. When β-hCG levels are too high, both the capture and tracer antibodies saturate, and the signal response is decreased. Talking inside the analytical part of immunoassay, the "hook effect" occurs when non-sandwiched tracer antibodies are washed away with the excess material resulting in a falsely low or negative test.[5]

This discordant result of the primary marker (β-hCG) for the diagnosis of molar pregnancy may delay diagnosis and lead to mismanagement of patients, may be with some fatal outcome. If molar pregnancy is suspected, a brief history regarding the case should be provided so that the laboratory personals can perform a 1:1000 dilution, with which an accurate value can be obtained.[5] This hook effect is also more commonly seen in assays for prolactin and thyroid stimulating hormone. The Access2 Beckman Coulter Immunoassay analyzer is used at our hospital, and has been shown to produce this effect with usually a β-hCG level of 700,000 mIU/dL. To eliminate the high-dose hook effect, the serum sample should be diluted before running the assay. Though rare, the hook effect can lead to delayed therapy or mismanagement of care. Therefore, clinicians should be aware of the limitations of laboratory measurements of extremely high levels of β-hCG, understanding that falsely low or negative tests may arise due to a hook effect, particularly in situations where a clinical scenario may not correspond to a potentially falsely low laboratory value.

CONCLUSION

False low β-hCG can give discordant and inconclusive results for the diagnosis of the complete molar pregnancy due to the hook effect. In such a case, clinicians and the laboratory professionals should be aware and the further and timely evaluation of β-hCG should be done after appropriate sample dilution. Although there are modern assay principles that have much improved reliability, but still clinicians and laboratory personals should be aware of the potential for false-negative urinary and serum β-hCG results due to the high-dose hook effect, especially in the setting of hydatidiform moles.

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