

Elevated  $\beta$ -hCG Outside of Pregnancy

Patient Presentation: 37 y/o G3P3 w/ previous BTL who presented with post-coital spotting and daily vaginal bleeding x 3 months associated with RLQ “pressure” and “cramping.” Normal periods until C-section 3 years ago. Patient also with dyspareunia and malaise. Physical exam was significant for mild discomfort in RLQ, 5cm posterior cervical mass noted on bimanual exam. B-hCG 19K, Hct 32.2.

Serum and urine  $\beta$ -hCG assays, most commonly used to diagnose pregnancy, can **also be elevated outside of pregnancy**. During pregnancy, hCG is produced by **syncytiotrophoblastic cells of placental villi** but several sources of positive hCG outside of pregnancy exist that are important to consider to prevent improper treatment of non-pregnant patients. The five causes of positive hCG outside of pregnancy are **pituitary hCG, “phantom hCG,” exogenous administration of hCG, nontrophoblastic malignancy, and trophoblastic malignancy**.

The pituitary gland secretes low concentrations in men and premenopausal women. HCG, like LH, is stimulated by gonadotropin releasing hormone and suppressed by estrogen and progesterone therapy; therefore, postmenopausal women (with lower estrogen levels) have higher levels of hCG compared to non-pregnant premenopausal women. Exogenous use of hCG preparations can be used to increase fertility (ovulation induction), expedite weight loss, and improve athletic performance. A good history might key in on recent exogenous use and the hCG level is normally only elevated for 24 hours. The term “phantom hCG” is synonymous with a false-positive test. This is important because false-positive hCGs lead to unnecessary treatments such as chemotherapy and surgery for presumed trophoblastic cancers. The estimated false-positive hCG is estimated to be between 1/1,000 and 1/10,000. Nontrophoblastic neoplasms can also cause hCG elevations. Classically, certain testicular cancers cause hCG increases but this isn't relevant since EM physicians would rarely order this assay on men. However, other tumors including bladder, uterine, lung, liver, pancreas, and stomach may secrete hCG. Historically, an elevated hCG outside of pregnancy placed gestational trophoblastic neoplasm (choriocarcinoma, hydatidiform mole) at the top of the differential diagnosis. These tumors can be both active and inactive tumors. Active gestational trophoblastic neoplasms will have greater increases in hCG levels than an inactive tumor.

A 2006 study evaluating elevated hCG outside of pregnancy showed the following distribution: 10% with pituitary hCG, **42% with false-positive hCG, 41% with quiescent GTN**, and 7.6% with active GTN. Several case reports also have shown that **women with ESRD may also have elevated hCG levels as well as certain medications including anticonvulsants, promethazine, and anti-parkinsonian drugs**.

Patient Outcome: Patient had TVUS in ED showing a highly vascular cervical mass with no IUP, adnexal mass, or free fluid. MRI obtained that day showing choriocarcinoma.

Emergency Medicine Take-Away: **Although the vast majority of pregnancy assays in the ED are accurate, we must be conscientious that up to 1/1,000 will show false-positive results and there are five main reasons for this with a disease as serious as choriocarcinoma being**

**a possibility.** If you have an elevated hCG with no IUP or adnexal mass, it might be wise to think of the possibility of elevated hCG outside of pregnancy. If this suspicion is high, OB/Gyn consultation needs to be activated early and don't forget to perform a bimanual exam.

### **References**

- Braunstein, G. (2002). False-positive serum human chorionic gonadotropin results: causes, characteristics, and recognition. *Am J Obstetr Gynecol*, 217-224.
- Montagnana, et. al. (2011). Human chorionic gonadotropin in pregnancy diagnostics. *Clinica Chimica Acta*, 412, 1515-1520.
- Olsen, T.G., et al (2008). Elevated hCG outside of pregnancy – diagnostic considerations and laboratory evaluation. *Obstetrical and Gynecological Survey*, 62(10), 669-674.