Important insights for non-molar choriocarcinoma. (Mini-commentary on BJOG-19-1824.R1)

Neil Horowitz[1], Ross Berkowitz[2], and Kevin Elias[2]

[1]BWH
[2]Brigham and Women's Hospital Department of Obstetrics and Gynecology

May 5, 2020

Mini-commentary on BJOG-19-1824.R1: Demographics, Natural History and Treatment Outcomes of Non-Molar Gestational Choriocarcinoma; A UK population study

Important insights for non-molar choriocarcinoma

Neil S. Horowitz,*[1] Ross S. Berkowitz,[1] and Kevin M. Elias[1]

[1] New England Trophoblastic Disease Center, Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, 02115, USA.

* Email: nhorowitz@partners.org

Although gestational trophoblastic neoplasia (GTN) is a rare event, particularly after a non-molar pregnancy, the true incidence of GTN is difficult to establish with certainty because data regarding the incidence of pregnancies and subsequent trophoblastic events are not available in most countries. This is not the case in the United Kingdom, where there is nearly a 50-year history of unified care of GTN at two major reference centres. The data generated from these centres has positioned them as world leaders in the care of women with GTN. In conjunction with national statistics on conceptions and birth, this data enabled the authors the unprecedented ability to estimate the incidence of non-molar choriocarcinoma. Furthermore, these reference centres had access to more granular demographic, clinical and cancer related data, not previously available in other studies, thus providing a more insightful understanding of non-molar choriocarcinoma.

In the current manuscript, the authors estimate that the incidence of non-molar choriocarcinoma was 1 in 66,775 births or 1 in 84,226 conceptions (BJOG 2020 xxxx). This is similar to other estimates and confirms the rarity of this disease (Hextan NYS Int J Gynecol Obstet 2018;143 (Suppl2):79-85). Approximately two-thirds of these cases (65.4%) presented after a term pregnancy and nearly 25% presented more than a year after the antecedent pregnancy. This delay in diagnosis is not surprising. Unlike hydatidiform moles that in the UK are mostly evacuated in the first trimester and followed with weekly hCG to allow early detection of persistent tumor requiring chemotherapy, term delivery and therapeutic abortions typically are not followed with serial hCG. GTN in these cases is only diagnosed when symptoms, like irregular bleeding, arise and when astute clinicians consider a very rare diagnosis. Given this delayed diagnosis, metastases were common with nearly 45% of women presenting with FIGO high-risk and 20% with ultra high-risk disease. Whether this reflects the biology of non-molar choriocarcinoma or whether it relates to duration of disease prior to diagnosis is not clear. Despite these risks, the overall cure rate was high, 100, 96 and 80.5% for low-risk, high-risk and ultra high-risk, respectively.

An important observation reinforced by this manuscript is the association of maternal age as a risk factor for GTN. Whether one considers the incidence of hydatidiform mole, the rate of postmolar GTN requiring

chemotherapy, or non-molar choriocarcinoma, advanced maternal age is associated with increasing risks (Elias KM et al. J Reprod Med 2012;57:354-8). Though one could speculate why there is this association with maternal age, (diminished immune surveillance, age-related changes to the microenvironment, etc.) the exact mechanism is not fully understood. This information can be useful however when considering non-molar choriocarcinoma in the differential of those with advanced maternal age who present with irregular bleeding postpartum or post-abortion.

Gaining insight into the incidence, natural history, and clinical outcomes of non-molar choriocarcinoma is a critical addition to the literature that will improve the counseling and care of women with this disease. For this, the authors should be congratulated.

No disclosures: Completed disclosure of interest forms are available to view online as supporting information.

Funding: The authors acknowledge support from the Donald P. Goldstein MD Trophoblastic Tumor Registry Endowment and the Dyett Family Trophoblastic Disease Research and Registry Endowment.