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Case report

Primary choriocarcinoma in postmenopausal women: Two case reports and review of the Texas Cancer Registry

Leslie F. Rafanan[a], Harvey Greenberg[a,*], Nancy U. Rondeau[a], Zuber D. Mulla[a], Darius A. Boman[b]

[a] Department of Obstetrics and Gynecology, Texas Tech University Health Sciences Center El Paso, Paul L. Foster School of Medicine, El Paso, TX, United States
[b] Department of Pathology, Texas Tech University Health Sciences Center El Paso, Paul L. Foster School of Medicine, El Paso, TX, United States

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1. Introduction

Gestational trophoblastic disease (GTD) encompasses a variety of interrelated conditions originating from the placenta, specifically, trophoblastic cells. There are five types of GTD which include non-invasive and invasive hydatidiform mole, choriocarcinoma, placental site trophoblastic tumors (PSTT), and epithelial trophoblastic tumors (ETT). Invasive hydatidiform mole, choriocarcinoma, PSTT, and ETT are further grouped into gestational trophoblastic neoplasia (GTN).

Choriocarcinoma is a highly malignant tumor that primarily occurs in women of reproductive age. The diagnosis of choriocarcinoma in a postmenopausal woman is rare (Desai et al., 2010). Prior to the 1970s, choriocarcinoma was almost always fatal, but due to early diagnosis and effective chemotherapy, it is now treatable and has up to a 90% survival rate (Ngan et al., 2012; Lurain, 2010). In low-risk trophoblastic neoplasia, single agent chemotherapy regimens are used (Stevens et al., 2015). High-risk patients are more prone to develop resistance to single-agent chemotherapy, and therefore, a multi-agent regimen is ideal (Lurain, 2010).

The reported incidence rates for choriocarcinoma vary in the literature due to methods of diagnosis (histology vs. clinical methods), and use of data sources (hospital-based vs. population-based) (Steigrad, 2003). Reporting methods for hydatidiform mole and choriocarcinoma are sometimes grouped into GTN, which interferes with the ability to accurately identify the occurrence of both diseases (Steigrad, 2003).

We identified two cases of primary gestational choriocarcinoma in women who were aged 50 years or older and postmenopausal at the time of diagnosis. Information from the Texas Cancer Registry, a population-based tumor registry, was reviewed to calculate the unadjusted incidence of primary choriocarcinoma in women aged 50 years or older in Texas for the period 1995–2012.

2. Case 1

A 50-year-old Hispanic female, G2P2002, presented with postmenopausal bleeding and abdominal pain in January 2005. Her last menstrual period (LMP) was one year prior to presentation. Antecedent pregnancies were term deliveries, the last being 15 years prior to presentation. A dilatation and curettage was performed and pathology demonstrated choriocarcinoma. A serum beta human chorionic gonadotropin (β-hCG) was 4668 mIU/mL. An exploratory staging laparotomy was performed and the patient was found to have an 8 × 7 × 6 cm mass in the lower uterine segment. A total abdominal hysterectomy and bilateral salpingo-oopherectomy were performed. The final pathology showed the tumor to be choriocarcinoma. Pelvic, paracolic and upper abdominal washings were negative.

Using the FIGO staging which incorporates a modified World Health Organization (WHO) prognostic scoring system (Barakat et al., 2002), the patient was found to have a high risk score of 11: age over 40 (1 point), antecedent pregnancy term (2 points), interval from index pregnancy over 12 months (4 points), pretreatment β-hCG 4668 (2 points), largest tumor over 5 cm (2 points). FIGO stage I:11 was assigned.

Multi-agent etoposide, methotrexate, actinomycin D, Cytoxan, and oncovin (EMA-CO) was given. She was followed with β-hCG levels and CT scans from 2005 to 2008. She remained disease free until February 2008, after which, β-hCG was found to be 7 mIU/mL, and progressively rose to 108 mIU/mL in April 2010. In May 2010, a pelvic mass in the

* Corresponding author at: 4801 Alberta Ave, El Paso, TX 79905, United States.
E-mail address: harvey.greenberg@ttuhsc.edu (H. Greenberg).

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cul-de-sac was noted on a CT scan and was found to be recurrent choriocarcinoma on biopsy. She received 7 additional cycles of EMA-CO from June to October 2010 with normalization of her β-hCG.

In February 2011, the patient presented with weakness and shortness of breath. CT scans confirmed the presence of a pelvic mass. She underwent a laparotomy and resection of the pelvic mass. Pathology revealed recurrent choriocarcinoma. Salvage chemotherapy with taxol and carboplatin was ineffective, and additional imaging studies revealed recurrence of the pelvic mass. A repeat laparotomy in April 2012 again showed choriocarcinoma. The β-hCG levels continued to rise in spite of additional salvage chemotherapy with cisplatin and etoposide. In 2013, the patient continued to decline despite two additional laparotomies and pelvic radiation therapy with 45 Gy. The patient expired in September 2015.

3. Case 2

A 51-year-old Hispanic female, G2P1103, presented with postmenopausal bleeding in March 2011. LMP was twelve years prior to presentation. Review of systems was negative. Her first child was a term vaginal delivery. Her second pregnancy was a twin gestation delivered at 36 weeks by cesarean section at age 26.

Laboratory studies showed normal CBC, LFTs, and renal panel. A β-hCG level was elevated at 396 mIU/mL. A chest radiograph was normal. A hysteroscopy and D & C revealed choriocarcinoma. A CT scan of the abdomen and pelvis revealed an enlarged uterus with a 3.3 × 3.9 × 5.8 cm craniocaudad mass. No enlarged lymph nodes or metastases were identified. A brain CT scan was negative. A repeat β-hCG two weeks following the hysteroscopy and D & C showed an increase to 613 mIU/mL.

Staging laparotomy with total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed in May 2011. The uterus was ten-week size. Pathology showed a choriocarcinoma invading from the fundus to the cervix (Fig. 1A–B). FIGO stage was 2:9 given the following: age over 40 (1 point), term antecedent pregnancy (2 points), interval from index pregnancy more than twelve months (4 points), and the size of the tumor over 5 cm (2 points).

She received two cycles of EMA-CO and remains disease free as of 2016.

4. Review of the Texas Cancer Registry

The Texas Cancer Registry (Department of State Health Services, Austin, Texas) provided demographic and epidemiologic information on women who were aged 50 years or older at the time of diagnosis with choriocarcinoma. Cases were residents of Texas and diagnosed between the years 1995 and 2012. Vital status as of December 2012 was determined by Texas Cancer Registry staff using multiple sources including state mortality data and the National Death Index (personal communication, David R. Risser, Ph.D.).

Primary site and morphology in the Texas Cancer Registry are coded using the *International Classification of Diseases for Oncology Third Edition* (ICD-O-3). The first four digits of the morphology code represent the histology of the tumor while the first digit after the slash indicates the behavior of the tumor (Fritz et al., 2000). According to the ICD-O-3, a value of 3 for behavior represents a malignant tumor (primary site). For our analysis, choriocarcinoma was defined as a morphology code of 9100/3.

Table 1
Cases of primary choriocarcinoma in Texas females age ≥ 50 years, diagnosed 1995 through 2012.
Source: Texas Cancer Registry.

Case	Age (years)[a]	Race	Hispanic?	Primary site	Vital status[b]
1	50	White	Yes	Other female genital organs	Alive
2	50	White	Yes	Other female genital organs	Alive
3	50	White	Yes	Uterus, not otherwise specified	Dead
4	50	White	No	Other female genital organs	Alive
5	51	White	No	Other female genital organs	Dead
6	51	White	Yes	Uterus, not otherwise specified	Alive
7	52	Black	No	Other female genital organs	Dead
8	55	Black	No	Corpus uteri	Alive
9	56	White	Yes	Corpus uteri	Dead
10	58	White	No	Ovary	Dead
11	80	Black	No	Ovary	Dead

[a] At the time of diagnosis.
[b] As of December 2012.

4.1. Data analysis

The unadjusted incidence of primary choriocarcinoma in women aged ≥ 50 years in Texas for the period 1995 through 2012 was calculated by dividing the number of primary choriocarcinoma cases found in the Texas Cancer Registry during this timeframe in women aged ≥ 50 years by the total female population of Texas (aged ≥ 50 years) during the years 1995–2012 (Texas Department of State Health Services, 2016). The incidence was reported as the risk per 10 million women.

5. Results

The query of the Texas Cancer Registry returned a total of 12 cases (Table 1). The unadjusted incidence of primary choriocarcinoma in women aged ≥ 50 years was 2.0 cases per 10 million. Twelve cases were identified, and we deleted one of these twelve cases whose primary site was outside the genital tract. Five cases were Hispanics of white race. Six (50.0%) of the cases had expired by December 2012.

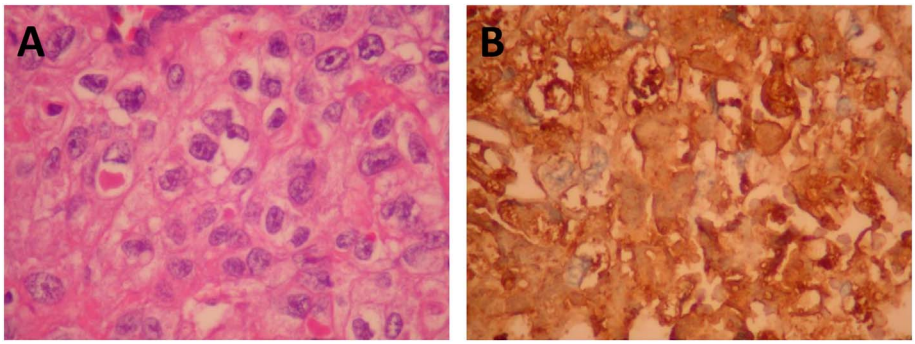

Fig. 1. Histological features of choriocarcinoma in Case 2 (A–B). (A) High magnification view of choriocarcinoma invading the uterine cervix. (B) High magnification view of choriocarcinoma in the cervix showing positivity for HCG immunostain.

6. Discussion

In premenopausal women, choriocarcinoma is a rare condition that can occur via abnormal proliferation of placental tissue, and commonly occurs within 12 months following a preceding pregnancy (Chittenden et al., 2009). However, it may present years after an antecedent pregnancy. Sixty percent of GTNs follow a molar pregnancy, 30% follow abortions, and 10% follow ectopic or term pregnancies (Chittenden et al., 2009). Common characteristics of GTN include abnormal vaginal bleeding, abdominal pain, or pelvic mass. However, it is estimated that up to 33% of patients may present with signs and symptoms related to distant metastasis (Chittenden et al., 2009).

Choriocarcinoma occurs in 1 in 40,000 pregnancies in the United States, whereas in Southeast Asia and Japan rates are significantly higher, i.e., 9.2 and 3.3 per 40,000 pregnancies respectively (Lurain, 2010). Gestational choriocarcinoma is even rarer in postmenopausal women, although the occurrence of choriocarcinoma in pregnancy is more common with advanced maternal age. Two cases from our institution consistent with gestational choriocarcinoma are reported with antecedent pregnancies which occurred 11 and 25 years prior to presentation. This is similar to pregnancy intervals reported by Tsukamoto et al. (1985) and O'Neill et al. (2008).

Our query of the Texas Cancer Registry revealed a woman (data not shown) with a primary site other than the reproductive system (soft tissue including heart). Primary extrauterine choriocarcinoma is extremely rare (Weiss et al., 2001). Several theories have been proposed to explain the occurrence of primary extrauterine choriocarcinoma. These theories include abnormal migration of retained primordial germ cells during embryonic development, metastasis from a primary gonadal tumor that regressed spontaneously, trophoblastic emboli related to molar pregnancy after a long period of latency, and dedifferentiation or metaplasia of nongonadal tissue (Di Crescenzo et al., 2013). Primary extrauterine choricarcinoma of the heart, lung, and gastrointestinal tract have been previously reported and tend to be nongestational in origin (Weiss et al., 2001).

While the diagnosis of choriocarcinoma in women over the age of 50 is very rare, the practitioner should consider choriocarcinoma as a differential diagnosis when evaluating a postmenopausal woman with an elevated serum β-hCG level.

Conflict of interest statement

The authors report no conflict of interest.

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