

Normal Production of Human Chorionic Gonadotropin in Menopause

TO THE EDITOR: A positive test for the presence of human chorionic gonadotropin (hCG) before menopause is an indication of pregnancy.¹ A positive hCG test in menopausal women poses a diagnostic challenge, despite available guidance in the literature.^{1,2} Erroneous assumptions regarding the presence of cancer have led to costly diagnostic testing, delays in necessary treatment, and even the initiation of toxic cancer treatments.

Pituitary production of hCG was first demonstrated 30 years ago, and many contemporary reports indicate that the pituitary produces hCG.¹⁻⁴ Low levels of hCG accompany the midcycle preovulatory surge of luteinizing hormone,¹⁻⁴ and pituitary hCG is normally produced with increasing menopausal production of luteinizing hormone, owing to the decreased production of estrogen and the suppression of progesterone.¹

In 2006, the USA hCG Reference Service consulted on the treatment of 120 premenopausal or menopausal women with serum hCG levels above 2 mIU per milliliter. Formal laboratory consultation was requested for 28 of these women; we present the results of the study here. Three women were prematurely menopausal due to primary amenorrhea or surgical oophorectomy at the ages of 29, 35, and 39 years; 25 were naturally perimenopausal or menopausal at the ages of 42 to 69 years. In most cases, hCG was detected during a preoperative or pretreatment evaluation (Table 1). The mean (\pm SD) level of hCG was 9.5 ± 6.5 mIU per milliliter (range, 2.1 to 32.0), and all 28 women had variably elevated levels of luteinizing hormone; 12 had levels of more than 200 mIU per milliliter. Although hCG levels ranged from 2.7 to 19.0% of luteinizing hormone levels, there was no correlation between measures of the two hormone levels ($r^2=0.78$).

Pending investigation of the hCG source, scheduled surgery was postponed for eight patients, including three who were scheduled to undergo renal transplantation. Six women had a history of gestational trophoblastic disease; therefore,

recurrent disease was assumed, and unnecessary chemotherapy given to three. In all cases, only pregnancy-type hCG was detected. Hyperglycosylated hCG, a marker of gestational trophoblastic neoplasm, and the hCG free β -subunit, the form of hCG produced by nontrophoblastic tumors, were absent in all patients.^{2,5} Results for all 28 patients support the hypothesis of normal pituitary function as the origin of the low level of hCG. Suppression of pituitary hCG production with a minimum of 2 weeks of treatment with estrogen-progesterone hormone-replacement therapy was recommended to all 28 patients. Outcome information was provided for 18 of the 28 patients (64%). In all 18 patients, hormone-replacement therapy suppressed the production of hCG to less than 2 mIU per milliliter.

Since measurement of serum or urinary hCG is increasingly performed in women as part of a preintervention assessment, positive results in menopausal women continue to create diagnostic problems that are potentially stressful. Low-level production of hCG is clearly normal in menopausal women. The finding of an hCG level of 32 mIU per milliliter or less in menopausal women may be sufficient to conclude that there is a pituitary source of hCG. However, the pituitary origin is easily confirmed by the resolution of hCG levels after the administration of hormone-replacement therapy for 2 or more weeks.

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Table 1. Histories of 28 Menopausal Women with Detectable Levels of hCG.*

Patient No.	Age yr	Level of hCG† mIU/ml	History	Result after Consultation
1	49	2.1	Recent history of persistent mole; administration of dactinomycin ineffective	≥2 wk HRT; hCG, <2 mIU/ml
2	51	3.3	Recent history of complete hydatidiform mole; administration of methotrexate ineffective	≥2 wk HRT; hCG, <2 mIU/ml
3	69	3.5	History (10 yr) of low hCG level; exploratory abdominal surgery unremarkable	Not available
4	52	3.7	Test before cosmetic surgery; procedure postponed	≥2 wk HRT; hCG, <2 mIU/ml
5	48	4.1	Abdominal pain; question of cancer	Not available
6	45	4.2	History of choriocarcinoma; lung nodule imaged; question of chemotherapy	Not available
7	55	5.3	Test before orthopedic surgery; procedure delayed	≥2 wk HRT; hCG, <2 mIU/ml
8	39	5.8	Suspected lung nodule (after oophorectomy); question of chemotherapy	≥2 wk HRT; hCG, <2 mIU/ml
9	53	5.9	Test before orthopedic surgery; procedure canceled	≥2 wk HRT; hCG, <2 mIU/ml
10	53	7.0	Test before pelvic surgery; procedure delayed	Not available
11	53	7.2	Test before renal transplantation; procedure postponed	Not available
12	53	7.3	History of ovarian cancer (after oophorectomy); question of recurrence	≥2 wk HRT; hCG, <2 mIU/ml
13	56	7.3	Test before elective surgery; procedure delayed	≥2 wk HRT; hCG, <2 mIU/ml
14	51	7.4	Incidental test; nodule imaged; question of extragonadal germ-cell tumor	≥2 wk HRT; hCG, <2 mIU/ml
15	57	7.9	Test before surgery; history of breast cancer; recurrence suspected	≥2 wk HRT; hCG, <2 mIU/ml
16	54	8.2	Test in emergency room; question of therapy	Not available
17	55	8.2	Suspected lung nodule; question of therapy	≥2 wk HRT; hCG, <2 mIU/ml
18	52	9.0	History of complete hydatidiform mole; administration of methotrexate ineffective	≥2 wk HRT; hCG, <2 mIU/ml
19	54	10.2	History of complete hydatidiform mole; administration of methotrexate ineffective	≥2 wk HRT; hCG, <2 mIU/ml
20	52	11.0	Left-quadrant pain (after oophorectomy)	Not available
21	48	11.4	Test before shoulder surgery; procedure postponed	≥2 wk HRT; hCG, <2 mIU/ml
22	35	12.4	Test before nasal surgery (after oophorectomy); procedure delayed	Not available
23	50	13.0	Test before renal transplantation; surgery postponed	≥2 wk HRT; hCG, <2 mIU/ml
24	29	14.2	Amenorrhea after administration of oral contraceptives; question of gestational trophoblastic disease	≥2 wk HRT; hCG, <2 mIU/ml
25	52	14.5	Test during annual evaluation with finding of elevated CA-125; question of ovarian cancer	≥2 wk HRT; hCG, <2 mIU/ml
26	59	16.0	Test in emergency room; question of therapy	≥2 wk HRT; hCG, <2 mIU/ml
27	42	23.8	Suspect lung nodule (postmenopause); question of cancer	Not available
28	60	32.0	Test before renal transplantation in patient undergoing hemodialysis; surgery postponed	Not available

* All patients were identified by the U.S. hCG Reference Service. HRT denotes hormone-replacement therapy.

† hCG was measured in the serum as pregnancy-type hCG.

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