

Elevated human chorionic gonadotropin HCG serum level in germ cell testicular tumor

Opinion

Testicular cancer is cancer that develops in the testicles, More than 90% of cancers of the testicle develop is germ cell tumors. These are the cells that make sperm. The 2 main types of germ cell tumors (GCTs) in men are:

- a. Seminomas
- b. Non-seminomas, which are made up of embryonal carcinoma, yolk sac carcinoma, choriocarcinoma, and/or teratoma.¹

One of the most important diagnostic methods is laboratory-based tests are potentially useful in screening for early malignancy, aiding cancer diagnosis, determining prognosis, surveillance following curative surgery for cancer, Tumor markers are playing an increasingly important role in cancer detection and management.

In case of testicular cancer diagnosis/case finding, staging, prognosis determination, alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), and lactate dehydrogenase (LDH) are recommended, they play an important role as serum tumor markers for in the staging and monitoring of germ cell tumors.²

But what the relationship between HCG serum levels and germ cell testicular tumors?

Human chorionic gonadotropin (HCG)

HCG is a glycoprotein hormone composed of two dissimilar subunits, α and β , joined noncovalently. It is produced by trophoblast tissue in pregnancy and trophoblast disease and in small amounts by certain poorly differentiated cancers. The α -subunit of HCG is similar to that of the pituitary glycoprotein hormones. It is produced principally by the trophoblastic cells of the placenta but may also be produced by nontrophoblastic tissues including normal pituitary and neoplastic cells.³ It is normal for non-pregnant women and men to make very small amounts of HCG, with blood levels less than 5mIU/mL. If HCG is high in non-pregnant women or men, it may indicate cancer.⁴ Where used in malignant causes as tumor marker which is secreted by some cancers including choriocarcinoma, endometrium, and ovarian carcinoma. HCG is elevated in most type of testicular cancer seminomas and non-seminoma germ cell testicular tumors.

It has been found that HCG possesses a role in the angiogenic process *in vivo* and *in vitro* by increasing capillary formation and endothelial cell migration, also, hCG-induced neovascularization. HCG may regulate vascular neof ormation through vascular endothelial growth factor (VEGF).⁵

HCG contains five acidic asparagines-linked sugar chains. These five sugar chains are derived by sialylation from three neutral oligosaccharides: two biantennary (N-1 and N-2) and one monoantennary (N-3) complex-type oligosaccharides. The malignant transformational change of the sugar moiety of HCG can be explained by an increase of a fucosyltransferase.⁶ Which indicate that N-acetylglucosaminyltransferase IV (GnT-IV) is abnormally expressed in the malignant cells.⁷

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There are independent variants of HCG, each produced by different cells with separate biological functions. Multiple molecular variants of HCG include intact HCG, nicked HCG (hCGn), free β -subunit HCG (hCG β), nicked free β -subunit HCG (hCG β n), free α -subunit hCG (hCG α), and the β -core fragment hCG (hCG β cf). In addition, HCG is differentially glycosylated in various tissues, resulting in a range of molecular forms from hypoglycosylated to hyperglycosylated. So-called hyperglycosylated HCG (hCG-h) is probably the best known of these glycosylated variants,⁸ each one of them sharing the common amino acid sequence but each differing in meric structure and carbohydrate side chain structure.

Hcg that produced by trophoblast cells take over corpus luteal progesterone production from luteinizing hormone (LH) Free β -subunit is the alternatively glycosylated monomeric variant of hCG made by all non-trophoblastic advanced malignancies. Free β -subunit promotes growth and malignancy of advanced cancers, Stimulates implantation by invasion of cytotrophoblast cells as occurs at implantation of pregnancy, blocks apoptosis, growth and malignancy of choriocarcinoma cells.⁹ Therefore, a question, Do all type of variants hCG linked with malignancy?

Unfortunately, studies on hCG-h in testicular cancer are limited, most studies have shown that the most variants of HCG that has related to testicular cancer is hyperglycosylated hCG (hCG-h). Most of the HCG expressed by testicular cancers is hyperglycosylated at diagnosis stage, preoperatively, at relapse, and shortly after treatment.¹⁰

Hyperglycosylated human chorionic gonadotropin (hCG-H) is a carbohydrate with double-sized oligosaccharide side chains; glycosylation variant of hCG, heterogeneous molecule produced is produced exclusively by stem cytotrophoblast cells, by trophoblastic cells in pregnancy and in gestational trophoblastic diseases including cancer of the trophoblastic cell or choriocarcinoma. It is also produced by other trophoblast sources including testicular germ cell malignancies. Regular HCG is produced only by differentiated syncytiotrophoblast cells.¹⁰⁻¹² it is also expressed as particular glycoforms by certain malignancies. These glycoforms, which are called "hyperglycosylated" HCG (hCGh), have been reported to contain more complex glycan moieties.¹³

A hyperglycosylated free beta-subunit is produced by a high proportion of all malignancies. This also functions as an autocrine

by promoting the growth and invasion of the malignancy, primarily hyperglycosylated HCG is produced in early pregnancy and in choriocarcinoma and germ cell testicular malignancies. Only free beta-subunits may be produced in other germ cell malignancies.¹⁴

Choriocarcinoma cells not only synthesize human chorionic gonadotropin (HCG), but also express LH/CG receptors on the cell membrane. HCG and LH/CG receptors may play a role in regulating the biological function of choriocarcinoma cells in an autocrine/paracrine manner. HCG, through its binding to the LH/CG receptor, may augment proliferation and inhibit apoptosis in choriocarcinoma JAr cells, and that the introduction of an antisense gene may be a potential approach to the inhibition of choriocarcinoma cell growth.¹⁵

Only small proportions of hCG-H are made in the absence of trophoblast invasion (<2% of total HCG), Four model systems have been used for studying the invasive functions of cytotrophoblast cells. All four cytotrophoblast models produce exclusively hCG-H and small amounts of HCG free b-subunit and no detectable regular HCG. Its established functions are autocrine rather than endocrine, modulating trophoblast cell apoptosis, more resembling those of a cytokine than a hormone.¹⁶

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Conflict of interest

The author declares no conflict of interest.

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