Clinical Chemistry
Trainee Council

PEARLS OF LABORATORY MEDICINE

Tumor Markers: alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG)

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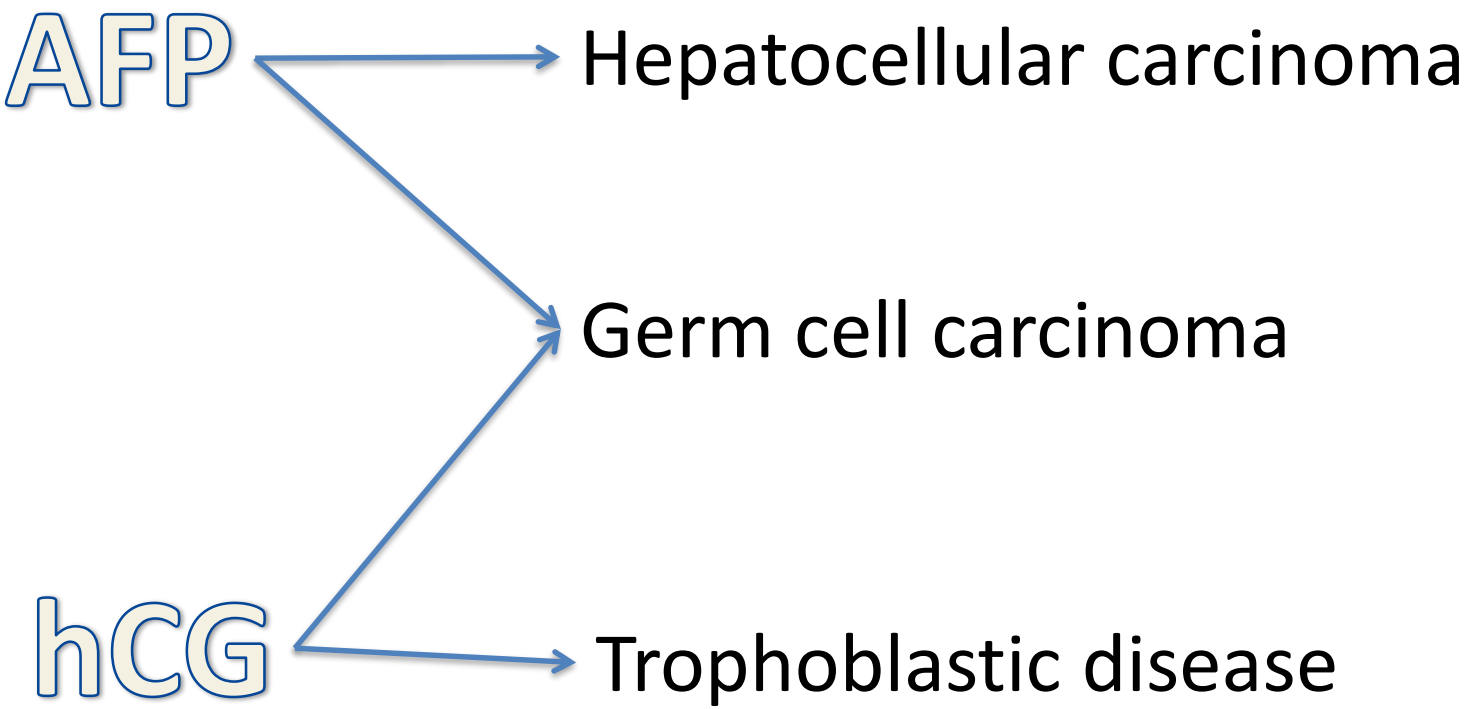
Alpha-fetoprotein (AFP)

- Oncofetal antigen
  - —High concentration in the sera of fetuses
  - —Related to albumin
  - —Low concentrations after birth; may be undetectable
  - —May increase in some malignancies (e.g., hepatocellular carcinoma)
- Glycoprotein with 70KDa and 4% carbohydrate
  - —Tumor-derived AFP composed of varying amounts of carbohydrate

Human Chorionic Gonadotropin (hCG)

- Glycoprotein secreted by the syncytiotrophoblastic cells of the normal placenta
- Elevated concentrations seen in pregnancy
  - —See the Pearls of Laboratory Medicine on Human Chorionic Gonadotropin by Dr. David Grenache for more details

AFP and hCG as Tumor Markers



AFP in Hepatocellular Carcinoma

- Diagnosis
  - AFP > 1000 µg/L → often increased in cancer
  - Can detect 50% of HCC at this cutoff
  - AFP of 500 µg/L → biopsy
  - Concentration of AFP approximates tumor size
    - To detect small tumors (< 5cm), a cutoff of 10 – 20µg/L is recommended
- Screening
  - Only for high-risk populations/countries (ex: China, Africa, Japan, Alaska)

AFP in Hepatocellular Carcinoma

- Prognosis
  - AFP > 10 µg/L and serum bilirubin > 2mg/dL → shorter survival time
- Monitoring of therapy
  - Post surgery → AFP decrease
  - A significant increase in AFP → metastasis
  - AFP can only be used in cases where AFP was elevated before treatment

Specificity of AFP for HCC

- Specificity is low
- Elevated AFP can also be seen in:
  - —Benign liver conditions (e.g., hepatitis and cirrhosis)
  - —Stomach, colon, lung, and breast cancers; lymphoma
  - —But typically (95%) with AFP < 200 ug/L

hCG in Trophoblastic Tumors

- Diagnosis
  - hCG frequently > 1 million IU/L
  - Concentration of hCG approximates tumor volume
  - hCG also elevated in:
    - 70% of patients with nonseminomatous testicular germ cell tumors
    - 45 – 60% of biliary and pancreatic cancers
    - 10 – 30% of bladder, renal, prostate, liver, colorectal, lung, breast, head, and neck cancers

hCG in Trophoblastic Tumors

- Prognosis
  - Hyperglycosylated form may help in:
    - Detecting new or recurrent trophoblastic malignancy
    - Discriminating active from quiescent trophoblastic neoplasia
  - Elevated hCG in CSF → metastasis to the brain

hCG in Trophoblastic Tumor

- Monitoring treatment and progression
  - Most useful:
    - During chemotherapy → weekly monitoring
    - After remission → annual monitoring
  - hCG concentration correlates with tumor volume and progression
    - hCG > 400,000 IU/L → high risk for treatment failure
    - Post surgery, slow decrease in hCG → presence of residual disease

hCG – Analytical Concerns

- Important to measure total β-hCG (intact hCG + free β subunit), as tumors may produce significant amounts of only the β subunit
- Equal molar recognition of hCG and hCGβ
- Cross-reactivity with LH < 2%
- hCG detection limit requires < 1 IU/L, although a challenging limit for most commercial hCG assays

AFP and hCG for Testicular Tumors

- Diagnosis
  - Seminoma patients
    - hCG < 300 IU/L (AFP not elevated)
  - Nonseminomatous germ cell tumors
    - hCG > 1000 IU/L
    - Or hCG < 300 IU/L and AFP elevated
- Prognosis
  - Good
    - hCG < 5000 IU/L and AFP < 1000 µg/L
  - Poor
    - hCG > 50, 000 IU/L and AFP > 10,000 µg/L

AFP and hCG for Testicular Tumors

- Monitoring of response to therapy
  - Weekly until concentrations within reference interval
  - Determining half-life is recommended
    - Normal $t_{1/2}$ hCG = 1.5 days, $t_{1/2}$ AFP = 5 days
    - During chemotherapy, $t_{1/2}$ hCG > 3.5 days or $t_{1/2}$ AFP > 7 days → recurrence and adverse prognosis
- Surveillance
  - Serial monitoring is recommended
  - Frequency is determined by tumor type, stage, treatment, and likelihood of relapse

Note: Lactate Dehydrogenase has also historically been used as a tumor marker for testicular tumors.

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Disclosures/Potential Conflicts of Interest

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