Falsely Elevated Testosterone Levels: Role of LC-MS/MS

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Abstract

- Immunoassays are commonly used in clinical laboratories for analyzing protein antigens and steroid hormones, including testosterone

- Advantages: availability as commercial kits, low cost, simplicity

- When there is discordance between clinical scenario and laboratory tests consider laboratory errors, including interfering substances

Case Report

- A 17-year-old female with facial acne was referred to us for elevated testosterone levels
- She was of Greek descent and reported having had coarse dark hair growth on upper lip, chin, chest for which she previously underwent laser therapy
- Her menstrual cycles were regular and predictable
- On physical examination, she was normotensive with BMI of 22kg/m². She had coarse dark hair on upper abdomen, lower abdomen and medial thighs with Ferriman-Gallwey score of 7, genital exam did not reveal clitoromegaly
- On initial testing, serum total testosterone was 417ng/dL (range: <75ng/dL)

Imaging Tests

- Pelvic and renal ultrasound: normal appearing ovaries, kidneys and adrenal glands
- MRI requested, not done prior to endocrine evaluation

Clinical Course

- Suspected falsely elevated testosterone levels since clinical scenario was discordant from laboratory test results
- On dilution, results were non-linear indicating interference
- Total testosterone levels after addition of heterophilic antibody blocking reagent resulted as 114ng/dL (from 422ng/dL) which indicated heterophile antibody interference.
- To obtain true testosterone levels, we repeated the test using liquid chromatography tandem-mass spectrometry (LC-MS/MS) which revealed total testosterone level as 19ng/dL
- Pending MRI was canceled

Heterophilic Antibodies: When to suspect interference?

- Patients with history of previous false results in immunometric assays
- Patients previously exposed to animal antibodies similar to assay antibodies
- Patients with seropositive rheumatic disease
- When results strongly impact treatment e.g. tumor marker hCG

Immunology Values

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Refernces

- Immunoassays, although widely used, are limited by cross-reactivity, matrix effects and heterophilic antibodies
- LC-MS/MS has superior performance and sensitivity for measurements at low concentrations including steroid hormones such as testosterone, estradiol, cortisol, 17-hydroxyprogesterone
- Repeat testing using LC-MS/MS for steroid hormones, such as testosterone, should be considered to prevent unnecessary repeat testing and imaging when clinical picture and laboratory tests are discordant

Discussion