

**"Close Shave": K-Case for K-C (Educational Exercise)**

**In the K-C mailing, we presented the following scenario and question related to specimen K-13:**

The patient is a 56 year-old man with increased weight gain and breast enlargement, especially over the past three months. The left breast is most affected and after several weeks of mild discomfort, the patient decides to consult his family physician.

The patient relates no recent history of changes in libido or erectile function. He is married with two children. He does admit, upon questioning, that recently he does not seem to have as much of a beard in the morning when he shaves. He denies headache and has no visual difficulties. He is a non-smoker but drinks four to five beers each day. On physical exam, his breasts appear enlarged bilaterally with a tender mobile mass under the left areola. There is no erythema or nipple discharge. The rest of the physical exam appears similar to his baseline. Both testes are soft and without masses. His physician orders some laboratory tests, including several hormone levels.

Review the results your laboratory obtained for estradiol, FSH, LH, prolactin and/or testosterone for specimen K-13. Using your laboratory's appropriate reference ranges, what would be the most likely cause of the patient's new problem?

- A. Primary hypogonadism
- B. Secondary hypogonadism
- C. Leydig cell tumor
- D. Liver disease
- E. Idiopathic gynecomastia

*We apologize for including this case in the K-C mailing.* It was meant for a Y survey (which includes the hormones mentioned above). Next year, we are renaming K-Kases "Chem-Cases", and they will begin to appear in other surveys managed by the Chemistry Resource Committee (see note below). A small number of participants did answer the question, however. The majority (39%) believed that the most likely cause of the patient's problem was idiopathic gynecomastia; 28% chose secondary hypogonadism; 13% chose primary hypogonadism; another 13% chose liver disease; and a small minority (6%) chose Leydig cell tumor.

Gynecomastia is the presence of palpable mammary tissue (not just fat) in the male breast. It is very common (and also commonly asymmetric). The differential diagnosis is very extensive but a common theme is alteration of the ratio of estrogens to androgens due to either an increase in estradiol or a decrease in testosterone production.

Most of the estradiol present in men arises from aromatization of testosterone in the periphery; this may be enhanced in liver disease because of a decrease in the metabolism of adrenal androgens (which are converted to estradiol in the periphery. Very rarely testicular tumors producing estradiol (such as Leydig cell tumor) or human chorionic gonadotropin (such as germ cell tumors) may elevate estradiol directly. This specimen should have had a normal estradiol level, making liver disease or Leydig cell tumor less likely. The gonadotropin levels (FSH and LH) should have been normal, making primary hypogonadism unlikely. The total testosterone should have been low for an adult male, and, without elevated gonadotropins, this finding should raise the possibility of secondary hypogonadism. The prolactin should have been normal, making hyperprolactinemia (or a pituitary tumor unlikely to be involved. Other causes of secondary hypogonadism include chronic illness, aging and

drugs. Further evaluation of this patient may be warranted, especially since he has symptoms (pain in the affected breast as well as reduced beard growth).

Like the ambulation of the character in the riddle of the Sphinx (who walks on four legs in the morning; two legs in the afternoon; and three legs in the evening), gynecomastia is common during early infancy, puberty, and in older men. It should not be surprising that the majority of the respondents chose idiopathic gynecomastia in our case. This is usually the most frequent diagnosis after other causes have been ruled out. If this patient is obese (his history includes recent weight gain), increased aromatization in adipose tissue may be the culprit and some have argued that the relatively high prevalence of mild gynecomastia in older men means that it may simply be part of the normal aging process. In any event, laboratory testing in gynecomastia should probably be focused on ruling out significant causes such as tumors, as it is unlikely that any specific diagnosis can otherwise be made.

Jim Faix MD, for the Chemistry Resource Committee

Read more about it: Braunstein GD: Gynecomastia. *New Eng J Med* 2007; 357:1229-1237.

*NOTE: Chem-Cases are educational exercises using CAP proficiency testing specimens to mimic real-life laboratory situations. Participation is optional. Responses will not be graded and will not be included in the individual laboratory reports. Beginning in 2009, cases will appear in many of the Surveys managed by the Chemistry Resource Committee. They will also appear on the Chemistry Resource Committee's webpage so that more laboratories may review them, even if they do not participate in the Survey in which the Chem-Case appears. Watch for an announcement of this new feature soon.*