Recurring Painful Ectopic Gynecomastia in a Young Male - A Case Report

Antonio Ochoa Pescador, Jr, MD, Celeste Ong Ramos, MD.
St. Lukes Medical Center, Quezon City, Philippines.

Painful lumps in the axillary area are relatively common and could normally be brought about by several etiologies, more commonly, lipomas, fibroadenoma, hidradenitis suppurativa, lymphoma, or breast cancer. However, recurring painful ectopic gynecomastia in the axillary area of a male patient is of rare occurrence with only few reports in the literature. Here, we report a case of a 25 year old male, who presented to our clinic due to recurring painful right axillary mass. He denied any prior history of trauma, infection, breast mass, or previous lymphadenopathy, decrease in libido nor erectile dysfunction. The mass appeared to be truly subcutaneous at the interface of skin between the superior axilla and the medial arm. Breast exam did not reveal any palpable masses nor abnormalities. Ultrasonography of the right axillary region revealed findings that may represent an accessory axillary breast tissue and histological evaluation revealed an accessory breast tissue with gynecomastia. For such cases, individual treatment requirements can range from simple reassurance to medical treatment or even surgery, all depending on the possible etiology. Due to the diversity of possible etiologies, performing a careful history and physical examination is imperative and the need for hormonal evaluation is warranted to be able to arrive at a certain diagnosis.

Reproductive Endocrinology
MALE REPRODUCTIVE HEALTH

Safety and Efficacy of Clomiphene Citrate in the Treatment of Secondary Hypogonadism. A Retrospective Study

Mariana Garcia-Touza, MD.
KCVA, Mission Hills, KS, USA.

"**Introduction:** Clomiphene (Clomid) has an off-label indication to treat hypogonadism in select populations. "Based on clinical practice, this medication in certain types of hypogonadism is equally effective as testosterone in treating hypogonadism. It will lead to less side effects, lower treatment cost, and will decrease rates of infertility in the male veteran population." Secondary hypogonadism can be most often caused by opioid use, obesity, sleep apnea, and diabetes." "**Aim of Study:** To evaluate the safety and efficacy of Clomiphene Citrate in Treatment of Secondary Hypogonadism in comparison with testosterone. "**Study Population:** Data was obtained from the Veterans Administration Data Warehouse through the Veterans Administration Informatics and Computing Infrastructure. Data was extracted using SQL. There were 405,824 male patients with a diagnosis of hypogonadism (87.1%)and infertility (12.9%). nationally at the VA. Of these, 9566 patients have been treated with clomiphene citrate and 232,123 with various testosterone therapy. " The two groups were then matched by propensity method to controls at a ratio of about 1:1 for Age, race, BMI and time for follow-up as potential confounding factors hat could have affected inclusion in the study controls. Patients without either Clomiphene or testosterone treatment were excluded. **Statistical Analysis:** SAS was used for propensity matching (PSM, greedy near) Categorical variables were evaluated as frequency counts with percentage within group, as well as ODDS ratio (OR) and differences were evaluated by a chi-square method. Comparisons of continuous variables were done were done by simple and paired t-test. Kaplan Meier plots and Cox Hazard ratio calculations were used to examine time dependent risk between treatments. Actual p-values are shown and p-values lower than 0.0001 are shown as such. All comparisons used a two-sided assumption. **Measurements:** Testosterone laboratory measures were recorded for start and end of trial. Survival was taken as the difference in days between start date and date of death. New diagnosis of Osteoporosis and Polycythemia was that which occurred after initiation of therapy. "**Results:** Clomid treatment normalized testosterone levels in 53.2% versus 46.8% in the testosterone group (OR 1.32 P<0.005). All-cause mortality was in the clomid group 0.16% and 1.62%in the testosterone group (OR 0.16 P<0.001). The incidence of new Osteoporosis for clomid was 3.9 % versus 5.9% for testosterone (OR 0.65 P<0.001)" **Conclusion:** This is a retrospective study comparing the efficacy and side effects of clomiphene versus testosterone for treatment of hypogonadism. The study showed that clomiphene is more effective than testosterone to treat secondary hypogonadism. We also found decreased overall mortality and incidence of polycythemia and osteoporosis.

Reproductive Endocrinology
MALE REPRODUCTIVE HEALTH

Serum Insulin-Like Factor 3 Levels Are Reduced in Former Users of Anabolic Androgenic Steroids Suggesting Persistent Impaired Leydig Cell Function

Jon Bjarke Jarløv Rasmussen, MD, PhD[1], Jakob Albrethsen, PhD[1], Mikkel N. Frandsen, Bsc[1], Niels Jørgensen, MD, PhD[2], Anders Juul, MD, PhD, DMSC[1], Caroline Kistorp, MD, PhD[1].
[1]RIGSHOSPITALET, Copenhagen, Denmark, [2]Rigshospitalet, Kobenhavn, Denmark.

Background: Illicit use of anabolic androgenic steroids (AAS) has emerged as a public health concern among men, but the long-term effect on gonadal function is still unresolved. Serum insulin-like factor 3 (INSL3) has emerged as a novel and potentially superior marker of Leydig cell function than serum testosterone per se. INSL3 synthesis and secretion exhibit far less daily variation than testosterone. Further, serum INSL3 levels are not related to body composition. The objective of this study was to investigate INSL3 as a marker of Leydig cell function in former AAS users. **Methods:** Community-based cross-sectional study including men aged 18 - 50 years, involved in recreational strength training and allocated to one of three groups: current (n = 46) or former AAS users (n = 42) or controls (n = 44). Mean age (SD) of all participants were 32 (7) years and the elapsed duration since AAS cessation, geometric mean (95% CI), was 32 (23; 45) months in former AAS users. All procedures were performed during one visit in the morning hours following overnight fasting. We drew blood through a cannula placed in an antecubital vein

following 30 minutes of supine rest. Medical records, testicular size, questionaries, and detailed history of strength training and AAS use were obtained in a structured interview. Serum INSL3 and testosterone were measured using liquid chromatography mass spectrometry. **Results:** Serum INSL3 was markedly suppressed among current AAS users compared with former AAS users and controls, P < 0.001. Additionally, former AAS users also displayed lower serum INSL3 concentrations than controls, mean (SD), 0.43 (0.31) versus 0.60 (0.22) μg/L, P = 0.006 and the difference remained significant in a multivariate linear regression, (B) (95%CI), -0.17 (-0.28;-0.55) μg/L, P=0.004, adjusted for plasma LH, plasma sexual hormone-binding globulin, age, body fat %, smoking and use of other illicit drugs. Longer accumulated duration of AAS use (log2) was associated with reduced serum INSL3 levels in former AAS users, (B) (95%CI), -0.08 (-0.14;-0.01), P=0.022, suggesting a dose-response relation between AAS use and suppression of serum INSL3. We evaluated the association between INSL3 and total testosterone levels and they were not associated among former users and controls in a multivariate linear regression, P=0.821. We noted recovery of serum inhibin B levels among former AAS users reaching the mean plasma level of controls after elapsed duration since AAS cessation of ≈ 21 months; (B) (95%CI), 2.2 (0.7; 3.7) months, P = 0.006. In contrast, we did not note any recovery of serum INSL3, P = 0.541, or total testosterone, P = 0.861, among former AAS users. **Conclusions:** Serum INSL3 is decreased years following AAS cessation in former AAS users, independently of plasma testosterone, suggesting persistent impaired Leydig cell function, which should be investigated further.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH

Use of a Lab-Ordering Pathway to Improve Adherence to Endocrine Society (ES) Guidelines for Early AM Timing and Testosterone Assay Method for Establishing Testosterone Deficiency

Emily Gammoh, MD[1], Alexandra Clark, MD[2], Erika Hoffman, MD[2], R Harsha Rao, MD, FRCP[2].
[1]University of Pittsburgh Medical Center, Pittsburgh, PA, USA, [2]VA Pittsburgh Healthcare System, Pittsburgh, PA, USA.

Introduction: Primary care providers (PCPs) prescribe the bulk of testosterone replacement therapy (TRT) at our institution, but our data show they are less likely than endocrinologists (ENDOs) to follow ES Guidelines for diagnosis of hypogonadism, based on two unequivocally low early AM [T] levels by tandem mass spectrometry (LC/MS/MS, PCP:213/783[27%]; ENDO:104/164[63%];p<0.0001). **Methods:** A lab ordering pathway was promulgated to direct PCPs to order 8AM T based on whether it was for monitoring therapy or diagnosing hypogonadism. The former leads to an order for Total T by electrochemiluminescence immunoassay (ECLIA), whereas the latter presents a choice between "*Initial (diagnostic)*" T or "*Confirmatory*" T. Ordering an initial diagnostic T requires a symptom to be chosen from a list of Low Libido, Loss of Early Morning Erections (EME), Fatigue, Erectile Dysfunction, or Other. Low libido or EME loss leads to an order for 8AM total T by LCMSMS, with a pop up reminder to instruct the patient to present at 8AM. Choosing any other symptom triggers a warning of non-specific symptoms, and an option to order 8AM total T by ECLIA, with the same pop up warning regarding timing. Ordering a confirmatory T requires a low initial 8AM T. **Objective:** To compare adherence by PCPs to ES guidelines based on timing and assay method for diagnosis of hypogonadism in the 6 months before (PRE) and 6 months after (POST) the date the pathway was promulgated. **Results:** There were 678 PRE and 884 POST lab orders for a diagnostic T for suspected hypogonadism. Although, adherence to 8AM timing was similar before and after promulgation (PRE 362/678[53.4%]; POST 452/884[51.1%]), there was a significant increase in the use of the accurate assay LC/MS/MS (PRE 39/678 [5.7%]; POST 105/884[11.9%];p<0.001). The 6.3% increase in LC/MS/MS use was reflected in a proportionate 7.3% reduction in ECLIA use (PRE 323/678 [47.6%]; POST (347/884 [39.3%]). Of note, all 105 patients in the POST cohort had a specific symptom (Loss of libido/EME) to justify the LC/MS/MS assay, whereas there was no such justification in the 39 in the PRE cohort. **Conclusions:** Promulgating a lab ordering pathway induced more appropriate use of LC/MS/MS in patients with specific symptoms associated with a high pre-test probability of hypogonadism. Although encouraging, it remains to be determined whether the more appropriate use of LC/MS/MS assays impacted testosterone prescribing practice. On the other hand, the lab ordering pathway did not improve adherence to early AM timing, despite the inclusion of pop up reminders to instruct patients to report early for blood draw. It is unclear whether that is attributable to PCPs not following through with the reminders, or to patients not following instruction due to ignorance, non-compliance, or practical problems, such as transportation and/or wait times at the lab. The lack of adherence to early AM timing has major implications for TRT.

Reproductive Endocrinology

OVARY, TESTES, AND IMPACT OF HORMONES ON METABOLIC FUNCTION

A Novel Mouse Model for Studying the Effects of Cyp17 Overexpression in a Temporal- and Spatial-Specific Manner

CHRISTIAN SECCHI, PhD, MARTINA BELLI, PhD, DWAYNE STUPACK, PhD, SHUNICHI SHIMASAKI, PhD.
UC San Diego, La Jolla, CA, USA.

Background: Cyp17 plays a key role in theca cells (TCs) to produce androgens, which, in turn, are converted to estrogens in granulosa cells. Intrinsic alterations in ovarian steroidogenesis contribute to excessive ovarian androgen production that characterizes polycystic ovary disease (PCOS)[1,2]. Hyperandrogenism has been associated with higher levels of Cyp17 in TCs, and correlate with increased numbers of antral follicles[3]. While androgen excess is one of the hallmark features of PCOS, its putative role in the follicular development and function remains poorly known. Most efforts have used androgen administration or Cyp19 blockade approach to study how androgens prolong folliculogenesis[4]. Although some insights have been made, it is not clear if these