Reproductive Endocrinology

CLINICAL STUDIES IN FEMALE REPRODUCTION

II

Undescended Testicle and Short Stature as Manifestation of Pituitary Stalk Interruption Syndrome a Report From Saudi Arabia

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SUN-LB2

Background

Pituitary stalk interruption syndrome (PSIS) is a congenital disease with isolated growth hormone deficiency or multiple anterior pituitary hormone deficiencies. Here, the authors report a case of PSIS from Saudi Arabia.

Clinical Case

A 16 year old Saudi boy presented to the endocrine clinic with short stature and undescended testis, status post bilateral orchidopexy. He was delivered by caesarean section because of breech presentation and birth asphyxia. Investigation revealed underdeveloped secondary sexual characteristics with decreased facial and pubic hair growth. The patient height was 134 cm whereas the bone age was 9 - 11 years. Pelvis examination showed a scrotum with bilateral 1 mL testes and the stretch penile length was 3 cm. The patient laboratory investigations showed hemoglobin level of 13 g/dL, serum sodium 140 mmol/L, serum potassium 4.1 mmol/L, serum chloride 102 mmol/L, calcium 9.1 mg/dL, random blood sugar 110 mg/dL and albumin 3.8 mg/dL. A pituitary hormone profile showed hypopituitarism with thyroid, and adrenal sparing. The patient free T4 was 17.3 pmol/L (9.25 pmol/L) and synacthen test revealed a morning baseline cortisol level of 6.5 µg/dL (normal = 4.3-22.4 ug/dL) with adrenocorticotropic hormone of 9.8 pmol/L (1.1 - 13.2 pmol/L). Insulin-like growth factor 1 level 50 ng/dL (normal = 193.0 - 731.0 ug/L), follicle-stimulating hormone 0.35 µU/mL (normal, 0.0-10.0), and leutinizing hormone 0.4 µU/mL (normal = 1.2-7.8). The patient’s morning testosterone level showed 8 ng/dL (normal = 280-800 ng/dL) and prolactin 116 mIU/L (normal = 86 - 324 mIU/L). There were no symptoms suggestive of posterior pituitary involvement like polyuria and polydipsia as urine and serum osmolality. The MRI examination showed no pituitary gland identified in the sella turcica and no clear pituitary stalk. A T1 hyperintense focus with post-contrast enhancement was identified posterior to the optic chiasma representing an ectopic posterior pituitary gland. The growth hormone and testosterone therapy were added to medical therapy of the patients and no thyroid or hydrocortisone replacement therapy was given.

Conclusion: Despite the fact that this is a rare disorder, it should always be kept in the differential diagnosis of a patient presenting with short stature. Patients with this disease have an excellent opportunity to reach normal height if they present before the joining of epiphyses.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Anti-Cancer Properties of RISUG Against Prostate Cancer Cell Line PC-3 - Invitro Study

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SAT-LB9

Title: Anti-cancer properties of RISUG against prostate cancer cell line (PC3) - invitro study

Abstract

Cancer cell lines were initially established for understanding the genetic, functional, and epigenetic properties of cancer cells. The PC3 cell line is a human-derived prostate cancer cell line from the metastatic bone site of the grade IV adenocarcinoma patient. With the invention of RISUG-a polymeric male contraceptive, and studying its astonishing properties such as anti-microbial activity, there have been multiple hypotheses stating its anti-cancerous effect based on its physical and chemical nature[1]. This study focuses on understanding the effect of RISUG on prostate cancer cell line from invitro study.

For our study, 10 mg/ml working concentration of RISUG in DMSO (solvent) was used for the treatment to the cells. The dosage given to the cells for three varying incubation periods of 24 hours, 48 hours and 72 hours were analyzed for there viable cells post treatment. The dose was delivered with the media such that the final concentration of DMSO in the media is 1.5% (optimized) to avoid vehicle toxicity. The MTT assay was employed to study the cytotoxicity effect by measuring the amount of viable cells post treatment. The observations were statistically significant for the anti-cancerous effect of RISUG on PC3 prostate cancer cells for 72 hours, the optimized minimum incubation time/ time of action for RISUG to exhibit significant anti-cancer effect against PC3 cells. However, further in depth research is necessary for the understanding of the mechanism behind these actions.
Keywords: RISUG, Prostate Cancer, DMSO, Cell line, Reference: 1. Subramanian, B., Agarwal, T., Basak, P., Maiti, T., & Guha, S. (2019). RISUG® based improved intrauterine contraceptive device (IUCD) could impart protective effects against development of endometrial cancer. *Medical Hypotheses, 124*, 67-71. doi: 10.1016/j.mehy.2019.02.026

**Pediatric Endocrinology**

**PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY**

**Novel Homozygous Mutation in BMP1 Causing Osteogenesis Imperfecta**

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**SUN-LB19**

**Background:** Osteogenesis imperfecta (OI) is characterized by bone fragility and increased fracture susceptibility. Most mutations occur in *COLIA1* and *COLIA2* genes. Rarely, mutations in *BMP1* have been reported in association with OI type XIII. Disease severity is generally more severe when the mutation affects both gene products encoded by *BMP1* that serve as procollagenases: bone morphogenetic protein 1 and mammalian tolloid (mTLD) [1].

**Clinical Case:** A 7-year-old Hispanic boy, with speech and gross motor delays, sustained five bilateral tibial fractures with minimal trauma since age 2.5 years. At age 6 years, he developed severe back pain after a minor fall. Diffuse spinal osteopenia and multiple vertebral compression fractures (VCF) at T9, L1, L3 were identified radiographically, with progressive vertebral height loss in the ensuing 9 months. Fatigue was reported after walking >10 min, with difficulty running and climbing stairs. There was no family history of musculoskeletal disorders.

Stature was consistently between 10-15th% for age. Subtle facial dysmorphism included micrognathia and small chin, with patchy blue-gray sclerae, and normal dentition. The lumbar spine was tender to percussion. Gait was slow and antalgic with external rotation of the right hip.

Laboratory evaluation revealed normal serum calcium, iPTH, magnesium, phosphate, 25-hydroxyvitamin D and alkaline phosphatase for age. PINP was slightly high (193 μg/L, 30-110 μg/L) and CTX was slightly low (554 pg/mL, n: 574-1849 pg/mL), the latter being atypical for OI. Total hip BMD (adjusted for height Z-score) was normal (Z-score = 1.76) and adjusted femoral neck BMD was high (Z-score = 2.67). VCFs precluded assessment of lumbar spine BMD. Genomic analysis revealed a homozygous missense mutation in exon 4 of *BMP1* resulting in an amino acid substitution (c. C505T; p.Arg169Cys) in both the bone morphogenetic protein 1 and mTLD gene products of *BMP1*. The mutation is predicted to be damaging to both proteins, and associated with this rare form of OI.

**Conclusion:** We report a novel homozygous mutation in *BMP1* identified in a child with autosomal recessive OI. Unlike most forms of OI, patients with type XIII often have normal or increased BMD [1], making a correlation between BMD and fracture risk difficult. While bisphosphonates (BP) may help reduce recurrent fractures and provide symptomatic relief, the broad phenotypic spectrum and concern for further increasing BMD complicate management. A high resolution peripheral quantitative CT scan to assess bone microarchitecture and quality may aid in the decision of BP therapy. As evidence is limited on the effectiveness of BP in this rare form of OI, it is important to consider each case individually.

1. Sangsin, A., et al., Two novel compound heterozygous BMP1 mutations in a patient with osteogenesis imperfecta: a case report. BMC Med Genet, 2017. 18(1): p. 25.

**Reproductive Endocrinology**

**MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES**

**Prevalence of Hypogonadism in Young Obese Males**

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**SAT-LB5**

Ageing, obesity, and chronic illness are major factors affecting serum testosterone (T) levels in men. The magnitude of the impact of ageing on serum T levels is well established, for obesity this is less clear. Severe obesity may lead to isolated hypogonadotrophic hypogonadism (IHH). Several explanations have been offered to clarify the presence of reduced T levels in obese men. One relates to the technique that is generally employed to measure serum androgen levels, i.e. measurement of total testosterone (TT) instead of free testosterone (FT). TT represents the sum of FT and T bound to albumin and sex hormone binding globulin (SHBG). A profound reduction in SHBG level is commonly found in obese men, and this is a major factor causing a decrease in TT. Measurement of free testosterone levels may provide a more accurate assessment of androgen status than the (usually preferred) measurement of total testosterone in situations where SHBG levels are outside the reference range. However, reference ranges for free testosterone levels are not well established, especially in older men, and some have argued that the measurement of free testosterone levels merely reintroduces age in a covert form. This is a cross sectional study to estimate prevalence of hypogonadism in young obese males. In this study 147 young obese men participated, of which we confirmed low total testosterone (TT) levels in 35.37% of subjects with a p value of 0.06. Since only Total Testosterone was measured for categorizing subjects with or without hypogonadism, Free Testosterone measurement would be a better indicator for the diagnosis of hypogonadism as in cases where the total testosterone is borderline-low or when SHBG concentrations are abnormal. As such, the study is valuable in the context of the ongoing controversy as to whether testosterone treatment should be limited to men with classical hypogonadism, or be considered for appropriately selected...