

109 A case of allergy to gelatin included in the gonadotropin-releasing hormone analog "depot leuporelin acetate"

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Introduction: Depot leuporelin acetate (leuplin®) have been frequently used to treatment of sex hormone dependent cancer such as prostatic cancer and breast cancer in adult, and central precocious puberty in childhood. Only a few adverse events to leuplin® have been reported. We report a patient with local reaction to gelatin included in leuplin®. **Case:** The patient is a 6 9/12 year- old girl. There is no past history of allergy to DPT and measles vaccine including gelatin. At 6 years of age, she was evaluated for obesity. Physical examination showed a rapidly increment of growth rate, breast swelling, and advanced bone age. She was diagnosed as having central precocious puberty based on hormonal examination. At 6 5/12 years of age, leuplin® was initiated. After third injection of the drug, she had local reaction with erythema, induration, and tenderness. The local reactions were repeated after fourth and fifth injection of the drug, which required change to buserelin acetate. Lymphocyte stimulation test showed predominantly positive reaction to gelatin and negative to leuporelin and polyethylene glycol used as a vehicle. RAST score to gelatin was 1.12 U_g/ml (>0.34). **Discussion:** Although there are a few reports of local reactions to leuplin®, the pathologic etiology remained obscure. Allergic reaction in the patient is elucidated to be due to gelatin used as a vehicle. Therefore, consideration should be given to allergic reactions to gelatin, if a patient has a local reaction after injection of leuplin®.

111 EFFECTS OF LONG-TERM TESTOSTERONE THERAPY ON BONE MINERAL DENSITY IN MALE WITH HYPOGONADOTROPIC HYPOGONADISM

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[Aims] We investigated effects of long-term testosterone therapy on bone mineral density (BMD) in male with hypogonadotropic hypogonadism(HH), and retrospectively studied factors related to the effects of the therapy.

[Subjects] Ten Japanese male with HH (2 isolated HH, 2 panhypopituitarism with invisible pituitary stalk, and 6 panhypopituitarism with brain tumor after surgery), 19.9-39.8(median 22.7) years old, were enrolled in this study. All of them received testosterone therapy with testosterone enanthate 25-125mg/dose/4weeks increased stepwise to 150-300mg/dose/4weeks, for a period of 1.8-12.8 (median 6.3) years. They reached final height and pubic hair of Tanner stage IV or V.

[Methods] 1) BMD were measured in L2-L4 with dual energy X-ray absorptiometry (DXA) XR-36. We calculated the Z-score of the BMD using the age-matched reference value in Japanese male, after changing to the data in DXA QDR-1000. 2) We also investigated the relationship between six factors and BMD in HH: ① the age at the start of the therapy ② pubertal stage at the start of the therapy ③ the duration of the therapy ④ total dose of testosterone ⑤ dose of testosterone per year ⑥ other hormone deficiencies.

[Results] 1) The range of BMD was from 0.699 to 1.106 (median 0.969) g/cm², and the BMD in 7 out of 10 subjects were more than -2SD of age-matched standard of Japanese male. 2) BMD was not affected by the above six factors.

[Discussion] Most of the BMD in HH received the long-term testosterone therapy was normal. We prospectively investigate, whether increasing of testosterone dose may be useful in normalizing BMD in HH with low BMD.

110 EFFECTS OF PERSISTENT MATERNAL EXPOSURE TO LOW DOSE 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN ON TESTICULAR FUNCTION IN MALE RAT OFFSPRING

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[Aim] 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is the most potent congener of the polychlorinated dioxins and is regarded as one of the important endocrine disrupters. Maternal exposure to TCDD causes many irreversible abnormalities in various organs of fetus and offspring. Many of these studies, however, took place using relatively high dose of TCDD. We evaluated the effects of extremely low-dose exposure of TCDD to maternal rats on the gene of the testis of the male offspring. **[METHOD]** The dams were treated subcutaneously from pregnancy to lactation. They received a weekly dose of 10 ng/Kg TCDD. The offspring rats were killed on postnatal days 21 and 42. The testis and liver were removed and weighed. The appearance of various mRNA levels was examined with the semi-quantitative RT-PCR method. **[RESULTS]** Total newborn rats number were 42 (M:F=17:25). The testis weights were increased in TCDD group on 21 days. A significant increase in CYP11A1 mRNA was detected in the liver of TCDD treated rats. The levels of AhR and ARNT mRNA were not influenced by TCDD treatment in the liver and testis. The low dose of TCDD produced no effect on the mRNA expression of subunits of inhibin(α,βA,βB). TCDD exposure increased estrogen receptor alpha mRNA levels on 21 days, but did not affect androgen receptor mRNA levels in testis. **[Conclusion]** Maternal exposure of the extremely low-dose TCDD throughout pregnancy and lactation alters the estrogen receptor mRNA levels in the testis of male offspring.

112 THE EFFECT TO BONE METABOLIC MARKERS DURING 5% TESTOSTERONE ENANTHATE OINTMENT THERAPY

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【Case】 A 3 years-old boy was mid primary hypogonadism with glanular type hypospadias. He had a micropenis, which was 2.0cm, and his testis was less than 1 ml×2. LHRH test was almost normal response, and HCG test showed mild primary hypogonadism. The DHT to testosterone ratio was 7.13.

【methods】 5% testosterone enanthate ointment with 10 g ointment delivering 150 mg testosterone enanthate was prepared by me with agreement of parents and my hospital. He applied the ointment on their skin of penis from days 1 to 21. On day 0 (before ointment application), and day 21 (after 21 days of daily the ointment application), the subjects were admitted to our hospital. Serum T, IGFBP3, and serum and urine bone metabolic markers were measured.

【Results】 The penile length changed 2.0cm to 4.5cm. Serum IGFBP3 levels increased 1.91 to 2.35. Urine Ntx levels increased 302.4 to 514.0 nmolBCE/mmol. Cr. Other bone metabolic markers also changed. The increment rate of height didn't change.

【Summary】 We have to take care of the effect to bone during 5% testosterone enanthate ointment therapy.