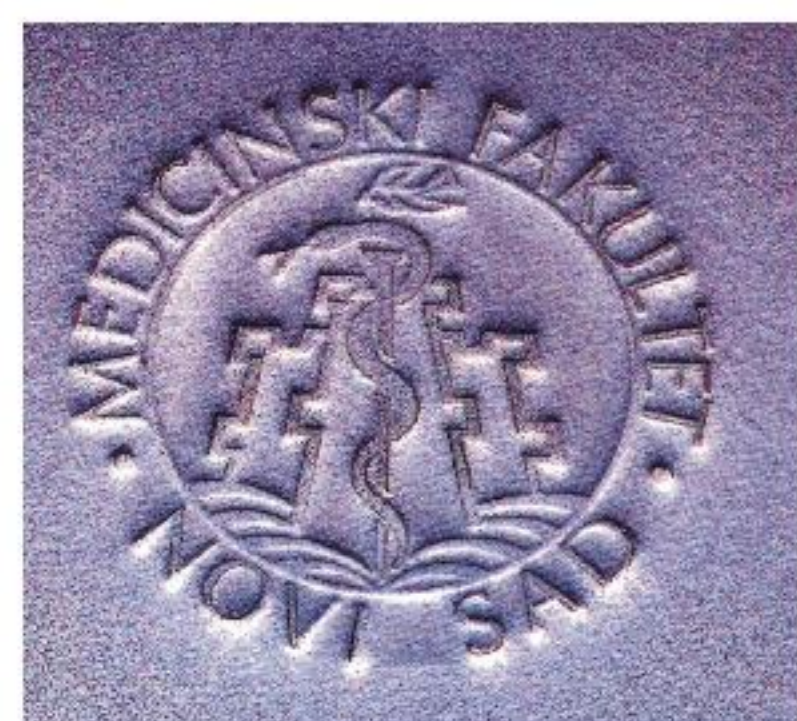


Should we initially manage young males with Kallmann's syndrome by stimulation treatment until the freezing and storage of sperm?

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Introduction: Hypogonadotropic hypogonadism(HH) is mandatory treated with testosterone(T). However, gonadotropin (hCG/FSH) administration might be the challenging optimal therapy.

Materials and methods:

Table 1: Main demographic characteristics of the case series patients assigned as Case No1,2,3 including the underlying pathology.

| | Case 1. | Case 2. | Case 3. |
|----------------------|--|---|---|
| Year at presentation | 2002.year | 2011.year | 2008.year |
| Gender | Male | Male | Male |
| Carotip | 46 XY | 46 XY | 46 XY |
| Age at presenttion | 23year old (1979.y.) | 19year old (1992.y.) | 26 year old (1982.y.) |
| Underlying Pathology | Hypophisectomy pp. adenoma hromophobum | Hypogonadism with anosmia - Sy Kallmann(KS) | Hypogonadism with anosmia - Sy Kallmann(KS) |
| BH (cm) | 187 cm | 182 | 174 |
| BW (kg) | 89 kg (+2kg) | 85 (+3kg) | 76 (+2kg) |

Table 2: History data in relation to reproductive problems

| | Case 1. | Case 2. | Case 3. |
|---------------------------------------|--|---|---------------------------------------|
| Mood -at presentation | Stable but physically „without enough energy”. | Without enough self confidence and swinging mood. | Without enough self confidence. |
| -after tetosteron or HCG therapy | Stable | Still swinging changes in mood. | New found sexuality. |
| -after HCG+HMG Tx | Stable | Still changes in mood. | Patient with full confidence. Stable. |
| Feeling physically well being. | On substitution or stimulation HCG therapy feeling well. | | |

Table 3: Physical examination findings included in Tunner stages of sexual development.

| | Case 1. | Case 2. | Case 3. |
|--|-------------------|---|---|
| HAIRINESS -face | Normally present. | Absent.Acne after Tx. | Absent. Beard, mustache on Tx. |
| -axillary | Normally present. | Absent. Developed on substitution Tx. | Relatively present!!! |
| -pectoralis | Normally present. | Absent. Scant on substitution Tx. | Absent. Developed on substitution Tx. |
| -pubic hair development | Stage 6. | Few darker hairs at base of penis (St. 2). On subst. Tx: St.6. | Stage ¼. On subst. Tx: St.6. |
| BREAST size | Stage 1. | Gynaecomastia, Stage 3 (for female). On subst. Tx: St.1. | Gynaecomastia, Stage 3 (for female). On subst. Tx: St.1. |
| TESTES length/ volume | 5cm (20ml). | 1.5cm (ultrasonogr.), 2ml (orchidometer) | 1.5cm (ultrasonogr.), 2ml (orchidometer) |
| | | without change on HMG Tx | 4x2cm (12ml) -after HMG+HCG Tx |
| PENIS -after testost./HCG Tx | Normal. | Stage 1 (2cm) | Stage 2 (2.5cm) |
| Libido and erection -ejaculation | | -longer and widened present | -longer and widened present |
| Male body shape | | without ejaculation. | without ejaculation. |
| | | normal after several month of therapy | similar phenotype as Case 2. |

Table 4: Laboratory values of endocrine tests, in basal staus and after the dynamic tests for hypothalamo- hypophyse- gonadal axis.

| | Case 1. | Case 2. | Case 3. |
|---------------------------------|---|--|--|
| FSH (U/L) | 1.5 U/L (one month after hypophisectomy) | FSH: 0.81U/L (basal) 3.27U/L (30.' LH-RH amp). | FSH: 0.57U/L (basal) 3.9U/L (60.' LH-RH amp). |
| LH (U/L) | one month later 1.5 | LH: 0.15U/L (basal) 2.81U/L (30.' LH-RH ampule). | LH: 0.10U/L (basal) 2.3U/L (30.' LH-RH amp). |
| Testosteronemia (nmol/l) | 0.day 0.069, 3.day 19.01 nmol/l . [each day 5000IU of Primogonyl (HCG)] | 0.day 1.32, 3.day 2.81nmol/L . [each day 5000IU of Primogonyl (HCG)] | 0.day 1 nmol/l |
| | | 13.9nmol/l . (3x3000i.u./w. HCG) | 14.4nmol/l . (3x3000i.u./w. HCG) |

Conclusion: Patients with HH should be treated until testes become enlarged and sperm conformed in ejaculate, initially. Beside eliminating psychosocial impact of small testes safety reasons (e.g. possible allergy on gonadotropins) should indicate the storage of a sperm before chronic testosterone therapy.

Results:

Figure 1: MR images of a cases (No2,3) with Kallmann syndrome and normal individual with this respect (No1). Coronal T2-weighted MR image: biltral agenesis of the olfactory bulbs and shortened olfactory tracts (arros).

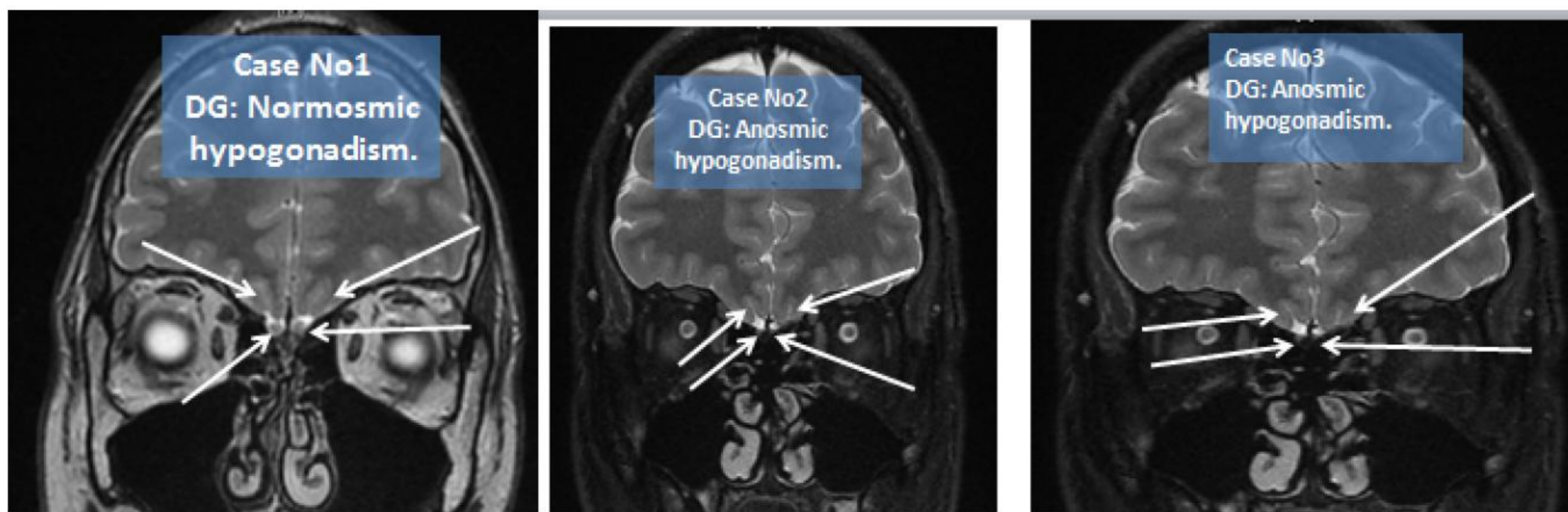
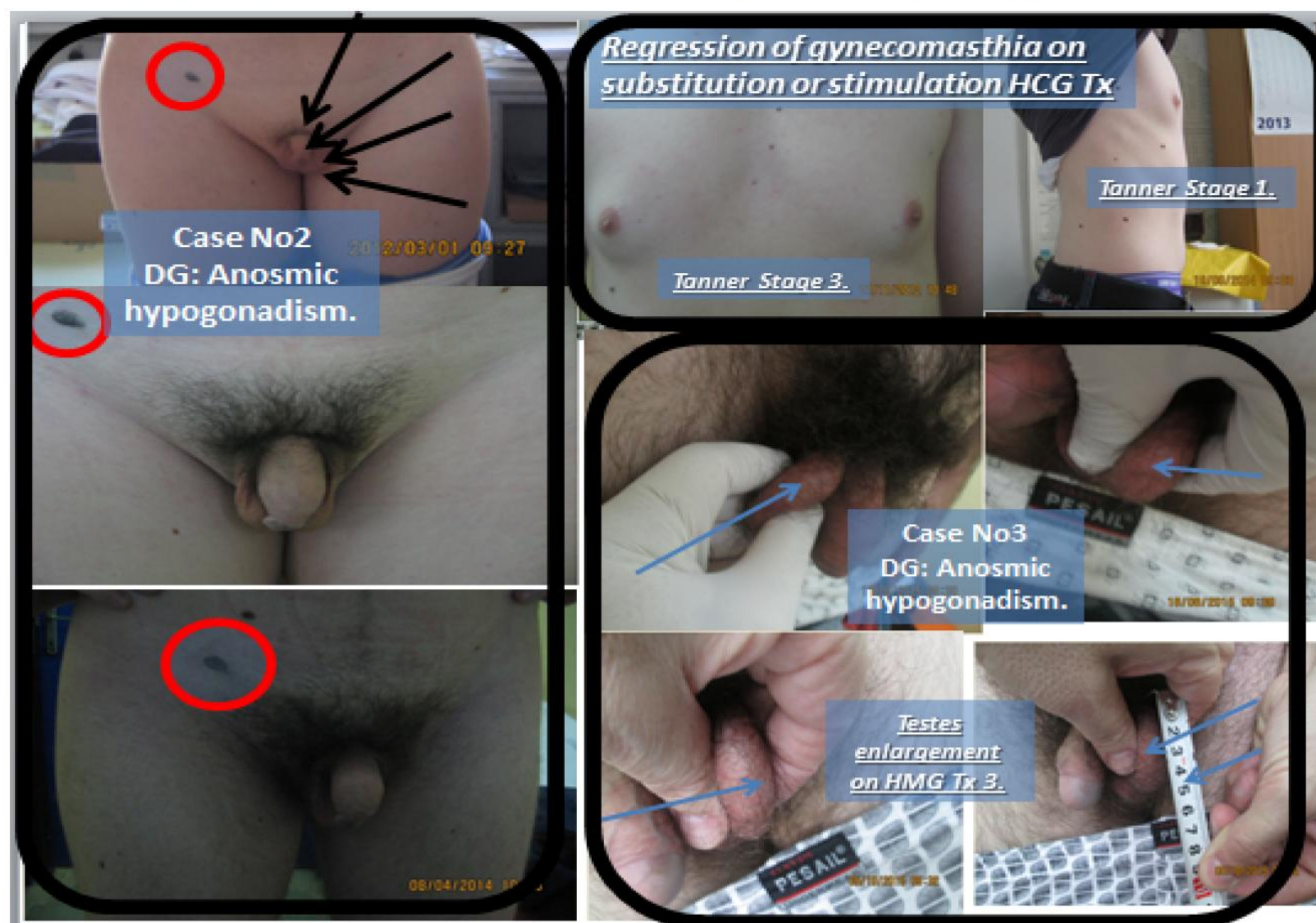


Table 5: Data showing semen analysis in both basal state and after gonadotropin therapies.

| | Case 1. | Case 2. | Case 3. |
|---|--|---|--|
| Semen analysis after substitution or „endocrine” stimulation therapy. | Azoospermia. (5m. after hypophysectomy). | Azoospermia. (Testosteron amp.) -ejaculation, voice deeper, libido: ?. | Azoospermia. (hCG 3000j./2-3day) - +ejaculation, voice deeper, libido: ?. |
| Semen analysis after specific stimulation therapy for „exocrine function”. | sperm reappeared, 22x10⁶/mL (5m. after HCG twice weekly 1,500i.u. + HMG 75i.u. tree times weekly) | „-” | Oligozoospermia 0.5x10⁶/mL , (2m. after HMG Tx) 3-(4.2; 9.2)x10⁶/mL , (4month after HMG 75i.u. tree times weekly) |
| | Oligozoospermia 3x10⁶/mL . (after 6m. on Testosteron amp.) | | sperm frozen !!! in storage tank with liquid nitrogen. |

Figure 2: In both patients(Case No2,3) effects of both testosterone or HCG therapy as associated with progression from Tanner 2 to 6 stage, except regarding testes. Introducing HMG therapy in Case No3 induced testes development and sperm appearance.



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