The aim of this study was to evaluate clinical and molecular aspects of a Brazilian cohort of pediatric patients with PPGLs. Out of 262 patients with PPGLs, 26 (9 %) were diagnosed before 19 yrs of age (16 males and 10 females), with a median age of 14.5 yrs (range, 4 to 18). Genetic investigation was performed in 19 patients: 14 by automated Sanger sequencing (*VHL, SDHB, SDHD* and *RET* genes) and 5 by a custom next-generation sequencing (NGS) panel including all genes previously associated with germline mutations in PPGLs. Median tumor size was 5.5 cm (1.7 to 16). Pheochromocytomas (PHEOs), paragangliomas (PGLs) or both were diagnosed in 46%, 31% and 23% of the patients, respectively. Bilateral PHEOs were diagnosed in 61% of the cases, most of them asynchronous (75%). Genetic diagnosis was confirmed in 14 out of 19 (74%) patients and all variants were found in heterozygous state: 8 *VHL* missense mutations from 6 kindreds (p.R167W in 2 kindreds, p.R167Q in one and p.G114S in 3); 3 *SDHB* mutations (p.C98Y, c.201-2A>G and p.L180L); 2 *SDHD* mutations (p.Y144_H145del and p.Q121*); and one *RET* mutation (p.C634R). All 8 VHL patients had bilateral PHEOs and 3 of them had also abdominal PGLs. All patients with *SDHB* mutations had abdominal PGLs. Two patients with *SDHD* mutation had head and neck paraganglioma (one of them had unilateral PHEO). Genetic investigation by NGS Panel was negative in all 5 cases: 2 malignant PPGLs (one PHEO and one PGL) and 3 PHEOs. Four out of 26 (15%) pediatric PPGLs were malignant: 2 with *SDHB* mutation and 2 with negative screening (one PHEO and one PGL). In conclusion, the majority of pediatric PPGLs (74%) were hereditary and almost exclusively caused by mutations in hypoxic genes. *VHL* (PHEOs) and *SDHB* (only PGLs) were the most frequent affected genes in this cohort of pediatric PPGLs.
Support: CAPES grant to Petenuci J.

Reproductive Endocrinology

MALE REPRODUCTIVE HEALTH - FROM HORMONES TO GAMETES

Adoption of an Age Adjusted Testosterone Reference Range Reduces Referrals to Endocrine Clinic and New Prescriptions of Testosterone

Charlotte Dewdney, MBChB, Heidi Mendoza, PhD, Rosemary Clark, MBChB, PhD, Sandra MacRury, MD, Rod Harvey, MBChB, Kenneth Muir, MBChB, Satinder Bal, MD, Catherine Anne Dorrian, PhD, FRCPath, David P. Macfarlane, Dr, MB, PhD.
NHS Highland, Inverness, United Kingdom.

SAT-047

Testosterone levels decline with age. However, until recently well defined harmonised age and/or obesity (BMI <30kg/m^2) adjusted reference ranges did not exist.[1] There is also a lack of international consensus on whether an age adjusted reference range (RR) should be used to define the syndrome of hypogonadism in men. Our local referral guideline suggests referral to endocrinology is appropriate if morning testosterone is <9.4nmol/L similar to the Endocrine Society Clinical Practice Guideline.[2] In mid 2018 our laboratory adopted the published *all men* age adjusted RR[1]. We sought to; i) investigate clinic referrals before and after adoption of the *all men* age adjusted RR and, ii) to model the impact on referrals and prescription of testosterone replacement therapy (TRT) had we adopted either the lower limit of either *all men* or *non-obese* age adjusted RR as our referral criteria. Despite similar numbers of testosterone levels being measured in the laboratory, referrals to endocrine clinic for investigation of male hypogonadism fell by 52% (n=101 vs 48) in the one year following the introduction of the new age adjusted RR, with a corresponding reduction in prescriptions for testosterone. Mean testosterone concentration (6.7±2.5 vs 6.4±3.9nmol/L [mean±SD], NS), and age (51±13.9 vs 50±17.9 years, NS) of individuals referred were similar before and after the change of RR. Of the 101 patients referred for investigation of hypogonadism prior to the new RR mean testosterone concentrations were 8.5±4.5, 7.3±4.1, 6.8±3.6, 6.7±2.1 & 6.6±1.6nmol/L, with 39, 71, 39, 40 & 17% of the 87 patients seen in clinic being prescribed TRT in age groups 19-39 (n=28), 40-49 (n=7), 50-59 (n=33), 60-69 (n=20) &70-79 (n=6) respectively, excluding those with a history of anabolic steroid use or Klinefelter's syndrome. Mean BMI was 30.9±4.4kg/m^2, which was similar between age groups. Had the lower limit of normal of the *all men* testosterone RR been employed as our referral criteria in the preceding year, 23.8% (24/101) of referrals would not have met referral criteria, and 26.2% (n=11/42) of those receiving a prescription would potentially not have received a trial of TRT. In contrast, had the *non-obese* age adjusted RR had been adopted for all men 13.9% (14/101) of referrals would not have met referral criteria and, of those prescribed testosterone, 2.4% (n= 1/42) would not have received a trial of TRT. In conclusion, adoption of the *all men* age adjusted RR for testosterone has been associated with a significant fall in referrals for investigation of male hypogonadism. However, modelling of historical clinic data would suggest that some non-obese individuals miss out on a therapeutic trial of TRT, especially if the *all men*, rather than *non-obese*, age adjusted RR is adopted.

Reference: (1) Travison et al, J Clin Endocrinol Metab, 2017,102(4):1161-1173, (2) Bhasin S et al,. J Clin Endocrinol Metab. March 2018;103(5):1715-1744.

Neuroendocrinology and Pituitary

PITUITARY TUMORS II

Long-Acting SSA Treatment Patterns in Sweden From 2005 to 2017: A Nationwide Study

Daniel S. Olsson, MD, PhD[1], Daniel Granfeldt, PhD[2], Åse Björstad, PhD[2], Antonio Ribeiro-Oliveira, MD,PhD[3], Anna Jonasson, MSc[4], John D. Whalen, MBA[5].
[1]Sahlgrenska University Hospital, Gothenburg, Sweden, [2]PharmaLex, Gothenburg, Sweden, [3]Ipsen, Cambride, MA, USA, [4]Ipsen AB, Kista, Sweden, [5]Ipsen Biopharma, Slough, United Kingdom.

MON-301

Background

Acromegaly is a complex disease, primarily treated with pituitary surgery or long-acting somatostatin analogues (LA-SSA). Few studies have examined real-world use of LA-SSA. This analysis evaluated LA-SSA treatment patterns in Sweden for patients with acromegaly.

Methods

Data were obtained from nationwide health care registers. Patients were included if they had diagnosis codes for acromegaly and neoplasm of the pituitary gland between Jul 1, 2005 and Dec 31, 2017, and at least one purchase of LA-SSA (lanreotide [LAN] 60, 90, or 120 mg, or octreotide [OCT] 10, 20, or 30 mg). Cox regression models were used for analyses of persistence and switching.

Results

The analysis included 176 pts treated with LA-SSA in 2005-2017. The cohort was subgrouped on year of initiation of LA-SSA (2005-2011, n=90, 51%; 2012-2017, n=86, 49%). In the first period, 36 pts (40%) initiated LAN while 54 pts (60%) initiated OCT while in the later period, 44 pts (51%) initiated LAN and 42 pts (49%) initiated OCT (p=0.17). No patients initiated pasireotide. Patient characteristics were similar between LAN and OCT initiators, but history of pituitary surgery was more common for LAN as compared to OCT (LAN 62%; OCT 46%, p<0.05). Similar results were seen for visual-field defects (LAN 20%, OCT 8%, p<0.05). Median (95%CI) follow-up was not significantly different [LAN 5.3 (3.7; 6.0) yrs.; OCT 6.4 (4.5; 7.6)].

The mean (95%CI) dose interval was not significantly different, 30.5 (28.7; 32.6) days for LAN vs 29.5 (28.5; 30.3) days for OCT. The median (95%CI) duration of 1st-line LA-SSA treatment was 14.4 (10.8; 21.6) months for LAN and 12.0 (7.2; 19.2) months for OCT. Fifty-one pts (64%) discontinued 1st-line LAN while 70 pts (73%) discontinued 1st-line OCT (hazard ratio (HR) LAN vs. OCT 0.80; 95% CI: 0.56-1.15). Due to the use of register data, the reason for therapy change could not be determined. Eight pts (10%) switched LAN to OCT while 29 pts (30%) switched OCT to LAN. Patients initiated on OCT were more likely to switch to LAN than the other way around (HR for switch for 1st-line LAN vs. OCT 0.33; 95% CI 0.15-0.72). Among patients who switched OCT to LAN, 67% of LAN dispensing was 120 mg, 21% 90 mg, and 12% 60 mg. Among patients who switch LAN to OCT, 84% of OCT dispensing was 30 mg, and 16% 20 mg.

Conclusions

There was no significant difference in the number of patients initiated on LAN or OCT despite the later introduction of LAN in Sweden. Patient characteristics were similar but LAN initiators were more likely to have undergone surgery and be diagnosed with visual field defects which could indicate that physicians initiate LAN in patients with more aggressive disease. Extended dose intervals with LAN (dosing every 6-8 w) do not seem to be commonly used in Sweden. In comparison to OCT, patients initiated on LAN were significantly less likely to change LA-SSA therapy.

Thyroid

THYROID DISORDERS CASE REPORTS II

A Case of Congenital Thyroid Hemi-Agenesis- Caution for Complications!

Sabah Patel, MD[1], Petra Krutilova, MD[2], Janice L. Gilden, MD,BA,MS[3].

[1]Rosalind Franklin University of Medicine and Science, Chicago, IL, USA, [2]Mount Sinai Hospital, Chicago, IL, USA, [3]Rosalind Franklin University of Medicine and Science/Chicago Med Schl, North Chicago, IL, USA.

SAT-478

Introduction: Congenital Thyroid hemi-agenesis is an uncommon clinical entity. We present a case highlighting the importance of awareness of this condition and the need to evaluate and manage co-existing hypothyroidism and risk of malignancy. Case: A 20 year old female known to have Hashimoto's thyroiditis (non-adherent to levothyroxine), and hemi-agenesis of left lobe of thyroid gland, presented with right-sided thyroid enlargement. She was clinically euthyroid. Physical exam: enlarged right sided thyroid gland with palpable anterior cervical lymphadenopathy. Left lobe could not be palpated. TFTs were notable for TSH 4.98 uIU/ml (0.358-3.74) and Free T4 0.79 ng/dl (0.76-1.46) consistent with sub-clinical hypothyroidism while Anti TPO antibody was positive at 8332.8 U/mL (0 - 60). CBC negative for leukocytosis. US thyroid: left-sided thyroid agenesis with intact isthmus and enlargement of right lobe of the thyroid 7.7 cm x 1.6 cm x 2.6 cm with 2 sub-centimeter hypoechoic solid nodules and 2 enlarged lymph nodes 1.5 cm and 2.3 cm (not found in US thyroid 2 years ago) Levothyroxine was re-started. ENT evaluation determined that her lymphadenopathy was benign and consistent with Hashimoto's thyroiditis. Subsequent TFTs improved. Discussion: Thyroid Gland embryogenesis occurs in the 4th week of fetal life. Subsequent abnormal bilobal differentiation of the thyroid gland is presumed to be the etiology of congenital hemiagenesis. Its prevalence in several studies is estimated to be between 0.05-0.25%. It is symptomatic pre-dominantly in females and may have familial origin with vast majority of cases having left hemi-agenesis with intact isthmus. It is helpful to know that most symptomatic patients have compensatory hypertrophy of the remnant lobe. It is important to remember that compensatory enlargement of the remnant lobe in the setting of hypothyroidism may be a sign of insufficient endogenous thyroxine production and/or replacement. Although rarely symptomatic, hemi-thyroid remnant may need to be evaluated for co-existing hyperthyroidism, hypothyroidism, carcinoma and multinodular goiter among others, with hypothyroidism thought to be the most common. US thyroid is a useful modality to help guide the evaluation of patients with hemi-agenesis. Awareness of this congenital condition is key in preventing unnecessary evaluations and interventions. Non-resolving lymphadenopathy in Hashimoto's thyroiditis must be evaluated for lymphoma, however, based on studies, no additional risk of malignancy was identified in patients with underlying thyroid hemi-agenesis. References: Y.H. Wu, R.O. Wein, B. Carter Thyroid hemiagenesis: a case series and review of the literature Am J Otolaryngol, 33 (3) (2012), pp. 299-302

Diabetes Mellitus and Glucose Metabolism

PREGNANCY, LIPIDS, AND CV RISK — IMPACT OF DIABETES ACROSS THE SPECTRUM

Increased Carotid Intima Media Thickness in Pediatric Type 1 Diabetes Is Associated with Disease Duration

Michal Cohen, MD[1], Meirav Oren, MD[1], Raya Gendelman, PhD[2], Hiba Yaseen, PhD[2], Ram Weiss, MD PhD[1], Anat Ilivitzki, MD[1], Nehama Zuckerman-Levin, MD[3], Murir Khamaisi, MD PhD[2], Naim Shehadeh, MD[2].