MON-LB84

Background: Thyroid nodules are exceedingly common, leading to costly interventions for many lesions that ultimately prove benign. Therefore, a reliable, noninvasive method to identify which nodules warrant fine needle aspiration and/or follow-up on the basis of a reasonable likelihood of malignancy is highly desirable. American College of Radiology (ACR) created a standard terminology (lexicon) to describe all thyroid nodules on sonography and standardized TI-RADS risk-stratification system to identify nodules that warrant biopsy and/or follow-up. Many healthcare institutions including UPMC adapted the TI-RADS scoring system in order to identify most clinically significant malignancies while reducing the number of biopsies and follow-up ultrasounds performed on benign nodules. According to ACR, TI-RADS category 3 nodules <1.5 cm and TI-RADS category 4 nodules <1 cm do not warrant follow-up imaging. There are no validation studies on TI-RADS follow-up recommendations.

Methods: We completed a retrospective chart review from UPMC endocrine surgery thyroid nodule database from 2002 to 2012. We identified 57 nodules that showed a change in size during follow-up and had surgical data. Patient demographics, nodule baseline TI-RADS category, size, follow-up volume change and histopathological data were recorded. We reviewed ultrasound images and calculated TI-RADS category at baseline and during follow-up.

Results:TI-RADS category 1-2 (TR1 and TR2) nodules(n=4) did not show any change in size over an average of 6.5 years confirming the recommendations that TR1 and TR2 nodules do not need follow-up.TI-RADS category (TR3) nodules (n=22) showed an average 225% change in volume over 4 years of follow-up. TR3 nodules <1.5 cm showed 397% volume change; 3 out of 15 (20%) nodules that showed a change in size proved to have thyroid cancer >1cm.

TI-RADS category (TR4) nodules(n=31) showed a 786% volume change over 2.6 years of follow-up. TR4 nodules <1 cm, 5/14(35%) proved to have thyroid cancer >1 cm in follow up.

Conclusions:TR1 and TR2 nodules did not show thyroid cancer during follow-up validating ACR recommendations not to follow these nodules. 3/15(26.5%) TR3 nodules <1.5 cm that showed a change in volume proved to have thyroid cancer. 5/14(35%) TR4 nodules <1cm that changed in volume were found to have thyroid cancer. Further studies are needed to identify nodules that require follow-up in order to decrease the misdiagnosis of thyroid cancer.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Increased In Vivo Pulsatile LH Secretion and Hypothalamic Kisspeptin, NKB, and Dynorphin RNA Levels in a PCOS-Like Mouse Model

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SUN-LB50

Polycystic ovary syndrome (PCOS) is a reproductive disorder in women characterized by hyperandrogenemia, anovulation, cystic ovaries, and LH hyper-pulsatility, but the mechanisms causing the pathophysiology remain incompletely understood. We recently reported a novel mouse model that recapitulates the majority of PCOS phenotypes in adulthood. Females given constant, long-term letrozole to reduce aromatase activity demonstrate PCOS-like phenotypes, including polycystic ovaries, anovulation, elevated circulating testosterone, and increased LH. *In vivo* LH pulsatile secretion, which is greatly elevated in PCOS women, was not previously studied, nor were possible changes in reproductive neurons known to control GnRH/LH secretion. Here, we used recent technical advances in the field to examine *in vivo* LH pulse dynamics of freely-moving LET female mice versus control and ovariectomized (OVX) mice. We also studied whether hypothalamic gene expression of several important reproductive regulators, kisspeptin, neurokinin B (NKB), and dynorphin, is altered in LET females. Compared to controls, LET females exhibited very rapid, elevated *in vivo* LH pulsatility, with increased pulse frequency, amplitude, and basal levels, similar to PCOS women. LET mice also had markedly elevated *Kiss1, Tac2,* and *Pdyn* expression along with increased *Kiss1* neuron activation in the hypothalamic arcuate nucleus. Although elevated, most hyperactive LH pulse parameters and increased arcuate mRNA measures of LET mice were significantly lower than in OVX littermates. Our findings demonstrate that LET mice, like PCOS women, have markedly elevated LH pulsatility which likely drives increased ovarian androgen secretion. Increased arcuate kisspeptin and NKB levels may be fundamental contributors to the enhanced stimulation of LH pulse secretion in this PCOS-like condition, and perhaps, in some PCOS women.

Healthcare Delivery and Education

EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE

Evaluating the Impact of a New Intake Process for British Columbia Children's Hospital Gender Clinic

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MON-LB302

Our pediatric Gender Clinic is receiving a growing number of referrals, yet continues to operate with limited resources. To try to address this issue, a new clinical pathway was developed in 2017, which included an inter-professional assessment clinic run by nurses and social workers as the entry point for new referrals (known as 'intake appointments'). These visits help to identify those youth who require urgent access to care (i.e. for imminent puberty), wayfinding to community supports and providers who can complete GnRH analog and hormone-readiness assessments, and information about potential medical interventions. The goals of this study were to (1) map out current processes, (2) evaluate wait times for patients referred in 2015-2016 (pre-intake) and 2018-2019 (post-intake), and (3) describe referral patterns and outcomes. Patients referred in 2017 were excluded, as this was a transitional year. In 2015-2016, 222 referrals were received, compared to 407 referrals in 2018-2019. Of the post-intake cohort, to date, 202/407

referrals have led to an intake appointment, of which 45 were via telehealth (a service not previously offered to families). Average wait time to physician visit was 171 days (range 10-1271; IQR 69-208) for patients in the pre-intake cohort, while the average wait time to intake appointment was 200 days (range 9-569, IQR 114-242) in the post-intake cohort. Wait time to physician visits cannot be assessed yet, due to the number of pending referrals. Fifty-four referrals were cancelled in the pre-intake, and 73 in the post-intake cohort. In both groups, the primary reason for cancellation was redirection by our team to other services (32% in both groups), and the second most common reason was cancellation by the family/no show to appointment (26% and 22% in the pre- and post-intake cohorts, respectively). Staffing resources and number of clinics per week have changed over the years, limiting our ability to attribute changes directly to the new clinical pathway. Moreover, most hormone-readiness assessments are completed by community providers. Therefore, wait times to physician visits partly reflect difficulty in accessing these community resources. However, using our new model of care, we have engaged with hundreds of patients and families within a similar time frame to the 2015-2016 cohort, despite an almost doubling of the number of referrals received by our clinic. Although these initial visits do not allow for initiation of medical therapy, they are a means to support patients and families through their gender journey. Moreover, the intake appointments have promoted inter-professional collaborative care, which is particularly beneficial in the face of limited resources. Thus, we believe this new model of care has led to improved quality of care for patients accessing our Gender Clinic.

Bone and Mineral Metabolism

BONE DISEASE FROM BENCH TO BEDSIDE

Oral Risedronate Treatment in Children With Osteogenesis Imperfecta

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SUN-LB66

Introduction: To date, there are no approved pharmaceutical therapies for children with OI. Intravenous bisphosphonates have been used for years to treat children with OI with variable efficacy and tolerability. However, a few studies have evaluated the effects and tolerability of oral risedronate in children with OI (1)(2). In this study, we aimed to present our experience with oral risedronate treatment in children with OI. **Methods:** A retrospective chart review of patients with OI and history of multiple fragility fractures, who were treated with oral risedronate and followed in our bone clinic between the years of 2013 and 2019. Primary outcomes included changes in fracture rate, urinary N-terminal telopeptide (uNTX), height z-scores, and lumbar and femur BMD z-scores. Safety and tolerability of risedronate were reviewed. Wilcoxon matched-pairs sign-ranks test was used to assess the medians (IQR) between pre- and post-treatment with p value of < 0.05 set as statistically significant.**Results:** A total of 17 patients ages 5—19 ys were reviewed (11 males, 65% type I OI, 12% type III, 18% type XI, and 5% unknown). At the time of the review, 69% were on weekly, 19% on daily, and 12% on monthly risedronate treatment. Mean duration of therapy was 2.7 y ± 2.3 y, ranging 0.5 to 8 ys. The bone resorption marker, uNTX, decreased > 30% from baseline in 93% of subjects within the first year of treatment, and was statistically lower by the end of treatment period [245 (159, 393) to 170 (39, 261), p=0.02]. Height z-score did not change with treatment, -0.80 (-1.20, 0.10) pre- and -0.85 (-1.60, -0.40) post-treatment, p = 0.2 in patients with Type I OI. There was a clinically significant reduction in the rate of fractures from baseline 0.6 per y (0.4, 0.8) to 0.24 (0, 0.5) by the end of the treatment period, though it did not reach statistical significance. Within a year of treatment, 80% of children were fracture free with improvement in bone pain and mobility. BMD pre- and on treatment for lumbar and femur were -2.5 (-3.43, -1.94) and -2.36 (-3.25, -1.35), and -2.05 (-2.95, 0.3) and -1.18 (-1.73, 2.13), respectively. However, there was no statistical significance. There was one case of reflux without erosive esophagitis, which resolved with reflux treatment. Overall, risedronate was well tolerated with no cases of clinically significant acute phase reaction, hypocalcemia, erosive esophagitis, or osteonecrosis of the jaw.**Conclusion:** Based on our experience, oral risedronate effectively decreased bone resorption, showed a trend towards decrease in fracture rate with improvement in symptoms, and was well tolerated in children with OI. More data are needed to systematically evaluate its long-term effects on growth, bone mineral density, fracture frequency, and quality of life in children with different types of OI. **Reference: (1)** Rauch et al., J Bone Miner Res. 2009; 24: 1282-1289 **(2)** Bishop et al., Lancet. 2013;382(9902):1424-32.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I

Thyroglobulin Stimulates the Secretion of Thyroxine From Thyroid Epithelial Cells in Suspension Culture via Nuclear Factor-κB Signaling Pathway

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SUN-LB129

The nuclear factor (NF)-κB signaling pathway controls a variety of biological functions such as cell growth and differentiation as well as immune and inflammatory responses. Two distinct pathways of NF-κB activation are known. NF-κB signaling via non-canonical pathway plays an important role in maintaining normal thyroid function, namely, thyroid cells survival and expression of thyroid-specific proteins, such as NIS, TPO and thyroglobulin (Tg). The primary function of thyroid cells is the production of