A Role for GNRH-II in the Control of Puberty?

Henryk F. Urbanski, MS,PHD,DSC.
OR Natl Primate Res Ctr, Beaverton, OR, USA.

SUN-035
Hypothalamic gonadotropin-releasing hormone (GnRH) neurons represent the primary neuroendocrine link between the brain and the reproductive system. Although they play a key role in stimulating the release of FSH and LH from the anterior pituitary gland, the underlying mechanism by which they trigger the onset of puberty is unclear. To address this issue, RT-PCR, in situ hybridization histochemistry, and Affymetrix gene arrays were used to profile hypothalamic GnRH gene expression in prepubertal and adult rhesus macaques (Macaca mulatta). Like humans, these nonhuman primates express two molecular forms of GnRH (GnRH-I and GnRH-II), both of which are highly effective at stimulating gonadotropin release via the same GnRHR1 receptor. However, only GnRH-II shows increased hypothalamic expression in the presence of elevated estrogen concentrations (i.e., positive feedback), whereas GnRH-I expression either remains the same or decreases (i.e., negative feedback). In the present study, the hypothalamic expression levels of GnRH-I and GnRHR1 were found to be no different between prepubertal and adult animals, despite marked differences in circulating sex-steroid hormone levels, whereas the hypothalamic expression level of GnRH-II was significantly higher in the adults than in the juveniles. Therefore, although the traditional GnRH-I neurons are likely to play a fundamental role in initiating FSH and LH release during the early stages of pubertal development, GnRH-II neurons may play an important role in maintaining elevated gonadotropin release during the final stages (i.e., at a time when the GnRH-I neurons are subjected to increasing negative sex-steroid feedback from the maturing gonads). Taken together, the data suggest that sexual maturation in primates is likely to be orchestrated by the concerted action of two distinct GnRH neuronal subtypes that respond differentially to sex-steroid feedback.

Tumor Biology
ENDOCRINE NEOPLASIA CASE REPORTS I
An Indolent Recurrent Parathyroid Carcinoma – A Case Report
Suetha Murthy, MD, MPH1, Maha B. Abdulla, DO2, Gady Har-EL, MD, FACP3, Elana Opher-Josifescu, MD4, Edward Merker, MD5.
1Northwell health Lenox Hill Hospital, New York, NY, USA, 2Lenox Hill Hospital, New York, NY, USA.

SUN-922
Introduction
Parathyroid carcinoma is a rare endocrine malignancy with reported incidence from 0.5 to 5% of primary hyperparathyroidism (1). Etiologies include prior neck irradiation, adenoma or hyperplastic parathyroid gland. Molecular pathogenesis includes RB gene overexpression, low P53, loss of APC and especially HRPT2 tumor suppressor gene. It has low malignant potential, but tends to recur locally or spread to contiguous areas. Here, we present a case of a recurrent parathyroid carcinoma that recurred after 17 years.

Clinical Case
The patient is a 56 YO female with Stage 1 breast cancer status post bilateral mastectomy who had undergone resection of a 2.5cm low-grade left lower parathyroid carcinoma in 1997 after 10 years of primary hyperparathyroidism. At that time of resection, iPTH was 2500 pg/ml and calcium level greater than 15 mg/dl. She presented with hypercalcemia (Calcium 11.5 mg/dl, PTH 67.1 pg/ml) again after 17 years. Work-up showed a 2.3 cm suspected parathyroid lesion in the left neck. She underwent removal of the left upper parathyroid gland along with a right enlarged parathyroid gland, as intra-operative PTH did not decline. Pathology confirmed parathyroid carcinoma with capsular invasion and muscle infiltration of the left gland and adenoma of the right gland. Repeat imaging in a month showed persistent parathyroid activity in the left neck. She had removal of the left upper parathyroid and a
left paratracheal mass excision with pathology confirming recurrent parathyroid carcinoma. After 4 years, her PTH and calcium levels rose. Sestamibi imaging showed abnormal activity in a 1.1 cm soft tissue mass near the sternal notch. The patient underwent complete excision of the left suprasternal mass and the left sternohyoid muscle with pathology confirming recurrent parathyroid carcinoma with lympho-vascular and perineural invasion. Follow-up Sestamibi imaging after a month showed no abnormal activity with recent labs of calcium level 10mg/dL and PTH 25 pg/ml.

Conclusion
Recurrent parathyroid carcinoma remains a challenge. Complete resection of the lesion along with care to avoid capsule rupture to prevent local seeding remains the treatment strategy. The main cause of morbidity and mortality is the sequelae of uncontrolled hypercalcemia rather than tumor burden. Management of hypercalcemia includes hydration, bisphosphonates and cinacalcet. Even though it is not radiosensitive, neck resection after surgery may be helpful in preventing tumor regrowth. Clinical trials using nivolumab and ipilimumab are being conducted to treat parathyroid carcinoma (2).

Reference
1. Givi, B., & Shah, J. P. (2010). Parathyroid carcinoma. Clinical oncology, 22(6), 498–507
2. Long, K. L., & Sippel, R. S. (2018). Current and future treatments for parathyroid carcinoma. International Journal of Endocrine Oncology, 5(01), IJE06

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORTS I
Renal Papillary Necrosis Associated with Normocalcemic Hyperparathyroidism
Mohamed K.M. Shakir, MD1, Vijay Kiran, BS2, Zachary Bloomer, MD1, Terry Shin, MD1, Vinh Q. Mai, D.O.3, Thanh Duc Hoang, DO1
1Walter Reed National Military Medical Center, Bethesda, MD, USA, 2Walter Reed National Military Medical Center, Gaithersburg, MD, USA, 3Walter Reed National Military Medical Center, North Bethesda, MD, USA, 4Walter Reed National Military Medical Center, Fayetteville, NC, USA, 5Walter Reed National Military Medical Center, Woodbridge, VA, USA.

SAT-363
Introduction
Hypercarnuriar is generally considered to be the most common identifiable metabolic risk factor for calcium nephrolithiasis. Important renal manifestations of primary hyperparathyroidism (PHPT) include asymptomatic nephrolithiasis, hypercalciuria, nephrocalcinosis, and chronic renal insufficiency. However renal papillary necrosis (RPN) occurring in PHPT has not been reported previously. We report a 50-year-old woman who manifested RPN associated with hypercalciuria and normocalcemic PHPT. Case Report
A 50-year-old Caucasian woman was evaluated in 2006 for hypercalcemia. She had no history of nephrolithiasis, fractures, or symptoms of hypercalcemia. Laboratory: serum calcium 11.8 mg/dL, ionized calcium 6.3 mg/dL, phosphorus 1.8 mg/dL, intact PTH 98 pg/mL (ref 15–65), urine calcium 543 mg/24 hrs (ref <235).

Renal ultrasound showed no evidence of nephrocalcinosis or nephrolithiasis. A parathyroid scan was consistent with a left superior parathyroid adenoma. Patient underwent parathyroidectomy and became normocalcemic with normal serum PTH levels postoperatively. One year later she was diagnosed with a left sided bronchial carcinoma. Surveillance Gallium-68 PET/CT scan done 2 years later was negative for any metastases. Twelve years later she reported to our clinic for follow up. She had no symptoms of hypercalcemia, fractures, nephrolithiasis, history of pyelonephritis, diabetes mellitus, analgesic use, or hypertension. Serum calcium was 9.1 mg/dL, serum phosphorous 3.8mg/dL, PTH 82 pg/mL, 25-OH vitamin D 34 ng/mL, 1.25-vitamin D 38 pg/mL, and a urorisk panel was normal except for a 24-hour urine calcium of 410 mg. However renal ultrasound showed bilateral RPN and this diagnosis was also confirmed by a CT scan. A urinalysis showed only microalbuminuria with no red cells. She had no history of any analgesic drug abuse, pyelonephritis, sickle cell disease, or diabetes mellitus. A glucose tolerance test was completely normal. Discussion
RPN is characterized by coagulative necrosis of the renal medullary pyramids and papillae brought on by several associated disorders and toxins that exhibit synergism toward the development of ischemia. Although the initial kidney US was normal, a repeat US done 12 years later showed evidence of RPN. This finding along with hypercalciuria and a diagnosis of normocalcemic PHPT suggests that RPN may be associated with hypercalciuria and normocalcemic PHPT. Furthermore she had no other risk factors for RPN. Additional studies with large number of patients are needed to confirm the association between these 2 disorders.

Healthcare Delivery and Education
EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE
Healthcare Services Utilization and Costs Associated with the Management of Patients Living with Acromegaly
Antonio Ribeiro-Oliveira, Jr, MD, PhD1, Kathryn A. Munoz, PhD1, Richard Alan Brook, MS, MBA2, Ian A. Beren, BS3, John D. Whalen, MBA4, Kevin C.j. Yuen, MD, FRCP (UK), FACE2
1Ipsen, Cambridge, MA, USA, 2Better Health Worldwide, Inc, Newfoundland, NJ, USA, 3HCMS Group, Cheyenne, WY, USA, 4Ipsen, Slough, United Kingdom, 5Barrow Neurological Institute, Phoenix, AZ, USA.

MON-141
Background: Acromegaly (ACRO) is a rare, chronic growth hormone hypersecretory disorder associated with increased morbidity and mortality. Limited information is available on the utilization and costs of healthcare by patients with ACRO.
Aims: To assess the impact of ACRO healthcare utilization and costs by locations of care (LoC).
Methods: A US database of prescription (Rx) drug and medical claims from Jan 2010 to Apr 2019 was analyzed. Patients with an ACRO diagnosis (Dx) were identified based on claims with ICD-9/-10 codes 253.0x/E22.0. The 12-month study period followed each patient’s first ACRO Dx in the database (the index date). ACRO patients