PD-L1 inhibitors, 42% were on combination PD-1/CTLA-4 inhibitors and 12% were on CTLA-4 inhibitors. Median time from CPI initiation to HP diagnosis was 95 days. Time to HP was shorter on a CTLA-4 inhibitor combination or monotherapy (median 82 days) compared to a PD-1/PD-L1 inhibitor monotherapy (median 220 days; Wilcoxon rank sum, p < 0.01). Central adrenal insufficiency was present in all patients not yet on steroids. Central hypothyroidism was common (10/19) in those without primary thyroid disease and was not associated with type of CPI (Fisher’s exact, p = 0.18).

Thirteen subjects had baseline MRIs, 18 had MRIs at HP diagnosis and 13 had MRIs in the follow up period. Baseline MRIs were normal in 12/13; one subject had an enlarged pituitary. At diagnosis, 10 had an enlarged pituitary, 7 a normal pituitary and 1 a partially empty sella. CTLA-4 inhibitor exposure was associated with pituitary enlargement at diagnosis: 9/11 compared to 1/7 on PD-1/PD-L1 inhibitor (Fisher’s exact, p < 0.04). Of the subjects who had follow-up MRIs, 3 had an enlarged pituitary, 7 a normal pituitary and 3 a partially empty sella. Follow up imaging did not differ between treatment types (Fisher’s exact, p > 0.05). Timing of MRI was significantly associated with pituitary appearance (Fisher’s exact, p < 0.01).

Conclusion: The MRI appearance of HP presents as a spectrum, from a partially empty sella, normal pituitary to an enlarged pituitary. HP diagnosed in the setting of CTLA-4 inhibitor treatment occurs earlier and is more likely to induce an enlarged pituitary gland compared to PD-1/PD-L1 monotherapy, which occurs later and is associated with a normal appearing MRI at diagnosis. This suggests that the pathogenesis of HP following CPI exposure may vary depending on the type of CPI.

Tumor Biology

TUMOR BIOLOGY: DIAGNOSTICS, THERAPIES, ENDOCRINE NEOPLASIAS, AND HORMONE DEPENDENT TUMORS

TMEPAI Inhibits SMAD 2/3 Mediated Muscle Wasting
Swati Kharoud, Honours1, Kelly Louise Walton, PhD2, Adam Hagg, Honours3, Georgia Goedch, Masters1, Justin Chen, BSc BA4, Rachel Thomson, PhD2, Hongwei Qian, PhD1, Paul Gregorevic, PhD3, Craig Anthony Harrison, PHD1.
1MONASH BIOMEDICINE DISCOVERY INSTITUTE, Clayton, Australia, 2Physiology/Monash Uni/Clayton, CLAYTON, Australia, 3University of Melbourne, Melbourne, Australia, 4Monash University, Clayton, Australia.

SUN-140
Inhibition of myostatin and activin activity using ligand traps, such as soluble receptors, follistatin and propeptides, can markedly increase skeletal muscle mass in healthy mice and ameliorate wasting in models of cancer cachexia and muscular dystrophy. Though effective, clinical translation of these approaches has been hindered by off-target effects. Toward the goal of developing tissue-specific myostatin/activin interventions, we explored the ability of transmembrane prostate androgen-induced (TMEPAI) to promote growth of skeletal muscle. TMEPAI, a transcriptional target of activin in muscle, is a known inhibitor of TGF-β1-mediated SMAD 2/3 signalling. In this study we show that TMEPAI also blocks activin A, activin B, myostatin and GDF-11 in vitro activity. Adeno-associated viral (AAV) gene delivery of TMEPAI into healthy mice increased local muscle mass by as much as 30%. Increased muscle mass was attributed to hypertrophy of fibres in TMEPAI-expressing muscles, and was coincident with an upregulation in markers of protein synthesis (pAkt, pMTOR, p70S6K). The ability of TMEPAI to block activation of the canonical activin/myostatin-SMAD 2/3 axis, was demonstrated by co-injecting AAV6:activin A and AAV6:TMEPAI into healthy mice. In this setting, TMEPAI blocked activin-induced phosphorylation of SMAD3 and associated skeletal muscle wasting. Finally, delivery of AAV6:TMEPAI into tibialis anterior muscles of mice bearing C26 tumours prevented muscle atrophy normally associated with this model. The results support that viral gene delivery of TMEPAI can effectively increase muscle mass via inactivation of the activin/myostatin-SMAD 2/3 pathway.

Adrenal

ADRENAL CASE REPORTS I

POEMS: A Medical Odyssey
Andrey Hacrylyan, MD1, Uzma Syed, MD2.
1Chicago Medical School at Rosalind Franklin University of Medicine and Science, North Chicago, IL, USA, 2Mount Sinai Hospital, Chicago, IL, USA.

SAT-205
Introduction: POEMS (polyneuropathy, organomegaly, endocrinopathy,-monoclonal plasma cell disorder, and skin changes) syndrome is a rare disorder with poorly understood pathogenesis. The incidence of endocrinopathy associated with POEMS syndrome has been recognized more frequently in the last two decades, ranging between 67-84%. The cause of endocrine dysfunction associated with the syndrome is not known, but has been described to include hypogonadism, hypothyroidism, abnormalities of glucose metabolism, hyperprolactinemia, gynecomastia in men, hyperestrogenemia, calcium abnormalities and adrenal insufficiency (AI).

Case: A 38 y/o Hispanic male was initially referred to nephrology with complaint of leg swelling. Subsequently, the patient was referred to endocrinology for abnormal thyroid function studies and ongoing fatigue. Patient had prior medical history of recently diagnosed hypothyroidism treated with levothyroxine 100 mcg daily. The most bothersome complaint was pitting edema in the lower extremities with associated pain. He also endorsed right shoulder pain exacerbated by use of the right arm. He reported unintentional weight loss of about 30 pounds in the past 2-3 years, denying night sweats. He did endorse feeling fatigued, skin darkening, and erectile dysfunction. On exam patient was afebrile, BP 120/71 mm/Hg, HR 87 bpm, no goiter, no gynecomastia, skin hyperpigmentation, darkening creases of the palms, pitting edema in lower extremities. Work up showed lytic lesion in right scapula. [prolactin 15.6 ng/ml (normal (NL)= 0-25], free testosterone 23.1 pg/ml (NL= 35.0-155.0), total testosterone 205 ng/dl (NL= 280-960)
250-1100), LH 8.2 MIU/ml (NL= 1.2-8.6), FSH 4.3 MIU/ml (NL=1.3-19.3), TSH 17.8 uIU/ml (NL= 0.45-5.33), free T4 0.62 ng/dl (NL= 0.58-1.64), free T3 3.05 pg/ml (NL=2.5-3.9), TPO antibody (AB) negative, IGF-1 41 ng/ml (NL=53-331), AM cortisol 8.2 ug/dl (NL=6.7-22.6), ACTH 99 pg/ml (NL=6-50), aldosterone 3 ng/dl (NL ≤28), renin activity 2.78 ng/ml/h (NL=0.25-5.82), 21-hydroxylase AB negative, 17-hydroxyprogesterone 54 ng/dl (NL=42-196), DHEA-S 88 mcg/dl (NL=106-464), ACTH stimulation test (250 mcg) was performed with basal cortisol 8.0 ug/dl (NL= 5.0-21.0), basal ACTH 93 pg/ml (NL=6-50), 30min cortisol 9.7 ug/dl (NL=13.0-30.0), 60min cortisol 10.2 ug/dl (NL=14.0-36.0). Pt was diagnosed with primary AI and started on hydrocortisone. CT abdomen and pelvis with contrast showed normal adrenal glands.

Discussion: Physicians should be cognizant of a unifying diagnosis in a syndrome of such a broad presentation. Endocrinopathies vary in extent of dysfunction and may fluctuate during the course of a POEMS syndrome. Multidisciplinary management as well as regular reassessment of endocrine function is integral in managing this complex disease.

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID II

Tyrosine Kinase Inhibitors Induced Thyroid Dysfunction: An Experience from a Tertiary Care Hospital

Subhash Kumar Wangnoo, DM FRCP FACE, Mohammad Asim Siddiqui, MD MRCP FRCP, Harsha Pammanni, MD, Khwaja Mohammed Usman, MD.
Indraprastha Apollo Hospital, New Delhi, India.

SUN-414

Tyrosine kinase inhibitors (TKI) belong to a new class of molecular multi-targeted anticancer therapy which targets different growth factor receptors and hence attenuates cancer cell survival and growth. TKI-induced thyroid dysfunction is recognized as a common adverse effect of treatment., but the onset of thyroid dysfunction is variable. This study analysed correlation between initiation of TKIs and the onset of thyroid dysfunction in non-thyroid cancers patients without any background thyroid dysfunction.

METHODS:
This was a retrospective cohort study to evaluate thyroid dysfunction in adult patients (n=227, M:F=13:24) with non-thyroidal cancers treated with TKIs. Patients having pre-existing thyroid disease including euthyroid goitres were excluded. Demographic, clinical, and cancer treatment data were collected. Thyroid function tests (TFTs) were done prior to initiation, at 2 months, 6 months and at 1 year. TFTs were classified as euthyroid (thyrotriptin [TSH] normal), subclinical (SCH; TSH 5-10 mIU/L, or higher TSH if free thyroxine normal), or overt hypothyroidism (OH; TSH >10 mIU/L, low free thyroxine, or requiring replacement).

RESULTS:
Of the 227 patients in the study, OH occurred in 57 patients (25.1%)(M:F = 19:38) and SCH occurred in 89 patients (39.2%) (M:F=39:50) with TKI therapy at the end of 12 months. 37 patients (M:F=13:24) developed OH in first 6 months after initiation of TKIs. Female patients were more likely to have OH in the first 6-month period following TKIs irrespective of type of TKI or the cancers. SCH was also more common after 2 months in female patients (n=23) (M:F=6:17) but the conversion of SCH to OH was more common in male patients at the end of 12 months. The symptoms were variable and most the patients did have any thyroid specific symptoms. After adjustment for age, sex, cancer type, cancer stage, performance status, and type of TKI, OH remained significantly associated with survival at 1-year (hazard ratio = 0.461; p<0.0001), whereas SCH did not (hazard ratio=0.591; p=0.165). Analysis of hypothyroid patients (SCH and OH) with TSH >5 and <10 mIU/L stratified by hormone replacement status showed improved survival associated with hormone replacement, although 1 year follow-up is too short to comment on overall survival rates.

CONCLUSIONS:
New onset hypothyroidism, both OH and SCH is common in non-thyroidal cancer patients treated with TKI. SCH is more common after 2 months and OH after 6 months following TKI initiation. Female sex is more predisposed to develop thyroid dysfunction irrespective of underlying cancer or type of TKI used but male patients progressed to OH at the end of 12 months.

Adrenal

ADRENAL CASE REPORTS I

Right Adrenal Mass: An Unusual Presentation

Lyan Gondin-Hernandez, MD, Jonathan Trejo, MD, MPH, Brenda Sandovel, MD, MPH, Jan M. Bruder, MD, Ramona Granda-Rodriguez, MD.
UTHSC-San Antonio, San Antonio, TX, USA.

SAT-183

Background: Adrenal masses may be incidentally found on imaging done for other reasons. The prevalence is 4.4% and up to 10% in older patients. Malignancy is an uncommon cause in patients without a known diagnosis of cancer. The frequency of primary adrenal carcinoma in patients with adrenal incidentalomas is approximately 2.0 to 5.0%; another 0.7 to 2.5% have non-adrenal metastases to the adrenal gland.

Clinical Case: 54-year-old man with Hepatitis C, prior alcohol abuse, and cirrhosis was found to have an increase in the alpha-fetoprotein (AFP) level from normal to 244 ng/ml (nl<15.1) over a 6-month period. Liver MRI was consistent with a cirrhotic liver without focal enhancing lesions and showed a new indeterminate 7.6 cm right retroperitoneal lesion arising from the adrenal gland compared to a prior CT of the abdomen a year early. Further imaging confirmed a 9.6 x 9 x 7.6 cm heterogeneously enhancing right adrenal lesion with a necrotic center, concerning for a primary malignancy; up to 11.1cm a month later. Patient referred to Endocrine for further evaluation. There were no symptoms suggestive of Cushing’s, pheochromocytoma or primary hyperaldosteronism. On exam there were no hypertension, dorsal fat pad, supraclavicular fullness, skin thinning or purplish striae. Biochemical workup was consistent with a non-functioning adrenal mass. DHEA-S was 11 (38-313

DOI: 10.1210/jendso/bvaa046 | Journal of the Endocrine Society | A803