metabolism, based primarily on intriguing animal studies. One prior trial of fecal microbiota transplantation (FMT) in obese men found that improved metabolic response after FMT was predicted by low baseline microbiome diversity. In the current trial, we investigated the safety and efficacy of weekly oral FMT capsules to improve glycemic outcomes in obese adults, and also explored determinants of successful microbiome engraftment and metabolic improvement after FMT.

Methods: FMT-TRIM was a double-blind randomized placebo-controlled pilot trial of weekly oral FMT vs placebo capsules for 6 weeks in 24 obese adults with mild-moderate insulin resistance. Each participant in the FMT arm received capsules derived from one of 4 metabolically healthy lean donors (BMI 18.5-23 kg/m^2). The primary outcome was change in insulin sensitivity assessed by hyperinsulinemic euglycemic clamp at 0 and 6 weeks. Secondary outcomes included body weight, metabolic labs, and body composition assessed by DXA over 12 weeks. 16SV4 rRNA sequencing was performed to assess microbiome composition and engraftment. Post-hoc exploratory analyses investigated metabolic outcomes after stratification by baseline microbiome diversity.

Results: FMT and placebo groups were well balanced in terms of age (mean±SD 40±9 yrs), BMI (40±6 kg/m^2), sex (72% female), and baseline metabolic measures. During the study, there were no statistically significant differences in insulin sensitivity between the FMT and placebo groups (+5 ± 12% FMT vs -3 ± 32% placebo, mean percent difference 9%, 95% CI -5% to 28%; p=0.16). There was a minor improvement in HbA1c at 12 weeks after FMT as compared to placebo (mean difference -0.1, 95% CI -0.3-0.01), but no significant differences in other metabolic labs, body weight, or body composition. Microbial engraftment varied by donor but was present in most FMT recipients, with persistence of engrafting strains throughout the 12-week study. Subgroup analyses of subjects with low microbiome diversity at baseline (FMT n=4, placebo n=7) showed a relative benefit of FMT over placebo at 12 weeks for HbA1c (mean difference -0.2, 95% CI -0.4 to -0.01), total cholesterol (-22 mg/dL, 95% CI -40 to -4 mg/dL), and fasting glucose (-10 mg/dL, 95% CI -19 to -1 mg/dL). There were no significant differences in adverse events between FMT and placebo groups.

Conclusion: Weekly administration of FMT capsules results in gut microbiota engraftment for at least 12 weeks but does not meaningfully alter human metabolism in an unselected population of obese adults. Future studies are needed to elucidate the role of baseline recipient microbial diversity and other factors on the impact of FMT.

Thyroid

THYROID DISORDERS CASE REPORTS I

Severe Hyperthyroidism in a Complete Molar Pregnancy

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SUN-513

Hydatidiform mole (HM), a type of gestational trophoblastic disease (GTD), is a rare cause of clinical hyperthyroidism. The development of hyperthyroidism requires an elevation of HCG >100,000 mIU/mL for several weeks. Complete mole has a marked HCG elevation compared to partial mole thus presents with a higher incidence of thyrotoxicosis. Surgical uterine evacuation is the treatment of choice for HM. However, untreated hyperthyroidism can pose a risk for the development of thyroid storm and high-output cardiac failure in the perioperative period. To our knowledge, there are no specific guidelines for management at this time. We present a case of hyperthyroidism secondary to complete molar pregnancy successfully treated with propylthiouracil (PTU), potassium iodide (SSKI), and atenolol in the preoperative period.

A 42-year-old female with history of migraines presented to her gynecologist with a 3-week history of lower abdominal cramping, vomiting, loss of appetite, and abnormal vaginal bleeding. She also endorsed a 6-pound weight loss, intermittent tachycardia, exertional dyspnea, and increased anxiety. Pregnancy test was positive, and ultrasound was concerning for GTD. Laboratory work up was significant for HCG 797,747 mIU/mL (< 5mlU/mL), TSH <0.005 mIU/mL (0.4-4.0 mlU/mL), Free T4 3.09 ng/dL (0.9-1.9 ng/dL), and Free T3 11.48 pg/dL (1.76-3.78 pg/dL). The patient was admitted to the hospital and started on PTU 100 mg Q6H, SSKI 200 mg TID following the first dose of PTU, and atenolol 25 mg daily. She underwent an uncomplicated D & C the next day. On post-op day 1, HCG decreased to 195,338 mIU/mL and Free T4 to 2.39 ng/dL. The patient was discharged on the aforementioned doses of PTU and atenolol. One-week follow-up labs showed HCG 8,917 mIU/mL and Free T4 1.22 ng/dL. Surgical pathology confirmed a complete hydatidiform mole. PTU was decreased to 50 mg TID. On post-op day 14, HCG had risen to 15,395 mIU/mL with onset of nausea and vomiting. Repeat Free T4 remained within reference range. Patient was taken back to surgery for a laparoscopic total hysterectomy with bilateral salpingectomy. Pathology confirmed an invasive hydatidiform mole. Two-week follow-up lab work showed HCG 155 mIU/mL, TSH 1.5 mIU/mL, and Free T4 1.19 ng/dL. PTU and atenolol were then discontinued.

The development of hyperthyroidism in molar pregnancy is largely influenced by the level of HCG and usually resolves with treatment of GTD (1). However, it's crucial to control thyrotoxicosis to avoid perioperative complications. This case also highlights the importance of monitoring HCG levels following a complete molar pregnancy due to an increased risk for invasive neoplasm.

1. Walkington, L et al. "Hyperthyroidism and human chorionic gonadotrophin production in gestational trophoblastic disease." British journal of cancer vol. 104,11 (2011): 1665-9. doi:10.1038/bjc.2011.139

Adipose Tissue, Appetite, and Obesity

RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Healthcare Utilization Patterns Among Commercially Insured Patients with Prader-Willi Syndrome: A Retrospective Analysis of Administrative Claims

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SUN-597

Prader-Willi syndrome (PWS) is a complex orphan endocrine disease characterized by hyperphagia and abnormal food-related behaviors that contribute to severe morbidity and early mortality along with a significant burden on patients and caregivers. Life-long medical care is required but the consistency of services rendered to this population has not been evaluated. This study characterized use of US hospital care, specialty physician care, and growth hormone (GH) therapy for PWS patients at different life stages.

Methods: PWS ICD-9 codes in the IQVIA™ Health Plan Claims Data from 1/2006 to 9/2015 were used to identify PWS patients. Inclusion criteria considered patients <65 years of age with ≥12 months of continuous enrollment who received ≥2 PWS diagnostic codes. Observation time was segmented into 12-month patient-years for analysis. Standardized billing code conventions were used to identify and categorize services of interest from 1/2006 to 11/2018.

Results: A total of 5,060 PWS patient years representing 1,461 unique patients were eligible. Mean annual visits to inpatient, emergency department, and physician office settings ranged by age-cohort in years from 0.2-1.6, 0.5-1.3, and 9.2-26.0, respectively. Younger (0-17) and older (50-64) age-cohorts utilized more services than early-mid adulthood age-cohorts. Use of pediatricians or endocrinologists ranged from 76% to 88% among patients under 18 years of age. Utilization of cardiologists, orthopedists, physical therapists, and otolaryngologists ranged by age-cohort from 8-44%, 7-21%, 3-21%, and 7-38%, respectively, with highest utilization among younger patients. GH use increased from 37% to 46% of PWS patients between 2007 and 2018. GH users <18 years of age were 3.0, 0.6, 1.9, 1.7, and 1.4 times as likely to utilize endocrinologists, cardiologists, orthopedists, physical therapists, and otolaryngologists, respectively, compared with non-GH users.

Conclusions: Use of hospital services for PWS patients was bimodal with higher use among the youngest and oldest age-cohorts. Change in the utilization level of select specialists reflects the complexity of care for age-related clinical sequelae, such as orthopedic concerns in infancy and early-onset cardiovascular disease due to hyperphagia and obesity in adolescents, as well as syndrome-specific treatment protocols (e.g., specialty consults needed for GH treatment). That less than half of PWS patients <18 years of age received GH therapy despite growing clinical evidence on the benefits and tolerability of GH suggests a potential gap in provider knowledge of the standard of care for PWS. Our analysis suggests that GH use may be a surrogate for better access to a multidisciplinary care team and specialty services. Considerable variation of services indicates that more effort is required to optimize care in PWS.

Tumor Biology

ENDOCRINE NEOPLASIA CASE REPORTS I

Immunotherapy Use in Adrenocortical Carcinoma with Encouraging Results- a Case Report.

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SUN-911

Adrenocortical carcinoma (ACC) is a rare cancer with a very poor prognosis with median survival of around 17 months. We present a patient with metastatic ACC in whom the response to PD1 inhibitor pembrolizumab has been promising. Case report: A Caucasian female patient presented at the age of 19 y with weight gain, hypertension, moon facies, supraclavicular fullness and increased hair growth on her upper back. Serum potassium concentration was 2.6 mmol/l, cortisol was 46 mcg/dL (nl = 3-12mcg/dL), and plasma ACTH concentration was < 5 pg/ml (nl = 6-58pg/ml). CT abdomen revealed a 5.4 cm right adrenal mass. For ACTH-independent Cushing's Syndrome, she underwent right adrenalectomy within 1 week of presentation. Pathology revealed a 6.5 cm ACC with negative margins, with sinusoidal invasion, but no vascular or capsular invasion. Mitosis rate was 15-20/HPF with atypical mitotic figures. Immunohistochemistry showed no loss of expression of mismatch repair gene products associated with microsatellite instability. She was unable to tolerate mitotane. Genetic analysis was negative for TP53 mutation, and she underwent radiation to the adrenal bed within 6 months following adrenalectomy. She remained without biochemical or structural evidence of disease recurrence until 2.5 years following adrenalectomy, when AM cortisol was 6 mcg/dL (nl < 1.8) after 1 mg and after 2 mg of dexamethasone the previous evening. CT scan of the pelvis, abdomen, and chest revealed 5 solid masses scattered within the lungs. The largest of these being 2.3 cm and 2 cm, and the other 3 being approximately 1 cm. Fine needle aspiration biopsy of the lung lesion revealed ACC metastases. Immunotherapy with pembrolizumab 200 mg every 3 weeks was initiated and continued for 2 years, with a side effect being grade 1 diarrhea. At 1 year after initiating pembrolizumab, she developed primary adrenal insufficiency that is being treated with 0.1 mg/d of fludrocortisone and low dose glucocorticoid replacement (hydrocortisone: 10mg in the morning and 5 mg in the evening), to avoid immune suppression. Pulmonary nodules decreased in size to 6 mm over the 2 years of pembrolizumab therapy and remained stable in size 1 year following completion of pembrolizumab therapy at which time the early morning serum cortisol concentration remained undetectable with a plasma ACTH concentration of 1177 pg/ml (nl = 6-50 pg/ml). In summary, this patient with ACC with normal mismatch repair gene expression demonstrated both structural and biochemical responses to 2 years of pembrolizumab therapy. The major side effect has been primary adrenal insufficiency. The biochemical and structural responses have been durable for 1 year after completion of pembrolizumab therapy.

Conclusion: This patient with microsatellite stable ACC has had a 36-month response to pembrolizumab.

Adrenal

ADRENAL CASE REPORTS I

Metastatic Paraganglioma Secondary to SDHB Gene Mutation: A Case Report and Review of New Therapies

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