Diabetes Mellitus and Glucose Metabolism

DIABETES DIAGNOSIS, TREATMENT AND COMPLICATIONS

Comparison of Phenotype and Metabolic Abnormalities Among Familial Partial Lipodystrophy Due to LMNA or PPARG Variants.

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Familial partial lipodystrophy (FPLD), a rare autosomal dominant disorder, is characterized by marked loss of subcutaneous (sc) fat from the extremities, and predisposition to insulin resistance, diabetes mellitus, dyslipidemia and hepatic steatosis. FPLD2 and FPLD3 due to causal variants in LMNA and PPARG, respectively, are the two most common subtypes. Due to extremely rare prevalence of FPLD3 and limited reports in the literature, whether there are phenotypic differences between the two subtypes remain unclear. Therefore, we compared the anthropometric measurements and prevalence of metabolic abnormalities among 32 FPLD3 subjects (4 M, 28 F; mean ± SD age, 41 ± 17.2 y; body mass index (BMI), 26 ± 4.0 kg/m²) with 271 FPLD2 subjects (66 M, 205 F; age, 37.4 ± 17.0 y; BMI, 26 ± 5.0 kg/m²) from two referral centers in the United States. As compared to those with FPLD2, FPLD3 subjects had borderline higher prevalence of hypertriglyceridemia (66% vs 84%; P = 0.063), but significantly higher prevalence of diabetes (44% vs 72%; P = 0.004), past history of acute pancreatitis (13% vs 52%; P <0.001), and polycystic ovarian syndrome (26% vs 52%; P = 0.011). As compared to FPLD2, FPLD3 subjects had similar fasting triglyceride levels (median 208 vs 255 mg/dL; P=0.15), but lower high-density lipoprotein cholesterol levels (median 37.5 vs 30 mg/dL; P <0.001), higher fasting glucose (median 95 vs 115 mg/dL; P = 0.05) and HbA1c (median 5.7 vs 7.0 %; P = 0.005) levels. Regional body fat was measured by dual energy X-ray absorptiometry in 19 FPLD3 and 105 FPLD2 subjects. In comparison to FPLD2, FPLD3 subjects had higher total fat (median 21.6% vs 26.1%; P = 0.018); upper limb fat (median 20.3% vs 27.3%; P = 0.003) and lower limb fat (median 16.0% vs 20.8%; P = 0.007). Skinfold thickness measurements by calipers also revealed less severe fat loss from both the upper and lower extremities in FPLD3 subjects compared to FPLD2 subjects. As compared to FPLD2, FPLD3 subjects had significantly higher triceps skinfold thickness (median 5.5 mm vs 7.5 mm; P = 0.015); and thigh skinfold thickness (median 5.8 mm vs 11.3 mm; P = 0.001). There were no significant differences in the prevalence of fatty liver, plasma alanine aminotransferase and aspartate aminotransferase levels in the two subtypes. We conclude that compared to FPLD2 subjects, those with FPLD3 have milder lipodystrophy phenotype but paradoxically present with more severe metabolic complications, especially diabetes, dyslipidemia and polycystic ovarian syndrome. It is likely that this discrepancy could be due to early recognition of FPLD2 because of severe fat loss versus initial diagnosis of FPLD3 subjects due to severe metabolic complications leading to discovery of milder fat loss.

Thyroid

THYROID DISORDERS CASE REPORTS II

Use of Weekly Levothyroxine Regimen for Rapid Normalization of Thyroid Hormone Levels: A Case Report

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SAT-LB85
Use of Weekly Levothyroxine Regimen for Rapid Normalization of Thyroid Hormone Levels: A Case Report
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Background: Hypothyroidism affects around 4.6% of the U.S. population. Non-adherence with thyroid hormone replacement is one of the biggest challenges in treating hypothyroidism. The half-life of T4 and T3 in hypothyroidism is about 7.5 and 1.4 days, respectively. A large dose once-weekly administration of levothyroxine (LT4) is possible. Recent publications suggest that once-weekly LT4 does not increase the risk of cardiovascular events and is well tolerated by most patients. Once-weekly LT4 produces similar results as daily LT4 as evidenced by thyroid function tests, and potentially improves patient compliance and satisfaction with the treatment.

Clinical Course: A 29-year-old female with a history of Hashimoto’s hypothyroidism, polycystic ovarian syndrome, depression, presented with irregular menses. Her symptoms included depression, fatigue, increased appetite. Her TSH was grossly elevated at 217 uIU/mL (0.27-4.20 uIU/mL). However upon re-visit, after increasing LT4 to 100 mcg daily her TSH increased to 280 uIU/mL. She admitted to non-adherence with her daily LT4 prescription. Physical exam was notable for sinus bradycardia and slow mentation, otherwise unremarkable. Blood count, basic metabolic panel and hemoglobin A1C were within normal limits. Liver function tests showed mild transaminitis, ALT 46 U/L (10-45 U/L). LT4 was started at 875 mcg per week. At five weeks, her TSH was 6.31 uIU/mL and at seven weeks, the patient was euthyroid with a TSH of 2.53 uIU/mL. Her periods have since normalized.

Conclusion: The current discourse on weekly dosing mainly focuses on its use for non-adherent patients. This case provides a clear time course also demonstrating rapid normalization of TSH using weekly dosing. Weekly LT4 dosing as first-line therapy in noncompliant depressed patients with severe hypothyroidism should be considered.

SAT-LB87
Thyroid
THYROID DISORDERS CASE REPORTS II
Golimumab Induced Thyroiditis
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Background: Subacute thyroiditis is caused by an inflammation and a destruction of the thyroid cells, leading to hyperthyroidism due to leakage of thyroid hormones, followed by possible hypothyroidism and/or full recovery of thyroid function. This is a case report describing a rare occurrence of drug-induced thyroiditis secondary to golimumab.

Clinical Case: A 79-year-old female with HTN, hyperlipidemia, dementia and rheumatoid arthritis was brought to the ER for abnormal behavior including visual hallucinating and insomnia. Initial ER evaluation showed UTI for which antibiotic therapy was initiated. Dementia workup was performed including a negative head CT, nonreactive RPR, and borderline low vitamin B12 level. TFT obtained showed low TSH of 0.2mIU/L, elevated serum FT4 of 1.72ng/ml (n=0.58-1.64ng/ml) and elevated serum FT3 4.38pg/ml (n=2.5-3.9pg/ml), suggestive of hyperthyroidism. The patient reported no heat intolerance, hyperdefecation, or weight changes, but had intermittent palpitations. She denied any history of thyroid problem and did not take thyroid medication, amiodarone, biotin, or any new drug. She reported no fever or URI symptoms within the few weeks prior to admission. In addition to prednisone and methotrexate, she was taking golimumab 50mg every 30 days for the last 22 months for RA. The patient had a family history of hypothyroidism of two daughters and sister. She denied smoking, alcohol, or any other recreational drug use. Her home medications included prednisone 5mg daily, methotrexate, folic acid, lisinopril, simvastatin, and golimumab. On physical examination, she did not appear thyrotoxic and had no exophthalmos, thyroid tenderness, thyroid enlargement or thyroid nodules. Her HR range was 80bmp. Further analysis revealed normal TSI, TPO, and TgAb levels. The thyroglobulin level was very high at 2505ng/ml (n=1.6-59.9ng/ml). Her thyroid sonogram revealed bilateral thyroid nodules, largest at 1.9cm in the right mid pole. A 24-hr RAIU scan showed very low uptake (1.8%) consistent with thyroiditis (hyperthyroid phase). Endocrinology team did not recommend any antithyroid medications. In addition, she did not warrant NSAIDs or beta blockers as she was not symptomatic or tachycardic. In the absence of an autoimmune or an obvious viral process, her subacute thyroiditis was thought to be induced by golimumab.

Conclusion: TNFα inhibitors used to treat chronic inflammatory diseases, have been rarely associated with subacute thyroiditis as described in case reports with adalimumab and