An Unusual Diabetes Variant; Beyond Type 1 diabetes

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Diabetes Mellitus (DM) is a clinical syndrome with multiple etiologies which inform the current classification system. While type 1, type 2, secondary and gestational DM are most commonly recognized, recent clinical observations are expanding the profile of secondary DM. Monogenic variants of DM (MODYs) have a prevalence of ~3-5% among type 2 DM cohorts. Recent reports suggest that the boundaries between DM types are largely artificial with the possibility of individual patients and/or cohorts having multiple underlying coexisting causes. We present the unusual case of a 39 yr old lady with features of both Monogenic (MODY5) and type 1 autoimmune DM.

The patient is 39 yr old African American lady referred for DM care. She had a history of DM presumably type 1 first detected at 6yrs in the setting of DKA. She had been insulin dependent (now Glargine+Lispro) since then and has complications including proliferative retinopathy, nephropathy requiring kidney transplantation 12 yrs ago and peripheral paraesthesiae suggestive of sensory neuropathy. She has an extensive family history of DM spanning three generations most presumed to be “type 1” as they were mostly thin and insulin dependent with early age of onset. Several affected relatives developed major renal disease requiring dialysis. Major examination findings included a BMI of 25.5, hypertension and no acanthosis nigricans. Lab evaluation showed a HBA1c of 8.5, undetectable random C–peptide and elevated GAD65 antibodies (0.06nmol/l). Genetic testing for MODY showed a mis-sense mutation of the HNF-1 beta gene consistent with MODY5 but also heterozygous sequence variants on the IPF 1 gene (associated with MODY4), the HNF -4 alpha gene (associated with MODY1) and the TCF-1 gene (associated with MODY3).

The possibility of multiple etiologies in the cause and type of DM should be considered in subjects with unusual history and/or clinical course. MODYs should be included in this differential diagnosis to enable genetic counseling and appropriate DM prognostication and classification.