Case Identification of Under-Diagnosed Monogenic Disease within a Large Clinical Database

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Gaucher disease (GD) is an autosomal recessive disorder which leads to an accumulation of sphingolipids in numerous organs due to a deficiency of the enzyme glucocerebrosidase. GD is most common in individuals of Ashkenazi Jewish ancestry, with an incidence of about 1 in 800, as compared to about 1 in 60,000 in the general population. There are approximately 200 known mutations in the *GBA* gene, which results in wide phenotypic variability. Continuing research suggests both that GD is under-recognized by providers and that the complete natural history of GD is not yet entirely understood. As treatment is available for GD, there is utility in widening recognition of the disease, especially as diagnostic delays may lead to irreversible damage. This study seeks to expand the understanding of the presentation of GD through the utilization of a large clinical database. The Partners Healthcare System Research Patient Data Registry (RPDR) is a centralized clinical data registry, with records from various hospital systems, such as electronic medical records, throughout the affiliated hospital network. Using the RPDR, symptoms and comorbidities of 51 GD patients were analyzed. Consistent with the variability of GD, the phenotype of the study population varied widely, with no single symptom affecting a majority of the patient population. Many patients had symptoms consistent with more recently recognized complications associated with GD, such as monoclonal gammopathy (20%). There was an increased risk for cancer in the GD patient population as compared to matched controls, and in particular an increased risk for malignant neoplasms of bone. This study may serve as a model for expanding the natural history of other monogenic disorders with wide phenotypic variability.