Metabolic Diseases Masquerading As Primary Progressive Multiple Sclerosis

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Introduction

Multiple sclerosis (MS) is a chronic demyelinating neurological disease primarily affecting young adults, with a prevalence of approximately 0.1% in the Caucasian population. In recent years some studies have raised concern over the possibility of misdiagnosis in MS, which could be as high as 6%, particularly among patients with primary progressive MS. Several single gene disorders share clinical and radiologic characteristics with MS, and have the potential to be overlooked in the differential diagnostic evaluation of both adult and pediatric patients. Diagnosis of primary progressive MS has special chalenges as there are no relapses and the MRI findings are different from those patients with relapsing onset MS. Clinically primary progressive MS is simillar to spastic paraparesis like hereditary spastic paraparesis or other metabolic disorders, such as lysosomal storage disorders, mitochondrial diseases or neurometabolic disorders, presenting with this predominant symptom.

Objectives

The overall aim of our research project* is to develop a Next Generation Sequencing strategy to identify metabolic disorders in patients with a presumptive diagnosis of primary progressive MS.

Methods

Next Generation Sequencing have been performed in a MiSeq Illumina instrument using a custom mitochondrial gene panel with around 250 genes. Libraries have been prepared using SureSelect QXT target enrichment system from Agilent.

Results and Conclusion

So far, panel validation has been performed on positive control DNA's and subsequently a cohort of 96 patients with primary progressive MS are being studied. The uniqueness of this project is to bring NGS technology to the bedside in the management of MS-like conditions, helping clinicians who have patients with diseases for which a diagnosis has been elusive. Recognition of a single-gene disorder as causal for a patient's 'multiple sclerosis-like' phenotype is critically important for effective patient management, and has broad genetic counseling implications for affected families.

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