Abstract

Congenital disorders of glycosylation (CDG) are a new, rapidly growing, and diverse group of inherited metabolic disorders comprising now more than 160 clinical entities, often with only a few described patients. As such, they can often be a diagnostic challenge for physicians, and for patients and their families, the time to find a diagnosis and proper care can be lengthy and burdensome.

This doctoral thesis aims to contribute to a better description of the clinical course and to improve clinical management of selected subtypes of CDG. At the same time, it aims to elucidate the aetiology of the disease in several patients with suspected CDG to enable appropriate care and early genetic counselling in affected families.

The work has resulted in eight articles, seven of them in impacted journals. These are three guidelines, including recommendations of an international expert group on the diagnosis and management of the most common/treatable CDG subtypes (PMM2-CDG, MPI-CDG and PGM1-CDG). These allow each treating physician to get to know the topic quickly and thus help to speed up the diagnosis and to reduce the number of preventable complications and unnecessary examinations. With the same aim, we published a review focusing on new discoveries in the field of CDG in 2017-2020. The next article summarizes the situation of PMM2-CDG patients in the Czech Republic. Two published case reports of the first Czech patients with rare SRD5A3-CDG and ALG3-CDG subtypes expand the phenotypic and genotypic spectrum of these diseases. As a part of my doctoral study, I have also collaborated on an international observational study of the most common subtype PMM2-CDG, in which we have so far published recommendations for the prevention of adrenal insufficiency, a potentially life-threatening complication of this disease, and more publications are in preparation.

The dissertation thus contributed to a better understanding of selected CDG subtypes and to the expansion of the known phenotypic and genotypic spectrum of these disorders. The results of the thesis provide useful guidelines for clinicians, allowing faster diagnosis, more appropriate care and early genetic counseling for affected families. Further research should be focused on finding effective therapeutic options for PMM2-CDG, establishing an international registry of CDG patients, and finding patients with mild forms of those diseases.