Abstract

Objective: Lysosomal storage disorders (LSD) represent a rare cause of neurologic impairment in childhood and adulthood. The aim of our study was to characterize patients with late-onset form of Tay-Sachs disease (LOTS) and alpha-mannosidosis (AM) and to identify typical brain MRI findings.

Methods: Patients with a genetically or enzymatically confirmed diagnosis of LOTS or AM and at least one brain MRI examination were included in the study.

Results: We have characterized the clinical manifestation in a unique cohort of 14 Czech patients with LOTS. As results of international cooperation, we also published analysis of neuroradiological findings in 16 patients with LOTS disease and 14 patients with AM.

Patients with LOTS clinically manifested by cerebellar symptoms, progressive motor neuron disease and psychiatric symptoms. A novel pathogenic variant *c.754C>T* in *HEXA* gene was described in two brothers. Disease was outlined by the slower disease course, milder weakness of lower limbs, milder cerebellar symptomatology and normal cognitive function in them.

The hallmark of neuroradiological findings was the cerebellar atrophy in both LOTS and AM. It was the pontocerebellar atrophy in LOTS, the finding which is also typical for spinocerebellar ataxia or multiple system atrophy. The concurrent presence of pontocerebellar atrophy with cerebellar symptoms imply that LOTS should be considered the differential diagnosis of adult-onset cerebellar ataxias.

We could confirm the decreased signal in basal ganglia and thalamus in T2 weighted brain MRI in AM, commonly interpreted as a result of iron accumulation. However, based on results of our study, AM should not be included in neurodegeneration with brain iron accumulation disorders. The signal intensity profiling demonstrated that the hypointense appearance of thalami and globus pallidus did not differ between AM patients and controls.

Conclusion: Our studies helped to identify the typical clinical and neuroradiological findings in patients with two rare LSD. This knowledge can help in early diagnosis of new patients and in accelerating their approach to the treatment and genetic counseling.

Key words: alpha-mannosidosis, late-onset form of Tay-Sachs disease, lysosomal storage disorders, pontocerebellar atrophy