

Neurological manifestations of Fabry disease

Abstract

The presented thesis deals with cerebrovascular manifestations of a rare X-linked disease, Fabry disease (FD). Screening programs can detect unrecognized disease and increase awareness of the disease with the goal of early diagnosis and initiation of therapy before developing an irreversible organ damage. Identifying vascular abnormalities and the influence of comorbidities on the cerebrovascular phenotype of FD patients may help to promote the knowledge of the pathophysiology of cerebrovascular involvement. The main objectives of the studies underlying this thesis were to determine the prevalence of FD and to evaluate the relevance of FD diagnosis in an at-risk group of patients with acute ischemic stroke, to analyse the cerebrovascular phenotype of patients with FD using ultrasound, and to identify predictors of significant cerebrovascular involvement. In this thesis we showed a relatively high prevalence of FD in adult patients with acute stroke, proposed to reclassify the G325S variant, and identified a novel R30K variant. We noted that the combination of aseptic meningitis with lacunar stroke in a young person should lead to suspicion of FD. We further demonstrated multiple differences in neurosonological parameters between patients with FD and a control group of subjects without FD. We confirmed a higher incidence of structural changes in the vascular wall of large arteries and found a lower cerebrovascular reactivity of the middle cerebral artery in patients with FD. As a possible new specific phenotype, we detected a higher variability of cerebral vascular reactivity in response to the breath-holding test. We demonstrated an increased pulsatile index, which could reflect increased vascular resistance and stiffness of the vasculature. Thus, the observed changes suggest a complex vascular involvement. We identified age and overall disease severity as significant predictors of these changes in a cohort of FD patients. The presence of classical vascular risk factors might also play a role.

Keywords: Fabry disease, stroke, intima-media thickness, vertebral artery, pulsatility index, cerebrovascular reactivity, white matter lesions