McLeod neuroacanthocytosis: genotype and phenotype.


Source

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Abstract

McLeod syndrome is caused by mutations of XK, an X-chromosomal gene of unknown function. Originally defined as a peculiar Kell blood group variant, the disease affects multiple organs, including the nervous system, but is certainly underdiagnosed. We analyzed the mutations and clinical findings of 22 affected men, aged 27 to 72 years. Fifteen different XK mutations were found, nine of which were novel, including the one of the eponymous case McLeod. Their common result is predicted absence or truncation of the XK protein. All patients showed elevated levels of muscle creatine phosphokinase, but clinical myopathy was less common. A peripheral neuropathy with areflexia was found in all but 2 patients. The central nervous system was affected in 15 patients, as obvious from the occurrence of seizures, cognitive impairment, psychopathology, and choreatic movements. Neuroimaging emphasized the particular involvement of the basal ganglia, which was also detected in 1 asymptomatic young patient. Most features develop with age, mainly after the fourth decade. The resemblance of McLeod syndrome with Huntington's disease and with autosomal recessive chorea-acanthocytosis suggests that the corresponding proteins--XK, huntingtin, and chorein--might belong to a common pathway, the dysfunction of which causes degeneration of the basal ganglia.

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