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An ITPR1 gene deletion causes SCA15 and 16; a genetic, clinical and radiological description.

Spinocerebellar ataxia (SCA) 15/16 is an autosomal dominantly inherited, almost pure cerebellar ataxia, which shows slow or no progression. (It has been designated variably SCA15 and SCA 16; we refer to it here as SCA15/16 to avoid confusion). Deletions in the inositol 1, 4, 5-triphosphate receptor 1 (ITPR1) on chromosome 3 have been shown to cause SCA15/16 in six families worldwide to date, with one further Japanese family identified as having an ITPR1 point mutation. We present a previously unreported SCA15/16 kindred. We describe the clinical phenotype of the family in detail; affected subjects display a remarkably slow, almost pure cerebellar syndrome. We also present genetic analyses for all subjects and longitudinal MRI data for one affected subject. Genetic analysis shows a deletion of 346,487bp in ITPR1 (the second largest ITPR1 deletion reported to date), suggesting SCA15 is due to a loss of ITPR1 function, and western blotting of lymphoblastoid cell line protein confirms reduced ITPR1 protein levels. Serial MRIs show progressive midline cerebellar atrophy with mild inferior parietal and temporal cortical volume loss in the absence of clinical disease progression. We believe that genetic testing for SCA15/16 should become a routine DNA screen available in all Neurogenetics clinics, which is likely to lead to an increased rate of the diagnosis. Familiarity with the phenotype is therefore important for all neurologists.