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KLEEFSTRA SYNDROME: NEUROPSYCHIATRIC SEQUELAE

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Introduction: Submicroscopic deletions of the distal long arm of chromosome 9q are relatively common and give rise to a clinically recognizable phenotype referred to as the Kleefstra Syndrome [OMIM 610253]. It was shown that haploinsufficiency of the EHMT1 (Euchromatic Histone Methyltransferase 1) gene is responsible for the core phenotype by identifying cases with intragenic EHMT1 loss of function mutations. Key features of the syndrome are mental retardation, childhood hypotonia and facial dysmorphisms. Congenital heart and renal defects, microcephaly, epilepsy, and behavioural problems are frequently present.

Objectives: Description of the developmental, behavioural and neuropsychiatric characteristics in 4 middle aged patients with recently diagnosed Kleefstra syndrome

Aims: Contributing to the putative behavioural phenotype of Kleefstra syndrome.

Methods: Detailed neuropsychiatric and neuropsychological assessment.

Results: In the 4 patients, conventional cytogenetic investigation showed normal karyotypes. With routine subtelomeric MLPA and additional 9q regional specific MLPA tests, a submicroscopic deletion of the long arm of chromosome 9 (9q34.3) was found. Both deletions comprised the EHMT1 gene, in agreement with the diagnosis of Kleefstra syndrome. In all patients a severe apathy and a marked dyssomnia were present. Although some motor symptoms could be assessed with a catatonia rating scale, these have to be considered as a consequence of the apathy and belong therefore not to the catatonic spectrum.

Conclusions: Kleefstra syndrome is constituted, in addition to its distinct phenotypic features, by a specific behavioural phenotype that comprises, apart from the absence of speech development, a specific sleep disturbance and severe apathy from the third decade on.

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