Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxi

Keywords: Clinical Genetics, Malformations and Dysmorphology, KW015 - CHARACTERIZATION OF DISORDERS, KW022 - CLINICAL HISTORY, KW099 - NATURAL HISTORY, KW110 - PHENOTYPE, KW131 - SPLICING MECHANISMS

Hereditary disorders of connective tissue may present with Chiari I malformation, occipitoatlantoaxial hypermobility, and functional cranial settling. *C. Francomano[1], T. Milhorat[2], P. Bolognese[2], M. Nishikawa[2], N. McDonnell[3]* 1) Greater Baltimore Med Ctr, Harvey Institute Human Genetics, Baltimore, MD; 2) The Chiari Institute, North Shore-Long Island Jewish Health System, Manhasset, NY; 3) National Institute on Aging, NIH, Baltimore, MD.

We report an association of hereditary disorders of connective tissue (HDCT) and Chiari malformation 1 (CM1), presenting with lower brain stem symptoms attributable to occipito-atlantoaxial hypermobility and functional cranial settling. The prevalence of hereditary disorders of connective tissue (HDCT) was determined in a prospectively collected cohort of 2,813 patients with CM1. All patients underwent a detailed medical and neuroradiological workup that included an assessment of articular mobility. Using reconstructed 3D-CT and plain x-ray images, osseus structures comprising the craniocervical junction were investigated morphometrically in 114 patients with HDCT/CM1 and compared to those in patients with CM1 alone (n = 55) and normal controls (n = 55). The diagnosis of Ehlers-Danlos syndrome (EDS) or other HDCT was made in 357 of 2,813 of patients with CM1 (12.7%). The clinical features of HDCT/CM1 were distinguished from those of CM1 alone by clinical stigmata of HDCT, a greater female preponderance (7:1 vs. 3:1), and a greater incidence of lower brain stem symptoms (0.43 vs. 0.05), retroodontoid pannus formation (0.71 vs. 0.16), and hypoplasia of the oropharynx (0.45 vs. 0.02). In patients with HDCT/CM1, upon sitting or standing there was

reduction of the basal-dens interval (3.6 mm), enlargement of the basal-atlas interval (3.0 mm), and reduction of the clivus-axis angle(10.8^{o}), clivus-atlas angle (5.8^{o}), and atlas-axial angle (5.3^{o}). These changes were reducible by cervical traction or returning to the supine position. In normal controls and patients with CM1 alone, these measurements did not change with position.

Conclusions: The identification of HDCT in 12.7% of patients with CM1 establishes an association between these previously unrelated disorders. Patients with HDCT and symptoms suggestive of CM1 should be evaluated with brain MRIs in the supine and upright positions.

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