ASSOCIATION OF AUTISM AND TUBEROUS SCLEROSIS

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Clinical Genetics: Characterization of Disorders (continued)

Usefulness of the Axial Mesodermal Dysplasia Spectrum concept as a pathogenetic diagnosis. I. Simonow(1), Y. Lacauna(1), (1) Medical Genetics and (2) Dept. Mental Health, Medical School, Foresterhill, Aberdeen, U.K.

We proposed and developed the concept of the Axial Mesodermal Dysplasia Spectrum. In 1990, Wulfsberg and Grigas reported a patient with Amand syndrome associated with the Pacio-Auriculo-Vertebral Sequence, which could be part of this mesodermal dysplasia spectrum, and reviewed several cases reported of associations of mesodermally derived sequences. We report 3 patients in whom we raised this diagnostic possibility. 3 Presented with features of the FAV spectrum, Treacher-Collins, Wilm's, Hemiplegia, Mesodermally-unusual facies, and Hay-Wells syndrome. 4 Presented with short stature, severe MR, microphthalmia, scoliosis, striking urogenital anomalies, kyphoscoliosis, short femurs, absent ribs, costal polydactyly left hand. MR was present in the maternal family. Presented with small ears, bilateral ambiguous anomalies, and skeletal malformations. These patients support the existence of this pathogenetic concept.


Grampian region in North East Scotland has the highest prevelence of Huntington's Disease in Europe. The Pre-symptomatic Predictive Test Programme has been in operation for 30 months and 38 results have been given. Exclusion testing has been requested by another 13 couples and 10 has been completed. The follow up of these patients groups has shown no significant psychiatric morbidity. The Beck's Hopelessness Scale is well as an assessment of lifestyle changes psychiatric interview.

The sex distribution of those receiving results, whether they had the gene or did not carry it, is approximately equal in both groups. This is in contrast to the affected population in Grampian, where an excess of females exists (38%). This unexpected ratio was also found in the affected individuals in Scottish psychiatric and general hospitals and in those dying from the diagnosis of Huntington's Disease over the last decade. This has not been explained by the local general population sex ratio, early death in affected males, early diagnosis in females, or a longer lifespan in affected females, nor does it appear to be a reflection of sample size. Five years of study has not revealed undiagnosed males in the population.

Late-infancy globoid cell leukodystrophy. S. Sklaver(1),* R. DeCarlo(1), K. Wiesiewicz(1), S. Gurdon(1), and D. Deshmukh(1). (1) OMRDD New York State Institute for Basic Research in Developmental Disabilities, Staten Island, NY and (2) St. Vincents Medical Center at Richmond, Staten Island, NY, USA.

Globoid-cell leukodystrophy (Krabbe Disease) usually presents between 6-12 months of age with rapidly progressive psychomotor regression. While other clinical forms have been described with later onset, only rare cases have been noted in 9 mo and 2 yrs and in only one case was MRI reported. We describe the clinical and phenotypic picture in two unrelated patients with onset at 10 and 15 months. Diagnosis was confirmed enzymatically using labelled galactocerebroside and lacto-oligosaccharide. Special emphasis was placed on previously attained motor milestones were the first observed findings and occurred over a period of about 2 months. In one child these symptoms developed following measles immunization at the development of a maculopapular rash and fever. Periodic extremity posturing and irritability were then noted. Neither child had visual disturbance at time of onset. CSF protein was elevated. The older child had mild dilatation of the ventricular system demonstrated on 2nd generation CT scan. The younger child had circumscribed and well defined bilateral regions of low density in the mid corona radiata from the lateral ventricles to the convexity on CT scan and 2-3 cm ovoid, poorly defined hyperintensities in the T2 weighted images in the deep white matter of the frontal and parietal lobes on MRI. These cases further delineate the phenotype and clinical heterogeneity in late-infantile Krabbe disease.

Association of autism and tuberous sclerosis. S. Smalley(1), F. Tanguay(1), and M. Smith(2). (1) Department of Psychiatry, UCLA, Los Angeles, CA and (2) Department of Pediatrics, UC Irvine, CA.

Tuberous sclerosis (TSC) is an autosomal dominant disorder characterized by hamartomas of multiple organs including skin and brain. Autism is a behavioral disorder that has been noted in patients with TSC. We are investigating the association of autism and TSC in an ongoing family/genetic study. In our first 27 families, 11 were classified through TSC probands and 11 through autistic probands, we have preliminary data on behavioral disorders in probands and their relatives. In this clinically based sample, 36% of TSC probands and 27% of all TSC subjects (11 probands and 4 controls) met or exceeded autistic symptom criteria for autism, a frequency significantly greater than the population frequency of 1%. Our data support a significant association of TSC and autism. The mechanism of this association is under investigation by our group. Using a family history interview, among 215 relatives of autistic probands, 3% have speech delay, 10% have cognitive deficits including mental retardation, and 4% have social deficits. Among 264 relatives of TSC probands, 3% have speech delay, 3% cognitive deficits, and none have social deficits. These findings suggest familial differences may exist between autism co-occurring with and without TSC.