Early Infantile Progressive Neurodegenerative Disease in a Gipsy family

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Abstract

Background: Dysmyelinating diseases, or leukodystrophies, encompass a spectrum of inherited neurodegenerative disorders affecting the integrity of myelin in the brain and peripheral nerves. They can be grouped into lysosomal storage diseases, peroxisomal disorders, and diseases caused by mitochondrial dysfunction. Distinctive clinical, biochemical, pathologic, and radiologic features enable the narrower differential diagnosis. We present a Gipsy family with a distinct phenotype present in a neonatal period. The infants presented with spasticity of the rigid type, difficulties with breathing, cry mimicking cock-a-doodle-doo and hearing loss. The deterioration was rapid to a severe bulbar palsy and death before the age of two years. Identical clinical findings were not found in any other disease. Chromosomal abnormalities and FISH subtelomeric deletions testing were normal. Most common genetic causes were excluded. Genetic heterogeneity is suspected and genetic linkage analysis considered. Cases/Group study: We present a Gipsy family with 6 affected infants. Their phenotype is very distinctive, suggestive of progressive neurodegenerative disorder. Laboratory findings and MR findings are suggestive of dysmyelinating disease, similar to metachromatic leucodystrophy or a milder form of Krabbe disease. Lysosomal diseases were excluded. Characteristics of infants encompass clinical features: spasticity, opistotonus, microcephaly, breathing troubles with a severe stridor and a distinctive cock-a-doodle-doo cry, some have umbilical hernia. They have early infancy seizures and bilat. deafness. Their pre- and perinatal history was unremarkable, with good Apgar scores and born AGA. Neonatal onset is profound with severe spasticity and neonatal seizures, progressing to death before the age of 2 years. Conclusions: The major feature of leukodystrophies is the lack of proper myelin formation during early development or the onset of myelin loss later which is described as
hypomyelination or dysmyelination. It is caused by a primary block in normal myelin synthesis because of a genetic mutation expressed in oligodendrocytes, or failure in myelination secondary to neuronal or astroglial dysfunctions. Our studied group displayed clinical characteristics of dysmyelinating disease, which we were not able to confirm more specifically. Mutations in the genes encoding the five subunits of eukaryocytic initiation factor 2B (eIF2B) are considered. However, we may be reporting a new syndrome hence linkage analysis in the Gipsy kindredship is considered.