

Mental Retardation in Tuberous Sclerosis Complex: Better Data Better Prediction

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Tuberous sclerosis was first described by von Recklinghausen in 1862 and named sclérose tubéreuse by Bourneville in 1880 for the potato-like firmness of the brain lesions⁽¹⁾. It is an autosomal dominant hereditary disease with frequent sporadic cases and variable clinical manifestations. It is a developmental disorder affecting nervous system, skin, retina and viscera by hamartomas, malformations and congenital tumors often early in life. The cardinal features of tuberous sclerosis are skin lesions, epileptic seizures and mental retardation, in accordance with a high incidence of pathological involvement in the skin and the CNS.

The clinical course of the disease depends upon the severity of disease manifestations and the age of disease onset. Patients with skin manifestations only or mild involvement often have a stationary course, whereas those with full-blown syndrome have a progressive course with increasing seizures, mental deterioration and other symptoms. There is a close relationship between mental retardation and the onset of seizures at an early age. In particular, young patients with infantile spasms are at great risk of developing mental abnormality later. In one study on 106 patients with tuberous sclerosis, seizure type on initial examination (i.e. infantile spasms) was the only risk factor which showed a consistent and independent association with poor mental outcome⁽²⁾. In two studies which counted the number of cortical tubers detected by MRI, cortical tuber was significantly more

numerous in patients who had mental disability and seizure onset before 1 year of age^(3,4). Furthermore, the cortical tube count was strongly associated with moderate-to-severe mental retardation and early, poorly controlled seizures, such as infantile spasms.

In this issue, Chou and Chang analyzed prognostic factors for mental retardation in 35 patients with tuberous sclerosis complex (TSC)⁽⁵⁾. Their ages ranged from 5 to 50 years with a mean of 15.9 ± 12.5 years. As expected, the most common manifestations were those of the skin (94.4%) and the CNS (seizure, 91.4%; mental retardation, 62.5%). Although mental retardation was correlated with the presence of cortical tubers and subependymal nodules on CT/MRI, it was highly correlated with poor control of seizures which was significantly higher in generalized tonic-clonic seizures than other seizure types including infantile spasm. Furthermore, there was no correlation between the age of seizure onset and the development of mental retardation.

It is conceivable that mental retardation is related to the presence of brain lesions which indicates the severity of the CNS involvement. However, the relationship between mental retardation and poor control of seizures needs to be clarified. Although poor control of seizures may indicate a more severe involvement of the CNS, it may be partly or entirely due to other conditions, including poor compliance, inadequate medication and improper selection of anti-epileptic drugs. Unfortun-

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ately, the latter conditions were not mentioned. To complicate the issue, how to define poor control of seizure was inadequate except that seizures occurred more than 3 times per year. Was it determined for the year of the study or the average over years? There are other questions that need to be clarified, including 1) How many patients with infantile spasm had mental retardation? and 2) How many patients had more than one types of seizures and how many patients with mixed types of seizures had mental retardation?

Mental retardation was evaluated by the diagnostic criteria of the DSM III-R. There was no mention who evaluated the patients using the criteria of the DSM III-R to diagnose mental retardation and what was the severity of mental retardation in those patients? Was poor control of seizure seen more frequently in patients with moderate-to-severe mental retardation than those with mild mental retardation? Because patients with poor control of seizures might be over-medicated, mental retardation might be related to the effects of medication.

In order to provide a more definite answer to the risk

factors for mental retardation in TSC, more comprehensive data collection and more detailed data analysis are required. Such study by the authors of this report is warranted and welcome.

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