Delayed onset dystonia secondary to neonatal anoxia

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Dystonia is a movement disorder, which is defined as an "involuntary" sustained muscle contraction affecting one or more sites of the human body. Frequently it originates twisting and respective movements or abnormal postures.[1] The dystonic phenomenon occurs during the wake state and increases with fatigue and stress, while it improves with relaxation, hypnosis, and sleep. Childhood dystonia is characterized by a heterogeneous group with strong inherited background. Dystonia is classified according to the etiology.[2] The dystonic phenomenon is the only symptom in primary dystonia. In dystonia-plus or secondary dystonia, other neurological abnormalities are also associated consisting of parkinsonism and myoclonus that are probably due to acquired exogenous causes and heredodegenerative disorders.[3] In addition, myoclonus, which is sudden and brief muscular contraction,[4] might be associated with dystonia in some conditions, including dystonia-plus, neurodegenerative disorders, and secondary dystonia caused by stroke, anoxia, infections, and toxins. We report a case of delayed dystonia associated myoclonus in an adolescent girl, which was secondary to a neonatal anoxia, and we discuss clinical and therapeutic features.

A 12-year-old girl was referred to our department for abnormal movement of the right arm. She was the fourth child of unrelated parents, no history of neurological problems was elicited in family members. She was born at term with prolonged labor, neonatal distress with cyanosis that required intensive care. Her psychomotor development was normal, no particular medical problem or school difficulties were noticed until her 12th birthday, thereafter, she developed abnormal posture of the right upper limb with sudden jerks of the hand making limited daily movements. The neurological examination showed dystonia of the right upper limb with myoclonic movements making prehension and writing difficult. This also consisted of adduction of the shoulder, extension, and internal rotation of the elbow and wrist with flexion of the metacarpophalangeal joints, and extension of the interphalangeal joints. The ophthalmological examination did not reveal Kayser-Fleischer ring. The abdominal examination did not reveal any hepatosplenomegaly, and the cardiac, pulmonary, and dermatological examinations were all normal. Magnetic resonance imaging showed high signals in the left caudate nucleus, rolandic, and occipital area involving both cortical and sub-cortical sites (**Figure 1**). Routine laboratory assessments including blood cell count, erythrocyte sedimentation rate, urea, creatine, glucose, transaminases, and prothrombin were all found normal. Considering dystonia etiology, investigating metabolic diseases including Wilson disease, organic aciduria, and mitochondrial disease were performed. Urinary and plasmatic copper, ceruloplasmin, CSF, and plasmatic lactic and pyruvic acids, showed all normal levels. The chromatography of urine organic acids was normal, and the anti-DNA autoimmune markers were negative. A muscle biopsy was performed and the histological study did not reveal any fibers disorder. The clinical examination and negative studies completed, suggested a late onset dystonia following neonatal anoxia. Therefore, levodopa treatment was decided with daily dose of 600 mg over 3 months. However, this treatment was interrupted later considering the negative response. Six months later, the symptomatology worsened and she stopped going to school as she became unable to write. The clinical examination found the initial dystonic posture more pronounced with extension to the left upper limb. In addition, dystonia of the left arm was less manifest than on the right side. Nevertheless, she was walking normally without any dystonia of lower limbs and without any extrapyramidal signs. Magnetic resonance imaging showed identical lesions to the first examination.

The first description of delayed onset dystonia was by Saint Hilaire et al,[5] and several reports have been published describing the clinical presentation with delay ranging from 1-21 years, and imaging abnormalities were

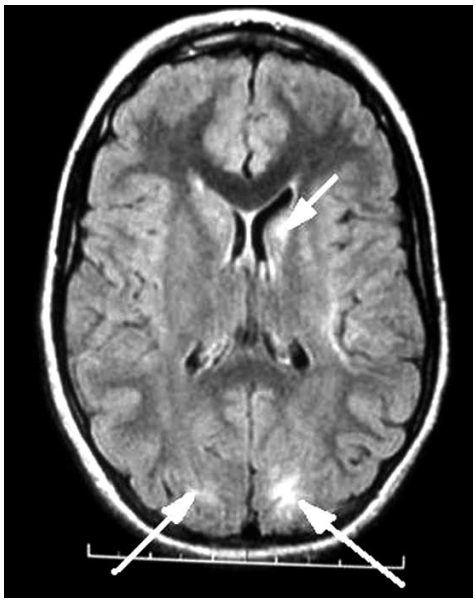

Figure 1 - Axial slices of FLAIR magnetic resonance imaging showing a bilateral symmetrical hypersignal in cortical and sub-cortical at the level of Rolando's area and caudate nucleus.

found in 50%.[5] Delayed onset dystonia diagnosis should be retained when other evident toxic origin and any other neurological features suggesting a neurodegenerative disease are not admitted. Perinatal suffering could be confirmed using the retrospective diagnostic criteria of neonatal asphyxia.[5] The association of delayed onset dystonia with myoclonus could be confused with a primary dystonia, this concerns myoclonic dystonia DYT 11, a dystonia-plus syndrome, which is inherited as a dominant autosomal characteristic starting in the first or second decade having a positive response to alcohol. In our patient, myoclonic dystonia is ruled out because this condition and the primary dystonia are not associated with any known anatomicopathological or imaging lesion.[3] The MRI abnormalities are often described with heredodegenerative diseases since the dystonia is part of widespread neurodegenerative syndrome with an inheritance pattern and morphological brain changes such as Wilson disease, organic aciduria, mitochondrial disease, and lysosomal diseases.[3] In our case, biological and metabolic assessments were negative for Wilson disease, mitochondrial disease, and organic aciduria, even though, lysosomal enzymes were not investigated as the clinical presentation did not support this affection. Treatments used in dystonic children are fairly efficient. Partial benefits might be recorded using levodopa with a daily dose of 600 mg. The anticholinergic trihexyphenidyl medication was used with good results in some children with dystonia. The maximum benefit required using high doses at 30-60 mg/day.[3] If there is unsatisfactory benefit from levodopa or trihexyphenidyl, baclofen, or benzodiazepines are prescribed since they can be helpful. Whenever oral medication is ineffective, botulinum toxin injections and intrathecal baclofen are recommended. Evermore, stereotaxic surgery could be suggested.[3] Finally, the diagnosis of dystonia in children is mostly difficult, especially at the early stage of the disorder associating focal forms. A meticulous review of the perinatal history would guide diagnosis, mostly, it consists of neonatal suffering of full-term neonate.

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