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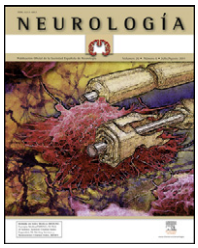

ORIGINAL ARTICLE

Prenatal encephalopathies of unknown origin. Our 19-years experience. To what extent must genetic and biochemical studies be carried out?☆,☆☆

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Prenatal encephalopathies;
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Abstract
Introduction: We examine those prenatal encephalopathies with clinical or neuroimaging data of encephalopathy before the birth. They affect a significant number of children seen by paediatric neurologists. They can be of disruptive origin (due to vascular problems, drugs, toxins or congenital infections), and genetically determined. We include cases of autism spectrum disorder and mental retardation with no history of perinatal of postnatal damages.
Material and methods: We analysed our 19-year neuro-paediatric data base in search of prenatal encephalopathies and their diagnostic origin. We also analyse the studies made in the cases with a diagnosis of unknown origin.
Results: The 19-year period of study in the data base included 11,910 children, and 1596 (13.5%) were considered as prenatal encephalopathies; 1307 children (81.4%) had a diagnosis of unknown origin, despite many investigations being done in a large number of them.
Discussion: Most of the children included in this study suffer a rare disease, and whether they are identified or not, they increasingly require an early diagnosis. Peroxisomal, mitochondrial, lysosomal diseases, carbohydrate glycosylation deficiency syndrome and other inborn error

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of metabolism, congenital infections and genetic encephalopathies, can be clinically indistinguishable in early life and require specific studies to identify them. Early diagnosis requires strategies using step-wise systematic studies, giving priority to those diseases that could be treated, and in many cases using an individualised approach. We believe that the potential benefits of early diagnosis, including savings on further studies, genetic counselling and prenatal diagnosis, overcome the financial costs.

PALABRAS CLAVE
Diagnóstico etiológico;
Diagnóstico precoz;
Encefalopatías prenatales;
Enfermedades raras;
Estudios bioquímicos;
Estudios genéticos;
Neuroimagen

Encefalopatías prenatales. Nuestra experiencia diagnóstica de 19 años. ¿Hasta dónde con los estudios bioquímicos y genéticos?

Resumen
Introducción: Consideramos encefalopatías prenatales las que tienen datos clínicos o prenatales de encefalopatía antes del nacimiento. Afectan a un número importante de niños controlados en las consultas de neuropediatría. Pueden ser disruptivas (por problemas vasculares durante el embarazo, drogas, tóxicos o infecciones congénitas), y genéticamente determinadas. Incluimos casos de trastorno del espectro autista y retardo mental sin historia de sufrimiento perinatal o postnatal.
Material y métodos: Se revisa nuestra experiencia en el diagnóstico etiológico de las encefalopatías prenatales durante los últimos 19 años. Se analizan los estudios realizados en los casos sin diagnóstico etiológico.
Resultados: En el periodo de estudio de 19 años y 5 meses, en la base de datos de neuropediatría figuran 11.910 niños. Tienen establecido el diagnóstico de encefalopatía prenatal 1596 (13,5%). De ellos no tienen diagnóstico etiológico preciso 1.307 niños (81,4%) pese a habérseles realizado múltiples estudios complementarios, fundamentalmente bioquímicos, genéticos y de neuroimagen.
Discusión: Muchos de los niños incluidos en este estudio presentan enfermedades raras, estén o no identificadas, que demandan crecientemente un diagnóstico precoz. Enfermedades peroxisomales, lisosomales, mitocondriales, defectos congénitos de la glucosilación, entre otras enfermedades metabólicas hereditarias, infecciones congénitas, cromosomopatías y genopatías, pueden ser indistinguibles clínicamente y necesitan estudios específicos para su identificación. Un diagnóstico precoz precisa estrategias de estudios sistemáticos de forma escalonada, priorizando las enfermedades que tienen posibilidades terapéuticas y en muchos casos es necesaria también una aproximación individualizada. Creemos que las ventajas potenciales del diagnóstico precoz, incluido el ahorro de más pruebas, y la prevención, probablemente sobrepasan el gasto financiero.

Introduction

The most frequent health care process that neuro-paediatric professionals are involved in begins with the motive for the first consultation, from which a diagnosis that can have up to four different levels is sought:

1. Topographic location of the problem: encephalopathy (which, in turn, may be exclusive or with associated involvement of the cerebral hemispheres, cerebellum, midline, etc.); we must always consider the possible involvement of the visual and auditory pathways, myelopathy, disorder of the neuromuscular unit (anterior horn, peripheral nerve [axonal or myelin]), neuromuscular junction or muscle involvement.
2. Temporal location of the origin of the problem: prenatal problems (genetically determined or disruptive), perinatal or postnatal (stroke, infection, etc.). Some problems do not have a specific temporal location: some cases of certain inherited metabolic diseases (IMD) and neurocutaneous syndromes combine central nervous system abnormalities that already began in the uterus.
3. Functional diagnosis: motor problems through malfunctions at any level of the central nervous system, cognitive and behavioural problems, and epilepsy due to brain dysfunctions and sensory problems (vision or hearing) from encephalopathy or sight or hearing organ disorders. The most frequent functional diagnoses are childhood cerebral palsy, mental retardation, autism and epilepsy. They are all the result of encephalopathies, but could be due to different aetiologies, which could be prenatal, perinatal or postnatal. A pure motor problem could arise from an encephalopathy as well as a spinal cord or neuromuscular unit disorder. Encephalopathy may be seen as isolated disturbances or associated to motor, cognitive, behavioural or sensory (visual or hearing deficit) ones. Visual impairment and hearing loss may be caused solely