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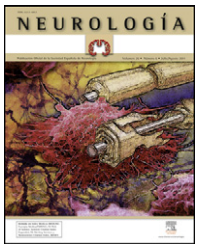

ORIGINAL ARTICLE

Neuroimaging findings in patient series with mucopolysaccharidosis☆

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Abstract
Introduction: Mucopolysaccharidoses (MPS) are a group of inherited disorders due to lysosomal enzyme deficiencies. The aims of this study are to describe the neuroimaging findings in children evaluated in our hospital with this diagnosis, looking for a possible correlation of these alterations with the type of MPS and clinical severity, and finally to compare these findings with those previously reported.
Material and methods: We retrospectively analysed the medical records of 19 patients who had been diagnosed with MPS between 1992 and 2010: 7 had type I (5 with Hurler syndrome and 2 with Hurler—Scheie syndrome), 10 had type II or Hunter syndrome (4 with the severe form and 6 with the mild form), 1 had type III or Sanfilippo syndrome and 1 had type VI or Maroteaux—Lamy syndrome. We assessed the brain neuroimaging studies: computed axial tomography (CAT) in 5 patients, and magnetic resonance imaging (MRI) in 15.
Results: We observed a broad spectrum of neuroimaging anomalies. In CAT: mega cisterna magna (3/5, 60%). In brain MRI: dilated Virchow—Robin perivascular spaces (11/15, 73%), white matter abnormalities (11/15, 73%), and ventriculomegaly (5/15, 33%).
Conclusions: Abnormal findings in neuroimaging studies are frequent in MPS (dilated Virchow—Robin perivascular spaces, white matter abnormalities and ventriculomegaly). Thus, given these abnormalities we should be aware of this possible diagnosis, particularly when typical signs and symptoms are present. However, we did not find a correlation between these findings and either any specific type of MPS or clinical severity.

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PALABRAS CLAVE
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Neuroimagen;
Síndrome de Hurler;
Síndrome de Hunter

Hallazgos neurorradiológicos en una serie de pacientes con mucopolisacaridosis

Resumen
Introducción: Las mucopolisacaridosis (MPS) son un grupo de enfermedades hereditarias de depósito lisosomal. El objetivo de esta revisión es describir las alteraciones neurorradiológicas en los niños evaluados en nuestro hospital con este diagnóstico, buscar la posible correlación de estas alteraciones con el tipo de MPS y con la gravedad clínica, y comparar nuestros hallazgos con lo descrito en la literatura.
Material y métodos: Revisamos retrospectivamente las historias clínicas de 19 pacientes diagnosticados de MPS en el periodo 1992—2010: 7 tipo I (5 con síndrome de Hurler y 2 con Hurler—Scheie), 10 tipo II o síndrome de Hunter (4 con la forma grave y 6 con la moderada), 1 tipo III o síndrome de Sanfilippo y 1 tipo VI o síndrome de Maroteaux—Lamy. Se analizaron las pruebas de neuroimagen: tomografía computarizada (TC) en 5 pacientes y resonancia magnética craneal (RMC) en 15.
Resultados: Encontramos un amplio espectro de alteraciones radiológicas. En la TC destaca la megacisterna magna (3/5, 60%); en la RMC el aumento de los espacios perivasculares (11/15, 73%), la alteración parcheada de la sustancia blanca (SB) (11/15, 73%) y la ventriculomegalia (5/15, 33%).
Conclusiones: Algunas anomalías neurorradiológicas son frecuentes en las MPS (aumento de los espacios perivasculares, alteraciones de la SB, ventriculomegalia), por lo que ante estos hallazgos debemos investigar esta posibilidad diagnóstica, especialmente en pacientes con clínica compatible. No hemos hallado datos específicos de cada tipo de MPS, ni relación de estas alteraciones radiológicas con la gravedad de la forma clínica.

Introduction

Mucopolysaccharidoses (MPS) are a group of congenital errors of metabolism characterised by the deficiency of one of the lysosomal enzymes catalysing the degradation of glycosaminoglycans (GAG) or mucopolysaccharides. This deficiency leads to abnormal accumulation of GAG in the lysosomes, and to it being excessively excreted in urine. There are 7 different types of MPS and their overall prevalence is estimated at 1 in 22 500 individuals. These diseases are multisystemic, degenerative, chronic and progressive, and entail a number of disorders, both physical and mental.[1,2] They are usually difficult to detect in newborns (unless other family members are affected) since these children are apparently normal at birth. They gradually develop a number of phenotypic abnormalities which include distinctive coarse facial features, changes in the skeletal system (dysostosis multiplex), small size, contractures, cardiovascular disorders (valvulopathy, myocardiopathy), visceromegalies, inguinal and umbilical hernias, skin infiltration disorders, corneal opacity, and hearing impairment.[2—4] Neurological manifestations may differ considerably depending on the type of MPS. Progressive cognitive impairment is very frequent in severe MPS types I, II, and VII, and also in type III.[5—7] Patients with neurodegeneration are extremely disabled, with death usually occurring in the first or second decade. Patients with milder forms of the disease may reach adolescence and adulthood, but high rates of morbidity are common.[5] All types of MPS are inherited by means of recessive autosomal transmission, except for MPS type II or Hunter syndrome, which is an X-linked recessive disease. MPS is diagnosed based on quantitative analysis of GAG levels in the patient's urine. In addition, an enzymatic study specific to the type of MPS and a molecular study are also performed. The treatment of MPS is a complex process.[5] Haematopoietic stem cell transplantation has been proven to be effective treatment for some forms of MPS. This is currently the treatment of choice for some patients with severe MPS I; however, morbidity and mortality rates are very high.[2] Enzyme replacement therapy has been proven effective for MPS I, II and VI. For all types of MPS, the complications that arise as the disease progresses must be treated correctly.[2,5,6]

The first neuroradiological studies to evaluate MPS were performed using computed tomography (CT), which revealed non-specific data suggestive of these diseases. Examples of such findings were as follows: hypodense areas in the white matter and dilation of the ventricles and subarachnoid spaces. Later studies showed that brain MRI is more sensitive than CT and offers more detailed information about changes in the central nervous system.[8]

The purpose of this study is to describe neuropathological alterations in children with any type of MPS who were attended in our hospital. We will search for potential correlations between these changes and the type or severity of MPS, and compare our results with those described in the literature.

Patients and methods

We retrospectively analysed the medical records of 19 patients who were either diagnosed with MPS or examined for that illness in our department between 1992 and 2010.