ALSTRÖM HALLGREN SYNDROME
SÍNDROME DE ALSTRÖM HALLGREN

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ABSTRACT

Introduction: Alstrom-Hallgren syndrome is an inherited condition in which the transmission of a double dose of a mutated gene leads to specific clinical findings. To the present time there has been only one gene detected which leads to this syndrome, the ALMS1 gene. Mutation of this gene leads to progressive blindness due to photoreceptor dystrophy, progressive sensorineural hearing loss, insulin resistant diabetes, morbid obesity and cardiologic abnormalities.

Clinical Case: We present the case of a four-year-old male who, after a cardiopulmonary shutdown in the fourth month of life, was diagnosed with a dilated cardiomyopathy. Nystagmus and photophobia followed, and, after ophthalmologic exploration and an electroretinogram, the results were consistent with Alström syndrome. The appropriate genetic studies were then performed.

Discussion: The diagnosis in this case was considered basically because of its uncommon clinical features, and the fact a multidisciplinary approach was used in its evaluation. We were only able to confirm the diagnosis by molecular biology techniques, with this resulting in the correct diagnosis in

RESUMEN

Introducción: El Síndrome de Alström es una enfermedad autosómica recesiva. Se conoce un gen (ALMS1) asociado al síndrome, caracterizado por ceguera causada por distrofia de conos y bastones, sordera sensorial, resistencia a la insulina, obesidad, y cardiopatías.

Caso clínico: Niño de cuatro años que tras una parada cardiorrespiratoria es diagnosticado de cardiomiopatía dilatada. Comienza con nistagmus y fotofobia. Se le realiza exploración oftalmológica y ERG, siendo los resultados compatibles con un Síndrome de Alström.


25-40% of cases. Treatment is symptomatic and the prognosis extremely variable (Arch Soc Esp Oftalmol 2007; 82: 649-652).

**Key words:** Photoreceptor dystrophy, Diabetes Mellitus, Cardiomyopathy, Obesity, ALSM1.

**INTRODUCTION**

Alström syndrome is an extremely rare disorder, described in approximately 350 cases around the world. It was first described by a Swedish doctor called Carl Henry Alström in 1959. Patients present a recessive genetic alteration in the short arm of chromosome 2-(2p12-13) (1). It may affect all races, but most cases have been reported in the Netherlands and Sweden (fig. 1).

Clinically, it is characterized by a series of sequential symptoms. The first tend to be cardiomiopathy and visual alterations that may appear even during the first year of life.

Visual alterations consist in cone-rod dystrophy together with nystagmus, photophobia and gradual loss of central and peripheral vision that may evolve into blindness during the first decade of life.

The onset of deafness takes place at four years of age and obesity appears during adolescence, when insulin resistance results in diabetes mellitus.

The diagnosis of this syndrome is based on clinical findings and molecular genetic studies. There is no characteristic diagnostic test. It is necessary to perform blood tests that should reveal hyperglycemia and hypertriglyceridemia; urine tests should reveal an increase in uric acid levels; and full ophthalmologic examination. In some cases, prenatal diagnosis is feasible.

There is no specific treatment for this disorder. The goal should be to correct and alleviate some of the symptoms and to bring diabetes under control.

**CASE REPORT**

Male, only child, born at forty weeks by Cesarean section. His personal history reveals that his mother suffered from non insulin-dependent diabetes mellitus from the age of 17 and that no affinity existed among the parents.

At four months of age, he suffered a cardiorespiratory arrest (diagnosed as a dilated cardiomyopathy) (1). During his stay in the hospital, he began to exhibit photophobia and intermittent nystagmus, prompting ophthalmologic check-up at his healthcare center.

Since the child exhibits psychomotor delay, a Nuclear Magnetic Resonance (NMR) is prescribed together with early stimulation treatment starting at one year of life, and achieving the proposed goals in eight months. The NMR reveals small T2 signal increase areas and FLAIR in the periatrial regions and temporal white matter (fig. 2).

At two years of age, he is referred to our hospital for ultrasound and ophthalmologic examination. The ERG performed reveals the lack of response and normal Visual Evoked Potentials (VEP). Ophth-

![Fig. 1: Gene map of chromosome 2p during Alström syndrome (2).](image-url)
halmoscopic examination shows nystagmus and intense photophobia. The anterior segment and eye fundus were normal (fig. 3).

Clinical diagnosis suggests an Alström syndrome, and subsequently a genetic study is advised. Analysis of exons 10, 16 and one segment of exon 8 for the ALMS-1 gene (3) reveals the mutations described so far; PCR amplification and automated sequencing do not reveal any mutations. Nevertheless, these findings do not invalidate diagnosis.

**DISCUSSION**

Alström syndrome is a rare disorder. It is characterized by the presence of cone-rod dystrophy, obesity, sensory hearing loss, resistance to insulin and cardiac alterations (table I).

The cone-rod dystrophy begins to emerge during the first year of life together with photophobia and nystagmus in a normal eye fundus though suffering from alterations under the ERG (1). In time, a chorioretinal atrophy appears.

The present case exhibits resistance to insulin, obesity, hypogonitalism and cardiac alterations. The patient does not exhibit neurosensory deafness, alt-

**Table I.**

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Other less frequent signs and symptoms</th>
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<tbody>
<tr>
<td>Photophobia and nystagmus during childhood</td>
<td>Acanthosis nigricans</td>
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<tr>
<td>Retinal degeneration of cones and rods</td>
<td>Hypogonadism with normal sexual development</td>
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<td>Insulin-resistant symptoms / NIDDM</td>
<td>Hypothyroidism</td>
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<td>Childhood obesity</td>
<td>Scoliosis</td>
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<td>Loss of bilateral hearing</td>
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<td>Dilated miocardiopathy</td>
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<td>Chronic nephropathy with tubular dysfunction</td>
<td>Asthma and respiratory ailments</td>
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<td></td>
<td>Muscular dystonia</td>
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<td>Portal hypertension and AHT</td>
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Fig. 3.
though it usually appears gradually and slowly and involves high frequencies from the age of four. On the other hand, renal function was normal.

Diagnosis is clinical, and only in 25 to 40 percent of cases do genetic alterations located in the only known gene (ALMS-1 (3,4)) appear (fig. 4).

The Bardet-Biedl syndrome presents the characteristic facies and polydactyly, a malformation not described for Alstrom Syndrome. Furthermore, visual symptoms appear later in time, at the age of eight.

Achromatopsia is a retinal pathology and reveals itself with a reduction in visual acuity, photophobia, nystagmus, central scotoma and loss of color discrimination.

Leber’s congenital amaurosis (LCA) is a retinal dystrophy involving the heart and brain. The ocular-digital sign is characteristic. The ERG is not detected. Our patient exhibited endocrine alterations including obesity, hypogonadism and insulin resistance, but no neurologic anomalies.

Clinical follow-up is crucial and action guidelines are used to monitor this disorder (table II).

From an ophthalmologic perspective, the use of tinted lenses with sun filters and learning Braille are advised.

Endocrine treatment includes diabetes management, hyperlipidemia and hormone deficiencies.

Prognosis and evolution for this disorder vary (5).

REFERENCES