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CASE REPORT

Achondroplasia and Down's syndrome – case report of a rare association

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KEYWORDS
Achondroplasia;
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Abstract
The association of achondroplasia and Down's syndrome is very rare and only five cases have been reported in the literature so far. These two genetic alterations have overlapping features such as short stature, developmental delay or hypotonia that complicate management and follow up.
We report the case of a girl that is unique since she was born from a mother with achondroplasia and a healthy father. Achondroplasia was dominantly inherited from the mother but at birth she had features of Down's syndrome as well, confirmed later by kariotype. We review her evolution regarding physical health, cognitive problems and adaptive behavior during her eight years of life.
To our knowledge this is the first report of the combination of both disorders in which the achondroplasia was inherited and not a "de novo" mutation. We address the problems resulting from the additional burden of having two disorders, and how they can be improved, aiming to help others in the future to deal with these cases.

PALABRAS CLAVE
Acondroplasia;
Síndrome de Down;
Trastorno del desarrollo

Acondroplasia y síndrome de Down: historia clínica de una asociación poco común

Resumen
La asociación entre acondroplasia y síndrome de Down es muy poco común y hasta hoy solamente se han descrito cinco casos en la bibliografía. Estas dos alteraciones genéticas tienen características que coinciden, como la baja estatura, el retraso en el desarrollo o la hipotonía, que complican el tratamiento y el seguimiento.
Presentamos el caso de una niña que es único, ya que es hija de una madre con acondroplasia y un padre sano. La acondroplasia la heredó predominantemente de la madre, aunque en el nacimiento también presentó rasgos de síndrome de Down, confirmados

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más adelante por cariotipo. Analizamos su evolución, en la que se observa la salud física, los problemas cognitivos y el comportamiento adaptativo a lo largo de sus 8 años de vida.
Hasta donde nosotros sabemos, este es el primer caso de la combinación de ambos trastornos en el que la acondroplasia es hereditaria y no una mutación "de novo". Abordamos los problemas derivados de la carga adicional de presentar dos trastornos y cómo pueden mejorarse con el fin de ayudar a otras personas a tratar estos casos.

Introduction

The association between achondroplasia and Down's syndrome was reported for the first time in 1970[1], and since then only four other were reported[2-5], but in all achondroplasia occurred as a "de novo" mutation. Achondroplasia is the most common form of human dwarfism and more than 85% occur as a "de novo" dominant mutation[6,7]. Down's syndrome is the most common chromosomal alteration in humans[8]. These alterations have distinctive phenotypic traits that characterize them and their concurrence permits to observe the consequences of overlapping features regarding physical and developmental phenotype.

Patient presentation

A white female child, was born from a 32-year-old mother with achondroplasia and a healthy 52-year-old father. She was the product of full term pregnancy and elective cesarean. Measurements at birth were: weight 2760g (5th to 10th percentile), length 44 cm (< 3rd percentile), head circumference 33 cm (10th percentile). Apgar scores were 5 and 7 at 1 and 5 minutes, respectively. Since achondroplasia is dominantly inherited, there was a high risk of having dwarfism but still the mother had opted not to have prenatal diagnosis. At birth she had evidence of achondroplasia but also features suggestive of Down's syndrome, such as hypotonia, up-slanting palpebral fissures, epicanthal folds, Brushfield's spots on the iris, flat occiput, short neck, short hands with transverse palmar crease and she also had a heart murmur.

Both disorders were confirmed by genetic studies, including a kariotype that confirmed 47,XX,+21.

Echocardiogram showed a small atrial septal defect that closed spontaneously.

Eyes examination showed no cataract, but strabismus.

During infancy, in addition to the frequent upper respiratory tract problems, she had frequent lower respiratory tract infections associated with wheezing and hypoxemia resulting in several hospital admissions.

At the age of four she revealed hearing impairment due to otitis media with effusion and she underwent tonsillectomy with ventilation tubes insertion. After the intervention her respiratory problems improved, reducing the number of admissions. However recently she is showing again signs of sleep apnea and may need surgery again.

As expected she has short stature, being below average both for Down's syndrome and for achondroplasia growth charts, and obesity. She has normal levels of growth hormone and growth hormone treatment was not considered a good option. Her thyroid function is normal. She shows no atlantoaxial instability or other spinal malformation.

Her developmental acquisitions were slower than expected for a child with Down's syndrome due to severe hypotonia, and also because of the frequent admissions that prevented a regular intervention to be held.

She was sitting at two years, walking at three, had her first words by age two and said small phrases by three. In the first three years of life she was at home with early intervention program, but it was very hard to implement for reasons involving her physical health.

After starting nursery, fortunately also coinciding with the improvement in general health, it was possible to have regular early intervention and speech and language therapy, and she showed then not only progress but real gains in her impairments. She is now eight (fig. 1) and she has a moderate cognitive impairment but she is in a regular school, having special education support, occupational therapy and speech and language therapy. She has a very good adaptive and social behavior, is well integrated and likes school and seems to live a happy life.

Discussion

Down's syndrome and achondroplasia is an extremely rare association and only a few cases have been reported[1-5]; however our case is the first report of a child having both disorders being born from a mother with achondroplasia.

Achondroplasia affects more than 250000 individual worldwide[6]. It is an autosomal-dominant with nearly complete penetrance[7]. Fifty percent of the offspring will be affected and therefore prenatal diagnosis was offered to the mother of our child. Her own perception and experience of the disorder made her decline it, since she had a fulfilling and well adapted life and felt happy disregarding of her condition. She was expecting a child with achondroplasia and the association of Down's syndrome was an unexpected event.

Down's syndrome affects nearly 1 in every 800 live births and is the most common and best known chromosomal disorder in humans[8]. The extra chromosome 21 affects almost every organ and system and causes a wide spectrum on consequences[8].

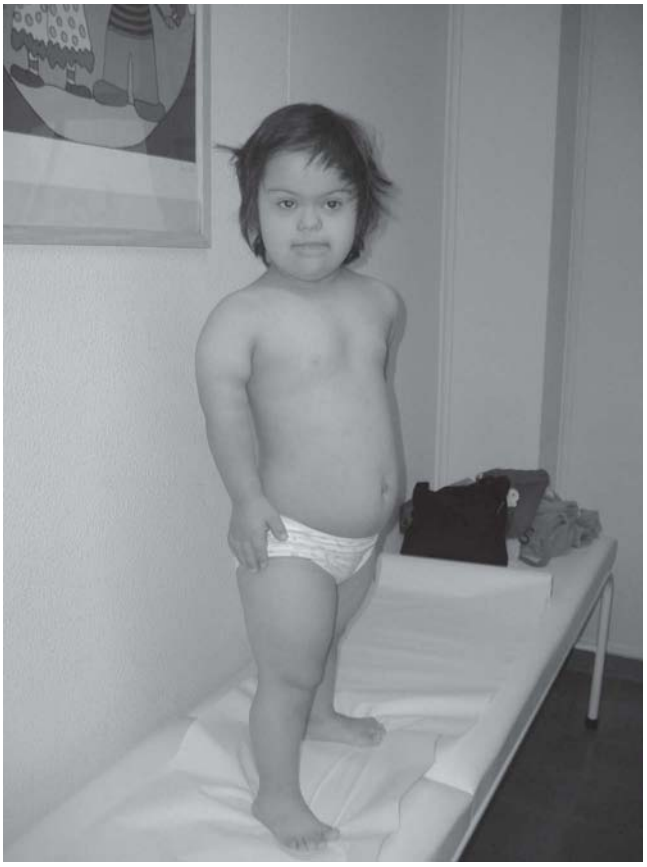

Figure 1 Pacient with achondroplasia and Down's syndrome.

Several problems are present in both diseases such as cervical spine problems that fortunately our patient didn't show and others were present such as otitis media with effusion, recurrent upper and lower respiratory problems, snoring and sleep apnea, midface hypoplasia causing orthodontic problems, speech delay and articulation problems, hypotonia, motor delays and an increased risk of obesity.

The disproportion between limbs and trunk sizes also made it more difficult for motor milestones to be achieved and respiratory and hearing problems also contributed to language impairment.

Due to these concurrent problems, her development was more impaired than we expect to see either in children with achondroplasia or with Down's syndrome. Motor and language skills were later to be accomplished and the frequent health problems didn't allow her to sustain a good and regular intervention program in her early years. This was only possible later and we consider it had some consequences in her abilities. However we have worked with the parents to minimize her problems and to help her to feel adjusted, in a regular school and to live a happy life.

It seems imperative that we try harder to stabilize these patients and to enable them to receive proper intervention as early as possible so that we can reduce the burden of having two diseases.

Conflict of interests

The authors affirm that they have no conflict of interests.

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