CASE REPORT

Spinal muscular atrophy type 2 treated with risdiplam at the Instituto Nacional de Salud del Niño - San Borja: a case report

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ABSTRACT

Spinal muscular atrophy (SMA) is a common pediatric neuromuscular disease characterized by progressive muscle weakness, hypotonia, and symmetrical muscle atrophy. In Peru, the treatment of SMA primarily involves the use of the drugs risdiplam and nusinersen. We present the case of a seven-year-old boy with SMA type 2 treated with risdiplam. The patient was referred to the cardiology department of a national pediatric referral center in Lima, Peru. The patient exhibited quadriparesis, hypotonia, preserved osteotendinous reflexes, intact sensory function, and the ability to stand with support. Risdiplam treatment was initiated under compassionate use. The response to treatment was favorable, with improvements in motor function scale scores and noticeable clinical enhancements in movement quality and speed. Follow-up radiographs revealed mild dorsal scoliosis (10° Cobb angle), while pulmonary function was preserved (FVC = 85 %). Despite its efficacy, access to risdiplam remains challenging for SMA patients due to its high cost, highlighting the importance of sharing this case with the scientific community.

Keywords: Muscular Atrophy, Spinal; Pediatrics (Source: MeSH)

Atrofia muscular espinal tipo 2 en tratamiento con risdiplam en el Instituto Nacional de Salud del Niño-San Borja: un reporte de caso

RESUMEN

La atrofia muscular espinal (AME) es una enfermedad neuromuscular frecuente en la edad pediátrica caracterizada por la presencia de debilidad muscular progresiva, hipotonía y atrofia muscular simétrica. El tratamiento de la AME en Perú se basa en el uso de los fármacos risdiplam y nusinersen. Presentamos el caso de un niño de siete años con AME tipo 2 en tratamiento con risdiplam. El paciente fue derivado al servicio de cardiología de un centro pediátrico de referencia nacional en Lima, Perú. Se evidenció cuadriparesia, hipotonía, reflejos osteotendinosos, sensibilidad conservada y bipedestación con apoyo. Se inició tratamiento con risdiplam en modalidad de uso compasivo. La respuesta al tratamiento fue favorable, evidenciándose un incremento en los puntajes de las puntuaciones de las escalas de función motora. Además, se observó una mejoría clínica en la calidad y rapidez de los movimientos. Las radiografías de control evidenciaron escoliosis dorsal leve (10° de ángulo de Cobb); mientras que la evaluación de la función pulmonar estuvo conservada (CVF = 85 %). A pesar de su efectividad, el tratamiento con ridisplasm es de difícil acceso para los pacientes con AME debido a su alto costo; de ahí la importancia de presentar este caso a la comunidad científica.

Palabras clave: Atrofia Muscular Espinal; Pediatría (Fuente: DeCS)

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INTRODUCTION

Spinal muscular atrophy (SMA) is a common pediatric neuromuscular disease, with an estimated incidence of 1 in 11,000 live births (1). Approximately 95% of cases are associated with an autosomal recessive disorder caused by a homozygous deletion or mutation in the SMN1 gene, located at 5q13. This gene regulates the expression of the SMN1 protein, which is essential for the survival of motor neurons in the anterior horn of the spinal cord and brainstem (2).

SMA is characterized by progressive muscle weakness, hypotonia, and symmetrical muscle atrophy. The severity of the disease is variable and is related to the number of copies of a secondary gene, SMN2, which encodes the same protein produced by the SMN1 gene (3). Therapeutic strategies have been developed to modulate SMN2 protein levels, as well as gene replacement therapies. In Peru, two medications that act on the SMN2 gene are available: risdiplam (Evrysdi®; Roche®) and nusinersen (Spinraza®; Biogen®). Gene therapy is currently in the process of being approved in the country, with onasemnogene abeparvovec (Zolgensma®; Novartis®) under evaluation. Internationally, these drugs have already been approved by the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA). Risdiplam was approved by the FDA in 2020 for the treatment of SMA in patients aged two months and older (4). In Peru, risdiplam was authorized by DIGEMID in July 2021.

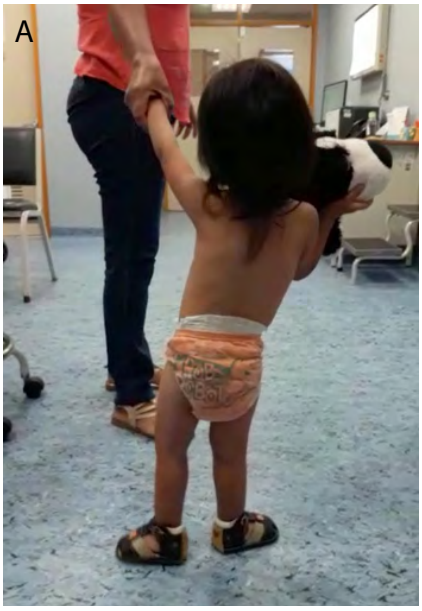
Clinical trials with risdiplam have demonstrated a significant improvement in motor function in patients with SMA type 2 and type 3 compared to those treated with a placebo after 12 months of therapy. Oral administration provides an advantage, allowing treatment to be continued on an outpatient basis (5,6). We present the case of a seven-year-old boy diagnosed with SMA type 2 who showed remarkable clinical improvement under treatment with risdiplam.

CLINICAL CASE

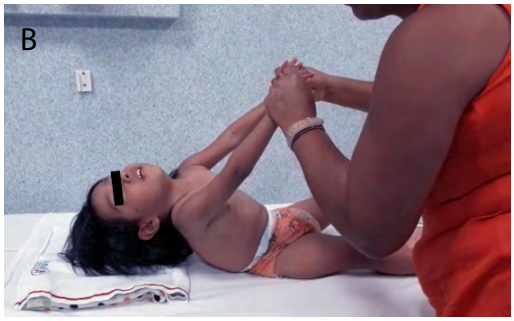
We present the case of a seven-year-old male patient from Tumbes, who initially exhibited good sucking and a strong cry at birth. He achieved trunk control around eight months of age, standing with support at 13 months, and walking with support at 15 months. However, due to the lack of independent walking, he was diagnosed with hip dysplasia and referred for physical therapy at the Regional Hospital of Tumbes. Unfortunately, his condition did not improve with physical therapy, and he began to show worsening hypotonia in the lower limbs. At two years of age, he started to present hand tremors, marked sweating, difficulty chewing, and poor weight gain. Another significant finding was the appearance of a purplish skin color during crying episodes. These symptoms led to his referral to the Cardiology Department of the Instituto Nacional de Salud del Niño – San Borja (INSN-SB). Upon admission in February 2019, it was noted that his height and weight were below age standards. Cardiac abnormalities and hip dysplasia were ruled out, and the patient was ultimately referred to the Neurology Department.

At two years and seven months, the patient underwent a comprehensive neurological evaluation. He was found to be alert, interactive, and able to follow simple commands. He had partial head control and a kyphotic posture and was able to stand with support. However, quadriparesis was observed, predominantly affecting the proximal region of the lower limbs. Deep tendon reflexes were absent, while sensation was preserved. Hypotonia was also noted, and the patient walked with support (waddling gait) (Figure 1).

Figura 1. Clinical evaluation before risdiplam treatment



A. The patient stands on both feet (with support)



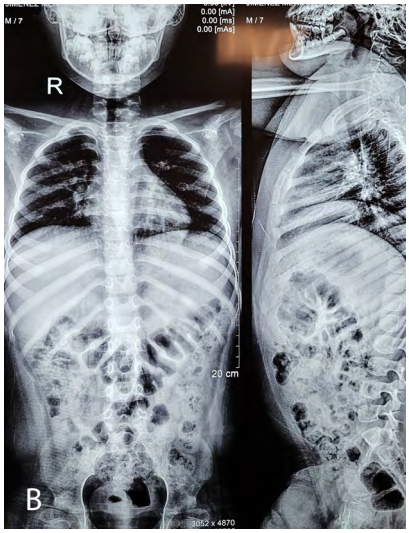
B. Poor head control is observed.

Creatine kinase levels were within the normal range (162 U/L). Electromyography and nerve conduction studies revealed findings consistent with motor neuron involvement. Subsequent PCR-based molecular testing showed the deletion of exon 7 in the SMN1 gene, confirming the diagnosis of SMA. Over the following years, the patient received physical therapy and continued follow-up by the INSN-SB multidisciplinary team. However, motor deficits progressed, leading to loss of independent standing and difficulties with head control, accompanied by worsening postural kyphosis.

At five years and eight months of age, the patient began risdiplam treatment under a compassionate use program, pending regulatory approval in Peru. During follow-up, the patient showed a remarkable response to treatment, with increased scores on the Revised Upper Limb Module for Spinal Muscular Atrophy (RULM) and the Expanded Hammersmith Functional Motor Scale (HFMSE). Figure 3 illustrates the variation in HFMSE scores over the course of treatment. After 26 months, the score increased by 17 points compared to the baseline (Figure 3 and Table 1). Additionally, clinical improvement was observed in the speed and quality of movements. Follow-up radiographs showed mild thoracic scoliosis (10° Cobb angle) (Figure 2), and pulmonary function was preserved (FVC = 85%).

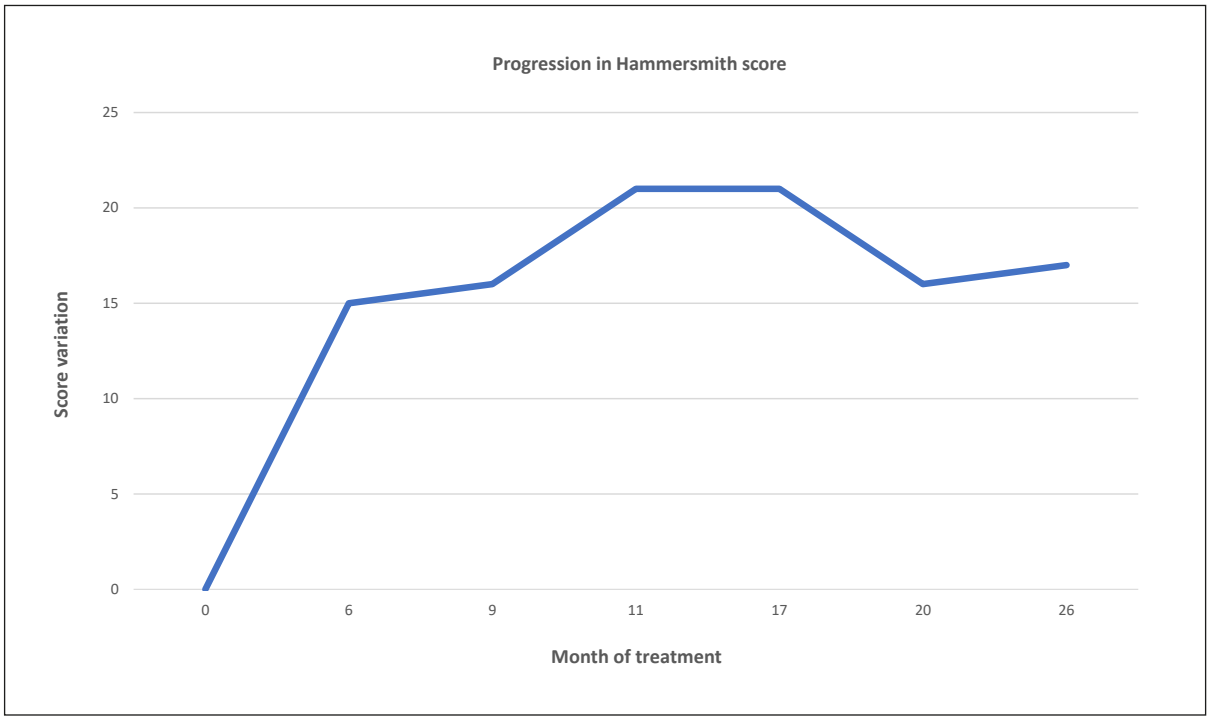
Figure 2. Clinical evaluation after starting risdiplam treatment

A. The patient walks with support.



B. Spinal X-ray shows no evidence of scoliosis.

Figure 3. Progression of scores on the Expanded Hammersmith Functional Motor Scale



DISCUSSION

SMA type 2 typically presents between 6 and 18 months of age. It is characterized by progressive muscle weakness, predominantly in the proximal lower limbs, hypotonia, reduced deep tendon reflexes, and tremor-like hand movements corresponding to polyminimyoclonus. SMA type 2 is further subdivided into types 2A and 2B, depending on whether or not the patient achieves independent standing. Some patients with SMA 2B, as in this case, can walk with support. As the disease progresses, patients may develop scoliosis and weakness of the intercostal muscles, affecting pulmonary function and reducing life expectancy (2). This report presents the case of a seven-year-old boy diagnosed with SMA type 2 who showed no scoliosis or respiratory involvement and responded favorably to treatment with risdiplam.

The efficacy of risdiplam in pediatric patients with SMA types 2 and 3 has been demonstrated in the randomized, double-blind, clinical trial SUNFISH. In this trial, treatment with risdiplam led to a significantly greater improvement in motor function compared to placebo. After 12 months, the RULM score increased by an average of 1.61 points in the risdiplam group, compared to 0.02 points in the placebo group (adjusted $p = 0.0469$). Additionally, risdiplam has been shown to improve motor function, with a significant increase in total scores on the Motor Function Measure (MFM) in a cohort of patients with SMA treated with risdiplam, compared to a control cohort (difference of 3.99 points; $p < 0.0001$) after 24 months of treatment (5). In our patient, the RULM score increased by 7 points from baseline, rising from 26 to 33 after 26 months of treatment.

In the natural history of SMA types 2 and 3, motor function progressively deteriorates. Previous studies have demonstrated a decline in HFMSE scores, highlighting motor function stabilization as a primary treatment objective (7). The patient in this case exhibited significant improvement in scores following the initiation of treatment (Figure 3 and Table 1).

The SUNFISH Working Group found that the natural history SMA cohort showed an average decrease of 3.03 points (SD = 3.77) in MFM32 scores after 24 months. In addition, RULM scores decreased by an average of 0.41 points (SD = 2.93) at 12 months, and HFMSE scores decreased by an average of 0.54 points (95% CI = −1.45 to 0.36) at 24 months. In contrast, efficacy analyses of risdiplam in the same study showed improvements in total MFM32 and RULM scores, along with stabilization of HFMSE scores after 24 months of treatment (8).

Table 1. Scores on the Expanded Hammersmith Functional Motor Scale during treatment

Score variation	Month of treatment
0	0
15	6
16	9
21	11
21	17
16	20
17	26

Advancements in current SMA treatments have significantly changed the prognosis of the disease. For patients with SMA type 1, the most severe and early-onset form, the disease has become a condition with more prolonged survival. For SMA type 2, the prognosis has shifted toward long-term stabilization of motor function. A key factor, in addition to the number of SMN2 copies, that predicts treatment success is the patient's age at the start of therapy. Improvements are primarily seen in children under five years of age (8–10).

The case presented showed a positive trajectory in HFMSE scores, with a significant improvement 26 months after beginning treatment with risdiplam. The patient experienced no adverse events. It is essential to highlight that this type of treatment remains difficult to access for patients with SMA due to its high cost. This patient began treatment at INSN-SB through a compassionate use program. Currently, the treatment is being provided by the Peruvian State via the Rare and Orphan Diseases Fund, marking it as the first documented case of SMA being treated in Peru. Therefore, sharing this experience with the scientific community is of significant relevance.

Author contributions

Conceptualization: PCME; data collection, management, and curation: PCME, RCMB, JCFZ, CTCG; data analysis: PCME, RCMB, JCFZ, CTCG; visualization: PCME, RCMB, JCFZ, CTCG; original draft writing: PCME, RCMB, JCFZ, CTCG; interpretation of results: PCME, RCMB, JCFZ, CTCG; review and editing of final version: PCME, RCMB, JCFZ, CTCG.

Conflicts of interest

The authors have no conflicts of interest related to the material presented in this manuscript.

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Ethical considerations

The authors declare they obtained informed consent from the patient's parents or legal guardians for the use of photographs.

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