

# RIGID SPINE SYNDROME

## CASE REPORT

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**ABSTRACT** - We describe a patient who had difficulty in walking since toddling stage and presented proximal upper and lower member weakness which have evolved to a progressive limitation of neck and trunk flexure, compatible with rigid spine syndrome. The serum muscle enzymes were somewhat elevated and the electromyography showed a myopathic change. The muscle biopsy demonstrated an active and chronic myopathy. The DNA analysis through PCR did not display any abnormality for dystrophin gene. The dystrophin by immunofluorescence was present in all fibers, but some interruptions were found in the plasma membrane giving it the appearance of a rosary. The test for merosin was normal.

**KEY WORDS:** rigid spine syndrome, merosin, dystrophin.

### **Síndrome da espinha rígida: relato de caso**

**RESUMO** - Relatamos o caso de um paciente com dificuldade de marcha desde o início da deambulação, com fraqueza proximal de membros, evoluindo com limitação progressiva da flexão do pescoço e tronco, compatível com a síndrome da espinha rígida. As enzimas musculares séricas estavam moderadamente elevadas e a eletromiografia revelou padrão miopático. A biópsia muscular indicou miopatia crônica e ativa. A análise do DNA por PCR não demonstrou alterações no gene da distrofina. A imunofluorescência para distrofina foi positiva em todas as fibras, apresentando interrupções na membrana plasmática, semelhante a um rosário e o teste para merosina mostrou positividade.

**PALAVRAS-CHAVE:** síndrome da espinha rígida, merosina, distrofina.

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First described in 1965 by Dubowitz, the rigid spine syndrome consists of proximal muscular member weakness as its main symptom; at that time he denominated it "pseudodystrophy"<sup>1</sup>. During the evolution of the disease, five years after its onset, was noted a progressive limitation of trunk and neck flexure and was redefined as "rigid spine syndrome". Even though other cases have been described, the diagnostic criteria have not yet been established<sup>2-12</sup>.

With the purpose of contributing to the elucidation of this entity, we relate a case presenting rigid spine syndrome in which we have the opportunity of studying the dystrophin and merosin by immunofluorescence and the dystrophin gene through polymerase chain reaction (PCR).

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## CASE REPORT

WPRO, a six years-old male, has walked with great effort and presented frequent falls since toddling stage (1 year and 7 months) tending to tiptoe gait. As the disease developed, he had difficulties in standing up and getting out of a chair. He only climbs stairs with the help of a rail. Gestation and familial history presented no particularities.

Physical examination: Blood pressure, pulse, cardiac frequency, respiratory frequency and temperature were normal. There was a lordosis (swayback) with thoracic and cervical column flexure limitations, but with preserved cervical extension. The paraspinal muscles had a retraction, mainly at neck and trunk level and he was not being able to turn his trunk. Also he had a bilateral winged scapula and retraction of the Achilles tendon (Fig 1).

Neurological examination: Normal cognitive functions. Cranial nerves were normal. Muscular strength was degree 4+ (MRCM) in the proximal muscles and degree 5 in distal muscles of the upper and lower limbs. There was a slight atrophy of lower limbs. The superficial cutaneous and deep tendon reflexes were absent, except for the Achilles reflex which was normal. Tactile, pain, vibration and position sense were normal, as well as the coordination. He had a myopathic gait and partial Gower's maneuver.

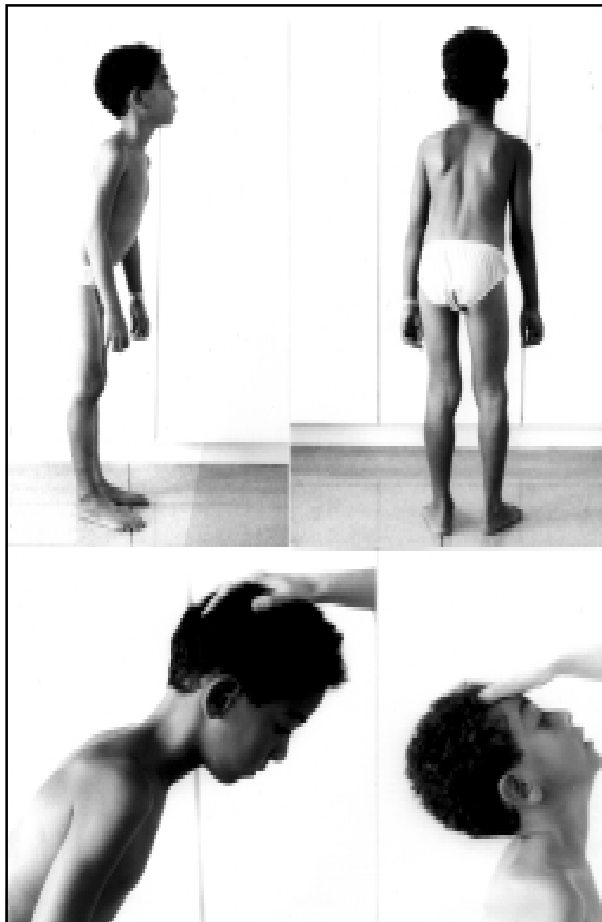


Fig 1. Photograph of the case: A. Lordosis. B. Bilateral winged scapula. C. Limitations of the thoracic and cervical flexure. D. Normal cervical extension.

Table 1. Electromyography.

Muscles (right)	biceps brachii	quadriceps femoris	tibialis anterior
Insertion activity	N	N	N
Fibrillation potentials	A	A	A
Fasciculation potentials	A	A	A
Positive sharp waves	A	A	A
Myotonic discharges	A	A	A
Duration of motor unit potentials	D	D	D
Amplitude of motor unit potentials	D	N	D
Short polyphasic motor units	++	+	++
Long polyphasic motor units	A	A	A
Recruitment pattern	I	I	I

N, normal; A, absent; D, decreased; I, increased; rare, +; occasional, ++.

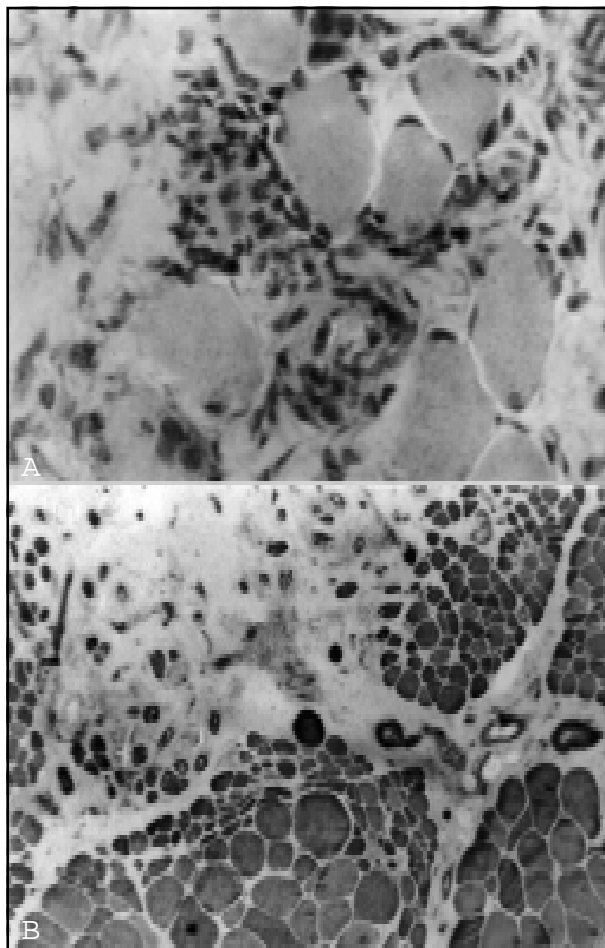
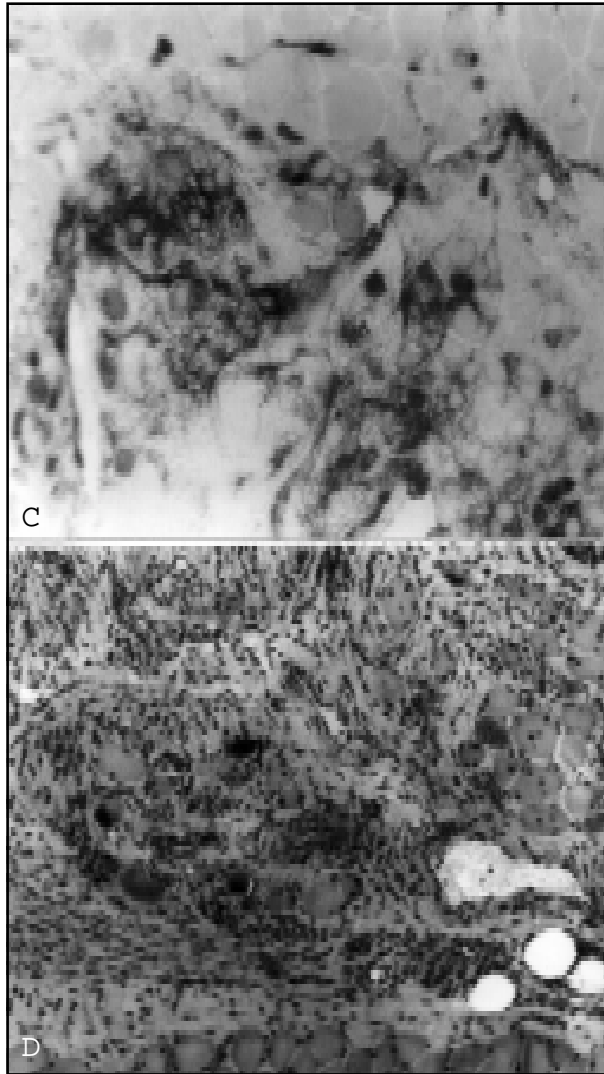


Fig 2. Muscle biopsy. A: Necrotic fibers (magnification x695; hematoxylin and eosin). B. Marked atrophy of the type I and II fibers (magnification x87; ATPase 9.4).



*Fig 2. Muscle biopsy. C. Increased activity in the interstice and positive fibers (magnification x87; alkaline phosphatase). D. Connective tissue proliferation and excessive internal nuclei (magnification x174; hematoxylin and eosin).*

Investigation: Hemogram, hemosedimentation rate, sodium, potassium, creatinine, BUN and glycemia were in the normal ranges. Creatinekinase: 413.5 U/L (normal 70); aldolase: 3.6 U/L (normal 3.1); lactate dehydrogenase 334.3 U/L (normal 240); aspartate amino transferase: 19 U/L (normal 22); Alanine amino transferase: 20 U/L (normal 25). Electrocardiogram and ecdopplercardiogram were normal. Electromyography done in biceps brachii, quadriceps femoris and tibialis anterior muscles recorded decreased duration, reduced amplitude of the voluntary potentials and increased recruitment, which represented primary muscle involvement (Table 1). The conduction velocities of peripheral nerves (right motor median, right deep fibular and right sural) were normal. A biopsy was done on quadriceps femoris muscle and was processed by histochemistry in fresh frozen sections (Fig 2 A-D). The results are shown in Table 2. The final analysis demonstrated an active and chronic myopathy. The dystrophin study by immunofluorescence, using anti-dystrophin antibody to carboxy

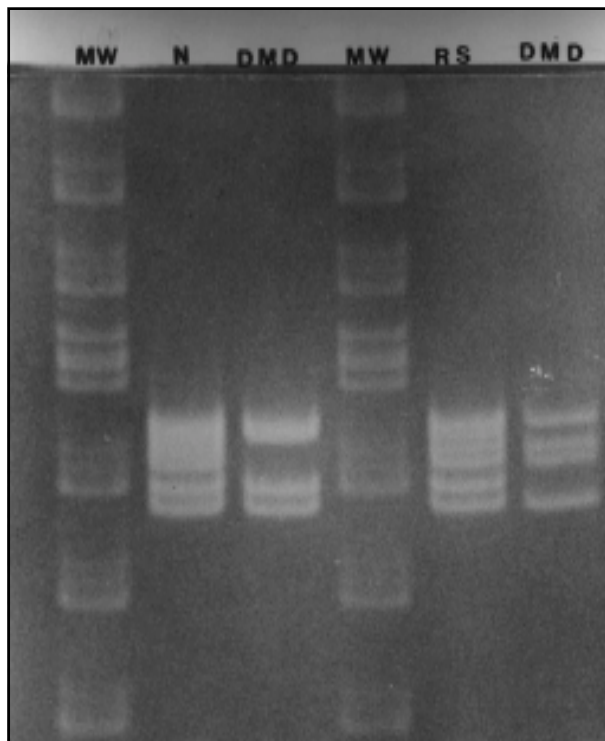


Fig 3. PCR analysis of the dystrophin gene: comparison with Duchenne muscular dystrophy (MW, molecular weight; N, normal; DMD, Duchenne muscular dystrophy; RS, rigid spine).

and amino terminal, as well as to the “rod” segment, demonstrated multiple small and large defects in several sarcolemmas of muscle fibers, with appearance of a rosary. The merosin was studied also with immunofluorescence technique and was normal. The dystrophin gene analysis was done by using DNA extracted from a muscular fiber sample amplified by a PCR technique that analysed 32 exons. No mutation, deletion or duplication were present (Fig 3).

## DISCUSSION

The rigid spine syndrome predominates in males and the child can have a history of delayed development or present the initial symptoms around 7 years of age<sup>1-4,7,11</sup>. Some reported cases have recessive autosomal inheritance<sup>1-4,7,19</sup>. There is proximal muscular weakness of the trunk and neck with posterior flexure limitation accompanied by progressive scoliosis (crookedness)<sup>10</sup>. Reflexes in general are diminished. Elbow and knee joint contraction were reported in many cases. The disease evolution is slow, without muscular strength reduction. Due to an alteration of the vertebral spine and restrictive respiratory failure, many cases ended in *cor pulmonale* and other cardiac alterations<sup>11</sup>. The serum muscular enzymes are slightly elevated<sup>5-7,11</sup>. The peripheral nerve conduction velocities frequently are normal<sup>2-4,6</sup>. The electromyography shows potentials of short duration and normal amplitudes or polyphasic potentials<sup>1,2,7</sup>. The muscle biopsy reveals nonspecific alterations of the myopathic type, with fibers in degeneration and regeneration, perimysial and endomysial connective tissue proliferation, type I fiber disproportion or hypotrophy<sup>4</sup>, atrophy and hypertrophy of type II fiber<sup>5,7</sup>. The differences in muscle histology are either most likely due to the fact that the biopsy has been done in different stages of the disease or that similar elementary lesions of muscle fibers were

Table 2. Histological alterations in muscle biopsy.

Alteration	Abnormality intensity
Connective tissue proliferation	+++
Variation of muscular fibers diameter	+++
Atrophic rounded fibers dispersed	++
Hypertrophic fibers dispersed	++
Internal nuclei	++
Necrosis	++
Phagocytosis	++
Splitting fibers	++
Basophilic fibers	++
Hipercontractile fibers	+
Type I fiber predominate	+
Type I fiber hypertrophy	+
Type II fiber hypertrophy	+
Type I fiber atrophy	+
Type II fiber atrophy	+
NADH-TR motheten fibers	+++
NADH-TR targets	+
NADH-cores (central cores)	+
Non-specific esterase increased activity interstice (macrophages)	+
Acid phosphatase - focal fibers activity	++
Acid phosphatase - positive fibers	++
Acid phosphatase - increased in mononuclear cells (macrophages)	+
Alkaline phosphatase - positive fibers	+++
Alkaline phosphatase - increased activity interstice	++

frequent +++ ; occasional ++ ; rare +

initiating their pathological process, which developed asynchronously in different muscles because of their different activity<sup>12</sup>. Ultramicroscopic studies showed the presence of autophagic vacuoles with membranous tangles with degenerative products in the muscular fiber without specificity<sup>4,5,7,11</sup>.

The differential diagnosis includes the muscular dystrophies<sup>10</sup> (Duchenne, Becker and Emery-Dreifuss); congenital myopathies<sup>4,9</sup>(central core disease, centro-nuclear myopathy, mitochondrial and multicore myopathy), nemaline myopathy<sup>13</sup> and ankylosing spondylitis<sup>7</sup>.

The reason for the involvement, mainly of paraspinal muscles, is not well known<sup>9</sup>. It is suggested that the increase of connective tissue in extensor muscles would result in their shortening which would inhibit the spine flexor muscles. Another possibility could lie on the weakness of the flexor muscles rather than the extensor muscles. The flexors would therefore be unable to resist the stronger group.

Our patient presents symptoms that are in accordance with literature, as well as the histological and histochemical alterations of muscle biopsies recorded by other authors<sup>4,5,7</sup>. The alterations are similar to the one observed in congenital muscular dystrophy<sup>14</sup>. The abnormal immunocytochemistry for dystrophin in this case is also similar to cases previously described in congenital muscular dystrophy<sup>7</sup>. The DNA analysis for the dystrophin gene in this patient did not demonstrate any alterations, suggesting that the genetic abnormality is not related to the dystrophin gene<sup>15-17</sup>. However in some cases of congenital muscular dystrophy is found a merosin (laminin-2 composed of  $\alpha 2$ - $\beta 1$ - $\gamma 1$  chains) deficiency<sup>18</sup> and one report call the attention for a reduction in the expression of the laminin  $\beta 1$  in the early onset autosomal dominant myopathy with rigidity of the spine, but this could be a secondary phenomenon and not the primary molecular defect<sup>19</sup>.

The 'rigid spine syndrome' still holds much heterogeneity and efforts are necessary to solve the nosological problem<sup>4,11,20</sup>. Future descriptions might add data, which will allow a better recognition of this syndrome.

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