Case report

Spinal muscular atrophy type I mimicking critical illness neuropathy in a paediatric intensive care neonate: Electrophysiological features

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Abstract

We report the case of a neonate with spinal muscular atrophy type I (SMA type I or Werdnig–Hoffman disease) who was initially misdiagnosis as having critical illness neuropathy. Electromyography (EMG) showed a moderate loss of voluntary and motor unit potentials of both neurogenic and myopathic appearance. Nerve conduction studies revealed the presence of a severe sensory–motor axonal neuropathy. Finally, a biopsy of quadriceps was compatible with the diagnosis of SMA type I. A genetic study confirmed the existence of a homozygous absence of exons 7 and 8 of the telomeric supervival motoneuron gene (SMN1 gene).

Keywords: Spinal muscular atrophy type I; Sensory–motor neuropathy; Critical illness neuropathy; Nerve conduction studies; Electromyography

1. Introduction

Nerve conduction studies and electromyography (EMG) are invaluable in the diagnosis and evaluation of newborn suffering from hypotonia and weakness. Spinal muscular atrophy type I (SMA type I or Werdnig–Hoffman disease) is a fatal autosomal recessive disorder, characterised by progressive degeneration of anterior horn cells that is a frequent cause of motor disability before 6 months of age [1]. The lack of significant motor and sensory nerve conduction abnormalities and the existence of neurogenic changes on the limb muscles are important electrophysiological criteria for suspecting its diagnosis.

We report the case of a neonate with SMA type I who was initially misdiagnosis as having critical illness neuropathy because electrophysiological studies revealed the presence of a severe sensory–motor axonal neuropathy.

2. Case report

This boy is the first child of healthy and nonconsanguineous parents. At 1 month of age, he was admitted to our hospital because of loss of appetite and vomiting. He was born at term in another hospital by spontaneous vaginal delivery. His birth weight was 2980 g. No remarkable events were mentioned during that period. The family history was negative for neuromuscular disorders. Physical examination showed a neonate with reduced
vitality and active contraction of accessory muscles. Chest radiography was compatible with complete atelectasia of the right lung and bronchiolitis. At that moment, he was transferred to our paediatric intensive care unit. At admission, body temperature was 37.0°C, respiratory rate 50/min, pulse 160/min and blood pressure 106/45 mm Hg. The following laboratory parameters were observed: leucocyte count (17,600/μL); C-reactive protein (0.4 mg/dl); sodium (132 mEq/L); potassium (5.30 mEq/L); Chloro (97 mEq/L); AST (37 U/L); ALT (45 U/L); gamma-GTP (68 U/L); creatinine (239 U/L); albumine (4.2 g/dl); and ammonia (40 μmol/L). Twelve hours later, he was intubated. Nasal and tracheal cultures detected the presence of respiratory syncytial virus as aetiology of his bronchiolitis. For the following days, he suffered from a picture of bacterial infection (Enterobacter taylorae), and sedation and muscle relaxation was necessary in order to obtaining adequate ventilation. On day 15, the clinical evolution was favourable, and the infant experienced a significant improvement of his respiratory symptoms. Although extubation was carried out in two occasions for the next 20 days, he was newly intubated because of respiratory failure. Then, an electrophysiological study was requested. One week later, a muscle biopsy was performed. A molecular genetic study revealed a homozygous absence of exons 7 and 8 of the telomeric supervivial motoneuron gene (SMN1 gene). Finally, on day 55, he experienced a cardiorespiratory arrest and died. Unfortunately, consent for a postmortem exam was not obtained.

Two electrophysiological evaluations were carried out with a Shappire 4ME electromyograph while the neonate was in the paediatric intensive care unit. These exams included needle EMG and motor and sensory nerve conduction studies from upper and lower limbs. EMG was recorded with disposable concentric needles from both tibialis anterior (TA) and deltoid muscles. Standard neurophysiological techniques were used. On the first exam, EMG showed a moderate loss of voluntary motor unit potentials in both TA muscles. Occasional fibrillations were detected in the right TA muscle. Spontaneous fasciculation potentials were not observed. Neurogenic motor unit potentials were intermixed with abundant short-duration, low-amplitude polyphasic potentials of myopathic characteristics (Fig. 1). High-frequency repetitive discharges were

![Fig. 1. Motor nerve conduction studies. (A) Left median nerve after stimulus at wrist and elbow. (B) Right tibial posterior nerve after stimulus at ankle and popliteal fossae. Note that the third trace is a retest obtained also after stimulus at popliteal fossae. Vertical division: 1 mV; sweep duration: 50 ms. (C) Motor unit potential from right tibialis anterior. Note the presence of abundant short-duration, low-amplitude polyphasic motor unit potentials of myopathic aspect. Vertical division: 100 μV; sweep duration: 50 ms. (D) Reduced recruitment in right TA muscle. Vertical division: 500 μV (upper trace) and 200 μV (bottom trace); sweep duration: 2 s.](image-url)
absent. There was a marked attenuation of CMAP amplitude (median nerve: 0.1 mV, normal >3.5 mV; ulnar nerve: 0.5 mV, normal >2.5 mV; peroneal nerve: 0.1 mV, normal >1.6 mV; tibial nerve: 0.2 mV, normal >3.5 mV) with slowing of MCVs in upper (median: 16.9 m/s, normal >25 m/s; ulnar: 27.3 m/s, normal >29 m/s) and lower limbs (peroneal nerve: 17.2 m/s; normal >29 m/s; tibial nerve: 13.0 m/s, normal >25 m/s) (Fig. 1). SNAPs were absent in upper and lower limbs. On the second exam, abundant fibrillations were detected in both deltoid and TA muscles. Abundant short-duration, low-amplitude polyphasic motor unit potentials associated with neurogenic potentials were also observed in upper and lower limbs. Biopsy of the quadriceps muscle was performed. Muscle biopsy was analysed microscopically after histological and histochemical staining. Severe atrophic fibers showing rounded form and peripheral nuclei were observed (Fig. 2). Types I and II (subtypes IIa and IIb) fibers were equally represented among the atrophic fibers. Small grouped hypertrophic fibers were also seen. The hypertrophic fibers were of histochemical type I. These findings were in keeping with the diagnosis of SMA type I.

3. Discussion

Our case report highlights the importance to bear in mind that, on rare occasions, SMA type I may coexist with a severe neuropathy and, therefore, the existence of marked abnormalities of the motor and sensory nerve conduction studies does not definitively rule out this fatal disorder.

The presence of a severe neuropathy associated with SMA type I is not a novel finding and it have been rarely mentioned in the past [2–6]. In general, severe hypotonia and minimal spontaneous movements are the main clinical presentation features in SMA type I. Indeed, muscle weakness severe enough to cause neonatal respiratory insufficiency is extremely infrequent [2]. However, we do not know the previously reported cases in which the clinical course and electrophysiological features had mimicked a picture suggestive of critical illness neuropathy. This fact is relevant because both entities pose a significant different outcome.

The patient describe here was severely ill as consequence of a viral respiratory process. He remained intubated and ventilated for several weeks in the paediatic intensive care unit, and electrophysiological studies were required because of the unexplained difficulty in weaning from mechanical ventilation. This clinical setting and some of electrophysiological findings such as the absence of SNAPs, marked attenuation of CMAPs, slowing of the MCVs and presence of abundant short-duration, low-amplitude polyphasic motor unit potentials intermixed with neurogenic changes led us to misdiagnose this picture as critical illness neuropathy. Indeed, in the appropriated clinical setting all diagnostic criteria for critical illness polyneuropathy were fulfilled [7].
Critical illness neuropathy is a primary axonal nerve disorder which occurs in intensive care patients with sepsis and multiple organ dysfunctions [7]. Although it has been typically described in adult subjects, it has been also seen in pediatric patients [8]. It is widely known that reduction in amplitude of CMAP and SNAP is the predominant electrophysiological finding [7]. Moreover, needle EMG may show a variable reduction of the number of motor unit potentials, some having myopathic features. These findings may result surprising in the context of congenital SMA, however, Hausmanowa-Petrusewicz and Karwanska [9] found, in addition to long potentials of high amplitude, some short and low-amplitude potentials in the quantitative EMG of patients with Werdnig-Hoffman disease. These authors concluded that it is possible to recognise bimodal histograms of amplitude and duration in SMA type I. These anomalies contributed, in our case, to the misdiagnosis. However, the biopsy of the muscles disclosing the typical pathological features described in SMA type I was the clue to request a genetic study and to obtain a precise diagnosis. Other rare entities such as SMA with respiratory distress type I [10] and severe infantile axonal neuropathy with respiratory failure [11] should have been included in the differential diagnosis in case of a negative genetic study for SMA type I.

It appears that severe congenital SMA shows larger deletion, including SMN and neuronal apoptosis inhibitory protein (NAIP) genes as well as the multicopy markers C212 and Ag1-CA [12]. Unfortunately, we do not have additional genetic data analysing these features in our case.

In summary, in those cases of critically illness neonates with unexplained difficulty in weaning from mechanical ventilation whose electrophysiological studies reveal marked motor and sensory abnormalities and combined neurogenic and myopathic changes, the possibility of a diagnosis of congenital SMA should be taken in account. In these patients, neuropathological and genetic studies should be considered.

References