Physical Medicine and Rehabilitation Research

Research Article ISSN: 2398-3353

A selective remarkably low M-wave amplitude in tibial nerve is characteristic in motor nerve conduction in spinal muscular atrophy type 2 and 3

Jun Jiang* and Sun Ruidi

Department of Electrophysiology, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology, China

Abstract

Introduction: Motor nerve conduction (MNC) in spinal muscular atrophy (SMA) type 2 and 3 had no characteristic change, and it may also occur in disorders that clinically mimic SMA type 2 and 3. There is little information about MNC in SMA type 2 and 3 and mimics.

Methods: Evaluation of MNC features from 90 patients with SMA type 2 and 3 mimics and 30 patients with SMA type 2 and 3.

Results: A selective remarkably low amplitude M-wave in tibial nerve as a marker in spinal muscular atrophy type 2 and 3, which can distinguish this type of disease from other mimic diseases.

Discussion: A selective M-wave with remarkedly low amplitude in tibial nerve was typical feature in SMA type 2 and 3 that can distinguish from other mimic diseases.

Abbreviations: MNC: Motor nerve conduction; SMA: Spinal muscular atrophy; DMD: Duchenne muscular dystrophy; MG: Myasthenia gravis; SMN: Survival motor neuron; NCS: Nerve conduction studies; MNCV: Motor nerve conduction velocity; CMAP: Compound muscle action Potential; GBS: Guillain-Barre syndrome; MCV: Motor conduction velocity; DML: Distal motor latency; SNAP: Sensory nerve action potential; LLN: Lower limit of normal; ULN: Upper limit of normal; AIDP: Acute inflammatory demyelinating polyneuropathy; AMAN: Acute motor axonal neuropathy; EV71: Enterovirus 71; AchR: Acetylcholine receptor; IgG: Immunoglobulin G.

Introduction

Spinal muscular atrophy (SMA) is an autosomal recessive disorder caused by mutations in the survival motor neuron (SMN)1 gene, and this condition is characterized by degeneration of the motor neurons in the spinal cord which resulted in progressive muscular atrophy and weakness [1,2]. SMA was classified into 4 types on the basis of age of onset and the degree of motor function achieved by the affected individual [1,2]. SMA type 1 patients are unable to sit without support, SMA type 2 patients achieve the ability to sit independently, and SMA type 3 patients at least for a time achieve the ability to walk independently.

The diagnosis of SMA is usually based on the typical clinical symptoms and genetic testing; it can be confirmed by nerve conduction studies (NCS) and neuropathy in electromyogram. The using value of neurophysiology examination in SMA is limited, and the change in motor nerve conduction velocity (MNCV) is from normal to significantly decreased in patients with SMA according to stage and type of disease [3]. In early stage of this disorder, neuropathy may not typical and needle electrodes may be a painful course to children. The signs and symptoms of SMA, especially in the early stage, are often vague and mimic those of other flaccid paralysis conditions, including muscle diseases, neuromuscular joint diseases, peripheral nerve diseases and spinal cord anterior horn cells diseases, thus, the differential diagnosis of SMA could be sometimes challenging. Therefore, it is needed to develop novel measures or validate previous ones for clinical diagnosis. Maximum ulnar compound muscle action Potential (CMAP) could be a feasible, valid, and reliable measure in paediatric SMA [4], and small M-wave amplitude had been reported in the tibial nerve in SMA type 2 and 3 in previous study with small sample size [3]. In order to validate these findings, the aim of this study is to investigate and characterize MNCV in SMA type 2 and 3 patients and its mimic diseases.

Methods

Data Acquisition: A retrospective chart review was performed on all patients at a single academic medical centre between 2010 and 2019 with approval by the ethical committee of Wuhan Children's Hospital. A total of 40 patients aged 2–96 months, who were definitively diagnosed as SMA according to clinical symptoms, typical electromyographic patterns, and genetic testing. Patients were diagnosed with SMA1, SMA2, or SMA3 according to the criterion [1-3]. The included criterion: patients were newly diagnosed based on gene examinations and had

Correspondence to: Jun Jiang, Department of Electrophysiology, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science & Technology. No. 100, Jiangan, Hongkong Rods, Wuhan of Hubei, China, E-mail: jiangjunzm@163.com

Key words: *nerve conduction studies, peripheral neuropathy, spinal muscular atrophy, m-wave, tibial nerve*

Received: January 10, 2020; **Accepted:** January 25, 2020; **Published:** January 31, 2020

electrophysiological results, and no respiratory muscle involvement. We review patient demographics (age, gender, the time from symptom onset to first electrodiagnostic examination, the age of assessment, genetic mutation).

Other flaccid paralysis diseases, including Duchenne Muscular Dystrophy (DMD), Myasthenia gravis (MG), Polio-like diseases and Guillain-Barré syndrome (GBS), were diagnosed according to clinical history, electromyographic patterns, auxiliary examinations and (or) genetic testing's [3,5-8]. Polio-like diseases should meet electrophysiology features in spinal cord anterior horn cells: CMAP in motor nerve was reduced while motor conduction velocity (MCV), distal motor latency (DML) and sensory nerve conduction were normal. All the patients were newly diagnosed without respiratory muscle involvement, age -match. Patients with coexisting other neuromuscular diseases, ocular MG only, Polio-like diseases with only upper limbs involvement or peripheral nerve involvement, GBS variation, other hereditary diseases, other neurologic diseases, preterm history and respiratory muscle involvement were excluded from this study. We review patient demographics (age, gender, the time from symptom onset to first electrodiagnostic examination, the age of assessment, genetic mutation).

Electrophysiology

On admission, all patients were evaluated by NCS, while the skin temperature kept higher than 34°C. Motor and sensory nerve responses were evoked and recorded using an electromyograph (Key point Four, Dendi, Denmark). Conduction studies were performed in each patient according to the standard procedure [9,10], and CMAP, DML, and MCV were obtained from 4 motor nerves (tibial, peroneal, median, and ulnar). For all motor nerves, the CMAP recorded was the amplitude for the response from the proximal stimulation site (if distal and proximal sites were both tested) in millivolts (mV). DML was measured from the onset (or rise of the negative deflection) of the CMAP, expressed in milliseconds (ms). The MCV was determined by using the distance between the distal and proximal stimulation sites, divided by difference in latency expressed in meters per second (m/s). Appropriate electrical stimuli, with a duration of 0.1-0.5 ms, were delivered to the median, ulnar, tibial and peroneal nerves, at the wrist and elbow (supramaximal electrical stimuli if necessary) in median and ulnar nerves, at the ankle and popliteal fossa (supramaximal electrical stimuli if necessary) in tibial nerve, and at the ankle and fibula capitulum (supramaximal electrical stimuli if necessary) in peroneal nerve respectively. We had done these tests at bilateral tibial and peroneal nerves, unilateral median and ulnar nerve. Sensory nerve action potential (SNAP) were evoked by orthodromic stimulation from a ring electrode placed on the second finger for median nerve recording, on the fifth finger for ulnar nerve recording, or by a two-pronged stimulator placed below the lateral malleolus for sural nerve recording. All SNAPs analysed were the average of approximately 10 responses evoked using supramaximal stimulus intensity. The latency of sensory conduction was measured from the stimulus artefact to the positive peak of the SNAP, and the SNAP amplitude was measured from the positive to the negative peak.

Normal values for nerve conduction were obtained from data from our laboratory data and previous studies [11]. In order to define the severity of MNCV, we classify the data in MNCV based on criterion in GBS [12]. In CMAP, 80% lower limit of normal (LLN) ≤ CMAP < 100% LLN was slightly reduced, 50% LLN ≤ CMAP < 80% LLN was moderately reduced, CMAP < 50% LLN was remarkably reduced. In DML, upper limit of normal (ULN) < DML ≤ 110% ULN was slightly prolonged. In MCV, 90% LLN ≤ MCV < LLN was slightly slow. Demyelination feature [12]: when patients had one of the following in two or more nerves: (1) MCV < 90% LLN; (2) DML > 110% ULN; (3) unequivocal temporal dispersion. Motor neuron or axonal degeneration feature was diagnosed when distal CMAP amplitudes were < 80% LLN in at least two nerves without evidence of demyelination [12]. If the patients were not cooperative with NCS, sedative medicine (10% Chloral hydrate) were given to make patients asleep during nerve conduction studies. Repetitive nerve stimulation at a frequency of 3, 5Hz shows a gradual decline in the CMAP in patients with MG and SMA. The examination nerves were median nerve: CMAP from abductor pollicis brevis. ulnar nerve: CMAP from abductor digiti minimi, accessory nerve: CMAP from trapezius. Repetitive nerve stimulation abnormal: A decrement more than 10% from the first to the fourth CMAP is regarded as abnormal in at least one muscle [6].

Control patients

We retrospectively investigated NCS of 90 paediatric patients with SMA mimics, including 20 DMD patients, 20 MG patients, 20 patients with Polio-like diseases, 20 GBS patients (13 patients with acute inflammatory demyelinating polyneuropathy (AIDP), 7 patients with acute motor axonal neuropathy (AMAN)), 10 SMA 1 patients.

Ethics

The study was approved by the ethical committee of Wuhan Children's Hospital. Written informed consent was obtained from their parents of these patients in our study.

Statistical analyses

All data were analysed by SPSS software, version 13.0 (SPSS, Chicago, IL). We performed chi-square (X^2 test) for categorical, and t test for continuous variables to identify differences in clinical parameters between SMA type 2 and 3 mimics and in SMA type 2 and 3.

Results

Demographic characteristics, clinical manifestations and genetic mutations: All the SMA patients had muscle weakness in varying degree, decreased or absent reflexes. Patients with SMA had more serious muscle weakness in lower limbs than upper limbs. The age of assessment for SMA1 patients was younger than that of SMA2 and SMA3 (t=5.458, p=0.000) (Table 1). In SMA 1, genetic testing showed homozygous deletion of SMN1 exons 7 and 8 in 8 SMA patients, homozygous deletion of SMN exons 7 alone in one SMA patient, and homozygous deletion of exons 7 and heterozygous deletion of exon 8 in one SMA patient. We also performed genetic testing for 30 SMA type 2 and 3 patients and found deletion mutations in 21 cases (55%), point mutations in 5 cases (25%), and duplication in 4 cases (20%) (Table 1).

In addition to SMA1, the information for other disorders mimicking SMA type 2 and 3 was shown in table 1. All 20 patients with Polio-like diseases was infected by Enterovirus 71 (EV71). 12 patients were lower limbs involvement, 8 patients were upper and lower limbs involvement. Faeces were extracted for EV71 diagnosis. All the diagnosis patients had to remove to disease Control centres.

Twenty patients were diagnosed with MG, 15 patients with MG have detectable antibodies against the acetylcholine receptor (AChR). No one had purely ocular weakness. A total of 20 GBS patients, including 13 AIDP patients and 7 AMAN patients, were included. Immunoglobulin G (IgG) antibodies were seen in 3 AMAN. 20 patients were diagnosed with DMD, gene deletion mutations were found in 11

cases (55%), point mutations in 5 cases (25%), and duplication in 4 cases (20%).

Electrophysiological findings at each group and the predictive value for diagnosis: Except for SMA 1, the sex (X^2=-0.347,P=0.556) and age(t=-0.802,P=0.425) were match between SMA type 2 and 3 and its mimics(DMD, MG, GBS, polio-like disease) (Table 2). Electrophysiological features that suggest demyelination and motor neuron or axonal degeneration could also be detected in varying frequency in patients with SMA type 2 and 3 and its mimics diseases. The most common abnormality was motor neuron or axonal degeneration which was observed in 30 SMA type 2 and 3, 20 polio-like patients, 7 AMAN patients. Demyelinating was another common abnormal finding which was found in 13 AIDP patients. A decrement of >10% in repetitive nerve stimulation was found in two SMA type 2, one SMA type 3, and 16 MG patients. Selective remarkably low M-wave amplitude in tibial nerve was defined as tibial nerve CMAP <50% LLN while other motor nerves CMAP ≥ 50% LLN. Selective remarkably low M-wave amplitude in tibial nerve was only seen in SMA type 2 and 3 diseases. All the motor nerves CMAP remarkedly reduced in SMA1. A slightly decrease in MCV was found in 3 SMA1 patients. We also compared unilateral CMAP in motor nerves between SMA type 2 ,3 and GBS, polio-like disease. It was found that CMAP in tibial nerve was lower in SMA type 2 ,3 than GBS, polio-like disease. In the contrary, CMAP in median nerve, ulnar nerve and peroneal nerve were lower than SMA type 2 ,3 (Table 3). It indicated that M-wave amplitude in tibial nerve in SMA type 2 and 3 was remarkably reduced.

Selective remarkably low M-wave amplitude in tibial nerve in SMA type 2 and 3 and its mimics: In SMA type 2 and 3, CMAPs in median, ulnar, peroneal motor nerves were in normal range, or slightly reduced (CMAP≥50% LLN), while in tibial nerve, CMAP was remarkably reduced (CMAP < 50% LLN) (Table 4). In 10 SMA type I, CMAP in all the motor nerves were remarkably reduced (CMAP < 50% LLN). In DMD and MG, CMAP in motor nerves were in normal range or slightly reduced. In mostly polio-like diseases and AMAN, CMAP in motor nerves were all equivalent moderately or remarkably reduced, based on diseases severity. Selective remarkably low M-wave amplitude in tibial nerve was only seen in SMA type 2 and 3 diseases. (Table 2).

Discussion

SMA is inherited motor neuron disease among children. It is a progressive neuromuscular disorder that involved the motor neurons of the anterior spinal horn. There were few studies to investigate motor nerve in SMA, and MCV were reported from normal to remarkably reduction according to the stage of the disease [13,14]. The main pathological changes in SMA involve motor neurons of the anterior spinal horn. The electrophysiological finding in patients with motor neuron or axonal degeneration is a decreased CMAP amplitude and but a normal or only minimally reduced MCV. In our study, SMA had a decreased CMAP amplitude in MNC and several SMA had slightly slow in MCV [3]. These slower conduction velocities could be caused by demyelination or by loss of fast-conducting myelinated axons.

The diagnosis of floppy infants is challenging in paediatrics. Many diagnoses should be considered. Anterior spinal horn, peripheral nerve, muscle and neuromuscular junction disease all could bring floppy as well as muscle weakness in children. To achieve diagnosis, neurophysiology is an important examination to help the direction of diagnosis. DMD (muscle diseases) and MG (neuromuscular junction disease) had no characteristic feature of MNC. DMD may had slightly

Table 1. Demographic characteristics and clinical manifestations

Type of diseases	SMA2+SMA3	SMA 1	DMD	MG	Polio-like diseases	GBS
No. of patients	25+5	10	20	20	20	20
Sex (M/F)	18/12	04/6	20/0	09/11	6/14	08/12
The mean time from symptom onset to first electrodiagnostic examination (range)	5 months (20 days - 30 months)	24 days (11 - 60 days)	4 months (2 - 10 months)	8 days (10 - 82 days)	19 days (12 - 28 days)	17 days (10 - 24 days)
The age of assessment (median) (month)	24.20 ± 19.90	4.10 ± 1.91	31.25 ± 17.04	24.85 ± 15.65	23.65 ± 8.88	27.75 ± 11.25
Genetic mutation	homozygous deletion of exon 7 and 8 in 25, homozygous deletion of exon 7 in 3, and homozygous deletion of exon 7 and heterozygous deletion of exon 8 in 1	-	deletion in 11, point mutation in 5, and duplication in 4			

Table 2. Statistical estimates for electrodiagnstic feature in SMA and its mimics (n=110). SMA: Spinal muscular atrophy

	Diagnosis (percentage)			
	SMA type 2 and 3(n=30)	SMA mimics(n=80)	t/ X^2	P
Age(month)	24.20 ± 19.90	26.88 ± 13.67	-0.802	0.425
Sex	18/12	43/37	-0.347	0.556
Demyelination feature	0 (0%)	13 (16.25%)	-	-
Repetitive nerve stimulation	3 (10.00%)	16 (20.00%)		
motor neuron or axonal degeneration	30 (100%)	27 (41.11%)	-	-
Selective reduced CMAP in tibial nerve	30 (100%)	0 (0.0%)	-	-

Table 3. CMAP in motor nerves in SMA and its mimics.

	SMA type 2 and 3 (n=30)	GBS and polio-like disease (n=40)	t	p
Age (month)	24.20 ± 19.90	25.70 ± 10.22	-0.411	0.683
Tibial nerve CMAP (mv,R)	1.71 ± 0.34	3.05 ± 1.32	-5.442	0.000
peroneal nerve CMAP (mv,R)	3.47 ± 1.14	2.44 ± 1.02	3.992	0.000
Median nerve CMAP (mv,R)	3.86 ± 1.41	2.47 ± 1.11	4.608	0.000
Ulnar nerve CMAP (mv, R)	4.29 ± 1.47	2.64 ± 1.03	5.541	0.000

CMAP: Compound Muscle Action Potential, R-right.

Table 4. SMA types and MNC studies

Case	Type	Age of assessment (months)	CMAP in median (mV)	CMAP in ulnar (mV)	CMAP in tibial (mV)(R)	CMAP in tibial (mV) (L)	CMAP in peroneal (mV) (R)	CMAP in peroneal (mV) (L)
1	II	9	2.4	2.7	1.4	1.1	2.5	2.4
2	II	10	2.3	2.2	1.3	1.5	2.2	2.0
3	II	10	2.1	2.5	1.5	1.6	2.3	2.2
4	II	10	3.1	3.3	1.2	1.2	2.1	2.0
5	II	12	2.7	3.2	1.6	1.5	2.3	2.2
6	II	12	3.4	3.5	1.5	1.7	3.5	3.2
7	II	14	3.2	3.9	1.4	1.4	3.3	3.4
8	II	14	3.4	4.2	1.5	1.7	3.5	3.2
9	II	15	4.2	4.5	1.8	1.8	4.2	4.0
10	II	15	4.1	4.1	1.6	1.7	3.9	3.2
11	II	16	3.1	3.8	2.2	2.0	3.4	3.5
12	II	16	3.2	3.6	2.1	1.8	3.2	2.8
13	II	16	3.1	3.3	2.0	1.7	3.0	2.8
14	II	16	2.8	3.8	1.7	1.7	3.5	2.8
15	II	16	3.2	3.9	1.5	1.4	2.9	3.7
16	II	17	3.8	4.2	1.8	1.9	3.7	4.5
17	II	17	3.4	4.1	1.9	1.8	3.8	3.6
18	II	18	2.5	3.7	0.8	1.0	2.5	2.6
19	II	20	3.2	4.0	1.8	1.4	3.0	3.0
20	II	21	3.1	3.2	1.4	1.2	2.6	2.8
21	II	22	3.6	3.7	1.9	2.0	2.6	2.6
22	II	23	4.1	3.7	1.8	1.8	3.5	2.8
23	II	24	4.2	4.2	1.7	1.9	3.2	3.6
24	II	24	4.1	4.1	1.6	1.7	3.5	3.9
25	II	25	4.2	5.4	1.8	1.8	4.1	4.2
26	III	72	6.4	6.8	2.1	2.0	4.8	5.2
27	III	96	6.1	7.5	1.8	1.9	5.2	5.5
28	III	38	7.6	7.8	1.9	1.7	5.9	5.4
29	III	49	6.9	7.7	2.1	2.0	4.5	5.3
30	III	59	6.2	6.1	2.5	2.5	6.2	5.9

CMAP: Compound muscle action potential; LLN: Lower limit of normal. SMA: Spinal muscular atrophy; MNC: Motor nerve conduction; R-right; L-left; Millivolts-Mv; CMAP LLN in motor nerve; 6 months-3 years: peroneal nerve: 3.5 mv; tibial nerve: 6.0 mv; ulnar and median nerve: 3.5mv; ≥3 years: peroneal nerve: 6.0mv; Tibial nerve: 6.0mv; ulnar and median nerve: 6.0 mv.

reduced CMAP in some cases and no characteristic feature in MNC in DMD. In MG, a decrement of >10% from the first to the fourth CMAP in repetitive nerve stimulation was characteristic feature, and this could also be detected in a few SMA. Neuromuscular junction is established at a normal frequency, there are structural as well as functional perturbations and a lack of maturation of the primitive synapse in SMA. These early defects are followed by loss of the Neuromuscular junction, denervation of the muscle and onset of muscle atrophy in SMA [15]. GBS is the most common peripheral nerve disease among children. It's had two main subtypes, namely AIDP and AMAN, with characteristic in demyelination and axon damage feature in MNC. A few cases in SMA could have slightly slower in MCV because of losing of fast-conducting myelinated axons. But the main pathological changes in SMA was degeneration motor neurons of the anterior spinal horn. The pathological changes in Polio-like disease was motor neurons of the anterior spinal horn involvement. Axon damage share the same features in MNC with motor neurons of the anterior spinal horn involvement. These electrophysiological findings in SMA can also be found in AMAN and Polio-like disease. Medical history and other auxiliary examinations could distinguish three different types of diseases, but selective remarkably low M-wave amplitude in tibial nerve was mainly found in SMA type 2 and 3. Pathological change in this electrophysiological finding was not clear. In previous studies, proliferation of the proximal anterior spinal roots and neuronal degeneration, selective loss of large myelinated fibers, retardation of motor fiber development and insidious motor neuronal degeneration in the clinical course may be the reason for selective reduced CMAP in tibial nerve [3]. As we all known, tibial nerve has more myelinated fibers than peroneal nerve. In SMA type 2 and 3, the initial lesion may be focal or patchy in anterior spinal horn and it occur preferentially in lower limbs, tibial nerve involvement represented more proximal anterior spinal roots and more degeneration of the motor neurons than peroneal nerve, so tibial nerve involvement had more possibility than peroneal nerve involvement. This may be the explanation in selective remarkably low M-wave amplitude in tibial nerve. In SMA type 1, all the motor nerve CMAP were remarkedly reduced, reflecting diffuse loss or axonal degeneration of the immature motor fibers in type 1 at a very early stage [3]. This may suggest that in types 2 and 3 the distribution of peripheral nerve involvement differs from that in type 1.

This is the first investigation to compare SMA with other flaccid paralysis diseases in MNC. In paediatric patients, the chief complain may be confusing, hereditary factors could delay and confused the diagnosis. In this condition, electrophysiological findings may be direct results in main pathological change and a direction to other laboratory examinations. In our investigation, selective remarkably reduced CMAP in tibial nerve was only seen in SMA type 2 and 3. Our results are in line with a previous report that tibial nerve CMAP amplitudes significantly reduced in SMA type 2 and 3 patients [3,16].

A clear limitation of our study is that electrodiagnostic features were found in stable patients without respiratory weakness and newly diagnosed patients. The MNC might vary with time elapse or respiratory weakness. Motor function of patients with SMA type 2 and 3 can improve as well as CMAP [17]. We had few follow-up cases with SMA to observe the change in CMAP and motor function. Another limit is that we did not analysis femoral nerve and sensory nerve conduction parameter in our study, recent studies have suggested that SMA may also affect sensory neurons [17]. Because of pathological changes in SMA 2 and 3, femoral nerve may have remarkably reduction in CMAP, it is valuable to investigate femoral nerve involvement in diseases.

Conclusion

In summary, initial lesion in SMA 2 and 3 may be focal or patchy in anterior spinal horn. Tibial nerve involvement represented more proximal anterior spinal roots and more degeneration of the motor neurons than peroneal nerve, so tibial nerve involvement had more possibility than peroneal nerve involvement. This may be explanation in selective remarkably low M-wave amplitude in tibial nerve. A selective M-wave with significantly low amplitude in tibial nerve was typical feature in SMA type 2 and 3.

References

1. D'Amico A, Mercuri E, Tiziano FD, Bertini E (2011) Spinal muscular atrophy. *Orphanet J Rare Dis* 6: 71. [Crossref]
2. Mercuri E, Bertini E, Iannaccone ST (2012) Childhood spinal muscular atrophy: controversies and challenges. *Lancet Neurol* 11: 443-452. [Crossref]
3. Miyanomae Y, Takeuchi Y, Nishimura A, Kawase S, Hirai K, et al. (1996) Motor nerve conduction studies on children with spinal muscular atrophy. *Acta Paediatr Jpn* 38: 576-579.
4. Lewelt A, Krosschell KJ, Scott C, Sakonju A, Kissel JT, et al. (2010) Compound Muscle Action Potential and Motor Function in Children with Spinal Muscular Atrophy. *Muscle Nerve* 42: 703-708. [Crossref]
5. Leigh F, Ferlini A, Biggar D, Bushby K, Finkel R, et al. (2018) Neurology Care, Diagnostics, and Emerging Therapies of the Patient with Duchenne Muscular Dystrophy. *Pediatrics* 142: 5-16. [Crossref]
6. Gilhus NE, Tzartos S, Evoli A, Palace J, Burns TM, et al. (2019) Myasthenia gravis. *Nat Rev Dis Primers* 5: 30. [Crossref]
7. Kim B, Moon S, Bae GR, Lee H, Pai H, et al. (2018) Factors associated with severe neurologic complications in patients with either hand-foot-mouth disease or herpangina: A nationwide observational study in South Korea, 2009-2014. *PLoS One* 13: e0201726. [Crossref]
8. Wakerley BR, Uncini A, Yuki N, GBS Classification Group, GBS Classification Group (2014) Guillain-Barre and Miller Fisher syndromes-new diagnostic classification. *Nat Rev Neurol* 10: 537-544. [Crossref]
9. Russell JW, Afifi AK, Ross MA (1992) Predictive value of electromyography in diagnosis and prognosis of the hypotonic infant. *J Child Neurol* 7: 387-391. [Crossref]
10. Jones HR (1990) EMG evaluation of the floppy infant. Differential diagnosis and technical aspects. *Muscle Nerve* 13: 338-347. [Crossref]
11. Ryan CS, Conlee EM, Sharma R, Sorenson EJ, Boon AJ, et al. (2019) Nerve conduction normal values for electrodiagnosis in pediatric patients. *Muscle Nerve* 60: 155-160. [Crossref]
12. Sekiguchi Y, Uncini A, Yuki N, Misawa S, Notturno F, et al. (2012) Antiganglioside antibodies are associated with axonal Guillain-Barre syndrome: A Japanese-Italian collaborative study. *J Neurol Neurosurg Psychiatry* 83: 23-28.
13. Moosa A, Dubowitz V (1976) Motor nerve conduction velocity in spinal muscular atrophy of childhood. *Arch Dis Child* 51: 974-977. [Crossref]
14. Ryniewicz B (1977) Motor and sensory conduction velocity in spinal muscular atrophy: follow-up study. *Electromyogr Clin Neurophysiol* 17: 385-391. [Crossref]
15. Goulet BB, Kothary R, Parks RJ (2013) At the "junction" of spinal muscular atrophy pathogenesis: the role of neuromuscular junction dysfunction in SMA disease progression. *Curr Mol Med* 13: 1160-1174. [Crossref]
16. Yonekawa T, Komaki H, Saito Y, Sugai K, Sasaki M (2013) Peripheral nerve abnormalities in pediatric patients with spinal muscular atrophy. *Brain Dev* 35: 165-171. [Crossref]
17. Yuan P, Jiang L (2015) Clinical characteristics of three subtypes of spinal muscular atrophy in children. *Brain Dev* 37: 537-541. [Crossref]