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Aims and Scope

Journal of Electrodiagnosis and Neuromuscular Diseases (*J Electrodiagn Neuromuscul Dis*, JEND) is a peer-reviewed journal concerning both normal and abnormal functioning of the muscle, the neuromuscular junction, and the peripheral motor, sensory and autonomic nerves. The journal publishes clinical studies, reviews, and case reports in the fields of electrophysiology, electrodiagnosis, imaging studies including ultrasonography, and management, about neuromuscular diseases. The journal is aimed to provide an open forum for original research in basic science and clinical research that will improve our fundamental understanding and lead to effective treatments of neuromuscular diseases.
JEND is the official journal of the Korean Association of EMG Electrodiagnostic Medicine.

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ORIGINAL ARTICLE

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정확하고 안전한 바늘근전도 검사를 위한 초음파를 이용한 요측수근굴근의 형태학적 평가

안준영, 김상현, 이승열, 조연희, 오백민, 석현

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Morphologic Evaluation of the Flexor Carpi Radialis Muscle Using Ultrasonography for Accurate and Safe Needle Electromyography

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Objective: This study aimed to determine the proper and safe needle insertion point in the flexor carpi radialis (FCR) muscle under ultrasonography guidance.
Methods: We identified the center point (CP) of the FCR as the optimal needle insertion point using ultrasonography. The location of the CP was analyzed using ratios and distances from other landmarks. The vertical distance (CP-VD) was measured by drawing an imaginary vertical line from the CP to the elbow crease. We measured the horizontal distance from the point where the imaginary vertical line from the CP meets the elbow crease to the biceps tendon at the elbow crease level (CP-HD). We presented the ratio of CP-HD to forearm circumference (HD ratio) and the ratio of CP-VD to forearm length (VD ratio) as percentages.
Results: The mean values of CP-HD and CP-VD were 2.0 ± 1.0 cm and 8.2 ± 1.1 cm, respectively. The mean HD and VD ratios were 8.4% ± 4.2% and 32.0% ± 3.1%, respectively.
Conclusion: When performing electromyography (EMG) of the FCR muscle, it is recommended to perform EMG at the point about 2 cm medial from the biceps tendon at the elbow crease level, to nearly the proximal one-third of forearm length.

Keywords: Flexor carpi radialis; Ultrasonography; Electromyography

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Introduction

The flexor carpi radialis (FCR) muscle is the forearm superficial muscle originating in the medial epicondyle of humerus and inserted into the base of the 2nd and 3rd metacarpal bones. As the name suggests, the contraction of FCR muscle located on the surface of volar side of forearm causes flexion and radial deviation of the wrist [1].

The FCR muscle plays an important role in the evaluation and diagnosis of the C6 and C7 nerve root lesions or pathologic conditions associated with median nerve innervations, such as pronator teres (PT) syndrome, in electromyography (EMG) [2]. Also, FCR muscle is vulnerable to myofascial pain syndrome caused by repetitive movements such as wrist flexion/ extension or ulnar/radial deviation [3]. Therefore, the FCR muscle is often targeted for trigger point injection. In addition, botulinum toxin is generally injected into the FCR muscle to manage spastic wrist flexors in patients with stroke or spinal cord injury, because FCR muscle is one of the muscles associated with forearm spastic postures under hypertonicity [4].

However, when botulinum toxin A injection was performed manually without instrumental guidance such as ultrasonography, the accuracy of needle entry into the FCR muscle was as low as 41.5% [5]. Also, it is difficult to penetrate the FCR muscle with a needle accurately along with serratus anterior, flexor carpi ulnaris (FCU), flexor pollicis longus, PT, and extensor indicis proprius muscles in the upper extremity [6].

Although the optimal needle insertion position for FCR muscle is clinically important, several needle EMG methods have been introduced [7-9]. In these studies, the needle insertion point was inaccurate using fingerbreadth, and the accuracy of needle insertion was not verified by ultrasonography. Also, the optimal needle insertion point varies with the patient demographic characteristics such as height. Song et al. [10] investigated the optimal area for FCR muscle injection in cadavers. However, the study had several limitations as living musculoskeletal structures differ from those of cadavers, and the sample size was small, which prevented discussion of proper depth of needle insertion. The aim of this study was to identify the center point (CP) of FCR muscle under ultrasonography guidance and to determine the most appropriate needle insertion point, considering the anatomical location.

Materials and Methods

1) Study design and participants

We enrolled 40 healthy subjects in this cross-sectional study. The study participants were prospectively recruited as volunteers. The sample size was calculated based on a previous study [10], which determined the anatomical localization of motor points of wrist flexors. In this previous study [10], the authors concluded that the motor point of FCR muscle was located at about proximal 27% of the FCR reference line connecting the medial epicondyle and the base of the 2nd metacarpal bone. Based on the primary outcome ($p = 0.27$), a power of 80% and a two-sided test ($\alpha = 0.05$) and, a margin of error of 20%, we determined that the sample size required was 76. Assuming a 5% loss, we estimated that the final sample size required was 80, for a total of 40 participants for the study. Subjects older than 19 years were included. Exclusion criteria were (1) inability to cooperate with the examination due to systemic disease or mental illness, (2) upper extremity amputation, and (3) a cast, splint or metal that create artifact in forearm. Both forearms were examined in all participants, and a total of 80 forearms were enrolled. Demographic characteristics including age, sex, height, weight, body mass index (BMI), and forearm length affect the morphology of FCR muscle, and therefore were collected. Especially, we analyzed data focusing on height. Because tall people have long forearms [11], we thought that height was a major factor in determining the CP of the FCR muscle. In addition, since height can be estimated approximatively, we thought it would be important during clinical examination. We defined forearm length as vertical distance from biceps tendon palpable at elbow crease to distal wrist crease, which is of sufficient consistency to be used as a reliable landmark [12]. The purpose and method of the study were explained to all subjects. All participants' informed consent was obtained. The Institutional Review Board of Soonchunhyang University Bucheon Hospital approved this study (approval number: 2020-05-029-001).

2) Sonographic examinations

A single physiatrist conducted the ultrasonography evaluation for FCR muscle using a linear array transducer (7-18 MHz, Xario SSA-660A; Toshiba, Minato, Japan). Ultrasonographic evaluation was performed in supine position with the forearm fully supinated, and the shoulder abducted about 30°. We obtained all measurable data in this supine position.

Since the shape of FCR muscle is fusiform, we assumed that the CP of the FCR muscle was an optimal needle insertion point in this study. To determine the location of CP, we located the musculotendinous junction and the origin of FCR muscle using sonographic long and short-axis views. Musculotendinous junction and origin of FCR muscle were indicated on the skin, respectively. As shown in Fig. 1A, the vertical location of CP was in the midline between origin of FCR muscle and musculotendinous junction, which was an imaginary line parallel to the elbow crease. To verify the horizontal location of CP, the FCR muscle was examined by moving the ultrasound probe horizontally over this midline. As shown in Fig. 1B, we defined the point in short-axis sonographic image where FCR muscle was located at the center of sonographic image as CP. Drawing an imaginary vertical line from CP to elbow crease, the vertical distance (CP-

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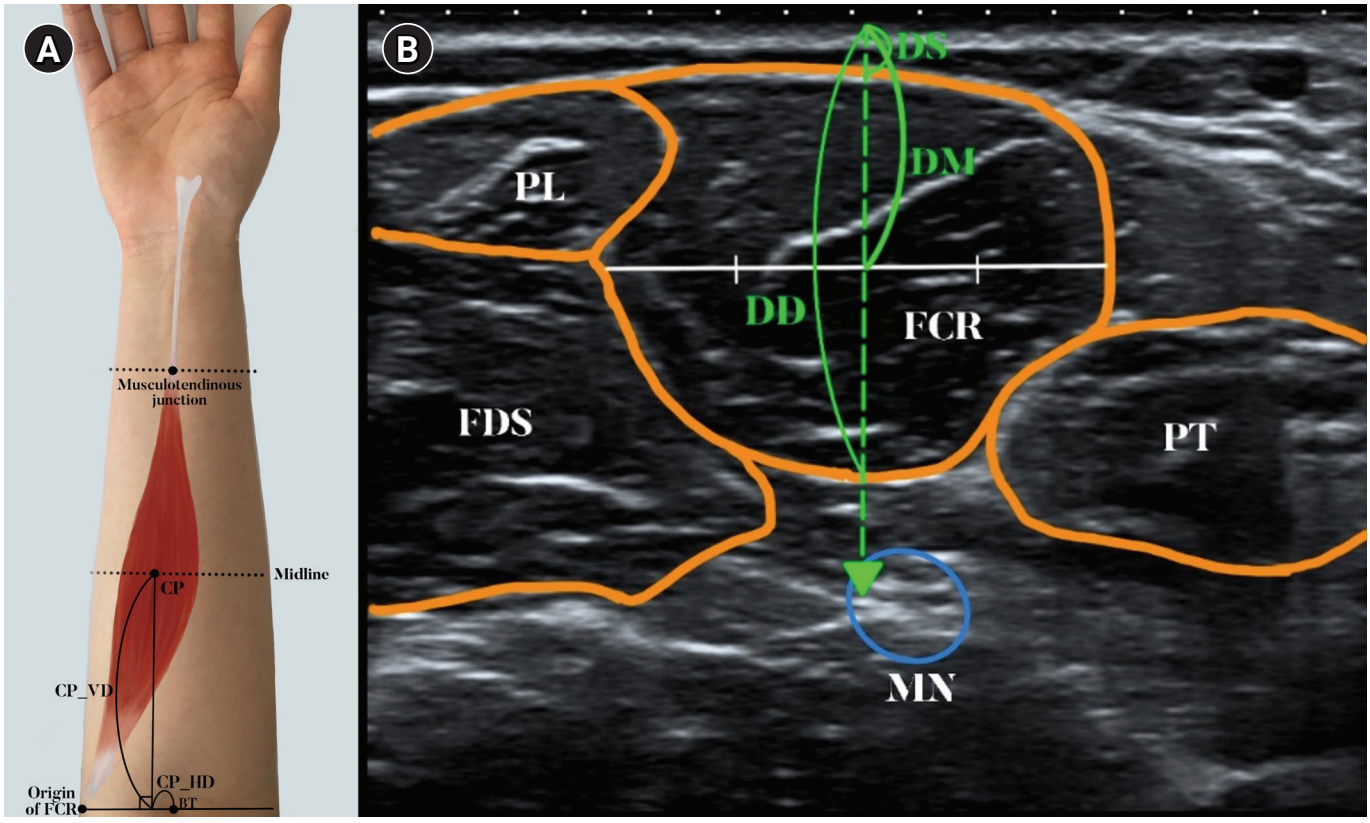

Fig. 1. (A) Schematic diagram of the center point (CP) of the flexor carpi radialis (FCR) muscle in the forearm. The vertical location of the CP was along the midline between the origin of the FCR muscle and the musculotendinous junction. The horizontal location of the CP was the point where the FCR muscle was located at the center of the sonographic image. (B) Short-axis ultrasonography image of the CP of the FCR muscle. Green arrow indicates the imaginary pathway of needle entrance. CP-VD, vertical distance from center point to the elbow crease; CP-HD, horizontal distance from the biceps tendon to point where the imaginary vertical line meets the elbow crease; BT, biceps tendon; DS, depth from the skin to the superficial margin of the FCR muscle; DM, middle value of depth from skin to the superficial margin of the FCR muscle and depth from the skin to the deep margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; PL, palmaris longus; FDS, flexor digitorum superficialis; PT, pronator teres; MN, median nerve.

VD) was measured. The horizontal distance was measured from the point where the imaginary vertical line drawn from CP meets elbow crease to biceps tendon at the level of elbow crease (CP-HD) (Fig. 1A). Also, forearm circumference at CP was measured. Each person has distinct CP-HD and CP-VD due to their unique demographic characteristics. In order to suggest a representative value that is equally applicable to all people, we presented the ratio of CP-HD to forearm circumference (HD ratio) and ratio of CP-VD to forearm length (VD ratio) as a percentage. The anatomical structures that could be penetrated by imaginary needle pathway were recorded on a short-axis sonographic image obtained in CP. If the median nerve was penetrated, the depth of the median nerve was recorded as a range from the depth of the most superficial part to the deepest part of the median nerve. Also, the depth from the skin to the superficial margin of FCR muscle (DS) and the depth from the skin to the deep margin of FCR muscle (DD) were measured. The mid-depth (DM) was defined as the median value of DS and DD (Fig. 1B).

Needle insertion points were previously suggested via 3 needle EMG methods [7-9]. Preston and Shapiro [7] and Perotto and Delagi [9] suggested that the needle should be inserted at a distance of 4 fingerbreadths distal to the center of the wrist from the midpoint between the medial epicondyle and biceps tendon at elbow crease level (point A). Lee and DeLisa [8] suggested that the needle should be inserted at the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle (point B). Perotto and Delagi [9] recommended that the needle should be inserted at a distance of 4 fingerbreadths distal from the midpoint between the medial epicondyle and biceps tendon at elbow crease level (point C). These 3 needle EMG methods and CP were marked on the skin as shown in Supplementary Fig. 1. At each point, we acquired a cross-sec-

tional sonographic image and analyzed the anatomical structures that could be penetrated (Fig. 2). The depth of penetration was measured if the imaginary needle pathway penetrated the FCR muscle or median nerve. To ensure that the middle portion of

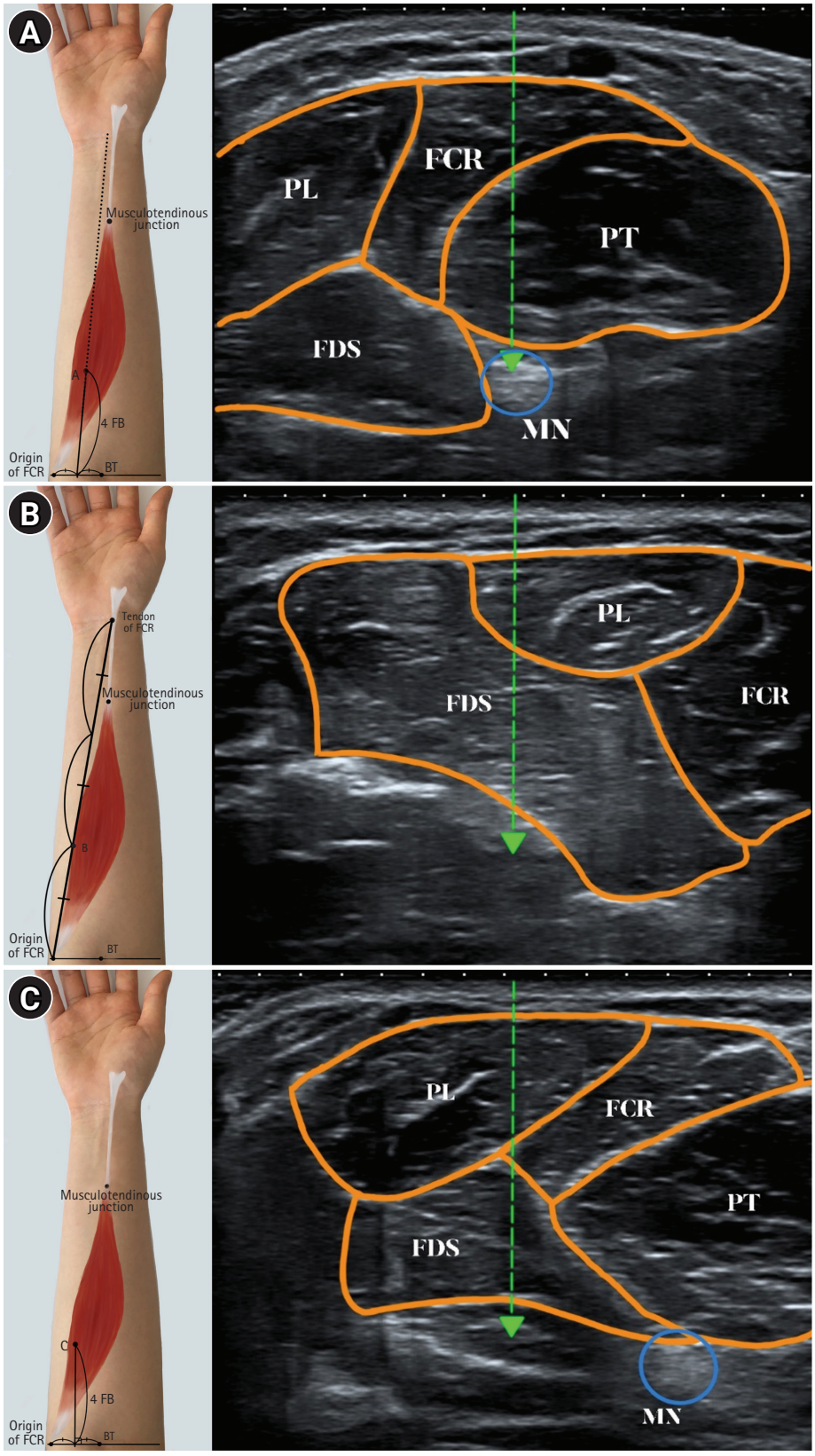

Fig. 2. (A) (Left) Schematic diagram of point A of the flexor carpi radialis (FCR) muscle in the forearm. Four fingerbreadths (FBs) distal to the center of the wrist from midpoint between the medial epicondyle and biceps tendon (BT) at the elbow crease level. (Right) Cross-sectional ultrasonography image at point A. Green arrow indicates the imaginary pathway of needle entrance. (B) (Left) Schematic diagram of point B of the FCR muscle in the forearm. Proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle. (Right) Cross-sectional ultrasonography image at point B. Green arrow indicates the imaginary pathway of needle entrance. (C) (Left) Schematic diagram of point C of the FCR muscle in the forearm. Four FBs distal from the midpoint between the medial epicondyle and BT at the elbow crease level. (Right) Cross-sectional ultrasonography image at point C. Green arrow indicates the imaginary pathway of needle entrance. PL, palmaris longus; FDS, flexor digitorum superficialis; PT, pronator teres; MN, median nerve.

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FCR was accurately penetrated by the imaginary needle pathway in each method, we defined the "middle portion" of the FCR muscle as the middle one-third when the muscle was divided into 3 segments in a horizontal axis. It was also recorded whether the middle portion of the FCR muscle was penetrated. In order to obtain accurate results, the ultrasound probe was carefully contacted with the skin with minimal pressure. The 4 fingerbreadths length of the physiatrist who conducted ultrasonography was about 7 cm.

3) Statistical analysis

Demographic characteristics and anatomical ultrasonography parameters are expressed as mean ± standard deviation, because the number of data (n = 80) was sufficient to ensure a normal distribution. Ultrasonography parameters (CP-HD, HD ratio, CP-VD, VD ratio, and DM) and demographic characteristics (height, weight, and BMI) were analyzed by correlation analysis. Sex differences were identified via Student t-test and Mann-Whitney was used for data that did not follow the normal distribution. Shapiro-Wilk test was performed to confirm normal distribution. A p-value of 0.05 or less was considered statistically significant. We used IBM SPSS Statistics ver. 26.0 (IBM Corp., Armonk, NY, USA) for all statistical analyzes.

Results

This study was performed on a total of 80 forearms involving 26 males and 14 females. The mean age was 31.4 ± 7.4 years; the mean height was 169.8 ± 9.5 cm; and the mean forearm length was 25.6 ± 2.0 cm. Other demographic data are summarized in Table 1.

Ultrasonography and anatomical parameters are presented in Table 2. The mean vertical distance from CP to elbow crease (CP-VD) was 8.2 ± 1.1 cm. The mean ratio of CP-VD to forearm length (VD ratio) was 32.0% ± 3.1%. The mean horizontal distance (CP-HD) was 2.0 ± 1.0 cm and the mean ratio of CP-HD to forearm circumference (HD ratio) was 8.4% ± 4.2%. The DS and DD of FCR muscle at CP were 3.7 ± 1.3 mm and 15.6 ± 2.2 mm, respectively. The DM of FCR muscle was 9.7 ± 1.3 mm (Table 2). Correlation analysis between ultrasonography parameters and demographic characteristics was performed (Table 3). CP-VD showed a significant positive correlation with height ($R = 0.550$, $p < 0.01$, Table 3). On the other hand, the VD ratio did not show a significant correlation with any demographic characteristics. Similarly, CP-HD and HD ratio did not show a significant correlation with any demographic characteristics. Among all variables, such as CP-HD, HD ratio, CP-VD, VD ratio, DD, DS and DM, only CP-HD, VD ratio and DM did not reveal significant differences between male and female (p-values 0.170, 0.052, and 0.947, respectively).

Table 4 demonstrates anatomical structures that could be penetrated by the imaginary needle pathway using each of the 4 different needle EMG methods [7-9]. Cross-sectional sonographic image of each point is presented in Fig. 1 and 2. The accuracy of penetration by the imaginary needle into FCR muscle was 82.5%, 20.0%, and 93.8% accuracy using methods A, B, and C, respectively. Methods A and C showed greater than 80% accuracy. However, the accuracy of penetration by the imaginary needle into the middle portion of FCR muscle was only 6.3%, 0%, and 38.8% in methods A, B, and C, respectively. Among the 3 methods, the probability of median nerve penetration was high in the order of A, C, and B (48.8%, 21.3%, 2.5%, respectively). Among the other structures, the PT, palmaris longus (PL) and flexor digitorum superficialis (FDS) muscles were also penetrated depending on the methods in question (Table 4). The median nerve penetration at CP was detected in 38 out of 80 (47.5%) forearms, showing a probability of 47.5%. In these 38 forearms, the mean

Table 1. Demographic Characteristics

Characteristic	Value (n = 40)
Age (y)	31.4 ± 7.4
Sex (male/female)	26/14
Height (cm)	169.8 ± 9.5
Weight (kg)	66.2 ± 11.2
Body mass index (kg/m^2)	22.8 ± 2.2
Forearm length (cm)	25.6 ± 2.0

Values are presented as mean ± standard deviation.

Table 2. Anatomical and Ultrasonographic Parameters

Variable	Total (n = 80)
CP-HD (cm)	2.0 ± 1.0
Forearm circumference (cm)	23.9 ± 2.2
HD ratio (%)	8.4 ± 4.2
CP-VD (cm)	8.2 ± 1.1
Forearm length (cm)	25.6 ± 2.0
VD ratio (%)	32.0 ± 3.1
DS (mm)	3.7 ± 1.3
DD (mm)	15.6 ± 2.2
DM (mm)	9.7 ± 1.3

Values are presented as mean ± standard deviation.
CP-HD, distance from the biceps tendon to the point where an imaginary vertical line meets the elbow crease; HD ratio, CP-HD/forearm circumference; CP-VD, distance from the center point to the elbow crease; VD ratio, CP-VD/forearm length; DS, depth from the skin to the superficial margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; DM, middle value of DS and DD; FCR, flexor carpi radialis.

Table 3. Correlation Coefficient (r) between Ultrasonographic Parameters and Demographic Characteristics

Parameter	Demographic characteristic						
	HD ratio	CP-VD	VD ratio	DM	Height	Weight	BMI
CP-HD	0.977*	-0.390*	-0.487*	0.096	-0.001	0.07	0.124
HD ratio	1	-0.412*	-0.461*	-0.008	-0.104	-0.085	-0.029
CP-VD		1	0.841*	-0.154	0.550*	0.361*	0.021
VD ratio			1	-0.150	0.078	-0.005	-0.083
DM				1	-0.003	0.399*	0.660*
Height					1	0.825*	0.305*
Weight						1	0.787*
BMI							1

CP-HD, distance from the biceps tendon to the point where an imaginary vertical line meets the elbow crease; HD ratio, CP-HD/forearm circumference; CP-VD, distance from the center point to the elbow crease; VD ratio, CP-VD/forearm length; DM, middle value of DS and DD; BMI, body mass index; DS, depth from the skin to the superficial margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; FCR, flexor carpi radialis.
*$p < 0.01$.

Table 4. Number of Structures Penetrated by an Imaginary Needle Pathway Using Four Different Needle Electromyography Methods (n = 80)

Method	FCR muscle (any portion of FCR)	Middle portion of FCR muscle	Median nerve	PT muscle	PL muscle	FDS muscle
A	66 (82.5)	5 (6.3)	39 (48.8)	73 (91.3)	4 (5.0)	7 (8.8)
B	16 (20.0)	0 (0)	2 (2.5)	0 (0)	72 (90.0)	78 (97.5)
C	75 (93.8)	31 (38.8)	17 (21.3)	30 (37.5)	18 (22.5)	48 (60.0)
CP	80 (100.0)	80 (100.0)	38 (47.5)	0 (0)	0 (0)	62 (77.5)

Values are presented as the number of penetrations (%).
FCR, flexor carpi radialis; PT, pronator teres; PL, palmaris longus; FDS, flexor digitorum superficialis.
Method A, 4 fingerbreadths distal to the center of the wrist from the midpoint between the medial epicondyle and biceps tendon at the elbow crease level [7]; method B, proximal third of the imaginary line connecting the flexor carpi radialis tendon of the wrist and medial epicondyle [8]; method C, 4 fingerbreadths distal from the midpoint between the medial epicondyle and biceps tendon at the elbow crease level [9]; method CP, about 2 cm medial from the biceps tendon at the elbow crease level, to nearly the proximal one-third of forearm length.

depth of the most superficial part of the median nerve was 18.61 mm and the mean depth of the deepest part was 21.31 mm.

Discussion

In the present study, 80 forearms were analyzed to propose safe and proper needle placement of FCR muscle in 40 healthy participants. According to our study, CP-VD and CP-HD were found to be approximately 8.2 cm distal, and 2 cm medial from the palpable biceps tendon at the elbow crease level, respectively. However, the precise location of FCR muscle may vary since each person has a variable forearm length. Since we hypothesized that forearm length was proportional to height [11], the correlation analysis was performed. As a result, only CP-VD showed a significant positive correlation with height, implying that as the height increases, the forearm length is longer, and accordingly, the CP-VD increases. Thus, unlike CP-VD, the CP-HD can be used regardless of height. However, the VD ratio showed no significant correlation with height, weight, and BMI. Therefore, the VD ratio can be used as a vertical distance of FCR muscle, instead of CP-VD. Consequently, we conclude that the CP of FCR muscle is located approximately 2 cm medial from the biceps tendon at elbow crease level horizontally, and the proximal 32.0% of the forearm vertically regardless of height. Also, the average value DM of FCR muscle was 9.7 mm.

In a previous study, the biceps tendon and medial epicondyle were used as landmarks to localize the FCR muscle, suggesting that the FCR muscle might be located 4 fingerbreadths distal from the landmark (point A, C). Another study proposed the proximal third of imaginary line connecting the medial epicondyle of humeral origin of the FCR muscle, and the FCR tendon palpable in the lateral part of the wrist with wrist flexion (point B). These previous needle insertion points for FCR muscle appear to have been determined approximately via empirical methods or anatomical cross-sections. Method A and method C, which were presented by Preston and Perotto respectively, seem to have suggested needle insertion points based on cross-sections and the authors' experiences. In these 2 methods, it is considered a problem to suggest a fixed position without considering forearm length. Method B, presented by Lee and DeLisa [8], seems

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that the needle insertion point was suggested based on the origin and insertion of the FCR muscle. In this method, they suggested that the needle should be inserted at the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle, considering forearm length. However, there was a problem that only the origin and insertion were considered and the accurate anatomy of the forearm flexors was not considered.

In the present study, we also used the biceps tendon, which is easily palpable at the elbow crease, as a landmark. However, we indicated the horizontal distance as a numerical value, and the vertical position as a proportional value based on ultrasonographic evaluation, which may be a more objective method than the other previous approaches, because our novel method did not use fingerbreadth that differs with each examiner. In addition, it considers variable heights for each examinee. VD ratio, which is approximately the proximal 1/3 of the forearm length, can be a good indicator for an intuitive approach. Additionally, the depth of FCR muscle, which was not mentioned in previous methods, was also suggested as 9.7 mm. Finally, these values did not show statistically significant differences according to sex as well as height.

As previously stated in the results, methods A and C had acceptable accuracy if used simply to penetrate FCR muscle. However, they were inaccurate if used to test or target the middle portion of FCR muscle (Table 4). Also, the accuracy of method B was substantially lower than that of methods A and C, given the anatomy of wrist flexor muscles. Wrist flexor muscles, such as FCU, PL, FCR, PT and FDS muscles, originate from medial epicondyle of humerus. The belly of FCU, PL and FCR muscles are formed proximal to the forearm, and turn into tendons distally, which are inserted into the bones of the hand. These muscles are located in the medial to lateral direction, in the order of FCU, PL, and FCR muscles in the narrow forearm space. The FCU muscle is located in the ulnar side, and the FCR muscle radially. Therefore, FCU muscle performs ulnar deviation in addition to wrist flexion, and the FCR muscle undergoes radial deviation similarly. Considering the anatomical structure, although the FCR muscle originates in the medial epicondyle similar to other wrist flexor muscles, its belly is not located on an imaginary line connecting the medial epicondyle and the FCR tendon palpable in wrist, but is located more radially from the imaginary line, because FCR muscle is pushed by PL and FCU muscles. Therefore, the point B, which is the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle, is more medially located from the muscle belly of FCR, resulting in very poor accuracy. Actually, ultrasonography reveals the muscle belly of FCR by moving the probe further radially from point B (Fig. 2B).

The methods A and C showed high accuracy in penetrating the FCR muscle, but low probability in targeting the middle portion of the FCR muscle, because the FCR muscle belly is usually located more distally than 4 fingerbreadths (A and C points). According to our ultrasonography analysis, CP-VD, which is the central point between musculotendinous junction and origin of FCR muscle, was found at about the proximal third (32%) of forearm length, and was more distally located than A and C points. Actually, in the sonographic short-axis image, the cross-sectional area of PT muscle was larger than that of FCR muscle at points A and C, whereas the FCR muscle was substantially larger at the CP (Fig. 1B, 2A, right; 2C, right).

The probability that the imaginary needle pathway in CP penetrates the median nerve was similar or higher than in the conventional method (A, 48.8%; B, 2.5%; C, 21.3%; CP, 47.5%). Therefore, it cannot be said that CP is a safer location than in previous methods. However, we can needle the FCR muscle more safely by adopting the depth established. The median nerve is formed by combining medial and lateral cords of the brachial plexus. It then passes through the arm, and the antecubital fossa to enters the forearm, driving between 2 heads of PT muscle. It traverses deeper than in the FDS muscle, and more superficially than in deep wrist flexor muscles of the forearm [2]. According to the data collected, the mean depth of the median nerve is in the range of 18.61 to 21.31 mm. The DM of CP of FCR muscle is 6.75 to 12.85 mm. The maximum DM was only 12.85 mm. Because FCR is more superficially located than the median nerve, no more than 1.3 cm depth is needed to target FCR muscle safely without piercing median nerve during needle EMG.

The study has several limitations. First, the mean age was 31.4 years old, and thus the study was targeted at relatively young people. Second, there might be slight difference between the suggested CP and the actual motor point of FCR muscle. We assumed that the actual motor point was close to the CP of the FCR muscle. Third, the average BMI of participants was 22.8 kg/m^2. The proper depth of needle insertion may differ in underweight or overweight and obese individuals. Fourth, we did not collect muscle mass data. Muscle mass measurement using dual energy X-ray absorptiometry is helpful in further studies. Fifth, in those without the PL muscle, the FCR belly is more likely to be located on the medial side. As mentioned earlier, this is because the FCR muscle is pushed laterally by FCU and PL muscles. Most standard textbooks of hand surgery report that the rate of absence of PL muscle was 15% [13-15]. Therefore, in such cases, it may be different from our findings. Sixth, we mea-

sured depth using ultrasonography without inserting the needle. However, when the needle is actually inserted, the shape of subcutaneous and muscle layers might be changed. Further studies involving more participants from variable age groups are required.

Conclusion

Several methods for proper needle placement have been suggested for FCR muscle. However, none of the methods have been evaluated in terms of safety and accuracy using ultrasonography. Accessing anatomical structures under ultrasonography guidance, we propose a novel method regardless of height. Also, we analyzed the accuracy of the previous methods and compared with our proposed strategy. These findings enable us to approach the CP of FCR muscle more accurately than previous methods. This study revealed that the CP of FCR muscle was approximately medial 2.0 cm from the biceps tendon at elbow crease, proximal one-third of forearm length, and at a depth of 9.7 mm. The method can be hopefully adopted more easily and safely in clinical applications.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Materials

Further details on supplementary materials are presented online (available at https://doi.org/10.18214/jend.2021.00017).

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밀러-피셔증후군과 중첩된 비전형 비대칭 길랭-바레증후군: 증례 보고

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Atypical Asymmetric Guillain-Barré Syndrome Overlapping with Miller-Fisher Syndrome: A Case Report

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Guillain-Barré syndrome (GBS) is an acute immune-mediated polyneuropathy that constitutes a heterogeneous syndrome with several variant forms. We experienced a patient who rapidly developed atypical variant GBS without a preceding history of infection. A 13-year-old female patient was admitted, presenting with left facial palsy and ophthalmoplegia. After a few days, right hand and ankle muscle weakness and paresthesia of both hands newly occurred. Electrophysiological findings revealed multifocal asymmetric motor and sensory axonal neuropathies compatible with multiple mononeuropathy. In blood testing, autoimmune-related antibodies were negative and anti-GQ1b antibodies were positive. We diagnosed the patient with overlapping Miller-Fisher syndrome and the acute motor sensory axonal neuropathy variant of GBS. After intravenous immunoglobulin therapy, the weakness of the limbs partially improved. Since the initial symptoms were similar to those of mononeuritis multiplex, it was difficult to recognize GBS. Electrodiagnostic studies and anti-ganglioside antibody screening tests are necessary for the early differential diagnosis of variant GBS.

Keywords: Guillain-Barré syndrome; Miller Fisher syndrome; Mononeuropathy multiplex

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Introduction

Guillain-Barré syndrome (GBS) is an acute immune-mediated polyneuropathy, characterized by progressive symmetrical weakness and areflexia [1]. Several variant forms of GBS have been revealed which present with extremity, facial or bulbar muscle involvement [2]. According to electrophysiological findings, GBS is classified by acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN), acute motor sensory axonal neuropathy (AMSAN) [3]. AMSAN is a rare axonal variant of GBS, characterized by involvement of motor and sensory fibers [3]. Miller-Fisher syndrome (MFS) is clinical variant, which is characterized by ophthalmoplegia, ataxia, and areflexia [1]. We experienced overlapping case of AMSAN variant of GBS and MFS with positivity for anti-GQ1b antibodies, whose initial presentation resembled mononeuritis multiplex.

Case Report

This study was conducted with informed consents of the patient and guardian. A 13-year-old female patient with no medical illness history presented at the emergency department with left facial palsy, diplopia, and paresthesia of right hand that had evolved over 24 hours. She didn't reported vomiting, diarrhea, or upper respiratory symptoms previously. Vital signs were within normal limits. Cranial nerves' examination was notable for limitation of abduction of the right eye and diminished left facial muscles' strength. Strength of all limbs was preserved and paresthesia of right hand disappeared at the time of examination. Deep tendon reflexes (DTRs) were preserved at all four limbs. The patient was negative for Hoffmann reflex and Babinski signs. Ataxia and symptoms of autonomic dysfunction were absent. Blood sample showed hemoglobin 12.9 g/dL (normal range, 11.5-15.5 g/dL); white blood cell 7,310/mm^3 (3,700-9,500/mm^3); C-reactive protein (CRP) 0.12 mg/dL (0-0.5 mg/dL); potassium 3.8 mEq/L (3.5-5.5 mEq/L), lactate dehydrogenase (LDH) 421 U/L (200-485 U/L); creatine phosphokinase (CPK) 125 U/L (33-211 U/L); urine analysis was normal. Serum IgM antibodies to Epstein-Barr virus, cytomegalovirus, varicella zoster virus, measles virus, mumps virus, and rubella virus were negative. Magnetic resonance image (MRI) of the brain was normal. There were no lesion with T1 high signal intensity on gadolinium-enhancement images. These presentations led to suspicion of left facial nerve palsy and right abducens nerve palsy. The patient was admitted to the pediatric neurology department and was empirically treated with valacyclovir 3,000 mg and prednisolone 50 mg for 14 days (Table 1).

An electrodiagnostic study was performed on 16 days from the onset (day 16). On the day of study, left facial palsy and ophthalmoplegia of right eye persisted. Right hand intrinsic muscle weakness developed with showing claw hand deformity, and left hand grip and release strength slightly weakened and right ankle and toe plantarflexion weakness and paresthesia of right 4-5th and left 1-2nd finger newly occurred; right hand intrinsic muscles were medical research council (MRC) 2/5; left hand grip and release strength was 4/5; right ankle and toe plantarflexion were 3/5. Muscle power of left lower extremity was normal. Sensory nerve conduction studies showed decreased amplitude of both median, right ulnar and right sural sensory nerve action potentials (SNAP) with normal peak latencies (Table 2). Motor nerve conduction studies showed markedly reduced amplitude of both median, right peroneal and right tibial compound muscle action potentials (CMAP) with normal latencies and conduction velocities. The right ulnar CMAP was not obtained from the abductor digiti minimi muscle. F-waves in right median and ulnar nerves were not formed. Electroneurographic study (ENoG) showed that the paralyzed/healthy side ratio of facial nerve was 26.1%. Bilateral blink reflex test was in normal range. Needle electromyography (EMG) study showed increased insertional activities and abnormal spontaneous activities, and decreased motor unit potentials recruitment pattern in right abductor pollicis brevis (APB), right first dorsal interosseous (FDI), right flexor carpi radialis, right flexor carpi ulnaris, and left APB (Table 3). Somatosensory evoked potentials after bilateral median and tibial nerves stimulation showed normal latencies. These electrodiagnostic findings were multifocal asymmetric motor and sensory axonal neuropathies compatible with multiple mononeuropathy.

For differential diagnosis, cerebrospinal fluid (CSF) studies, MRI of the whole spine and auto-immune related antibodies screening were performed on day 17. CSF studies showed normal range without albuminocytologic dissociation. The CSF oligoclonal band screening test was negative. MRI of the whole spine was normal. There was no enhancement of the nerve roots after gadolinium administration on fat-saturated T1-weighted image and was no spinal cord lesion with T2 high signal intensity on MRI of the whole spine (Fig. 1). Antineutrophil cytoplasmic antibody (ANCA), antinuclear antibody (ANA), rheumatoid factor (RF), anti-dsDNA, anti-RNP, anti-Sm, anti-SSA, anti-SSB antibodies were in normal range. In anti-ganglioside antibodies screening, anti-GQ1b IgM antibodies were positive, and anti-GM1, anti-GD1b were negative. Based on these findings, this patient was diagnosed with MFS with multiple mononeuropathy, and received methylprednisolone 1,000 mg for 3 days and intravenous immunoglobulin (IVIG) injection at a dose of 1 g/kg for 2 days.

On day 29, left facial palsy, right eye ophthalmoplegia and

Table 1. Laboratory Test Results

Parameter	Result (normal value)
Hemoglobin (g/dL)	12.9 (11.5-15.5)
White blood cell (/mm^3)	7,310 (3,700-9,500)
C-reactive protein (mg/dL)	0.12 (0-0.5)
Potassium (mEq/L)	3.8 (3.5-5.5)
Lactate dehydrogenase (U/L)	421 (200-485)
Creatine phosphokinase (U/L)	125 (33-211)
Oligoclonal bands	Negative
Antineutrophil cytoplasmic antibody	Negative
Antinuclear antibody	Negative
Anti-GQ1b	Positive*
Anti-GM1	Negative
Anti-GD1b	Negative

*Abnormal value.

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Table 2. Results of the Nerve Conduction Studies

Nerve	Day 16						Day 67					
	Latency (ms)		Amplitude		CV (m/s)		Latency (ms)		Amplitude		CV (m/s)	
	R	L	R	L	R	L	R	L	R	L	R	L
Sensory												
Median	2.76	2.86	10.8*	11.8*	-	-	3.49	2.71	4.4*	12.0*	-	-
Ulnar	2.34	2.19	3.0*	27.6	-	-	3.07	3.02	2.9*	12.5*	-	-
Radial	1.61	1.88	17.6	23.1	-	-	1.88	1.88	5.7*	25.9	-	-
Sural	2.97	2.97	4.5*	11.3	-	-	2.97	2.81	4.0*	7.6*	-	-
SPN	2.97	3.07	12.6	20.5	-	-	3.18	2.86	8.5*	15.3	-	-
Motor												
Median wrist	3.18	2.66	0.4*	4.4*	-	-	4.01	3.07	1.2*	6.4	-	-
Median elbow	7.24	6.77	0.4*	4.2*	56.6	58.3	8.96	7.60	1.0*	5.7	46.5	59.6
Ulnar wrist	NR*	1.93	NR*	14.7	-	-	3.07	2.19	0.4*	11.5	-	-
Ulnar below elbow	NR*	5.78	NR*	14.6	NR	62.3	7.71	6.46	0.2*	11.1	51.8	67.9
Radial forearm	1.93	2.03	4.1	4.7	-	-	1.51	1.56	3.9	4.8	-	-
Radial elbow	4.69	4.79	3.8	4.4	58.0	58.0	3.70	3.96	3.7	4.7	59.4	58.4
Peroneal ankle	3.59	2.76	2.2*	9.6	-	-	3.96	3.49	2.6*	5.5*	-	-
Peroneal fibular head	10.68	9.32	1.4*	8.3	48.0	51.8	12.29	11.15	1.6*	4.3*	42.0	43.1
Tibial ankle	3.28	3.75	6.9*	14.8	-	-	3.23	3.65	7.3*	7.7*	-	-
Tibial knee	11.04	10.94	5.0*	11.6	49.0	52.8	12.66	12.71	4.8*	6.6*	44.6	46.3
Facial nasalis	3.75	4.11	2.6	0.6*	-	-	3.65	3.54	2.6	1.3*	-	-

Amplitudes are measured in microvolt (μV, sensory) and millivolt (mV, motor).
CV, conduction velocity; R, right; L, left; SPN, superficial peroneal nerve; NR, no response.
*Abnormal value.

Table 3. Results of Needle Electromyography

Muscle	Day 16								Day 67							
	Fibrillation		PSW		MUAP		Recruitment		Fibrillation		PSW		MUAP		Recruitment	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
APB	1+	1+	1+	1+	N	N	Dis	Red	3+	3+	3+	3+	N	N	Red	Red
FDI	1+	NT	1+	NT	N	NT	Dis	NT	3+	1+	3+	1+	N	N	Dis	Red
FCR	1+	N	1+	N	N	N	Dis	Red								
FCU	1+	NT	1+	NT	N	NT	Red	NT								
Biceps	N	NT	N	NT	N	NT	Full	NT								
Triceps	N	NT	N	NT	N	NT	Full	NT								
TA	N	N	N	N	N	N	Full	Full	1+	3+	1+	3+	N	N	Red	Red
GCM	N	N	N	N	N	N	Full	Full	1+	1+	1+	1+	N	N	Red	Red
CPS	N	N	N	N	N	N	NC	NC	N	N	N	N	N	N	NC	NC
LPS	N	N	N	N	N	N	NC	NC	N	N	N	N	N	N	NC	NC

PSW, positive sharp wave; MUAP, motor unit action potential; R, right; L, left; APB, abductor pollicis brevis; N, normal; Dis, discrete; Red, reduced; FDI, first dorsal interosseous; NT, not tested; FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; TA, tibialis anterior; GCM, gastrocnemius; CPS, cervical paraspinals; NC, not checkable; LPS, lumbar paraspinals.

right ankle plantarflexion weakness improved slightly, and bilateral hand weakness was similar. Bilateral ankle dorsiflexion weakness and paresthesia of all distal limbs newly occurred; right hand was MRC 2/5 and left hand was 4/5; bilateral ankle dorsiflexion was 4/5. There were differences in the severity of left and right, but eventually, symmetric paralysis and paresthesia appeared in all limbs as in the general course of GBS. The patient began to receive physical therapy to strengthen distal upper and lower extremities.

Follow-up electrodiagnostic study was performed on day 67. Left facial palsy and right eye ophthalmoplegia fully improved, and bilateral ankle dorsiflexion strength was 4/5, and right hand

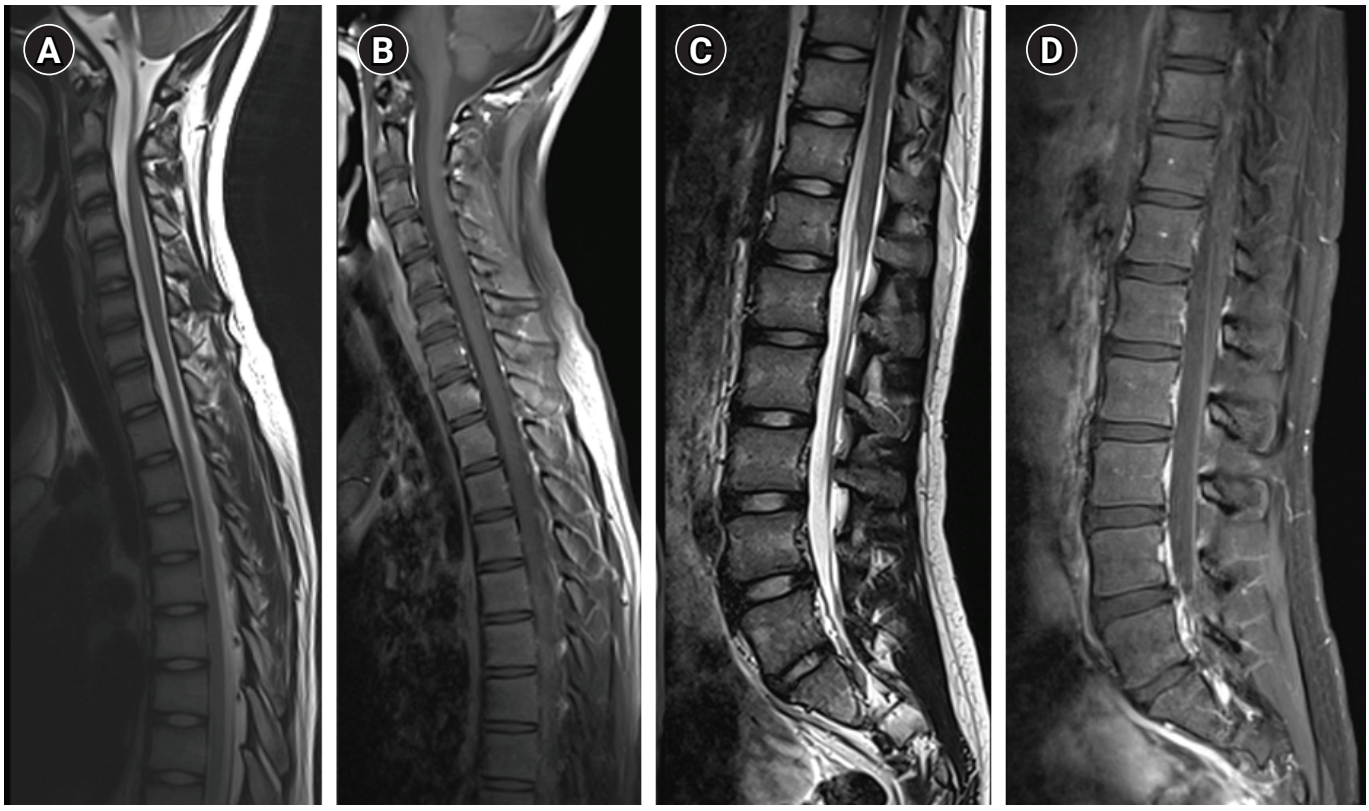

Fig. 1. Magnetic resonance imaging of the spine. (A) A T2-weighted image and (B) a T1-weighted image with gadolinium enhancement in the upper spine. (C) A T2-weighted image and (D) a T1-weighted image with gadolinium enhancement in the lower spine.

was able to use chopsticks. DTRs were preserved at all four limbs. Compared to previous examination, the amplitude of SNAPs of right median, right radial, right superficial peroneal, left ulnar, and left sural nerve more decreased with normal peak latencies. The amplitude of CMAPs of both median and right ulnar nerve increased showing reversible conduction block. The decreased amplitude of CMAPs of left peroneal and left tibial nerve newly appeared. The paralyzed / healthy side ratio of facial nerve ENoG increased from 23.1% to 50.0%. Needle EMG showed increased insertional activities and abnormal spontaneous activities, and decreased motor unit potentials recruitment pattern in bilateral APB, FDI, tibialis anterior and gastrocnemius muscles. In conclusion, these electrodiagnostic findings were consistent with symmetric motor and sensory axonal polyneuropathy compatible with GBS, and we diagnosed the patient with GBS overlapping AMSAN and MFS. At 14 weeks of symptom onset, muscle strength of all limbs improved for 4/5 and mild paresthesia of all limbs still remained.

Discussion

GBS is an acute immune-mediated polyneuropathy that occurs after infection. GBS is characterized by symmetric ascending paralysis, areflexic paralysis, and albumin-cell dissociation [1]. This patient initially presented with unilateral facial palsy, ophthalmoplegia, asymmetric paralysis, and DTRs of all limbs were preserved. She had no history of infection/vaccination. CSF test was normal. Although GBS is a common cause of acute paralytic peripheral weakness, this patient had an atypical course, which made it difficult to suspect GBS. Therefore, we performed an EMG to determine the patient's electrophysiological condition, and revealed findings consistent with multiple mononeuropathy.

Multiple mononeuropathy is a form of peripheral neuropathy in which one or more non-adjacent peripheral nerves are asymmetrically invaded over the upper and lower extremities. It is the most common clinical presentation of vasculitic neuropathy, which is one feature of a systemic vasculitis and is associated with connective tissue diseases such as polyarteritis nodosa, Churg-Strauss syndrome, and rheumatoid arthritis [4]. Vasculitic neuropathy is caused by multifocal peripheral nerve infarction due to obstruction of blood vessels distributed in the nerve [4]. Ischemic injury initially occurs in the distal part of the nerve and induces pain, weakness or sensory abnormality in the distal ex-

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tremities [5]. Although other organ systems are often involved, initial clinical manifestation of systemic vasculitis may only appear in the peripheral nervous system and in that case, diagnosis is difficult [6].

The finding of multiple mononeuropathy is suggestive of but not specific for vasculitis. Various non-vascular etiologies should be considered, such as infection, hereditary neuropathies, and neoplasm [4]. For differential diagnosis, medical history, physical examination, laboratory tests, and electrophysiologic study with nerve conduction studies and EMG were required. The patient had no medical illness, vaccination, and previous infection history. Complete blood count and differential, serum creatinine and estimation of glomerular filtration rate, liver function tests, urinalysis, erythrocyte sedimentation rate, CRP, CPK, LDH and autoimmune-related serologic assays, such as ANA, ANCA, RF, anti-dsDNA, anti-RNP, anti-Sm, anti-SSA, anti-SSB to evaluate for underlying systemic rheumatic or infectious diseases are helpful and all were within normal range in this patient.

GBS typically exhibits symmetric paralysis, but asymmetric paralysis has been reported in some variants [7]. Since the proportion of axonal variant GBS is high in East Asia [3], if asymmetric paralysis is shown as in this patient, the electrophysiological findings may be similar to multiple mononeuropathy, making it difficult to diagnose. Preserved tendon reflexes are mostly associated with the AMAN subtypes, but all GBS subtypes and MFS may present with hyper-reflexia [8]. Some variants of GBS invade the cranial nerves and may exhibit facial palsy, dysphagia symptoms, and MRI of the brain and electrophysiological examinations should be performed to discriminate brain-stem stroke, Wernicke's encephalopathy, myasthenia gravis [1]. In general, the axonal type of GBS showed history of infection with *Campylobacter jejuni* [3], but there were no signs of infection in the patient's report and we didn't perform stool examination for *C. jejuni* infection. CSF studies can be normal for the initial one week, and albumin dissociation is observed in 75% of patients after 3 weeks [1]. Our patient underwent CSF test 2 weeks after symptom onset, but it was normal.

In the past, GBS was used as a synonym for AIDP, and Brighton's diagnostic criteria using electrophysiological findings were widely used [2]. Since the 1990s, with the report of axonal variant GBS, immune-mediated pathology involving anti-ganglioside antibodies was revealed [1]. In recent years, anti-ganglioside antibodies have been used to diagnose and classify various subtypes of GBS, such as axonal, MFS, and pharyngeal-cervical-brachial variant [2]. Anti-ganglioside antibodies screening revealed that anti-GQ1b IgM antibodies were positive and anti-GM1, anti-GD1b were negative. Anti-GQ1b antibodies are found in 83% of MFS [2]. Based on the clinical features, electrodiagnostic evaluation and antibody test, it could be diagnosed by overlapping of MFS and AMSAN variant of GBS. A study in Korea reported that anti-ganglioside antibody tests in children with GBS showed a lower positive rate (20%) than adults [9]. However, since the number of cases reviewed (10 cases) was small and information on clinical features and whether the MFS cases were included was limited, further studies are needed to determine the diagnostic value of anti-ganglioside antibodies in children with GBS.

IVIG injection and plasma exchange are well-established treatments, and equivalent effects have been reported [1]. This patient was administered IVIG 1 g/kg for a total of 2 days and showed a response. The weakness and numbness of the limbs gradually recovered from 4 weeks after the onset of symptoms. After receiving the rehabilitation treatment of the limb strength training, the strength of all limbs recovered to 4/5 at 14 weeks.

Previously, one case of overlapping of MFS and AMSAN variant of GBS was reported in Korea but did not showed an asymmetric feature [10]. In another case, asymmetric GBS, which was mistaken for cauda equina syndrome, was reported [11], but there was no detailed description of electrodiagnostic findings. We performed nerve conduction test and needle EMG repeatedly, and it was confirmed that the pattern of asymmetric multifocal axonal neuropathy initially progressed symmetrically after time.

In summary, the most important point we want to emphasize is that variants of GBS are so diverse that GBS should be suspected despite atypical symptoms. When physicians face a patient with atypical symptoms of asymmetric weakness in the cranial nerves or limbs, early electrophysiologic study should be performed to discriminate for type of peripheral neuropathy. Considering that axonal variant of GBS is frequent in East Asia, anti-ganglioside antibodies screening test should be considered to discriminate GBS, and IVIG or plasmapheresis treatment must be performed without delay to prevent serious complications such as respiratory system invasion. This diagnostic approach is thought to be helpful in the early diagnosis and treatment of GBS.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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연소성 재발성 만성염증탈수초다발신경병증 1예

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Juvenile-Onset Relapsing Chronic Inflammatory Demyelinating Polyradiculoneuropathy: A Case Report

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Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired, immune-mediated condition. It is a symmetric, motor-predominant neuropathy that results in both proximal and distal limb muscle weakness and is characterized by electrodiagnostic or pathologic features of demyelination. CIDP is a treatable disease that is known to be rare in the pediatric population. This case report describes a 12-year-old female who presented with gait disturbance and progressive upper and lower limb weakness. The electrophysiologic findings were compatible with demyelinating polyneuropathy. Combined with the clinical features, the diagnosis of CIDP was made and treatment was administered. The first-line immunomodulatory treatment seemed to be effective, as shown by improvements in electrophysiologic and clinical parameters, but the relapsing-remitting clinical course required additional immunomodulatory treatment. Herein, we describe the patient's clinical and electrophysiologic course according to the treatment.

Keywords: Child; Polyradiculoneuropathy, chronic inflammatory demyelinating; Electrodiagnosis

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Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a progressive, symmetric and motor-predominant neuropathy that results in both proximal and distal muscle weakness in the limbs. Although CIDP was initially documented by

Dyck and Tracy in 1975, its pathogenesis is still poorly understood, except about autoreactive T-cells which are known to play a dominant role in CIDP [1]. Inflammatory responses are triggered in motor and sensory nerves which cause damage to Schwann cells and myelin sheath surrounding axons [2].

CIDP is a rare disease entity with prevalence ranging from 4.8 to 8.9 cases per 100,000 persons. CIDP can occur at any age, even in early childhood and its prevalence among children is estimated to be 0.5 cases per 100,000 persons [3]. According to previous cases, juvenile-onset CIDP has more rapid onset and relapsing-remitting disease course, but more favorable long-term outcome than adult-onset CIDP. Several cases of juvenile-onset CIDP has been published in the literature, however, due to the rarity of juvenile-onset CIDP, only few cases were reported in Korea.

Although the European Federation of Neurological Societies/Peripheral Nerve Society (EFNS/PNS) consensus guideline for CIDP diagnosis is known to be most sensitive, the diagnosis of CIDP is often conflicting due to its wide spectrum of disease [4]. Intravenous immunoglobulin (IVIG), corticosteroids, and plasmapheresis are often considered as major treatment and also apply to the juvenile-onset CIDP. Juvenile CIDP shows superior response to the treatments, but a substantial proportion remains as refractory CIDP. In this case report, we described clinical and electrophysiological changes of a 12-year-old female who showed relapsing-remitting symptoms of CIDP and briefly reviewed juvenile-onset CIDP in the viewpoint of rehabilitation.

Case Report

A previously healthy 12-year-old girl was presented with a 6-month duration of progressive bilateral lower extremities weakness and gait disturbance. She did not take any medical treatment at the beginning of the symptom. However, 5 months after the symptom onset, symptom aggravated, and she started to have difficulty in walking. She was initially admitted for evaluation and treatment to the Department of Orthopedic Surgery.

Clinical examination revealed the symmetrical motor weakness of the Medical Research Council (MRC) grade 4 to 5 in the upper extremities and grade 4 in the proximal/distal lower extremities, and the Gower's sign was positive. Hypoesthesia was examined in both medial calves. The straight leg raise test was negative, bilaterally. Diminished deep tendon reflexes were examined in the lower extremities, and there were no pathologic reflexes. Romberg test was positive and finger-to-nose test was negative, indicating no impairment of cerebellar function. There was no history of any antecedent infection and no family history of comparable symptoms. She had a history of uveitis 8 years ago. With this information, clinical impressions such as myopathy, peripheral polyneuropathy, and less likely motor neuron disease or neuromuscular disease were made.

Imaging studies, including lumbar spine magnetic resonance image, found no abnormal radiological findings. In the initial nerve conduction study (NCS) (Table 1), the compound muscle action potentials (CMAPs) showed prolonged latencies with temporal dispersion (Fig. 1), low amplitudes, and decreased conduction velocities in all the nerves tested. The sensory nerve action potentials (SNAPs) were unobtainable, with all the nerves examined. In the initial needle electromyography (EMG) (Table 1), abnormal spontaneous activities of fibrillation potentials and positive sharp waves were noted in all the right upper and lower extremities examined muscles examined. Increased proportions of polyphasic to complex polyphasic motor unit action potentials with reduced recruitment patterns were noted in the same muscles. Combined with the clinical presentation, electrophysiological findings of demyelinating disease were fitted to the CIDP criteria: (1) motor distal latency prolongation ($\geq$ 50% above upper limit of normal) in 2 nerves, (2) reduction of motor conduction velocity ($\leq$ 30% below lower limit of normal) in 2 nerves, and (3) abnormal temporal dispersions ($>$ 30% duration increase between the proximal and distal negative peak CMAP) in $\geq$ 2 nerves. Also, the cerebrospinal fluid (CSF) protein elevation (Table 2) and negative result of *PMP22* gene analysis for differential diagnosis of hereditary motor and sensory neuropathy, supported the diagnosis of CIDP. Due to the patient's young age, a nerve biopsy was not performed, but it was able to meet the diagnostic criteria for CIDP.

After the diagnosis of CIDP was made, combination of IVIG therapy (400 mg/kg/day for 5 days) and steroid pulse therapy (1,000 mg/day for 5 days) were done as the initial treatment. Also, the acyclovir therapy (10 mg/kg/dose IV3/day for 8 days) targeting varicella-zoster virus (VZV) was done. The second NCS/EMG (after 17 days from the 1st study) revealed somewhat improvement in CMAPs. She was discharged from the ward with the improvement in the gait performance, muscle power (MRC grade 5), and balance (Berg balance scale [BBS] score of 55) (Fig. 2, Table 3).

However, she was re-admitted 3 weeks after the discharge, due to aggravation of the weakness in limbs (MRC grade 4) and gait impairment. Second-line therapy of IVIG (400 mg/kg/day for 5 days) was done and improvement of weakness was observed from MRC grade 4 to MRC grade 5. Follow-up (third) NCS/EMG after the second treatment (48 days from the 1st study) revealed continuous improvement in both CMAPs and SNAPs,

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Table 1. Initial (6 Months after Onset) Nerve Conduction Study and Needle Electromyography

Nerve conduction study						
Motor		Stimulation site	Recording site	Latency (ms)	Amplitude (mV)	NCV (m/s)
Side	Nerve					
Right	Median	Wrist	APB	15.8*	1.8*	36*
	Ulnar	Wrist	ADM	10.1*	2.9*	25*
		Below elbow	ADM	18.5*	1.8*	11*
		Above elbow	ADM	27.5*	1.5*	
	Tibial	Ankle	AH	30.0*	0.2*	24*
	Peroneal	Ankle	EDB	18.4*	0.6*	23*
		Fibular head	EDB	30.4*	0.3*	18*
		Popliteal fossa	EDB	32.6*	0.3*	
Sensory		Stimulation site	Recording site	Latency (ms)	Amplitude (μV)	Distance (cm)
Side	Nerve			Onset peak		
Right	Median	Wrist	III digit	-	NR*	14
		Palm	III digit	-	NR*	7
	Ulnar	Wrist	V digit	-	NR*	14
	Sural	Calf	Ankle	-	NR*	14
	Sup. peroneal	Leg	Ankle	-	NR*	14
Needle electromyography						
Side	Muscle		Insertional activity	Spontaneous activity	MUAPs	Recruitment pattern
Right	Brachioradialis		Increased	F&P(+)	Increased polys	Reduced
	Flexor carpi radialis		Increased	F&P(+)	Increased polys	Reduced
	Vastus medialis		Increased	F&P(+)	Polys	Reduced
	Tibialis anterior		Increased	F(+)	Complex polys	Reduced
	Gastrocnemius medialis		Increased	F&P(+)	Polys	Reduced
Left	Tibialis anterior		Increased	F(+)	Complex polys	Reduced

NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor halluces; EDB, extensor digitorum brevis; NR, no response; Sup. peroneal, Superficial peroneal nerve; MUAPs: moto unit action potentials; F&P, fibrillation potentials and positive sharp wave; Polys, Polyphasic motor units.
*Abnormal values.

but the evidence of demyelination was still noted. The SNAPs were measured in the upper extremities for the first time; onset, peak latency (ms) and amplitude (mV) were 3.7/5.0/6 and 6.8/8.9/6 in the right median (palm stimulation) and ulnar nerves, respectively. However, 2 weeks after the second discharge, the symptoms aggravated, and the patient was re-admitted. She received plasmapheresis (7 days) and immunosuppressants (azathioprine) therapy. The fourth NCS/EMG (after 99 days from the 1st study) revealed more improved results than the third one. However, the SNAPs were still unobtainable in the lower extremities. Serial NCS revealed fluctuating results in both CMAPs and SNAPs with the evidence of demyelination remaining. This pattern with relapsing and remitting symptom was continued until the last (8th) study. The motor grades of both lower limbs showed fluctuation between MRC grade 4 to 5 and the BBS score ranged from 30 to 55.

Discussion

As the patient presented with a 6-month history of progressive upper and lower extremities weakness and gait disturbance, the NCS/EMG results showed demyelinating features and met the electrodiagnostic criteria of CIDP; additionally, the clinical symptoms, high protein level of CSF analysis, and response to consequent IVIG treatment supported the diagnosis of "definite CIDP" according to the EFNS/PNS guideline of CIDP.

A previous study [5] revealed juvenile-specific clinical and electrophysiological features of CIDP compared to adults and elderly. Predominant weakness in lower extremities and deep sensation or proprioception impairment are common features of all spectrum of ages. But moderate motor weakness was noted in the juvenile-onset CIDP. Usually the decreased conduction velocity of the median nerve and prolonged distal latency of the tibial nerve is observed in electrophysiologic study of juvenile-

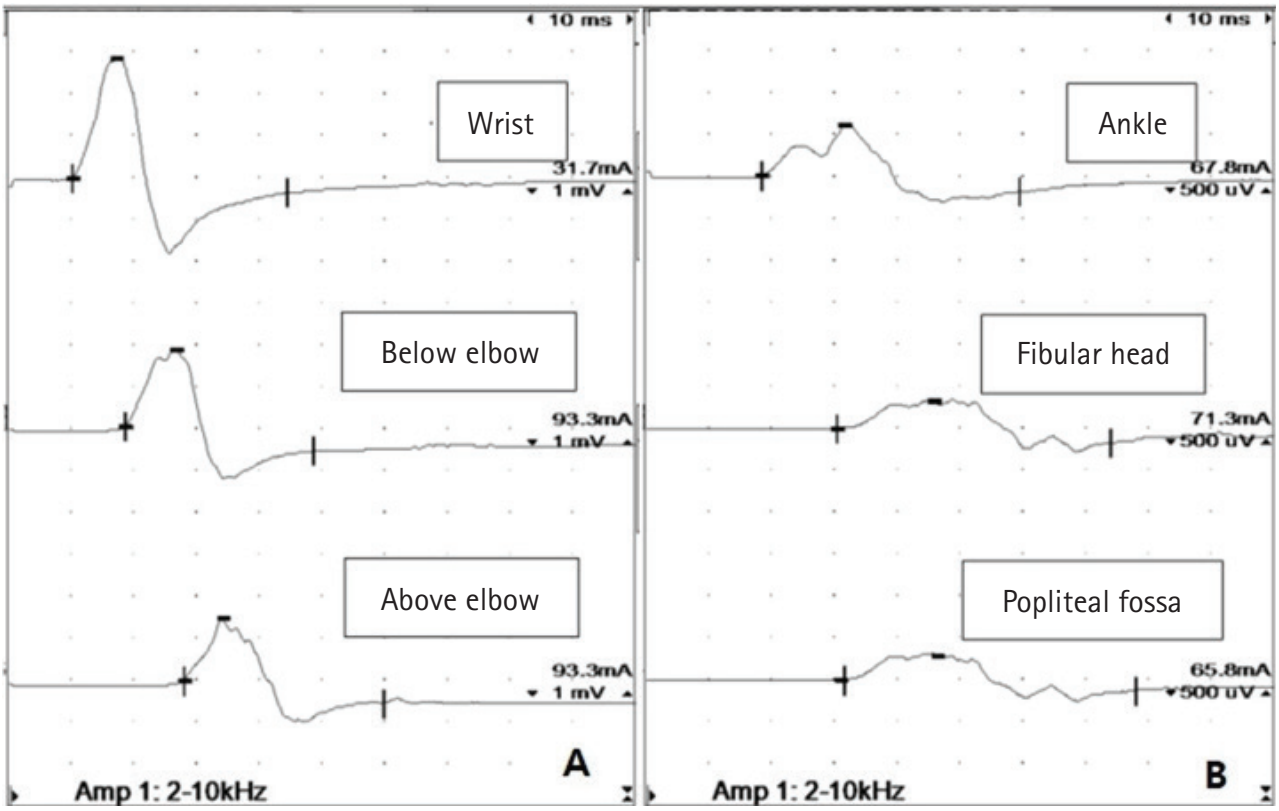

Fig. 1. Waveform morphologies of right ulnar and common fibular nerve motor conduction studies showing prolonged latencies and prominent temporal dispersions. Amp, amplitude.

onset CIDP, and similar results were found in our case. The motor strength of both proximal/distal lower extremities showed less fluctuation, however the gait function showed more fluctuations. This phenomenon is typical findings of CIDP since it primarily affects large myelinated fibers observed in the skin and nerve biopsy [6]. Large myelinated fibers are usually associated with proprioception, which is crucial for balancing, movement coordination, and gait function.

The differential diagnosis with hereditary motor and sensory neuropathy (e.g. Charcot-Marie-Tooth disease) is very important due to their pathophysiologic similarities. At first, CIDP presents unequal multifocal demyelination in contrast to uniform demyelination of hereditary motor and sensory neuropathy [1]. Therefore, the temporal dispersions are less-likely identified in the hereditary neuropathies. In addition to these electrophysiologic differences the disease course, CIDP shows more relapsing and remitting clinical feature compared to the hereditary neuropathy.

Conventionally, IVIG and corticosteroids are considered as first-line therapy in childhood CIDP [7]. The addition of plasmapheresis or immunosuppressant is considered if the treatment response is poor. In the previous studies of typical adult-onset CIDP, about 60% to 80% of patients were able to control disease severity with conventional therapies [1]. Children are more likely to response better to treatments. The large cohort study [7] revealed that about 80% of juvenile CIDP patients showed good responses to the first-line treatment with IVIG (79%) or corticosteroids (84%). Response to first-line plasma exchange was poor (only 14% of patients improved) although it may offer some transient or partial benefit as adjuvant or temporary therapy for selected patients [7]. However, despite this incomplete response, it is being used as an alternative treatment for patients who are ineffective with conventional treatments, such as in our case. Immunosuppressant drugs are often used for these refractory patients, and were also used in this case [6].

Guillain-Barré syndrome (GBS), which is similar to CIDP but different in onset duration, is often associated with preceding infections such as *Campylobacter jejuni*, *Mycoplasma pneumoniae*, Epstein-Barr virus, and VZV. In contrast, antecedent infection is rarely found in the CIDP. This might be because development of GBS is more influenced by environmental factors than that of CIDP. The immune system of CIDP patients are more genetically permissive, letting autoreactive T-cells to remain viable, and once activated, it causes a chronic autoimmune disease [6].

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Table 2. Initial (6 Months after Onset) Laboratory Findings

Lab category	Results
Routine labs	Hemoglobin 12.5, WBC 6,300/μL, platelet 341,000/μL
	Aspartate transaminase 17 IU/L, alanine aminotransferase 8 IU/L
	Blood urea nitrogen 11.3 mg/dL, creatinine 0.68 mg/dL
	erythrocyte sedimentation rate 7 mm/h, C-reactive protein 0.25 mg/dL
	Urine analysis: within normal limits
Muscle enzymes	Creatinine phosphokinase 99 IU/L, lactate dehydrogenase 259 IU/L
CSF analysis	Red blood cell 840/μL, WBC 0/μL
	Glucose 62/dL
	Protein 65.7 mg/dL*
	Viral markers(-), bacterial growth(-)
Autoimmune	Anti-Sm Ab(-), anti-RNP Ab(-)
antibody studies	Anti-SSA Ab(-), anti-SSB Ab(-)
	P-ANCA(-), C-ANCA(-)
	FANA(-), RF < 5 IU/mL
	Lupus anticoagulant(-)
	Anti-Hu Ab(-), anti-Ri Ab(-)
	Anti-Yo Ab(-), anti-amphiphysin(-)
	Anti-CV2(-)
	Anti-GM1 Ab IgG & IgM(-/-)
	Anti-GD1b Ab IgG & IgM(-/-)
Pathogen workup	HIV Ag(-), HIV Ab(+)
	Respiratory virus(-), gastroenterologic virus(-)
	EBV IgM(-), EBV IgG(-)
	Mycoplasma pneumoniae IgM(-)
	CMV IgG(-), CMV IgM(-)
	HSV IgG(-), HSV IgM(-)
	VZV IgG(+): 820.00 mIU/mL*
Protein electrophoresis, immunofixation electrophoresis	Normal pattern
	Monoclonal gammopathy(-)

WBC, white blood cell; CSF, cerebrospinal fluid; Sm, Smith; Ab, antibody; RNP, ribonucleoprotein; SSA, Sjogren's-syndrome-related antigen A; SSB, Sjogren's-syndrome-related antigen B; P-ANCA, perinuclear anti-neutrophil cytoplasmic antibody; C-ANCA, antineutrophil cytoplasmic antibody; FANA, antinuclear Ab titer; RF, rheumatoid factor; Hu, ANNA1, human anti-neuronal nuclear autoantibody 1; Ri, neuronal nuclear antibody; Yo, Purkinje cell cytoplasmic antibody type 1; Ig, immunoglobulin; HIV, human immunodeficiency virus; EBV, Epstein-Barr virus; CMV, cytomegalovirus; HSV, herpes simplex virus; VZV, varicella-zoster virus.
*Abnormal values.

However, some previous cases reported the serologic marker of VZV found in CIDP patients. Therefore, acyclovir treatment was applied in addition to IVIG treatment in our case.

In addition to pharmacological therapy, physical therapies also benefit CIDP patients. The principal goals of rehabilitation therapy are to help the patients to achieve optimal muscle use at a tolerable pain level as nerve supply returns, and to use supportive equipment and other functional adaptations for daily activities [8]. From the acute exacerbation stage to maintaining stage, physical therapy can help the patients maintain the patients' function and the level of daily living.

There are some proven favorable long-term prognostic factors of CIDP; subacute onset, symmetrical symptoms, good response to initial corticosteroid treatment, and predominance of nerve conduction abnormalities in the distal nerve terminals [9]. In contrast, insidious onset, asymmetric symptoms, and electrophysiological evidence of demyelination in the intermediate nerve segments are known to be associated with poor response to treatment or treatment dependent relapse. Unfortunately, this case was fitted to the latter conditions. Indeed, the onset-to-diagnosis time duration was about 6 months, which meant that the disease onset was insidious rather than subacute. The patient's mother thought her symptom as just 'lack of fitness training' at the early stage and sent the patient to the fitness center. Therefore, the symptoms aggravated continuously, and we can suppose that one of the leading causes for her poor disease course is late

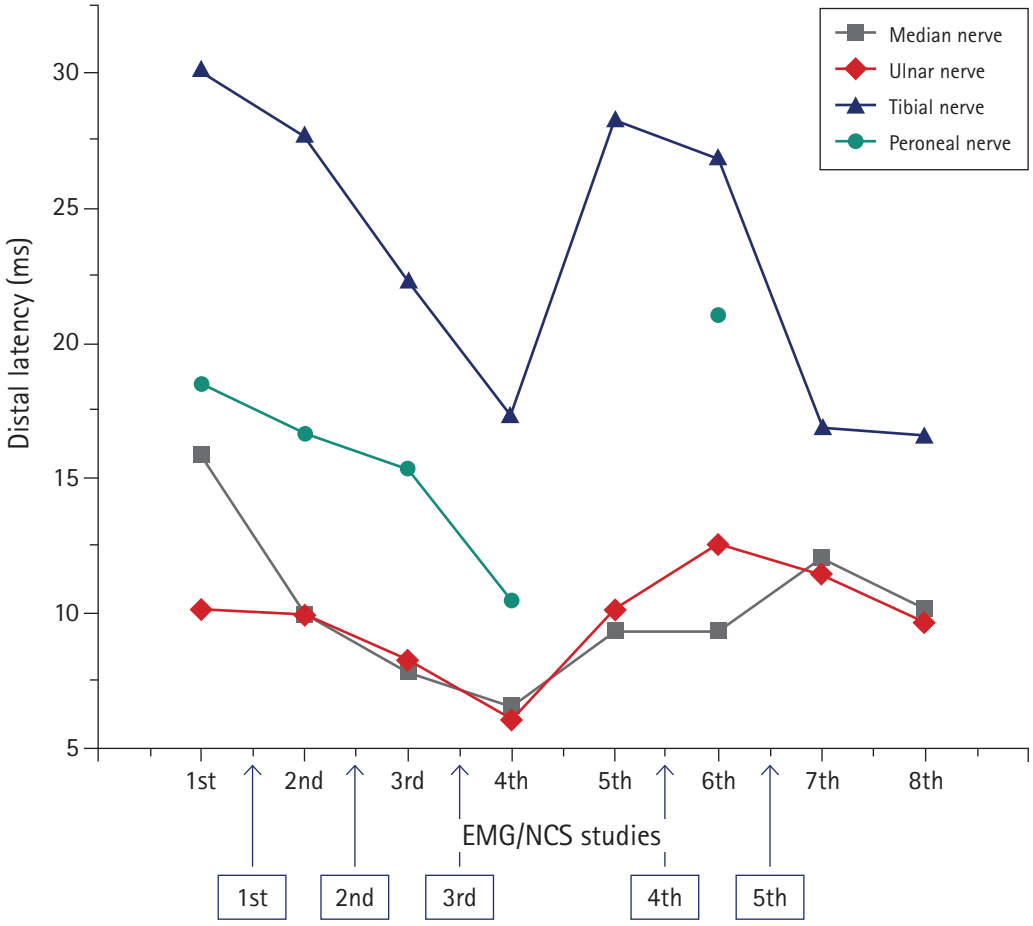

Fig. 2. Serial distal latencies of the right ulnar nerve and timetable of serial treatments. The 5th, 7th, and 8th distal latencies of the peroneal nerve were unobtainable. The rectangular boxes with arrows denote admission events with treatment. EMG, (needle) electromyography; NCS, nerve conduction study.

Table 3. Serial Distal Latencies of the Right (Left) Ulnar Nerve and Timetable of Serial Treatments

Admission	Treatment
1st (2019/12/16)	1st IVIG therapy (400 mg/kg/day, 5 times)
	Acyclovir therapy (10 mg/kg/dose, IV 3, 8 times)
	Steroid pulse therapy (1,000 mg/day, 3 times)
2nd (2020/1/24)	2nd IVIG therapy (400 mg/kg/day, 5 times)
3rd (2020/2/13)	1st plasmapheresis (7 times)
	Immuno-suppressant agents
4th (2020/4/13)	Low-dose steroid therapy (1.05 mg/kg/day, IV 3, 6 times)
	Immuno-suppressant agents
5th (2020/5/5)	2nd plasmapheresis (7 times)
	3rd IVIG therapy (400 mg/kg/day, 5 times)
	Immuno-suppressant agents
	Per oral steroid medication therapy

IVIG, intravenous immunoglobulin; IV, intravenous.

diagnosis of CIDP. There were some case reports of miss diagnosis or delayed diagnosis of CIDP, and the disease courses were poor in that case [10].

In conclusion, as in previous studies on juvenile CIDP, our patient showed remitting and relapsing clinical course and through the precise analysis of electrodiagnostic findings and physical examinations, the diagnosis and treatments of juvenile-onset CIDP were made appropriate and the medical and rehabilitative treatments were done. Juvenile CIDP is a very rare disease and appropriate differential diagnosis is crucial for suitable treatment. Future research should be considered to make more effective and additional lines of treatment to this relapsing and remitting rare disease.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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CASE REPORT

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저칼륨혈증 마비: 서로 다른 두 증례의 보고

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Hypokalemic Paralysis: A Report of Two Different Cases

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Hypokalemic paralysis is a cause of acute paralysis that can be classified as primary (familial) or secondary according to its etiology. Routine electrodiagnostic examinations can be normal between attacks, potentially interfering with the diagnosis. We report two cases of hypokalemic paralysis with different etiologies. The first case involved secondary hypokalemic paralysis due to pharmacologic potassium shift, which was diagnosed by an electrodiagnostic study within the symptomatic period. The second case provides information on the diagnostic approach to primary hypokalemic periodic paralysis during the inter-attack period, as the diagnosis was made using the long exercise test. This case report highlights the need for a proper combination of routine electrodiagnostic studies and special techniques, such as the long exercise test, in patients suspected of hypokalemic paralysis to evaluate the disease state and exclude other possible causes of paralysis.

Keywords: Hypokalemic periodic paralysis; Electromyography; Long exercise test

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Introduction

Hypokalemic paralysis is characterized by symmetric muscle weakness due to low serum potassium levels, which is completely disappeared when the potassium levels become normalized. It can be classified into primary (familial) or secondary depending on the etiology. Primary hypokalemic paralysis, which is called hypokalemic periodic paralysis (HPP), is mostly caused by a gene mutation that codes calcium or sodium channel in skeletal muscle. It is quite rare, with an estimated prevalence of 1 in 100,000. Secondary hypokalemic paralysis can be caused by potassium ion loss through the gastrointestinal or renal system. It can also be developed by an intracellular shift of potassium ion by pharmacologic causes such as insulin and beta-adrenergic agonists [1-3].

Although hypokalemic paralysis can be suspected with clinical features, electromyography (EMG) can be used to help to establish the diagnosis. During the attack of paralysis, compound muscle action potential (CMAP) amplitude declines and increased small polyphasic motor unit action potentials (MUAPs) with decreased interference pattern can be observed on the needle EMG. However, the routine electrodiagnostic examination can be normal between the attacks. Therefore, many provocative tests have been proposed. Among them, the long exercise test

(LET) has been regarded as the most useful and sensitive diagnostic test for HPP in the inter-attack state and is recommended by muscle channelopathies guidelines [4-6].

In this article, we reported two cases of hypokalemic paralyses. The first case is a secondary hypokalemic paralysis in diabetic ketoacidosis, and the second case is the HPP. The EMG study was performed during the paralytic attack in the first case, while it was performed between attacks in the second one. Therefore, each case presented distinct electrodiagnostic findings. We reported diagnostic approaches to hypokalemic paralysis according to symptoms and intended to emphasize the timely diagnosis of EMG study and utility of the LET.

Case Reports

Case 1

A 27-year-old male was admitted to the emergency department because of dyspnea. He had a medical history of diabetes. The initial arterial blood gas analysis was confirmed as metabolic acidosis of blood pH 7.09 (normal range, 7.35-7.45), bicarbonate 3.2 mmol/L (normal range, 22-26 mmol/L), and anion gap 28 (normal range, 14-18). The serum glucose level was 340 mg/dL (normal range, 70-100 mg/dL when fasting) and the HbA1C level was 10.6% (normal range, < 5.7%). The intravenous insulin supply was carried out under the diagnosis of diabetic ketoacidosis.

The muscle weakness of bilateral upper and lower extremities occurred, four days after the initiation of insulin therapy. On physical examination, the Medical Research Council (MRC) grades of proximal and distal extremities were grade 2/5 and 3/5, respectively. There was no sensory loss and the deep tendon reflexes were hypoactive. On the laboratory findings, the serum potassium level was 2.0 mmol/L (normal range, 3.5-5.0 mmol/L), which was 4.6 mmol/L at the time of admission. The thyrotropin level was 0.48 μIU/mL (normal range, 0.4-4.0 μIU/mL), and free T4 level was 1.17 ng/dL (normal range, 0.7-1.4 ng/dL); which is euthyroid state. The thyroid function test results excluded the possibility of thyrotoxic periodic paralysis.

The electrodiagnostic study was performed one day after the onset of muscle weakness. On the motor nerve conduction study (NCS), most of the CMAP responses showed prolonged latencies with decreased amplitudes (Table 1). On needle EMG, decreased insertional activities were noted in deltoid and brachioradialis muscles; and increased insertional activities were noted in the first dorsal interossei muscle. MUAPs were not observed in the deltoid muscle and showed reduced interference patterns in the biceps brachii, brachioradialis, and gastrocnemius muscles (Table 2). The patient denied any family history that could lead to muscle weakness. Along with the patient's medical history, laboratory testing, and EMG findings, we made the diagnosis of secondary hypokalemic paralysis due to insulin therapy. Oral potassium replacement therapy had started, and the serum potassi-

Table 1. Nerve Conduction Study Findings for Case 1

	Nerve, side	Stimulation site	Recording site	Latency (ms)	Amplitude	NCV (m/s)	F wave (ms)	Distance (cm)
Motor	Median, left	Wrist	APB	5.1*	1.8*	-	29.8	-
		Elbow	APB	9.8*	1.7*	47*	-	-
	Ulnar, left	Wrist	ADM	5.9*	3.5*	-	31.5*	-
		Below elbow	ADM	9.7*	3.4*	47*	-	-
		Above elbow	ADM	11.8*	3.2*	48*	-	-
	Tibial, left	Ankle	AH	5.3*	6.1	-	NR*	-
		Knee	AH	13.4*	4.1	40	-	-
	Peroneal, left	Ankle	EDB	5.9*	0.4*	-	NR*	-
		Fibular head	EDB	12.6*	0.4*	37*	-	-
		Knee	EDB	14.5*	0.4*	37*	-	-
Sensory	Median, left	Wrist	III digit	3.0/3.7	32	-	-	14
		Palm	III digit	1.0/2.0	52	-	-	7
	Ulnar, left	Wrist	V digit	2.8/3.4	31	-	-	14
	Sural, left	Calf	Ankle	3.2/4.0*	20	-	-	12
	Superficial peroneal, left	Calf	Ankle	2.6/3.3	13	-	-	12

Soleus Hoffman reflex: right side, NR; left side, NR.
Amplitudes are measured in millivolt (mV, motor) and microvolt (μV, sensory); onset/peak latency used in sensory nerve conduction.
NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor halluces; NR, no response; EDB, extensor digitorum brevis; -, not applicable.
*Abnormal value.

Table 2. Needle Electromyography Findings for Case 1

Side	Muscle	Insertional activity	Spontaneous activity	Motor unit action potentials	Interference pattern
Left	Deltoid	Decreased	-	-	Absent
	Biceps brachii	Normal	-	Normal	Reduced
	Brachioradialis	Decreased	-	Normal	Reduced
	First dorsal interossei	Increased	-	Normal	Normal
	Vastus medialis	Normal	-	Normal	Normal
	Tibialis anterior	Normal	-	Normal	Normal
	Gastrocnemius	Normal	-	Normal	Reduced

-, not applicable.

um level returned to normal of 4.0 mmol/L in one day with the full recovery of the muscle strength.

Case 2

A 63-year-old male visited the emergency department due to the sudden onset of motor weakness. The MRC grades of proximal and distal extremities were grade 2/5 and 3/5, respectively. The sensory examination was normal and deep tendon reflex was hypoactive. He has a family history of his son diagnosed with HPP. Routine laboratory study and arterial blood gas analysis were normal except for hypokalemia of 2.1 mmol/L. Oral potassium replacement was begun under the probable diagnosis of HPP, resulting the remission of muscle weakness with serum potassium level 4.5 mmol/L.

The electrodiagnostic study was performed one day after the recovery of motor strength. On the NCS, all the motor and sensory responses were within normal limits (Table 3). On needle EMG, polyphasic and small amplitude MUAPs with reduced interference patterns were noted in the deltoid and biceps brachii muscles, but there were no abnormal findings in other muscles examined (Table 4).

For accurate differential diagnosis, LET was performed. First, CMAPs recorded from the left abductor digiti minimi muscle were monitored every 30 seconds for 3.5 minutes before exercise to stabilize the baseline. Then, the patient was asked to contract the muscle as strong as possible for 5 minutes with monitoring CMAPs every 30 seconds. After the 5 minutes of exercise, the patient was asked to relax while CMAPs were recorded every 2 minutes for 40 minutes. During exercise, CMAP amplitude and area showed increment from baseline; 14.2% and 32.2%, respectively. Additionally, the prolonged gradual decline of CMAP amplitude and area was noted with the periods of rest; up to 34.8% and 57.5%, respectively (Fig. 1). The patient refused genetic testing for confirmatory diagnosis of HPP due to the cost of the test. However, based on the LET findings and the family history, we diagnosed the patients as HPP.

Discussion

Hypokalemic paralysis has heterogeneous etiologies with a final common clinical symptom which presents as an acute systematic weakness. An electrodiagnostic study is a valuable diagnostic tool and should be conducted to differentiate other possible causes of weakness [7]. In this article, we described two cases of hypokalemic paralysis; one is secondary hypokalemic paralysis, and the other is the HPP, a hereditary type. This case report is meaningful in that it provided a comprehensive review of hypokalemic paralysis that occurred after insulin treatment for diabetic ketoacidosis.

There are several reports about the mechanisms of muscle weakness due to hypokalemia. One of them is paradoxical depolarization. When hypokalemia is occurred, paradoxical depolarization is triggered and the resting membrane potential of muscle fiber is sustained at -60 mV, resulting in sodium channel inactivation. Another is hyperpolarization. Hypokalemia results in the hyperpolarization of the cell membrane potential, which leads to depolarization block of the muscle fiber membrane. The blockage of membrane depolarization decreases muscle fiber excitability, resulting in reducing CMAP amplitude and decreased insertional activity in EMG study. Also, increased insertional activities and spontaneous activities may be observed in the early attack of paralysis [8,9]. In the first case, most of the CMAP amplitudes were very small, and decreased insertional activities were observed. Especially, there were no MUAPs on the deltoid muscle. The prolongation of motor and sensory latencies and absent or prolonged F wave and H reflex was considered to be due to the early phase of diabetic polyneuropathy. This electrodiagnostic result was compatible with the prior reports of hypokalemic paralysis on its maximal period of paralytic attack [2].

In HPP, which has muscle channelopathies, underlying muscle fiber membrane instability exists. The LET reveals a progressive loss of muscle fiber excitability in the asymptomatic phase of the patient with HPP. It is known that there is an abnormal incre-

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Table 3. Nerve Conduction Study Findings for Case 2

	Nerve, side	Stimulation site	Recording site	Latency (ms)	Amplitude	NCV (m/s)	F wave (ms)	Distance (cm)
Motor	Median, left	Wrist	APB	3.2	9.7	-	27.4	-
		Elbow	APB	7.7	9.2	54	-	-
	Ulnar, left	Wrist	ADM	2.7	10.4	-	28.7	-
		Below elbow	ADM	6.3	9.8	57	-	-
		Above elbow	ADM	8.3	9.2	50	-	-
	Tibial, left	Ankle	AH	5.3	16.4	-	48.6	-
		Knee	AH	12.8	10.8	51	-	-
Sensory	Median, left	Wrist	III digit	2.7/3.4	28	-	-	14
		Palm	III digit	1.3/2.0	39	-	-	7
	Sural, left	Calf	Ankle	3.4/4.0	11	-	-	14

Soleus Hoffman reflex: right side, 29.2 ms; left side, 29.6 ms.
Amplitudes are measured in millivolt (mV, motor) and microvolt (μV, sensory); onset/peak latency used in sensory nerve conduction.
NCV, nerve conduction velocity; APB, abductor pollicis brevis; ADM, abductor digiti minimi; AH, abductor halluces; -, not applicable.

Table 4. Needle Electromyography Findings for Case 2

Side	Muscle	Insertional activity	Spontaneous activity	Motor unit action potentials	Interference pattern
Left	Deltoid	Normal	-	Polyphasic, small	Reduced
	Biceps brachii	Normal	-	Polyphasic, small	Reduced
	First dorsal interossei	Normal	-	Normal	Normal
	Vastus medialis	Normal	-	Normal	Normal
	Tibialis anterior	Normal	-	Normal	Normal
	Peroneus longus	Normal	-	Normal	Normal

-, not applicable.

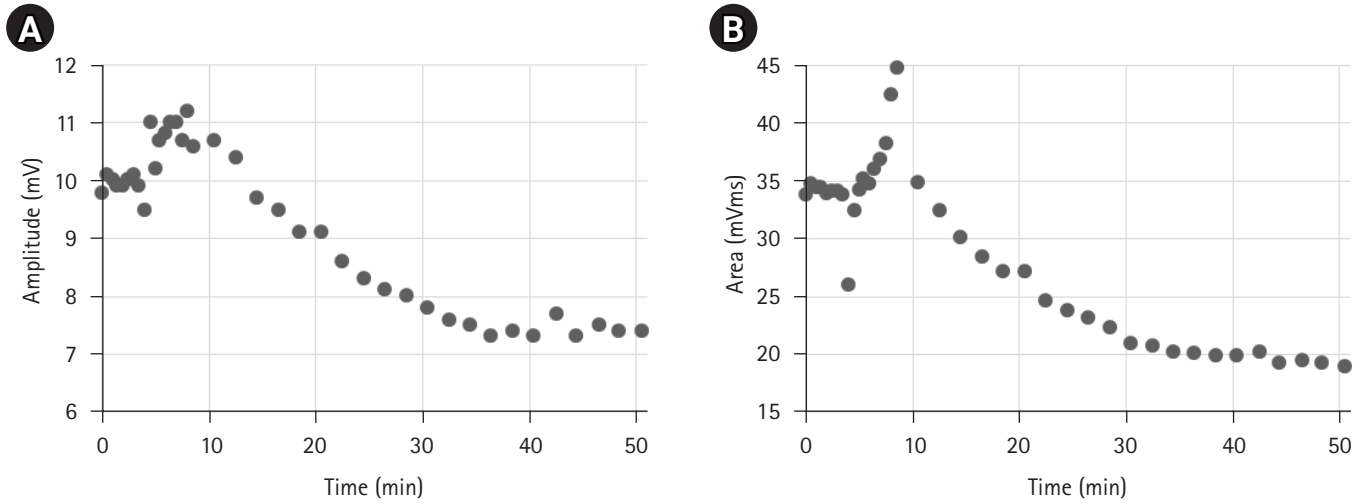

Fig. 1. Long exercise test findings from the abductor digiti minimi muscle recording. (A) The compound muscle action potential (CMAP) amplitude showed a 14.2% increment and a 34.8% decrement during and after exercise, respectively. (B) The CMAP area showed a 32.2% increment and a 57.5% decrement during and after exercise, respectively.

ment of CMAP during the exercise period, followed by a prolonged gradual decrement during the post-exercise phase [5]. This increment and decrement of CMAP may appear in the normal population. However, based on recent research, 40% amplitude or 50% area decrement with the peak-to-nadir method is suggested as optimal cutoff points for diagnosis [10]. In the second case, the CMAP area decreased to 57.5%, which corresponds to the suggested cutoff values. The LET takes consider-

able time and has an obstacle that is accompanied by discomfort due to repetitive stimulation to the same nerve. Therefore, the examiner should set stimulation intensity to the just supramaximal to minimize the patient's discomfort from stimuli. Since the genetic testing for HPP may require several weeks for results and the cost of analysis is prohibitively high, the importance of LET is once again highlighted.

The limitation of our report is that the completeness of the data has been compromised. First, we could not perform a follow-up EMG study due to the patient's refusal. Also, in the second case, we did not conduct peroneal nerve motor conduction study, and ulnar and superficial peroneal nerve sensory conduction studies. Considering that the patient's weakness was fully recovered at the time of the examination and the rest of the nerve conduction studies were within normal limits, the above conduction studies were thought to be less diagnostic but to increase the patient's discomfort. Another limitation was that we could not perform the genetic testing to exclude or confirm HPP in both cases. Although it is a very rare circumstance, in the first case, the possibility that underlying HPP may exacerbate hypokalemia due to insulin treatment cannot be completely excluded. Early diagnosis and management of hypokalemic paralysis is important since it can prevent life-threatening complications. However, periodic symptoms may resolve when patients visit a hospital, and the serum potassium level may be normal, which makes the diagnosis difficult. This case report highlights that the EMG study is a useful and sensitive diagnostic test for hypokalemic paralysis. A proper combination of routine EMG study and LET should be performed in patients suspected of hypokalemic paralysis to evaluate the disease state and exclude other possible causes of paralysis.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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CASE REPORT

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염증성 근육병증으로 오인된 신경유극세포증: 증례 보고

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Neuroacanthocytosis Syndrome Misdiagnosed as Inflammatory Myopathy: A Case Report

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Neuroacanthocytosis syndromes are a category of diseases characterized by progressive basal ganglia degeneration and acanthocytosis. Chorea- acanthocytosis (ChAc), a core neuroacanthocytosis syndrome, is characterized by chorea, psychiatric symptoms, and cognitive decline. It is also associated with neuromuscular abnormalities, including myopathy and axonal neuropathy. Herein, we describe a case of ChAc that was misdiagnosed and inappropriately treated as an inflammatory myopathy due to lower extremity weakness and hyper-creatine kinase (CK)-emia. Careful clinical and laboratory evaluations are always warranted to rule out neuroacanthocytosis in patients with myopathy presenting with chorea and peripheral neuropathy. Although rare, it is necessary to consider ChAc as a potential cause of hyperCKemia. A prompt differential diagnosis can prevent unnecessary treatment with steroids or immunomodulating agents.

Keywords: Myositis; Neuroacanthocytosis

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Introduction

Neuroacanthocytosis syndromes are a group of diseases characterized by progressive basal ganglia degeneration and acanthocytosis [1]. Chorea-acanthocytosis (ChAc), a core neuroacanthocytosis syndrome, is characterized by chorea, psychiatric symptoms, and cognitive decline. It is also associated with neuromuscular abnormalities, including myopathy and axonal neuropathy. Approximately 85% of all patients with ChAc have elevated serum creatine kinase (CK) levels, termed as hyperCKemia [2], which is a nonspecific marker of muscle damage. Differentiation from other hyperCKemia-causing lesions, especially those of primary muscular diseases, is required when a patient presents with other clinical features indicative of ChAc.

Here, we describe a case of ChAc that was misdiagnosed and inappropriately treated as inflammatory myopathy (IM) due to lower extremity weakness and hyperCKemia. Furthermore, we discuss the points of differentiation between ChAc and potentially treatable acquired IM.

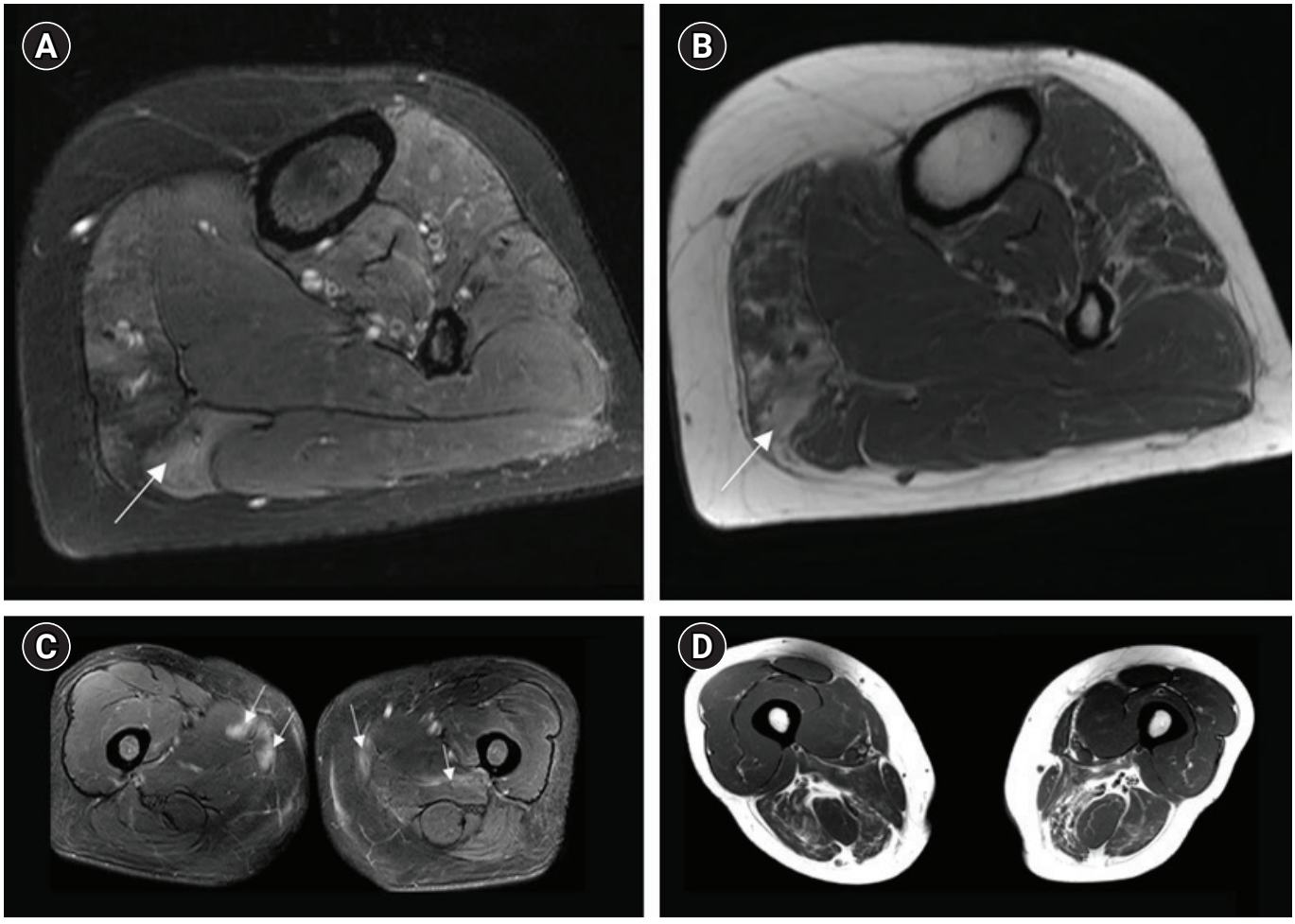

Fig. 1. Left lower extremity magnetic resonance imaging (MRI) showing (A) focal T2 hyperintensity in the medial head of the gastrocnemius muscle (arrow) and (B) fatty degeneration in the medial head of the gastrocnemius and pretibial muscles (arrow). Thigh MRI showing (C) patches of T2 hyperintensity in the bilateral gracilis, right adductor longus, and left adductor magnus muscles (arrows) and (D) fatty degeneration and atrophy in the bilateral biceps femoris, semimembranosus, and adductor magnus muscles. (A) T2 spectral attenuated inversion recovery, (B) T1 turbo spin echo (TSE), (C) T2 fat saturation, and (D) T1 TSE.

Case Report

A 45-year-old female presented at a local community hospital with a 1-year history of bilateral lower extremity weakness, dysphagia, and mastication difficulty. Laboratory and electrodiagnostic testing revealed hyperCKemia and a mixed myopathic neuropathic pattern with polyneuropathy, respectively. Because of suspected myopathy, muscle biopsy was performed at the left medial head of the gastrocnemius muscle, in which magnetic resonance imaging (MRI) showed a T2 hyperintensity on the lower leg (Fig. 1A, B). She was diagnosed with autoimmune IM and treated with oral steroids and additional intravenous immunoglobulin G for 3 years. She was referred to the locomotor medicine clinic of Samsung Medical Center after showing no symptom improvement. Written informed consents were obtained.

According to her medical history, her initial symptoms were swallowing/chewing difficulty and truncal instability during walking, which appeared at the age of 43 years. She also reported tingling in both knees. She experienced difficulties in holding small objects because of the impaired fine hand movements. Her elder brother had generalized chorea and died in his early 40s.

Neurological examination revealed bilateral hip, ankle, wrist, and finger weakness without overt atrophy. She had a bilateral positive Trendelenburg sign and an uncompensated gluteus medius gait pattern. No Gower sign was observed. The anterior neck flexor and knee extensors on both sides had normal muscle strength. She had touch hypoesthesia with a stocking-glove distribution. Deep tendon reflexes were absent in all four extremities. Tongue dyskinesia and facial oromandibular dystonia were observed, and frequent tongue biting resulted in poor ingestion

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of solids.

Her laboratory findings included hyperCKemia (CK level, 816 IU/L; reference range, 0-170 IU/L), with acute phase reactants, antibodies for necrotizing autoimmune myositis, and HLA B51 all within normal limits. Electrodiagnostic tests revealed symmetrical sensorimotor axonal polyneuropathy. However, there was no history of systemic diseases, such as diabetes, that could cause polyneuropathy. Reduced motor unit action potential (MUAP) recruitment was observed in the muscles of the upper and lower limbs and the tongue. However, there was no denervation potential or myopathic MUAP.

The paraspinal muscles were normal on lumbar spine MRI. Additionally, thigh MRI revealed fatty degeneration and atrophy of the bilateral hamstring and adductor magnus muscles (Fig. 1C, D). Therefore, an electrodiagnostic test was additionally performed on the muscles and patchy T2 hyperintensities were noted. Denervation potential was observed in the right gracilis and left semitendinosus muscles, with no typical neuropathic or myopathic MUAP. A reexamination of the previous muscle biopsy showed no evidence of an IM (Fig. 2A).

Considering the family history of chorea and physical and laboratory findings, neuroacanthocytosis was suspected. Peripheral blood smear and brain MRI were performed, which revealed acanthocytosis and bilateral caudate nucleus atrophy with T2 hyperintensity in the bilateral basal ganglia (Fig. 2B, C).

Next-generation sequencing for dystonia revealed two likely pathogenic variants of the *vacuolar protein sorting 13 homolog A* (*VPS13A*) gene. The patient was finally diagnosed with ChAc

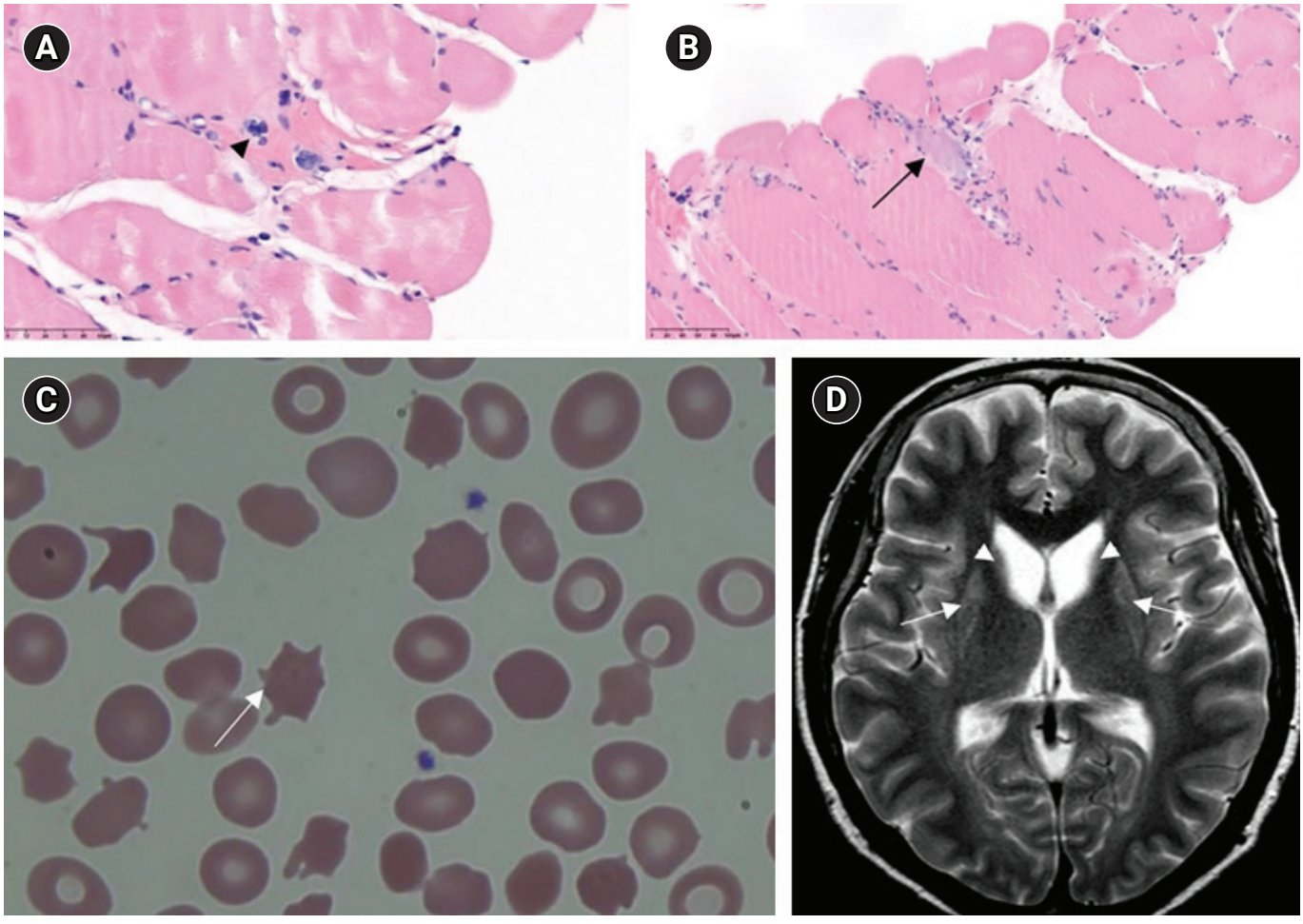

Fig. 2. (A, B) Muscle biopsy performed at the left medial head of the gastrocnemius muscle showing mild size variation in myofibers, a few extremely atrophic myofibers with multiple clumped nuclei (arrowhead), a few regenerating myofibers (arrow), and mild fatty ingrowth (H&E: A, ×50; B, ×100). (C) A peripheral blood smear showed normocytic and normochromic anemia, with anisopoikilocytosis and polychromasia. Acanthocytes (arrow), burr cells, and elliptocytes are seen as poikilocytosis. (D) Brain magnetic resonance imaging showing bilateral caudate nucleus atrophy (arrowheads) and T2 hyperintensity in the basal ganglia (arrows). T2 turbo spin echo.

[1]. She was administered haloperidol, following which her feeding dystonia and lingual dysarthria improved slightly, but with no change in hyperCKemia and gait disturbance.

Discussion

ChAc is an autosomal recessive neurodegenerative disorder. Most patients with ChAc present with choreatic movement disorders, including orofaciolingual dystonia, and various neuromuscular manifestations, including muscle weakness, atrophy, and areflexia [1]. Because its neuromuscular manifestations have not been sufficiently investigated, it can be initially mistaken as a primary myopathy. In early-stage ChAc, abnormal hyperkinesia is not severe. Proximal and distal muscle weakness usually appear late (age, 20-40 years), often with accompanying hyperCKemia. These characteristics may lead to erroneous diagnoses, particularly autoimmune IM.

Based on the characteristics of this case, several differentiating points between ChAc and IM may be suggested. First, the distribution of muscle weakness is different; the latter generally shows axial and symmetric proximal girdle muscle weakness. Although this patient had bilateral hip abductor muscle weakness, the anterior neck flexor and knee extensor had normal strength, and the Gower sign, which is a hallmark of proximal girdle muscle weakness, was not found. Moreover, lumbar spine MRI did not show fatty atrophy of the lumbar paraspinal muscles, which is often seen in muscular dystrophies. Second, sensory hypoesthesia with a stocking-glove distribution was observed, which was later confirmed as symmetric axonal polyneuropathy through a nerve conduction study. Third, no definite evidence of myopathy was found on the electrodiagnostic test. In a study by Rampoldi et al. [2], 67% of patients with ChAc showed neuropathic features in an electrophysiological study, but none showed myopathic features. This could differentiate ChAc from IM, in which the electromyographic characteristics of myopathy, such as short duration, small amplitude, polyphasic MUAPs, and an early complete recruitment pattern on volition are generally observed. Fourth, MRI showed asymmetrical focal patchy involvement of several thigh muscles. In contrast, the muscle involvement in IM is usually diffuse and symmetric [3]. Finally, chorea is frequent in neuroachantocytosis, and orofaciolingual dystonia is a specific finding of ChAc. In this case, mandibular symptoms played an important role in the differential diagnosis.

Previous studies have reported that the muscle histology of ChAc (increased number of internal nuclei, increased fiber size variation, and mild endomysial fibrosis) is consistent with that of moderate myopathy. However, these myopathic findings may be secondary to chronic denervation changes, and the main findings could be small-group atrophy, increase of small fibers on diameter analysis, and frequently angulated fibers [4]. Therefore, muscle biopsy finesenting with chorea and peripheral neuropathy. Although rare, it is necessary to consider ChAc as the cause of hyperCKemia [5]. Early differential diagnosis can prevent unnecessary treatment with steroids or immunomodulating agents.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Authorship is credited to those who have direct involvement in the study and have made significant contributions to (a) conceptualization and design of the research, or acquisition, analysis, and interpretation of the data, (b) drafting of the manuscript or critical revision, and (c) approval of the submitted and final versions of the manuscript. The primary investigator is designated the first author of the study unless contested by the other authors. The corresponding author is directly responsible for communication and revision of the submitted manuscript.

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2. Preparation of the Manuscript

2-1. Forms of the manuscript

Use Microsoft Office Word (versions after 2003) and ensure correct spelling and grammar. Set up the MS Word document for 1-inch margins on a letter or A4-sized paper. The manuscript must be written in 12-point font, and the sentences must be double-spaced including tables and figure legends. The length of the manuscript should not exceed 20 pages in original articles, 7 pages in the case report, and 30 pages in review article except for the tables and figures.

2-2. Use of language and unit

Draw up a manuscript in proper and clear English as per the orthography. When there is no appropriate translation of foreign medical terms, proper nouns, drug names, units, etc., use their originals in the manuscript. If foreign-language words are needed, capital and small letters should be clarified: in principle, proper nouns, place names, and names of persons should be written with a capital letter as the first letter and then small letters for the rest. If an original term has its translation whose meaning is unclear, place the original in a small parenthesis after its translation when it appears for the first time and then uses its translation alone.

Numbers should be written in Arabic numerals, and measurements should be reported using the metric system, and hematologic and biochemical markers should be reported in the International System (SI) of Units. (http://physics.nist.gov/cuu/Units/index.html)

2-3. Use of abbreviations

The use of abbreviations should be minimized and restricted to those that are generally recognized. When using an abbreviated word, it should be spelled out in full on the first usage in the manuscript, followed by the abbreviation in parentheses.

2-4. Word-spacing

In manuscripts, leave one space for each side, using arithmetic marks as ±, =, +, - (minus), ×, etc. (ex. 25.3 ± 1.2). Leave no space for "-" (hyphen) between words (ex. post-stroke). Leave one space after ",", ";", ":" and ":". Using parentheses, leave 1 space each side in English. And brackets in parentheses, apply square brackets. Ex) ([ ])

2-5. Order of manuscripts for original articles

The manuscript for original articles should be organized in the following order: 1) title page as a separate file, 2) Title of the manuscript 3) abstract and keywords, 4) introduction, 5) materials (or subjects) and methods, 6) results, 7) discussion, 8) conflict of interest, 9) acknowledgements (if necessary), 10) references, 11) figure legends 12) tables as separate files, and 13) figures as separate files.

Figures should be submitted with an online submission system as separate files, named as the number of figures of the text and figure legends in JPEG, TIFF, GIF format (ex: Fig1.jpg)..

Title page

The title page should be uploaded online as a separate file and should describe the title of the article, full names of authors, institutional affiliation(s) with each author. English names should not be described in initials. All authors' ORCIDs should be described.

If authors belong to different organizations, the chief research organization should be specified in the first place, and the other one's shoulder is specified in the order of Arabic numerals (e.g., 1,2,3).

In the title page, the corresponding author must be identified, and his or her contact information (postal address, e-mail, telephone, and fax numbers) should be listed, and if necessary, financial support might be described as a footnote. Running title with 50 spaces maximum should be described.

Title of the manuscript

The title of the manuscript page should contain the only title. Do not include author information on the title page for a blind peer review. The author names should not appear on this page.

The title should be short, specific, and informative to present clearly the objective of the study and should not use the expressions, such as "study about---" or "clinical study about---." The title should contain less than 20 words. The first letter of words ex-

cept article, preposition, and conjunction should be capitalized. Drug names in the title should be written with generic names, not product names.

Title of the manuscript

Abstract should summarize the content and should not exceed 250 words in the original article and 150 words in the case report. In the original article, a structured abstract with the headings of Objective, Methods, Results, and Conclusion must succinctly describe the paper. Use complete sentences and do not number the results. At the end of the Abstract, list up to 5 relevant Keywords which are in accordance with the Medical Subject Headings (MeSH) in the Index Medicus (http://www.nlm.nih.gov/mesh). Keywords should be written with a capital letter as the first letter and then small letters for the rest and separate each word by a semicolon (;). The abstract of the case report should be non-structured, with no more than 5 Keywords attached. Brief communications should not describe abstract and keywords.

Introduction

Introduction should clearly present the objective of the study, and a brief background to inform the readers of the relevance of the study may be necessary.

Materials & Methods

Describe the participants or research materials of the study, divided by subsection titles, and describe the experimental methods in a logical and systematic manner so that they can be reproducible by another investigator. Explain in detail the inclusion and exclusion criteria for both the experimental and control groups. Experimental drugs should be stated in the generic name. When proprietary brands are used, include the brand name and the name of the manufacturer in parentheses after the first mention of the generic name. When using experimental devices or other products, state the brand name then follow with the name of the manufacturer, city (state), and country in parentheses, e.g., Flow Cytometer (Coulter Electronics Inc., New York, NY, USA). To ensure anonymity during the peer review process, the authors' affiliations or the institutional setting of the study should not be revealed. Subsection titles should be listed in order to 1), (1), A), (A).

Precisely describe the statistical analysis methods, computer programs, and criteria for determining significance.

(Description of participants)

Ensure correct use of the terms sex (when reporting biological factors) and gender (identity, psychosocial or cultural factors), and, unless inappropriate, report the sex or gender of study participants, the sex of animals or cells, and describe the methods used to determine sex or gender. If the study was done involving an exclusive population, for example, in only one sex, authors should justify why, except in obvious cases (e.g., prostate cancer). Authors should define how they determined race or ethnicity and justify their relevance.

Results

Results should be summarized and described logically the significant findings and trends observed in the results, giving the main or most important objective. Results can be sectioned by subsection titles listed in order to 1), (1), A), (A). Avoid extensive repetition of contents of the tables and figures in the text. In statistical expression, mean and standard deviation should be described as mean ± SD, and mean and standard error as mean ± SE. The letter 'p' in p-value is written in the lower case.

Discussion

Refrain from an excessive review of historical studies, textbook facts, or irrelevant references. Interpret the results with respect to the objective of the study, and describe differences with previous studies and significant findings, which lead to the deduction of the conclusion. Accentuate newly obtained observations from the study and include significant limitations of the study. Do not repeat the results in detail or other information that is given in the Introduction or the Results section.

Conclusion

Conclusions should avoid unqualified statements that are not adequately supported by the data and describe briefly novel findings of the study, according to the purpose of the study.

Acknowledgment

If necessary, persons who have made contributions to the study, but who are not eligible for authorship may be named in this section. Their contribution must be specified, such as data collection, financial support, statistical analysis, or experimentation.

References

References must be written only to the cited body. It is recommended that only important references are recorded, and the number of references is within 40. References should be numbered in order of appearance in the text using Arabic numerals in square brackets such as [1], [2-4], and [5,7,9]. A bracket is placed after the author's name, or before the period in a sentence. In case the author should be mentioned, write only "last name" and list the first two author and add "et al." if the authors are more than three (e.g., one author: Kim, two: Park and Jeong, more than

three: David et al.). The English name is written the last name in conjunction with capital letters of first and middle names. If the reference is Korean, then list the English version in the reference section. List all authors when they are six or fewer; when there are seven or more, list only the first six and add 'et al.". If an article has been accepted but not yet published, the assigned month to be published could be written. Journal titles should be abbreviated in style used in the Index Medicus. If the reference is not listed in Medicus, use the full name of the journal. All other references should be listed, as shown in the "Uniform Requirement for manuscripts submitted to Biomedical Journals" (2008).

Sample References

1) Journals:

Authors: full title of the article. journal name year;volume:the first and last page number.

(e.g., Curr A, Dietz: Traumatic cervical spinal cord injury: relation between somatosensory evoked potentials, neurologic deficit and hand function. Arch Phys Med Rehabil 1996;77:48–53.)

2) Book:

Authors: Book title. edition. place: publisher; year, the first and last page number.

(e.g., Cailliet R: Shoulder pain. 3th ed. Philadelphia: FA Davis; 1991, pp32–35.)

3) Book chapter

Authors: title of the chapter. In: editor. The book title. edition. place: publisher; year, the first and last page number.

(e.g., Kottke FJ: The neurophysiology of motor function. In: Kottke FJ, Lehmann JF, editors. Krusen's handbook of physical medicine and rehabilitation. 4th ed. Philadelphia: Saunders; 1990, pp234–269.)

4) Online resource

National Library of Medicine: Fact sheet: AIDS information resources [Internet]. Bethesda: National Library of Medicine; 2003 [cited 2007 Mar 26]. Available from: http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html.

Tables

Tables should be uploaded online as separate files and numbered in order of appearance in the main text (Table 1, Table 2, etc.). Table should be easy to understand and unique. The total number of tables should not exceed more than five. Title of table should be briefly written as a phrase or sentence. The first letter except article, preposition, and conjunction, should be capitalized. The title of table is written above the table, and footnote should be described below the table. All abbreviations should be spelled out in footnote in order of abbreviation, colon, and unabbreviated name (e.g., NCS: nerve conduction study). The symbols (*, †, ‡, §, ||, ¶, **, ††, ‡‡) should be superscripts and be used in the indicated sequence (e.g., * $p < 0.05$).

Figure legends

Figure legends must appear on a separate page at the end of the manuscript written in the Microsoft Word file. Write sentences to be understood fully without relying on the main text. Only the first sentence written in capital letters. The second sentence should be set on the starting line of the first sentence. Explain any abbreviation and symbol in the legend. Figures containing histologic slides should be accompanied by legends explaining tissue origin, stain method, and microscopic amplification.

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Figures should be uploaded online as separate files and numbered in order of appearance in the main text (e.g., Fig. 1). If more than two figures are used in the same number, insert the alphabet after Arabic number (e.g., Fig. 1A, Fig. 1B) and record as a single file. Arrows should be inserted to be easily understood. All images should be saved in JPEG, TIFF, GIF or PPT format within 3 MB. The minimum resolutions required are 300 dpi. At online submission, set a file name as the same title as written in main text and legends (e.g., Fig1.jpg).

When already published figures or graphs are inserted, the written consent of the author should be attached and acknowledged in the manuscript.

2-6. Articles other than the original manuscript

The general guidelines abide by the original article section.

Invited review

An invited review is a contemplation focused on a certain topic appointed by the Editorial Board. The abstract is limited to less than 250 words, the number of main text less than 30 pages, and the references no more than 60.

Case Report

Case report deal with any unique features, novel diagnosis or treatment, or others accepted in Editorial Board. The abstract should be non-structured and limited to 150 words, with no more than 3 keywords attached. Introduction should be briefly written about background and significance of the case. Main texts are

composed of the course of clinical features, diagnosis, and treatment. Discussion should focus on the significance of the case, and tedious review should be avoided. The number of table and figure is limited to five in total, and the number of references should not exceed more than ten. The maximum word count is limited to 1,500 words, excluding references, tables, and figure legends.

Brief communication

Brief communication deal with already reported findings or cases, but with any unusual features, or features that are considered to be important. Abstract and keywords are not required. The text is limited to 700 words. Up to seven references should be listed. Only one table or figure is allowed, and acknowledgment should not be written.

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The author is responsible for disclosing any financial support or benefit that might affect the content of the manuscript or might cause a conflict of interest. When submitting the manuscript, the author must describe the conflict of interest statement. Examples of potential conflicts of interest are financial support from or connections to companies, political pressure from interest groups, and academically related issues. In particular, all sources of funding applicable to the study should be explicitly stated.

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Clinical trial defined as "any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome" is recommended to be registered to the primary registry to be prior publication. ARM accepts the registration in any of the primary registries that participate in the WHO International Clinical Trials Portal (http://www.who.int/ictrp/en/), NIH ClinicalTrials.gov (http://www.clinicaltrials.gov/), ISRCTN Resister (www.isrctn.org), University Hospital Medical Information Network (www.umin.ac.jp/ctr/index/htm), Netherlands Trial Register (http://www.trialregister.nl/trialreg/index.asp) or The Clinical Research Information Service (http://cris.nih.go.kr/). The clinical trial registration number will be published at the end of the abstract.

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