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Review Article

For how long do denervated muscles in children retain the ability to regenerate?: Restoration of elbow flexion and shoulder function by partial nerve transfer in a child with long-standing poliomyelitis-like paralysis☆

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A R T I C L E I N F O

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A B S T R A C T

Background: In infant poliomyelitis or poliomyelitis-like paresis, there has been no means of treating residual paralysis and the policy has been to wait until an affected infant has grown sufficiently to enable tendon transfer or arthrodesis. However, recent reports have described relatively good results for early surgical intervention in the form of nerve transfer.
Methods: In a 4-year and 6-month-old child we transferred a partial ulnar nerve for elbow flexor reconstruction even 3 years and 10 months after the onset of poliomyelitis-like palsy and also transferred partial accessory and radial nerves for shoulder function restoration 6 months after the first operation.
Results: Elbow flexor restored M4 on the British Medical Research Council scale. The shoulder subluxation resolved, however, the strengths of the deltoid and infraspinatus remained almost M1. At the most recent clinical examination, the patient was 18 years old and the active range of motion of patient's left elbow was 0°–125°, and those of the whole shoulder girdle were abduction 35°, flexion 60°, extension 30° and external rotation 0°.
Conclusions: The outcomes we achieved may support partial nerve transfer techniques as viable treatment options for persistent long-standing motor deficits following poliomyelitis-like palsy in children. However, we recommend performing partial nerve transfer as early as possible after recovery from flaccid paralysis and also use of nerves that derive from narrow spinal cord segments. After denervation, children's neuromuscular systems seem to have the ability to regenerate after a much longer period than has generally been believed. This speculation is based on only a single case report; thus, more experience is needed before this generalization can confidently be made.

1. Introduction

In Japan, poliovirus vaccination led to the eradication of poliomyelitis by 1980. However, there are sporadic cases of poliomyelitis-like paralysis caused by enterovirus 71 infection, which causes hand, foot, and mouth disease in infants.

We experienced a child with long-standing poliomyelitis-like paralysis whose elbow flexor was restored by partial ulnar nerve transfer to the musculocutaneous nerve (the Oberlin method) performed 3 years and 10 months after onset of paralysis. Consent was obtained from a parent of the patient prior to publication.

1.1. Case report

A 13-month-old girl was brought to a university hospital because of paresis of her left upper extremity. She had a history of hand, foot, and mouth disease at the age of 8 months. After a high fever for 2 days, her left upper extremity had become completely paralyzed. A

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neutralization test revealed that serum antibody titers to enterovirus 71 were high (positive at ×360 dilution; normal < ×4).

Clinical examination showed that she had recovered the function of her wrist and fingers; however, she had a frail shoulder joint and was unable to bend her elbow. The deltoid, infraspinatus, latissimus dorsi, pars clavicularis of the pectoralis major, and biceps were completely paralyzed. The triceps strength was M3 on the British Medical Research Council (BMRC) scale and the trapezius strength M2. She seemed to have normal sensation.

Magnetic resonance imaging (MRI) of the cervical spinal cord showed a linear high signal intensity region from C2 to C6 on sagittal T2-weighted images (Fig. 1a) that was located in the left anterior horn on axial T2-weighted images (Fig. 1b). A diagnosis of poliomyelitis-like paralysis caused by infection with enterovirus 71 was made.

The initial plan was to treat her conventionally by a combination of arthrodesis of the shoulder joint and Steindler elbow flexorplasty when her growth plate had closed and she was old enough to cooperate. She was followed up at 3 monthly intervals. Fig. 2 shows the timing of recovery of the muscles in her left upper limb (Fig. 2). When she was 4 years and 4 months old, the possibility of nerve transfers was considered. To this end, the volumes of her biceps and shoulder girdle muscles were measured by MRI and needle electromyogram (EMG) examination of the biceps, deltoid, and infraspinatus muscles performed. The MRI showed that these three muscles were extremely atrophic but had retained some volume and had almost the same signal intensity in both T1 and T2-weighted images as her healthy muscles (Fig. 3). EMG showed positive sharp waves and fibrillation voltages with no voluntary spikes, indicating complete denervation of the muscles with retention of the physiological characteristics of denervated striated muscles. It was therefore decided to perform a nerve transfer for her elbow flexor and, if this was successful, subsequently attempt restoration of shoulder girdle function by nerve transfer.

The first operation was performed when the patient was 4 years and 6 months old, that is, 3 years and 10 months after denervation. The Oberlin method, which entails transferring a fascicle of the ulnar nerve to the musculocutaneous nerve in the mid arm, was performed. Very weak electrical stimulation was used to distinguish the function of the selected fascicle; however, this was ineffective because stimulation of various fascicles induced almost the same responses in the hand. Neurorrhaphy was performed by Ochiai's method because the musculocutaneous nerve had a much larger diameter than the transferred fascicle (Fig. 4a and b) [1]. No abnormal hand movements were detected postoperatively. Three months later, the biceps began to contract.

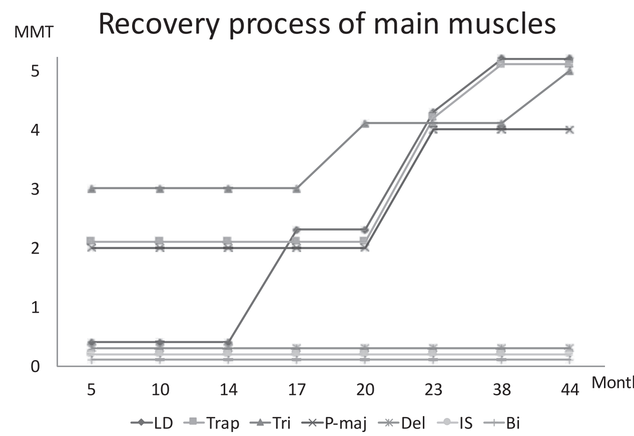

Fig. 2. Timing of recovery of main muscles from denervation. The trapezius and triceps took about 2 years to recover strength of MMT 4 on the BMRC scale.

The second procedure was performed when the patient was 5 years old, that is, 6 months after the first operation and 4 years and 4 months after denervation. With the patient in a supine position, the accessory and suprascapular nerves in the supraclavicular fossa were explored and a branch of the accessory nerve innervating the lower part of the trapezius was selected for transfer to the suprascapular nerve in an end-to-end fashion. With the patient's upper extremity on her chest, the quadrilateral region was explored via a posterior approach and a motor branch of the axillary nerve and motor branches of the radial nerve to medial head of the triceps were identified. The branches were electrically stimulated to verify contraction of the medial head. Three branches of the radial nerve innervating the medial head of the triceps were transferred to the

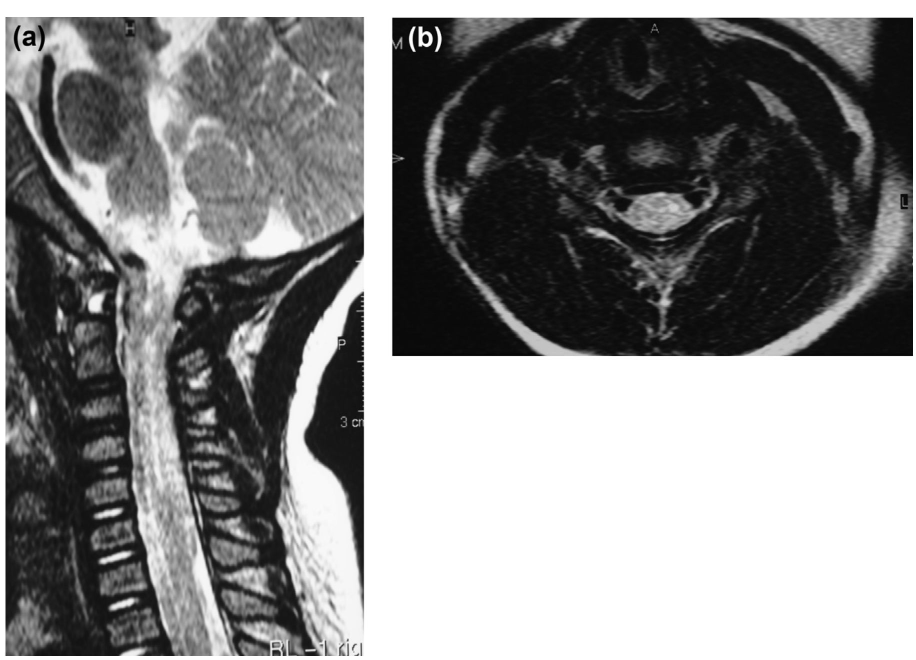

Fig. 1. MRI of the spinal cord 6 months after onset. (a) T2W sagittal view. (b) T2W axial view at C4 level.

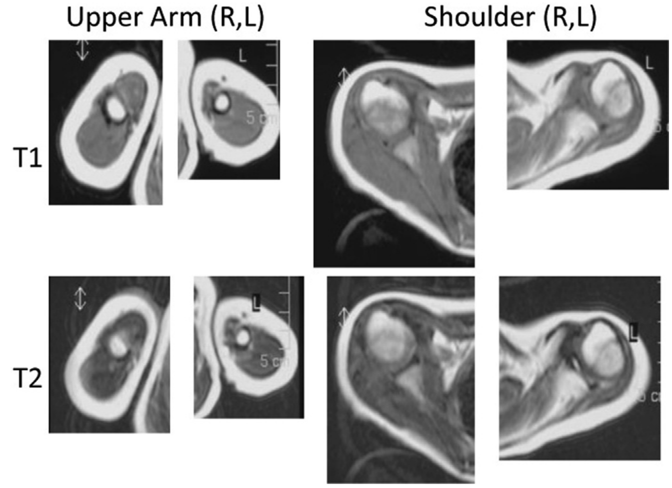

Fig. 3. MRI of both upper arms and shoulders 3 years and 10 months after denervation showing extreme atrophy of the left deltoid, infraspinatus and biceps muscles. These muscles have the same intensity in both T1W and T2W as the healthy side.

axillary nerve, neurorrhaphy being performed in an end-to-end fashion.

Eleven months after the Oberlin method, the strength of the elbow flexor was M4 on the BMRC scale. Seven months after the shoulder reconstruction, the shoulder subluxation had resolved; however, there was little subsequent improvement (Fig. 5). The strengths of the deltoid and infraspinatus remained almost M1 on the BMRC scale; however, the patient was able to abduct in a full arc in the supine position. When she was 13 years old, she was enjoying playing tennis at junior high school. At the most recent clinical examination, she was 18 years old and studying to become a medical clerk. The range of motion (ROM) of her left elbow was 0°–125° and muscle strength of the elbow flexor M4 on the BMRC scale (Fig. 6). Her left shoulder joint was stable. The ROMs of the whole shoulder girdle were abduction 35°, flexion 60°, extension 30° and external rotation 0°. She had a slight co-contracture between the intrinsic muscles of the hand and elbow flexor and recurrent anterior dislocation of the radial head at the elbow. However, these did not hinder her activities of daily living and she did not want further operative interventions.

1.2. The dawn of early surgical intervention for infant poliomyelitis or poliomyelitis-like paresis

In infant poliomyelitis or poliomyelitis-like paresis, there has been no means of treating residual paralysis and the policy has been to wait until an affected infant has grown sufficiently to enable tendon transfer or arthrodesis. However, recent reports have described relatively good results for early surgical intervention in the form of nerve transfer [2,3]. Funahashi et al. reported an infant

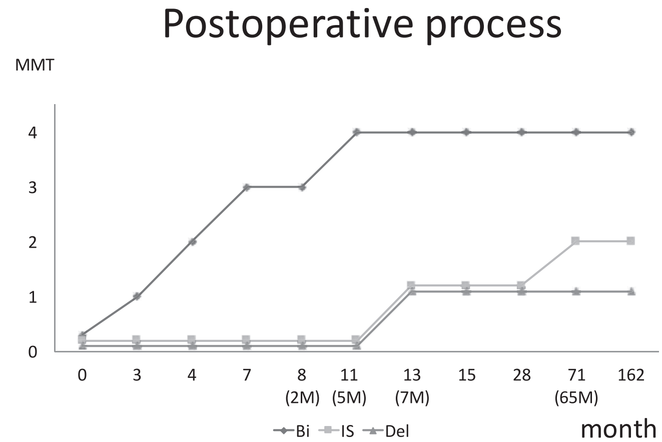

Fig. 5. Postoperative course. The numbers immediately under the horizontal axis denote months since the first operation and those below them in parentheses denote months since the second operation.

Fig. 6. Elbow flexion and shoulder abduction at 18 years old.

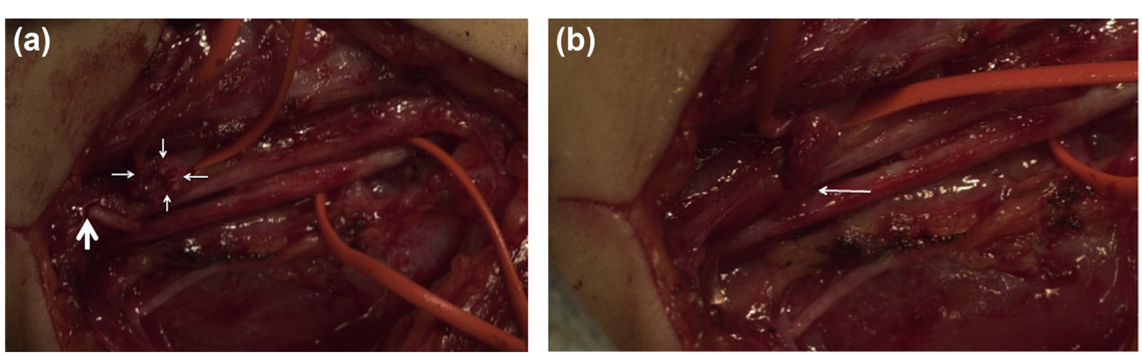

Fig. 4. Nerve transfer by Ochiai's method. (a) Large difference between diameter of the musculocutaneous nerve (surrounded by four small allows) and the ulnar fascicle (large arrow). (b) After neurorrhaphy.

with poliomyelitis-like paralysis whose shoulder function and elbow flexion were successfully restored by partial accessory nerve transfer to the suprascapular nerve and transfer of intercostal nerves to the musculocutaneous nerve. Their patient had become paralyzed at age 8 months and underwent surgery at age 1 year and 2 months, 6 months after onset of the paralysis. Liao et al. reported nerve transfer to restore shoulder abduction in six patients (aged 1 year and 4 months to 5 years and 10 months), five of whom were operated on within 1 year of paralysis and whose strength improved to stage V (normal in Gilbert's classification). The remaining patient, who was operated on 3 years after onset of paralysis, had no recovery. These authors also used functioning free muscle transfer (FFMT) to restore elbow function in four patients (aged from 3 years and 6 months to 15 years and 5 months). Strength was restored to M4 on the modified BMRC scale (able to oppose the examiner's single finger force for longer than 30 s) in all four patients; however, they did not try direct neurotization to the biceps because their regimen for the elbow was to await recovery for one year after onset of paralysis. El-Gammal et al. performed shoulder arthrodesis followed by FFMT and succeeded in restoring elbow function in six patients with long-standing paresis (7–16 years old) [4].

Nerve transfers following traumatic brachial plexus injuries are infrequently performed more than 6 months after injury because myoneural degeneration may set in before nerve regeneration can occur. Because the myoneural end plate begins to degenerate 12–18 months after a denervating injury and the rate of axonal regeneration is less than 2.5 cm per month, most brachial plexus surgeons operate only on patients who present within 6 months after injury [5].

We succeeded in restoring elbow flexion by partial ulnar nerve transfer 3 years and 10 months after the onset of poliomyelitis-like palsy. However, nerve transfers to the suprascapular and axillary nerves that we performed 6 months after the first operation did not completely restore shoulder function. Our experience with this patient informs the following suggestions for neurotization to muscles with long-standing denervation, especially in children.

1.2.1. Timing of surgery

Preoperatively, we performed EMG to ascertain the denervated potentials of the biceps, deltoid, and infraspinatus muscles. The results indicated that these muscles still had the physiological characteristics of denervated striated muscle and had not progressed to complete degeneration or fibrosis as described by Aird and Naffziger [6]. The elbow flexor recovered voluntary contracture 3 months postoperatively, that is, 4 years and 1 month after denervation as a result of virus infection of the anterior horn cells. Because we had ascertained that nerve transfer to this long-standing denervated muscle could restore function, we also attempted to restore shoulder function by nerve transfer. We directly transferred part of the accessory nerve to the suprascapular nerve in the supraclavicular region and part of the radial nerve to the axillary nerve in the posterior quadrilateral space area. The second procedure was performed 6 months after the first one, that is, 4 years and 4 months after denervation. The strengths of the deltoid and infraspinatus had recovered to M1 on the BMRC scale by 7 months after operation. The shoulder joint was thus partially stabilized; however, there was little subsequent improvement and function was not restored.

Leechavengvongs reported that it took 6–8 months to restore deltoid strength to M2 on the BMRC scale after nerve transfer with a branch to the long head of the radial nerve; however, they did not report how long it took to achieve grade M1 strength [7]. It must be at least less than 6 months. Such recovery usually takes 4–6 months in free nerve grafting in brachial plexus injuries [8]; however, these data are for adults. Thus far, no precise data are available for children; however, a much shorter period would likely be needed in children.

The results obtained in our patient's biceps suggest that children's neuromuscular systems can recover useful function after re-innervation performed as long as 4 years after denervation. However, after 4 years and 6 months the shoulder reconstruction was unsuccessful; thus, 4 years after denervation may be a critical point in children.

Aird and Naffziger investigated denervated human striated muscles from both the atrophy and fibrosis points of view and recommended surgical intervention should not be delayed beyond 3 or 4 months, this being the time they identified as providing a reasonable chance of successful re-innervation of the involved muscle. They concluded that surgical intervention performed more than 11 months after peripheral nerve injuries would likely achieve poor functional recovery because of fibrosis of the denervated muscles [6]. However, their biopsy specimens were taken from 3 to 9 months after nerve injury and they provided no data on the clinical results of neurorrhaphy, nor did they report their patients' ages. A recent report described performing FFMT by nerve transfer more than 1 year after onset of paralysis [9]. In particular, a CC7 procedure for brachial plexus injuries using FFMT achieved better functional recovery of finger flexion than procedures without FFMT [10]. However, children's muscles, unlike those of adults, have a greater potential to regenerate. How long denervated muscles in children retain the ability to regenerate is an important topic for future research.

1.2.2. Which nerve should be selected as the donor?

Consideration must be given to the particular pathological processes involved. Poliomyelitis-like lesions spread longitudinally in the anterior horn cells of the spinal cord. Our patient had initially presented with complete paralysis of her left upper extremity. During follow-up, her hand and forearm function, but not elbow extension, showed early recovery (Fig. 2). She eventually lost function associated with innervation by C5 and C6. We transferred branches of the radial nerve to medial head of the triceps to the axillary nerve, the triceps muscle usually being innervated by C6–8 segments. We confirmed muscle contracture by electrical stimulation intraoperatively; however, this does not necessarily ensure good physiological quality of the transferred branches. Sharrard reported a relationship between muscle strength on the BMRC scale and number of anterior horn cells in a patient with poliomyelitis [11]. It seems likely that the branches to medial head of the triceps were not healthy in our patient because restoration of triceps strength took more than 2 years (Fig. 2). Given that an MRI showed longitudinally spread lesions, the branch of the accessory nerve used, which consists of both cranial nerve XI and cervical branches, may have been incomplete. The trapezius and triceps muscles are innervated by rather broader segments of the spinal cord than are ulnar-innervated muscles. The ulnar-innervated muscles recovered much earlier than the triceps in our patient, suggesting that the quality of the ulnar nerve was much better than that of the radial and accessory nerves. We suggest selecting a donor nerve that innervates a narrow myotome area and will restore strength to M5 by an early stage of convalescence.

1.2.3. Considerations concerning time required for re-innervation

Duration of re-innervation is the time that the regenerative axons need to reach the denervated muscle. In consideration of this, in patients with long-standing denervation we prefer the Oberlin method for restoring elbow function. Both our experience and many published reports [5,12–17] indicate that the time between surgery and re-innervation is shorter with this method than with direct intercostal nerve transfer.

However, Teboul et al. have reported that regeneration takes an average of 5 months (range 3–9 months) after the Oberlin method and Nagano et al. have reported that it takes 4–8 months after direct intercostal nerve transfer [18,19].

One disadvantage of the Oberlin method is that it involves intra-brachial plexus nerve crossing and therefore results in some degree of contracture between the biceps and ulnar nerve-innervated muscles. Our patient demonstrated this phenomenon between the biceps and hand intrinsic muscles to a degree; fortunately, this did not impair her activities of daily living. From this point of view, intercostal nerve transfer is superior to the Oberlin method. Even so, we recommend that, if possible, the Oberlin method should be selected for patients with long-standing denervation.

In conclusion, the outcomes we achieved may support partial nerve transfer techniques as viable treatment options for persistent long-standing motor deficits following poliomyelitis-like palsy in children. However, we recommend performing partial nerve transfer as early as possible after recovery from flaccid paralysis and also use of nerves that derive from narrow spinal cord segments. After denervation, children's neuromuscular systems seem to have the ability to regenerate after a much longer period than has generally been believed. This speculation is based on only a single case report; thus, more experience is needed before this generalization can confidently be made.

Conflicts of interest

None.

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