Nerve Root Replantation

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KEYWORDS

- Brachial plexus injury • Spinal nerve root avulsion
- Spinal cord replantation • Functional recovery
- Pain • Plasticity

Spinal nerve root avulsion injury is a lesion where the nerves linking the spinal cord to the muscles or various sensory receptors have been torn or avulsed from the spinal cord (**Fig. 1**). This is a "longitudinal spinal cord injury," as motor and sensory fibers within the affected spinal cord segments are interrupted. The root avulsion injury is most frequent in severe brachial plexus lesions from high-energy trauma such as a motorbike accident at high speed, in which the forequarter has been violently impacted or has become dissociated from the trunk. Avulsion of at least one spinal nerve root of the brachial plexus has been estimated to occur in about 70% of all brachial plexus lesions.[1] The lower roots of the plexus, ie, C8 and T1, are more easily avulsed than the upper roots C5 to C7, because the latter are supported by ligaments at the exit foramina. Traction forces strong enough to overcome those ligaments can cause a complete C5-T1 brachial plexus avulsion injury.

Although the exact process leading to root avulsion is not completely understood, two mechanisms have been described (**Fig. 2**). The *peripheral mechanism* is a lateral or peripheral traction force onto the root and spinal nerve that, when forceful enough, pulls the root off the spinal cord and displaces the roots with the ganglia out of the spinal canal and the intervertebral foramina.[2] This is prevalent in adult trauma cases. After such a traction, the roots and the dorsal root ganglion can be found in between the scalene muscles or, even further distally, underneath the clavicle. In the *central mechanism,* the roots have been detached from the spinal cord, but the ganglion and the roots have not been displaced out of the spinal canal or the foramen. This paradoxical situation is thought to depend on an axial rather than a lateral force occurring during a shift in the spinal cord from excessive lateral flexion of the cervical spine.[2] In that movement, the spinal cord pulls in cranial direction away from the roots that are anchored at the intervertebral foramina. This type of root avulsion is likely to occur when there has been an impact to the cervical spine, sometimes with vertebral fractures, rather than trauma to the shoulder. A mixture of peripheral and central mechanisms of root avulsion is often seen in the obstetric brachial plexus injury.

The clinical effect of the root avulsion injury is loss of movements and sensory dysfunction in the affected limb, ie, a monoplegia. Early, in many cases on the day of injury, there is a typical severe excruciating pain. It consists of two components: one is constant as dull ace and the other is intermittent as shooting severe jolts of a burning and compression sensation.[3] In about 10% of severe brachial plexus avulsion injuries there is a Brown–Sequard syndrome most likely from compromised circulation in the affected spinal cord segment. Other severe conditions may follow spinal nerve root avulsion. Spinal cord tethering or herniation through the dural defect after the root avulsions can give rise to tardy Brown–Sequard syndrome as well as myelopathy with spastic paraplegia, which has been reported to occur late after this injury.[4–7] The onset of such symptoms ranged from 6 months to 37 years after root avulsion. Adhesions and arachnoid cysts, in some cases from singular root avulsion, cause compression of the spinal cord and interference with circulation, particularly a chronic venous congestion resulting in ischemic insults. Significant

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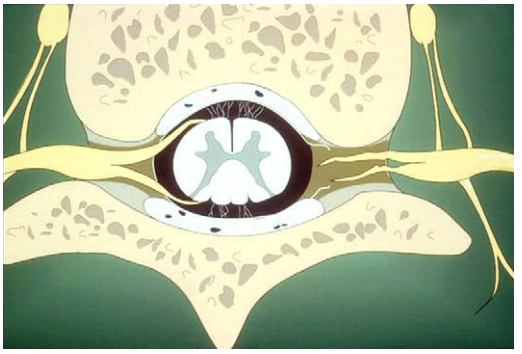

Fig. 1. Avulsion of spinal nerve roots. The connections between the CNS in the spinal cord and the extensions in the nerve roots and PNS are interrupted. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

improvement of long tract symptoms with arrest of progression of the motor dysfunction followed surgical decompression. Other rare phenomena late after root avulsion injury includes hemosiderosis, which can be progressive and fatal.[8]

BASIC SCIENCE

At the cellular level, the root avulsion injury triggers a cascade of molecular events that leads to degeneration of nerve fibers and death of nerve cells within the spinal cord. The early response in motoneurons to avulsion means a shrinkage in size of the soma and dendrites. The number of synaptic connections with the injured neuron is diminished, especially on the cell body and proximal dendrites.

There is a preferential loss of excitatory inputs to the motoneuron in this situation, probably leaving the cells under an inhibitory influence during the repair process.[9] These events mirror a shift in the metabolism of the severed motoneurons from subserving the role for the motoneuron as a commander of motor activity to a state where the primary goal is to survive and produce new axons. This is reflected in an increase in mRNA expression of proteins linked with cell survival such as growth factors (ie, brain derived neurotrophic factor [BDNF]) and receptors[10] as well as proteins for axonal growth (ie, growth associated protein [GAP-43]).

Motor as well as sensory neurons within the spinal cord are rapidly killed by root avulsion.[11,12] Disconnection from the periphery, meaning an interrupted supply of neutrotrophic factors together with vascular trauma leading to excitooxicity, drastically reduces the number of motoneurons up to about 90% of the normal population.[9,11] Other mechanisms to motoneuron death, such as an inflammatory response to avulsion by means of microglia activation from cytokines, has also been described.[13] Two weeks after such an injury about half of all motoneurons in the pertinent spinal cord segment have disappeared whereas an almost instantaneous 15% death of dorsal horn neurons occurs.[12] There is a further motor neuron death over time.[14] In contrast, a dorsal root avulsion does not induce any significant nerve cell death in the dorsal root ganglion.[12] Obviously the

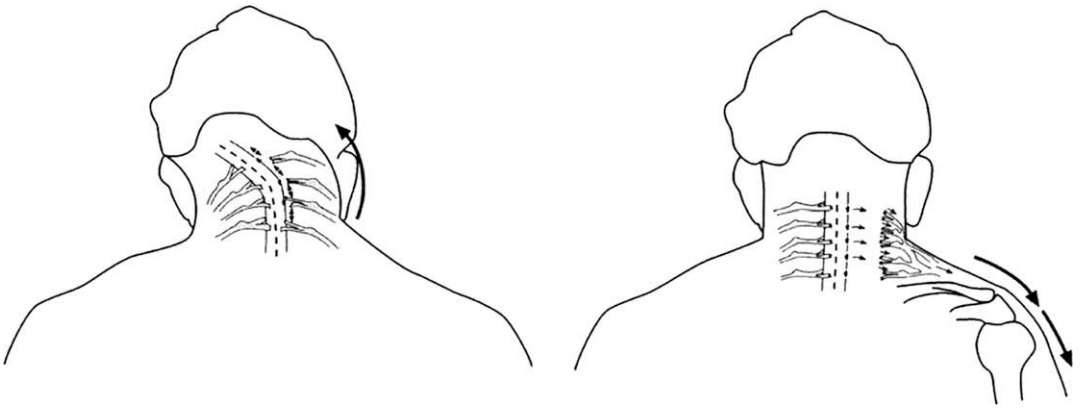

Fig. 2. Root avulsions. The central (*left*) and peripheral (*right*) mechanisms of root avulsion. In the central mechanism there is a forceful lateral flexion of the cervical spine and spinal cord (*large arrow*).There is a longitudinal shearing force that separates the roots from their attachments with the spinal cord (*small arrows*) without the roots being displaced outside the spinal canal. The spinal cord is pulled in a cranial direction in relation to the spine, whereas the roots are held by their attachments to the spine at the intervertebral foramina. The loose suspension of the shoulder girdle makes the brachial plexus particularly susceptible to traction injury when there is a trauma that separates the shoulder from the neck (*large arrows*). Root avulsions with displacements of the roots outside the spinal canal (*small arrows*) occur if the force is of significant magnitude. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

central but not the peripheral sensory neuron is more sensitive to root trauma. The loss of dorsal horn neurons is of course of importance for the development of the classical brachial plexus avulsion pain.

The recent development and gain in knowledge from studies of molecular biology has demonstrated the importance in timing of repair of nerve injuries. One month after injury the expressions of growth factors and their receptors have already declined to the extent that outcome of repair is less favorable than if done immediately after the injury (for review see Gordon and colleagues).[15] With regard to root avulsion injury, time-dependent neuron death adds to the urgency in reconstructing these injuries as replanting the avulsed ventral root to some extent maintains the population of spinal cord neurons.

The spinal cord injury that follows from root avulsion can today be repaired with a functional outcome in humans.[16–21] The surgical strategy is based and developed from a long series of laboratory experiments. The basic requirements for regeneration of function after a spinal nerve root avulsion injury are the survival of nerve cells situated close to the injury and the regrowth of new nerve fibers along a trajectory consisting of central nervous (CNS) growth-inhibitory tissue in the spinal cord and peripheral nervous (PNS) growth-promoting tissue in nerves. This is the first example of a spinal cord lesion that can be treated surgically leading to restoration of activity and alleviation of pain (for a full description, see Carlstedt).[16]

ASSESSMENTS

Clinical

The ''classical'' history of a brachial plexus avulsion injury is that from patients involved in a motorcycle accident where the forequarter has been impacted resulting in a monoplegia. The patient is often able to describe the typical root avulsion pain as a constant dull, crushing, or burning pain with superimposed lightening jolts of severe sharp pain shooting down the arm.

On inspection, a Bernard-Horner sign suggests but is not a proof of avulsion of the lower roots to the plexus. Bruising and swelling at the base of the neck are ominous signs of a lesion of the longitudinal neurovascular structures.

Examination can reveal spared muscle function, but activity in the serratus anterior muscle is possible in spite of a complete brachial plexus avulsion injury. Some fascicles to the long thoracic nerve can be spared at the C5 root, although the roots are found pulled out of the foramen. The brachial plexus can, if in situ, be palpated as a ridge just lateral to the sternocleidomastoid muscle. Tapping on this site can elicit a sharp electric sensation shooting down the arm, ie, the Tinel's sign, if there are some root or nerve stumps still in continuity with the spinal cord. In cases of a complete brachial plexus avulsion injury there is no Tinel's sign to be found, which of course is a bad sign.

Ancillary

Without any ancillary examinations, it can be initially assumed that the patient has a total brachial plexus avulsion injury if no Tinel's sign can be proved in a patient with a complete paralysis, a Bernard-Horner sign, and typical avulsion pain. Electrophysiology is of little value in the immediate posttraumatic period. It is 2 to 3 weeks later when typical denervation signs, ie, positive sharp waves and fibrillations, become obvious in the affected muscles. The presence of a sensory nerve action potential (SNAP), together with loss of sensation is, however, a useful sign of root avulsion, as the sensory neurons in the avulsed dorsal root ganglion will be alive and conducting distally but not centrally for perception.

Radiographs of the neck and upper thorax give valuable information regarding fractures and the possibility of cervical spine instability. Fractures of the transverse processes are often associated with avulsion injury to the pertinent spinal nerve roots and traumatic insult to the vertebral artery. Fracture dislocation of the first rib indicates a severe proximal or intraspinal lesion to the lower trunk of the plexus and to the subclavian artery. A raised hemidiaphragm on a chest radiograph reveals a most proximal C5 lesion.

Magnetic resonance imaging (MRI) is at present not optimal for considering individual roots.[22] Myelography followed by computerized tomography (CT) appears still to be the current imaging of choice for the assessment of roots;[23] however, it does not allow a full assessment of C8 and T1 roots because of beam-hardening artifacts from the shoulder. False or overdiagnosis of root avulsions is possible and the outcome could be difficult to understand in cases of severe contrast leakage.

SURGERY

The Exposure

The patient is in a ''strict'' lateral position.[24] The head is supported in a Mayfield clamp with the neck slightly flexed toward the opposite side (**Fig. 3**). The head-up position of the operating table is used to prevent venous congestion, particularly of the epidural veins. During the procedure, the operating table's tilting facilities can be used

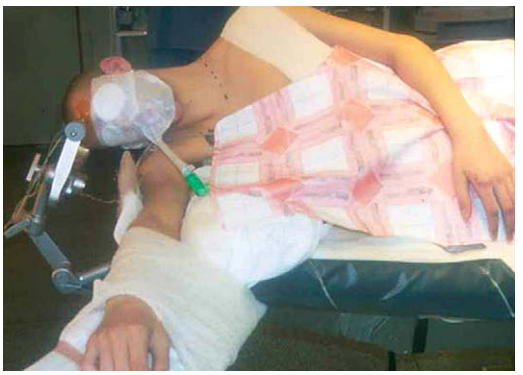

Fig. 3. Patient in a lateral position with head fixed in a Mayfield clamp and shoulder pulled down by Elastoplast. Skin incision is indicated.

when going from medial to lateral exposures of the brachial plexus. A skin incision from the jugulum into the posterior triangle of the neck toward and passing the spinous process of the C5 vertebra is performed (see **Fig. 3**). Platysma and skin flaps are raised and held either by stay sutures or a thyroid retractor. Dissections first are performed in the posterior triangle of the neck of the injured extraspinal part of the brachial plexus and the spinal accessory nerve as it emerges from the posterior aspect of the sternocleidomastoid muscle (**Fig. 4**). The accessory nerve can be cut as distal as possible to be used later for transfer to the suprascapular nerve.

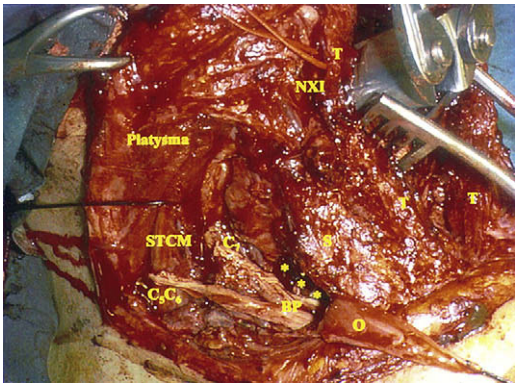

Fig. 4. Intraoperative picture of exploration of brachial plexus. The platysma has been elevated and the sternocleidomastoid muscle, the scalenei (S) and the trapezius (T) muscles are indicated. The omohyoid (O) muscle has been divided. The upper nerve roots, C5-C7, have been avulsed from the spinal cord. Asterisks indicate the empty foramina. A sling is applied around the accessory nerve (NXI). Retractors in the posterior part of the wound to expose the cervical spine. (*From* Carlstedt T, Anand P, Hallin R, et al. Spinal nerve root repair and replantation of avulsed ventral roots into the spinal cord after brachial plexus injury. J Neurosurg (Spine 2) 2000;93:237–47; with permission.)

Endoscopy

When there are avulsions and the spinal nerve and roots have been pulled out from the spinal and intervertebral canal, it is possible to introduce an endoscope through the empty foramen. A small 2 mm in diameter joint arthroscope has been used. The lower foramina, ie, the C7-T1 intervertebral canal, are best suited for this maneuver as they are larger than the foramina above and do not contain the vertebral vessels (**Fig. 5**).With this technique, more information regarding remaining intradural root stumps or full root avulsions can be gained than through ancillary investigations (ie, electrophysiology or CT-myelography), particularly regarding the lower roots to the brachial plexus without proceeding to a full inspection after a laminectomy.

The second part of the dissection is to reach the cervical spine in the posterior part of the incision. No further skin incision is needed to perform this dissection. The posterior tubercles of the transverse processes of C4 to C7 can be palpated, and they are followed in the dissection through a connective tissue plane between the levator scapula and the posterior and medial scalene muscles (**Fig. 6**). The longissimus muscle deep to this plane must be split longitudinally to expose the posterior tubercles of the transverse processes and the hemilaminae (see **Fig. 6**). The paravertebral muscles are detached from the hemilaminae and pushed dorsomedially. After a standard hemilaminectomy taking away the medial part of processes for the facet joints using drills or rongeurs and breaching the periosteum (which could be confused with the dura mater), hemostasis of epidural veins, which laterally can cause irritating bleedings, is achieved. Sometimes a rent in the dura mater has been caused by the avulsion trauma and cerebrospinal fluid (CSF) starts to leak before the dura has been formally opened. The dura mater is incised longitudinally and stay sutures applied (**Fig. 7**). The denticulate ligaments that are preserved are cut from their lateral attachments. Stay sutures are applied to the part of the denticulate ligament that runs along the side of the spinal cord to gently rotate the cord (see **Fig. 7**). With this approach and with the help of the stay sutures in the denticulate ligament, it is possible to reach to the anterior aspect of the spinal cord at the ventral root exit zones. At this stage it is possible to see if the roots have been completely avulsed and displaced outside

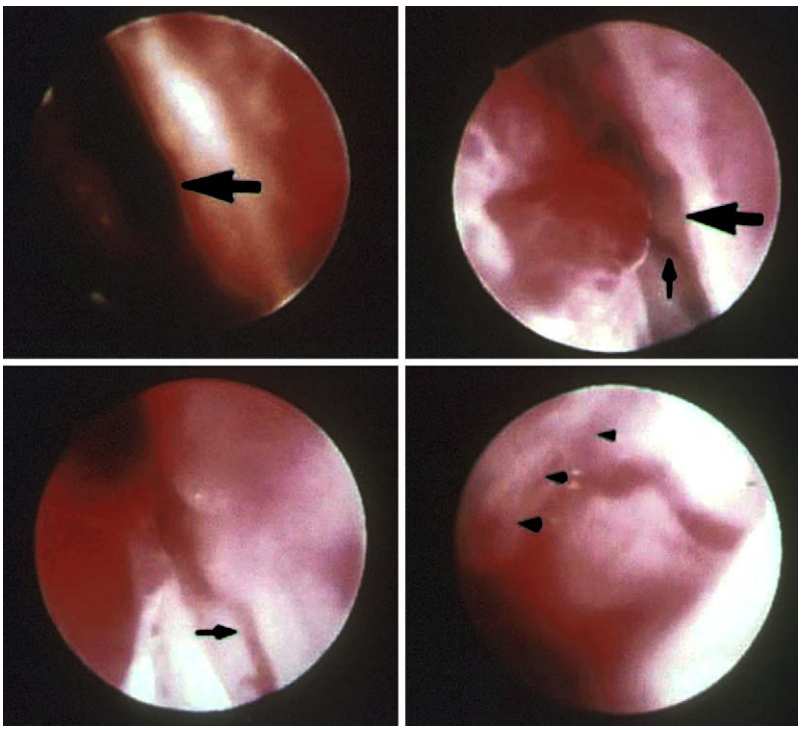

Fig. 5. Endoscopy of cervical spinal cord through empty intervertebral foramina after brachial plexus avulsion injury. Top left: at the external foramen (*arrow*). Top right: blood vessel (*arrow*) within the canal. Lower right: view of the spinal cord with blood vessel (*arrow*) on its surface. Lower right: arrows indicate site of ventral root avulsion. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

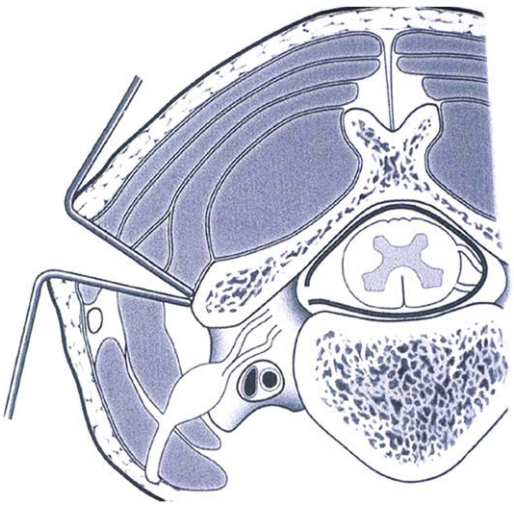

Fig. 6. Schematic drawing of a transverse section through the lower part of the neck illustrating the lateral approach to the cervical spine. The nerve roots have been avulsed from the spinal cord and the subdural space. (*From* Carlstedt T, Anand P, Hallin R, et al. Spinal nerve root repair and replantation of avulsed ventral roots into the spinal cord after brachial plexus injury. J Neurosurg (Spine 2) 2000;93:237–47; with permission.)

the spinal canal (see **Fig. 7**) or still remain within the subdural space in the spinal canal.

The Repair

Detached nerve roots can be retrieved through the intervertebral foramen if the surgery is performed within days after the accident. This is done with great care using a tube or a catheter, avoiding injury to the vertebral vessels (see **Fig. 7**). This is not possible if the surgery is delayed more than 2 weeks, as the displaced roots will be scarred and the intervertebral foramen sealed by scar tissue. In some cases, the avulsed roots can be situated within the subdural space allowing for a direct replantation. In most cases, however, nerve grafting is the only possibility to reconnect the spinal cord to the avulsed roots (**Fig. 8**). The nerve graft (taken preferentially from the superficial radial, the medial cutaneous nerve of the ipsilateral forearm, or the sural nerve) is split into separate fascicles for two to four different spinal cord segments and introduced to a depth of about 1 to 2 mm by means of a probe, leaving another 2 mm of white matter to the ventral horn and the motoneuron pool. Useful in this maneuver is a small Rhoton instrument in the shape of a hockey stick, the

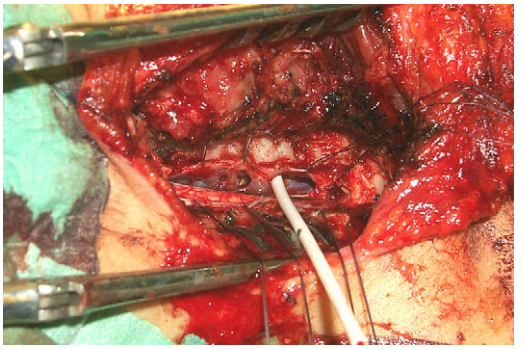

Fig. 7. Intraoperative picture. The partly torn dura has been opened. No remaining roots are seen in the subdural space. A catheter is introduced through C7 intervertebral canal, with the other end in the posterior triangle of the neck ready to apply nerve grafts. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

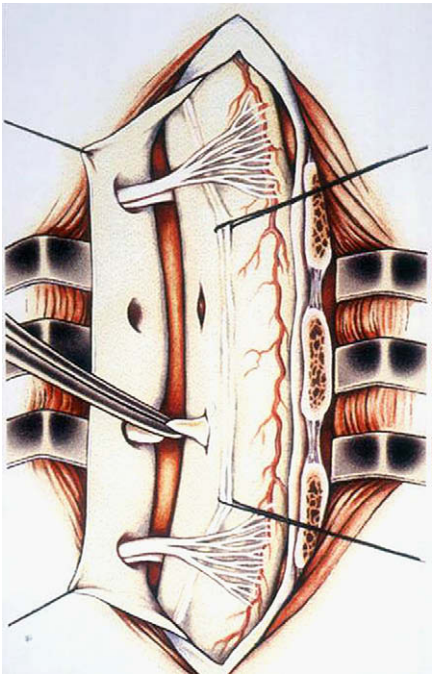

Fig. 8. Drawing depicting the exposed spinal cord after a lateral approach and hemilaminectomy. The dura mater has been opened, and by stay sutures in the denticulate ligament, the spinal cord has been slightly rotated for access to its ventral part. Through slits in the pia mater and the spinal cord surface, nerve grafts are implanted superficially into the spinal cord. (*From* Carlstedt T, Birch R. Management of acute peripheral nerve injuries. In: Winn R, editor. Youmans neurological surgery. Philadelphia: Saunders; 2004; with permission.)

"blade" of which being 1 to 2 mm in length can be used as a depth gauge when implanting the root or the nerve graft. The position of the implanted grafts is retained by glue (Tisseel). Stitching the graft to the pia mater can also be done, but is difficult. In case of root ruptures the nerve graft is directly apposed to the trimmed end of the ventral root stump. The nerve grafts are pulled trough the intervertebral foramen for C7 or C8 spinal nerves (see **Fig. 8**). If the foramen is blocked, the grafts are passed through the incision in the dura and outside the vertebral canal. The grafts are connected to the avulsed roots in the posterior triangle of the neck where they have been displaced by the traction trauma. During the intraspinal procedure, spinal cord monitoring of motor tract function (MEP) together with somatosensory-evoked potential (SSEP) is performed. The dura is not usually closed but the opening in the dura is covered by artificial dura or a vein patch and Tisseel glue. A lumbar drain could be applied for about 1 week to prevent the development of CSF leakage. The patient is mobilized after a week but the arm is kept in a sling for a total of 6 weeks.

Outcome

Motor recovery

Most patients started to recover muscle function within 1 year after the injury, seen as muscle twitches (Medical Research Council [MRC] grade 1/5) in the pectoral muscle.[17,18,21] Muscle activity returned first in shoulder muscles followed by upper arm muscles about a year later and in a few cases as far distally as to one or two forearm muscles during the third year. There was an eventual increase in power in shoulder girdle muscles, ie, serratus anterior, pectoral, and supraspinatus muscles to a significant power, in many cases reaching a normal magnitude ie, MRC 4-5/5 (**Fig. 9**).

There was less power in upper arm muscles that never reached a normal but a useful level ie, MRC 3-4/5. Obviously there is not a specific motoneuron to the original target regeneration. The regrowing new axons try to reinnervate the first possible muscle target, which are the shoulder muscles.

Consequently, there is less reinnervation in more distal muscles (**Fig. 10**). Muscle power in some forearm muscles reached only about MRC 2/5, ie, not functional. However, spinal cord replantation after a complete avulsion injury in a preadolescent boy resulted in recovery of hand function together with useful activity in shoulder and arm.[21] Intrinsic muscle recovery was verified by electromyography (EMG) and he developed a transverse palm and pinch grip (**Fig. 11**) that is useful in many daily

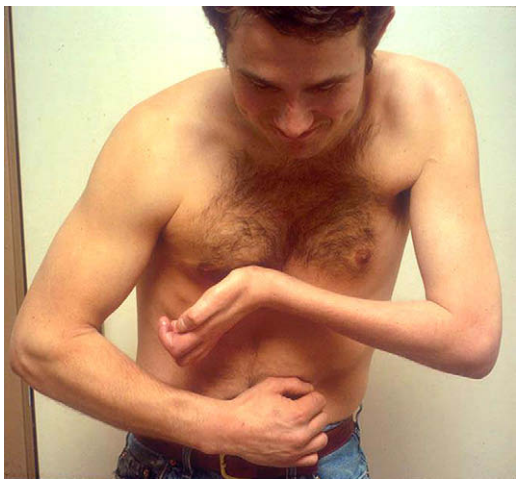

Fig. 9. Photograph showing return of function 3 years after replantation surgery in a case of complete brachial plexus avulsion injury. Good muscle activity in shoulder and upper arm muscles with some muscle contraction in radial forearm muscles.

activities as well as making it possible for him to play drums with the affected hand.

The final muscle power in major proximal muscles of MRC Grade 4/5 was noted only in patients who had been operated within a moth or earlier after the trauma. Patients operated late recovered very little or nonuseful muscle power. This is consistent with the experimental findings of time-dependent motoneuron loss after avulsion injury.[14] Moreover, motoneuron programs for repair are available for a limited period after injury and are effective only if the severed axons are offered a conduit for regrowth.[15] When reconstruction is delayed, the growth-associated genes are downregulated and the neurons become atrophic or die. With delay of repair there is also an impairment of Schwann cell ability to support regeneration[25] as well as the deterioration of the denervated muscles.[14] In spite of a considerable motoneuron loss from the root avulsion trauma, there was a consistent recovery of muscle power, which in proximal muscle groups was near to normal. Of importance in this recovery is obviously the ability of surviving motoneurons to establish larger than normal motor units that can compensate for an 80% loss of neurons.[26]

Magnetic cortical stimulation demonstrated and verified the clinical observation of connectivity from motor cortex to the previously denervated muscles through the reconstructed spinal cord–peripheral nerve trajectories. The latency of the muscle response was generally longer than in the intact arm, indicating that the regenerated nerve fibers were not fully developed and less myelinated than on the normal side.

Severe co-contractions or synkinesis between agonistic and antagonistic muscles such as biceps and triceps occurred in most patients. Nonspecific recruitment of motoneurons through the implanted PNS conduit and lack of guidance or misdirection of axons causes aberrant muscle reinnervation.

Inappropriate muscle reinnervation applies also to the phrenic motoneurons regenerating to arm muscles after replantation of ventral root or PNS graft, causing respiratory-related limb muscle contractions. This peculiar type of synergism was noted in some patients where the implantation into the C5 spinal cord segment provoked spontaneous contractions of arm muscles in synchrony with respiration, ie, "the breathing arm" phenomenon.[21] Muscle contractions synchronous with spontaneous inspiration were generally related to recovery of volitional function but could also occur in muscle without voluntary function, ie, MRC 0/5. Different combinations of muscles mainly in the C5 myotome showed this activity, ie, pectoral, deltoid, biceps, and triceps muscles.

The occurrence of the breathing arm phenomenon in patients after complete brachial plexus avulsion injury with subsequent spinal cord replantation is caused by CNS or spinal cord regeneration. The anatomic background to this is the caudal part of the phrenic motoneuron nucleus is extending into the C5 segment. These neurons are situated most medially in the ventral horn and after reimplantation of an avulsed ventral root or

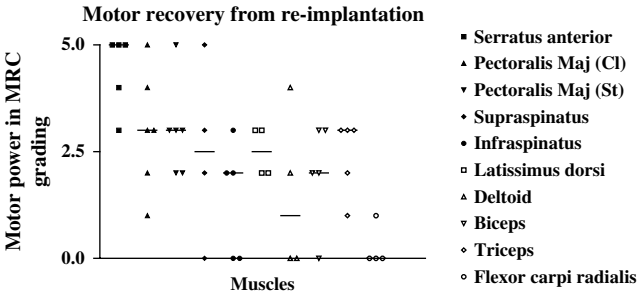

Fig. 10. Diagram showing recovery of muscle power after spinal cord replantation of avulsed ventral roots. Power decreases in distal direction. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

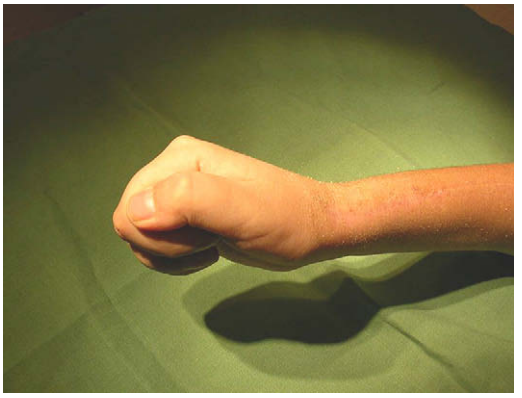

Fig. 11. Recovered transverse hand and pinch grip in a preadolescent boy who sustained a complete brachial plexus avulsion injury. Hand function returned 3 years after replantation surgery.

a peripheral nerve conduit into this segment phrenic motoneurons are recruited to extend axons along the peripheral nerves to the arm rather than into the phrenic nerve to the diaphragm (**Fig. 12**).

The lack of sensory reconnection with the pertinent spinal cord segment after intraspinal repair means lack of muscle proprioception. In such a situation without Ia afference there is no reciprocal inhibition of antagonistic muscles. A mass movement without the ability to activate individual joints is a sign of supraspinal-led activity without proprioceptive feedback and to some extent this deficient afferent control over muscle function leads to co-contractions. Some degree of muscle proprioception would be necessary for good muscle function. A central motor program alone may, however, be sufficient to execute learned simple movements such as elbow flexion. Limb function and, in particular, purposeful movements have been described in a rare example of sensory neuropathy with loss of muscle afferents.[27]

Sensory recovery

After complete C5-T1 root avulsion injury, sensation is poor after this type of surgery, where only motor conduits have been reconstructed.[20] Pinprick sensation was usually subnormal in the C5, diminished in C6, and absent in C7-T1 dermatomes. Sense of joint position could be appreciated at the shoulder but also at the elbow. The return of some sensory function such as proprioception, temperature, and pain in avulsed dermatomes is unexpected and difficult to explain, as only the ventral roots have been reconnected to the pertinent spinal cord segments. Whether this function depends on extensions of new processes from dorsal horn neurons along the implanted ventral root or whether it is related to collaterals from adjacent spinal cord segments is at the present unknown.

Sensory stimulation within the avulsed dermatomes was mostly perceived abnormally and or experienced at remote sites as referred sensation.[20] Intraspinal afferent sprouting producing terminal fields extending into spinal cord segments that have sustained root avulsion and deafferentation[28] could explain such phenomena as referrals of sensation from the region of the neck to the hand or the other way around. Classical "right way" referral of sensation when sensory

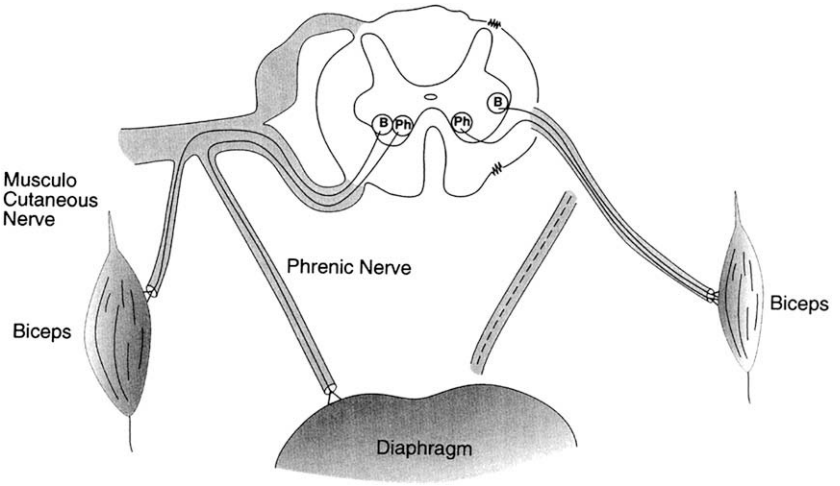

Fig. 12. Diagram showing erroneous spinal cord regeneration of axons from the phrenic motoneuron nucleus in the spinal cord, causing the "breathing arm" phenomenon. Ph, phrenic motoneurons; B, biceps motoneurons. (*From* Carlstedt T. Central nerve plexus injury. London: Imperial College Press; 2007; with permission.)

stimulation of the hand was perceived at the trunk, neck, or face or ''wrong way'' referral of sensation from the face, neck, or trunk to the affected arm occurred (**Fig. 13**).[20,29] In the early weeks after injury and repair there was referral of sensation from central parts of the body, even viscera to the affected arm.

Pain

The severe pain sustained by patients suffering from brachial plexus injury is typical[20,30] and is presumed to be caused by the generation of abnormal activity in deafferented spinal cord segments.[31] There is a correlation between number of roots avulsed and severity of pain.[20] Remarkable is that in patients with complete avulsion injury to the brachial plexus followed by ventral root replantation there is reduction of pain correlated to return of muscle activity rather than other qualities of function.[20,29] In patients who had recovery of motor function limited to the upper part of the extremity there is persisting pain in the hand. In a case of a preadolescent boy with complete plexus avulsion and after replantation there was motor recovery in all parts of the arm and the hand. There was a complete alleviation of the severe pain when motor function recovered. The mechanism behind this is difficult to explain, but selective loss of motor fibers after ventral rhizotomy can provoke pain in animals[32,33] and humans.[34] In some patients there was allodynia to mechanical and/or thermal stimulation.[20] The area of allodynia was at the border zone of affected and unaffected dermatomes, usually at the border of T1 and T2 dermatomes, at the back of the elbow. The allodynia was not bothersome and minor in comparison with the deafferentation pain.

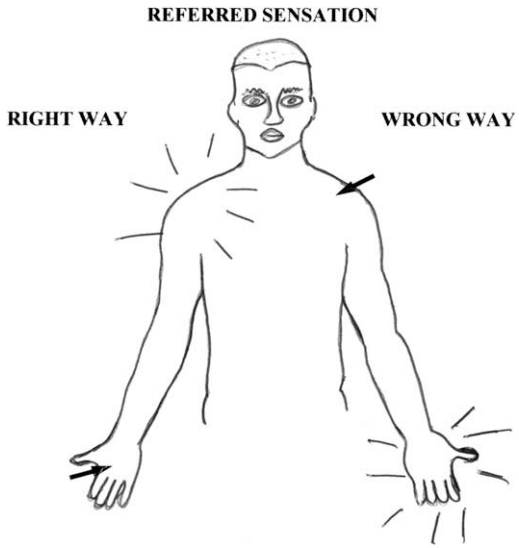

Fig. 13. Referral of sensation. "Right way" referral of sensation: Touching the hand is perceived in the upper part of the trunk because of growth of transferred nerves into the hand. "Wrong way" referral of sensation: Touching an area at the base of the neck or the face is perceived in the hand because of cortex plasticity.

Plasticity

In cases of muscle co-contraction there was an eventual tendency for one of the antagonistic muscles—the biceps or the triceps—to dominate and for the antagonistic to be functionally suppressed indicating a degree of plasticity, but isolated contraction in individual muscles could still not be performed. Synkinesis and breathing arm phenomena were noted in long-term follow-up indicating a stationary condition.[21] In general there was no sign of spinal cord plasticity to modulate muscle activity to become purely voluntary. The lack of plasticity as well as methods to correct the misdirection of motoneurons is known also from children with obstetric brachial plexus injury.[35] In experimental studies, this lack of modification of spinal motoneurons connected inappropriately even in the young or immature animal has been documented.[36] There seems to be an inability of motor programs to change when innervating a new target and that motor circuits are usually maintained, even after the motoneurons innervate a foreign muscle.[37]

Contrary to the lack of spinal cord plasticity is the well established fact that supraspinal parts of the central nervous system can become reorganized after deafferentation, which may explain the ''wrong way'' referred sensations (see **Fig. 13**).[38] Plasticity and reorganization of the somatosensory cortex, which may underlie referred sensation, have been demonstrated by imaging studies.[38,39] The hand, trunk, and face cortical representations are situated adjacent to each other. After dennervation of the hand, expansion of inputs from the face or trunk into the former hand territory can occur. Reorganization of the somatosensory cortex by expansion of the adjacent sensory area of the cortex area may explain referred sensation, but larger scale reorganization could also occur in different levels, including the thalamus.[40]

The ''right way'' of referral of sensation (see **Fig. 13**) appears as an early sign of recovery. It seems as if cortical circuits within the somatosensory system are not easily corrected for deafferentation and eventual misdirectional growth of sensory fibers can occur. The ''wrong way'' referral of sensation (see **Fig. 13**) on the other hand

indicates plasticity rather than recovery. This is obvious in patients who even a long time after surgery have not developed sensation in the hand but perceive sensation in the hand when the neck, trunk, or face is touched. This phenomenon could occur early after the injury, suggesting unmasking of preexisting connections.[41] Intracortical sprouting could be the reason for later-appearing ''wrong way'' referral of sensation.[38]

Cortical reorganization has been correlated with severity of neuropathic pain.[42] There is no relationship between alleviation of pain and referral of sensation in these patients, although both phenomena are thought to be due to plasticity in the central nervous system.[20] Instead, there is correlation between pain alleviation and motor recovery. Successful motor recovery could lead to reestablishment of normal inhibitory processes that reveres the cortical process leading to pain.

Border zone allodynia could depend on abnormally sensitized peripheral nociceptic fibers that induce secondary changes in reorganization of the dorsal horn and central processing, leading to spinal cord hyperexcitability and pain.[43,44] The intact nociceptors of the adjacent uninjured spinal nerves may acquire abnormal spontaneous activity and chemical sensitivity may play a role in creating, or maintaining, an abnormal pain state.[34,45]

COMMENTS

The root avulsion injury is a spinal cord injury that interrupts defined populations of neurons, ie, the ''final common pathway'' for motor command and the sensory pathway from the peripheral sensory neurons. Patients with such spinal cord injuries from brachial or lumbosacral plexus injuries including cauda equina lesions can recover function from the reimplantation spinal cord surgery. This relatively less complicated injury compared with a ''classical'' transverse spinal cord lesion is obviously advantageous regarding chances for recovery.

Spinal cord surgery to restore connectivity after spinal nerve root avulsion injury can recover function and alleviate pain, as well as rescue spinal cord nerve cells and reestablish spinal cord circuits. In my opinion, this surgical technique is therefore today the most promising treatment in cases of longitudinal spinal cord or root avulsion injury. This strategy has encouraging prospects for future treatment of brachial and lumbosacral plexus injuries and possibly the most caudal transverse spinal cord injury, ie, conus medullaris injury. A transverse lesion of the conus medullaris would affect mostly the lower motoneurons and CNS parts of the peripheral sensory neurons together with nervous control over bladder and bowel function. A transverse caudal spinal cord injury at a conus level has therefore many similarities with the root avulsion or the longitudinal type of spinal cord injury and could in the future be considered for similar type of surgical strategy. Avulsed roots could be implanted cranial to the site of the transverse spinal cord lesion to reverse lower extremity paralysis with return of locomotion and reinnervate pelvic targets to reverse bladder and bowel dysfunction.

The original observations in laboratory experiments have taken a long time to become applied to human clinical practice. At present, the shortcomings of this technique are proportionate to the delay of surgery with death of nerve cells and incomplete and unpredictable sensimotor recovery. To reach further, to recover useful sensorymotor function and to alleviate pain, it is of course necessary to pursue research and development of basic and clinical science. Surgical and imaging refinements are also obligatory to achieve a full or near normal functional restitution after brachial plexus and lumbosacral plexus avulsion injuries with minimal risks and efforts for the patient. A number of already available pharmaceutical substances, molecular products, and cellular therapies will be applied in the future to continue the achievement of recovery of injuries at the spinal cord surface but also to help in finding cure for the more complete spinal cord injuries (for further reading see Carlstedt).[16]

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