Preserved spinal dorsal horn potentials in a brain-dead patient with Lazarus’ sign

Case report

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The case of a brain-dead patient with complex movements of the extremities (Lazarus’ sign) is reported. This is the first description in the literature of short-latency somatosensory evoked potentials (SSEP’s) following median-nerve stimulation by a nonencephalic reference method. The scalp P14 wave (a far-field positivity with a peak latency around 14 msec that originates from the cervicomedullary junction) disappeared, and the spinal N13 wave (a near-field negativity with a 13-msec peak recorded on the posterior neck and generated by the cervical dorsal horn) was preserved. Respiratory-like movement was also seen in this case. The SSEP findings support the hypothesis that both Lazarus’ sign and respiratory-like movement have a spinal origin.

Key Words: brain death, Lazarus’ sign, spinal respiration, somatosensory evoked potentials

In the brain-dead state, spinal reflexes may be either present or absent, the disappearance of spontaneous respiration is an essential criterion. Complex movements of the extremities, called Lazarus’ sign, or respiratory-like movements in brain-dead patients have been reported. However, there have been no reports on short-latency somatosensory evoked potentials (SSEP’s) recorded on a nonencephalic reference method in Lazarus’ sign since our first report in 1988. Use of nonencephalic references is essential when studying the individual functions of the cervical cord and the cervicomedullary junction near the cuneate nucleus. After our 1988 report, we observed two brain-dead patients with Lazarus’ sign; an SSEP study was completed on one of these patients. The mechanism of Lazarus’ sign and the respiratory-like movements seen in brain-dead patients are discussed.

Case Report

This 67-year-old woman suddenly developed a severe headache on January 30, 1991. A computerized tomography (CT) scan was obtained at a nearby hospital, and subarachnoid hemorrhage was diagnosed. She was transferred to our hospital the same day.

Examination. Neurological examination was normal except for a mild headache and stiff neck. Angiography showed a large aneurysm arising from the left vertebral artery-posterior inferior cerebellar artery junction in a high location.

Operation. On February 14, the aneurysm was clipped via the left suboccipital approach. Postoperatively, the patient’s state of consciousness deteriorated to somnolence. The next day, a subdural hematoma in the posterior fossa was detected and immediately evacuated. She suddenly entered a state of deep coma 1½ hours after surgery, requiring artificial ventilation as spontaneous respiration disappeared. A repeat CT scan disclosed a huge pontine hemorrhage. Continuous intravenous infusion of dopamine hydrochloride was begun on February 16 to maintain the patient’s blood pressure, but she continued to deteriorate.

Hospital Course. On February 18, the patient fulfilled all the criteria of brain death. At 10:40 a.m., the electroencephalography (EEG) recording was flat, axillary temperature was 35.6°C, pulse rate was 130 beats/min, and blood pressure was 80/60 mm Hg. The pupil diameters were 5 mm bilaterally. All of the brain-stem...
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reflexes, including light, corneal, oculocephalic, vestibular, ciliospinal, gag, cough, and mandibular, were absent. Of the deep-tendon reflexes, the biceps, triceps, and brachioradial reflexes were present bilaterally, but the patellar and Achilles tendon reflexes were absent. Of the superficial skin reflexes, both the abdominal and the plantar reflexes were missing, and no pathological reflexes were found. Apnea testing was performed via administration of 7 liters 100% O2 per minute by insertion of an aspiration tube into the trachea. Observation for 13 minutes disclosed neither spontaneous respiration nor movement. The PaCO2 level rose from 35.5 to 63.3 mm Hg during the test.

At 11:05 a.m. on February 19, repeat EEG revealed the same flat recording, and the patient's vital signs showed no marked change. The pupils were markedly dilated bilaterally (to 7 mm in diameter); all other neurological findings were the same, except for the disappearance of the biceps reflexes. An apnea test was performed. The PaCO2 was 45.3 mm Hg before the test. Six minutes after removal of the respirator, movement appeared in the right upper extremity; the right arm flexed at the elbow, elevated from the bed, abducted, and then returned to its original position. The apnea test was stopped, and an evoked potential study carried out. The apnea test was repeated twice more, but no spontaneous movements were observed although the test period was prolonged to 20 minutes.

At 11:15 a.m. on February 20, brain death was declared and consent for final respirator removal was obtained from the patient's family. The possibility of the appearance of Lazarus' sign was explained to the family, and a video recording was made. Five minutes after respirator removal, respiratory-like movements occurred three times; both shoulders adducted and slow cough-like movements were identified. Lazarus' sign immediately followed these respiratory-like movements. The forearms were pronated and the wrist joints extended bilaterally. Fingers on the left hand were extended, but those on the right were flexed as if grasping. Subsequently, flexion and extension in the knee and foot joints were repeatedly observed. Slow supination of both feet occurred. Finally, the left forearm was adducted to the side of the body, and the right hand pronated. These movements continued for about 3.5 minutes, during which time blood pressure was 46/35 mm Hg and pulse rate was 90 beats/min with a regular sinus rhythm. Cardiac arrest occurred at 11:35 a.m.

Evoked Potential Test. Auditory brain-stem responses after 95-dB auditory click stimuli were absent for both ears. Short-latency SSEP's were recorded following median-nerve stimulation. The contralateral Erb's point was used as the noncerebral reference. Figure 1 shows SSEP test results in a normal subject. These consist of the N9 wave at Erb's point (brachial plexus potential), the spinal N13 wave (cervical dorsal horn origin) at the posterior neck, the far-field P4 wave (brachial plexus origin), the P11 wave (cervical dorsal column), the scalp P14 wave (cervicomedullary junction), and the N18 wave (brain-stem activity below the thalamus) recorded at the frontal and parietal scalp and the N20 wave (primary cortical response) at the parietal scalp.6,7,17,23

Our normative data and those in the literature show that the latency of the scalp P14 component is almost the same as, or slightly longer than, that of the spinal N13 component.6,18 Figure 2 shows the SSEP results in the present case. Right median-nerve stimulation elicited the N6 wave at Erb's point and the spinal N13 components; no responses were identified on the scalp electrodes, except for the far-field P4 and P11 components. Left median-nerve stimulation also showed preservation of the N9 wave at Erb's point and the spinal N13 component. On the scalp electrodes, three positive potentials were present that were identified as the P9, P11, and "P13" components (but not the P14 component), since the last component appeared 1.2 msec earlier than the spinal N13 wave.

Discussion

Literature Review

Spinal reflexes are observed in about 30% to 70% of brain-dead patients.10,11 Studies have demonstrated abnormal complex movements of the extremities in brain-dead patients.9,14,16,17 Mandel, et al.,12 reported a case in which there were complex movements of the upper limbs combined with leg motions similar to walking. Ropper14 designated these movements "Lazarus' sign" after the man in the Bible story who was resurrected by Jesus Christ. Our patient showed movements after removal of the ventilator that were not elicited by noxious...
stimuli and neck flexion, whereas movements were elicited by such stimuli in the patients reported by Mandel, et al., and Turmel, et al.16

Evoked Potentials

There has been only one other report of an SSEP study of two brain-dead patients with Lazarus' sign who showed preservation of the P/N13 component and the absence of the following SSEP components.14 The P/N13 component in that study was thought to be derived from dorsal column nuclei located in the medulla oblongata.3,14 The difference between the SSEP findings and the brain-dead state that includes loss of the medulla oblongata function is considered to be due to the use of a cephalic reference in the SSEP study.3,14 The cephalic reference (Fz) electrode picks up the far-field P4 component activity, and the neck electrode records the near-field spinal N13 component.5,10 Therefore, it is not certain whether both the scalp far-field P4 and the spinal near-field N13 components were recorded when the neck-scalp montage was used.5,7,14 A non-cephalic reference method must be employed to isolate the two SSEP components.5,7,14 Our study, using a non-cephalic reference method, showed SSEP's in a patient with Lazarus' sign in whom the spinal N13 component was preserved despite loss of the scalp P4 component. These findings agree with those of our previous report.17

The spinal N13 component is a fixed generator with a horizontal axial dipole; the main contribution to the spinal N13 component is input from the C-6 dermatome.18,19,22,23 Results of spinal intramedullary SSEP tests in man showed that the spinal N13 component is similar to the postsynaptic activity in Rexed layers IV and V of the dorsal horn in animals.22

The scalp P14 component originates close to the cuneate nucleus,18,21 sometimes showing bilobed peaks.20,21 The component that precedes it has been referred to as "scalp P13", which was also found in the present case. We hypothesize that the scalp P13 component originating from nonsynaptic activity below the cuneicomedullary junction would appear clearly after the loss of the true P4 component.20 Therefore the loss of the scalp P14 component but preservation of the spinal N13 component in Lazarus' sign is in agreement with the concept of brain death; that is, loss of the cuneicomedullary junction near the cuneate nucleus and preserved cervical dorsal horn function. Somatosensory evoked potentials reflect only activity in the medial lemniscal pathway, but the findings described above suggest that Lazarus' sign is associated with the complex spinal polysynaptic reflex elicited by hypoxia or hypercapnia.17

Respiratory-Like Movements

Respiratory-like movements in our patient appeared only a few times; however, they were prolonged in the brain-dead patients reported by Ropper, et al.,15 and in our 1988 case.17 Why do respiratory-like movements appear as a spinal reflex? The medulla oblongata is the dominant center for producing spontaneous respiratory rhythm,8 but spinal reflex in respiratory muscles25 and phrenic nerve activities of spinal origin have been recorded.4,5 Animal experiments have shown that spinal respiratory movements develop spontaneously even when there is transection between the medulla and the spinal cord.1,2,8 Although rhythmic afferent inputs from peripheral receptors in cutaneous and thoracic muscle triggered by the ventilator may activate phrenic motoneuron discharges when the posterior roots remain intact,2,8 spontaneous rhythmic spinal activities have also been shown to exist for a short time in animals when reflex afferents were abolished.2,8 Aoki and his
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coworkers clearly demonstrated that respiratory neurons are distributed in the upper cervical segments (C-1 and C-2) in cats and that these neurons send descending axons to lower cervical (C-5 and C-6) and thoracic segments and sometimes to the lumbar levels. These findings suggest that the respiratory-like movements originate from complex spinal reflexes and/or activities of the cervical intrinsic respiratory center that are elicited by hypoxia or hypercapnea during apnea.

The relationship between spinal respiration and Lazarus' sign, which might be similar to locomotion, must also be considered. In our previous report, the former was followed immediately by the latter, an inverse time course was seen in the patient reported here. Viala, et al., found that the spinal phrenic rhythm is driven by the spinal hindlimb locomotor generator. Spinal respiratory and spinal locomotor generators exist independently, but the hindlimb afferents of movement increase breathing. Our present patient and our previously reported case support the hypothesis that these spinal generators are tightly coupled.

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References


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