Evidence of Axonal Reinnervation in Two Arthropod-Borne Viral Encephalomyelitis Patients

Flaviviruses are the main cause of epidemic encephalitis, yet the ratio of inapparent to apparent infections is high, ranging from 20:1 to 1,000:1 [1,2]. When symptomatic, some viruses may cause severe encephalomyelitis that may lead to lasting disability with lower motor neuron paralysis masquerading as poliomyelitis [review in 3, 4]. This syndrome is known as ‘Amyotrophy in Russian spring-summer encephalitis’ (A83) in the classification of neuromuscular disorders of the World Federation of Neurology [4]. We here report 2 patients with such a syndrome, also the subject of another, but clinically-epidemiological, report [5].

The features of our patients are summarized in Table 1. Both had neck stiffness with headache, fever greater than 39 ° C, and their cerebrospinal fluid (CSF) showed a lymphocytic pleocytosis with an elevated protein content. Ceftriazone (2 g/day) was started intravenously and the patients improved within 2 days. Both gave a history of insect bite 3 weeks prior to admission. The 3rd day after admission, the patients developed, within hours, bilateral neck, periscapular and brachial muscle weakness and respiratory failure. Both patients required intubation at the end of the 1st week. At the nadir of the disease, examination revealed ventilatory failure, bilateral are-flexic asymmetrical upper limb and neck flexor muscle weakness with atrophy, fasciculations, and absence of abdominal cuta-
neous reflexes. Patient 1 had superimposed bilateral facial weakness and transient bilateral up-going plantar responses with slight distal muscle weakness of the left lower limb. Patient 2 experienced fluctuating numbness in the left proximal lower extremity. The patients underwent normal conventional chemical, hematologic and EKG studies. The thoracic roentgenograph revealed bilateral asymmetrical diaphragm muscle weakness. The VDRL and TPHA tests were normal. Cultures of blood and CSF for bacteria were sterile, and serologic tests of serum and CSF were negative for recent infection (including *Borrelia burgdorferi*), except for specific antibodies to *Flavivirus*. The antibody titers were determined by ELISA using a commercially available kit (Immuno®) in a reference laboratory (Institut de Zoologie, Neuchâtel, Switzerland). Serological conversion, with 6-fold change in IgG, was demonstrated by repeating tests (Patient 1: week 3 IgM++, IgG 70 U, week 24 IgM-, IgG 700 U. Patient 2: week IgM++, IgG 60 U, week 12 IgM-IgG 480 U). Over the next 18 months, the patients improved progressively, but both had initially prolonged apneic dyspnea. On examination one and a half years after onset, there was diffuse wasting of periscapular muscles. Deep reflexes were present, but weak. Muscle strength was weak and asymmetrical, but arm abduction, flexion and extension were possible against slight resistance.

Electrodiagnostic studies were carried out 3 weeks and 8 months after onset in the 2 patients. Nerve conduction studies were performed on facial, spinal, axillary, musculocutaneous, median, ulnar, peroneal and sural nerves on the weaker side. Conventional needle EMG was performed in head, neck, trunk, arm and leg muscles. In the initial studies, marked reduction of motor areas recorded on scapular and proximal arm muscles, normal nerve conduction and normal sensory responses were seen. Needle EMG showed signs of widespread acute denervation, and reduced recruitment patterns in all muscles tested, except in the lower limb muscles, where only rare signs of denervation were found. In the final studies, signs of chronic denervation at rest, with scarce fibrillation potentials and complex repetitive discharges, were seen in proximal upper limb muscles. The motor unit potentials morphology was polyphasic in all muscles tested in the upper limbs, with enlarged potentials in scapular and brachial muscles. Abnormal rhythmic activation of infraspinatus, upper trapezius, and anterior portion of deltoid muscles was seen coupled with inspiration (fig. 1). Electrical stimulation of the radial nerve at the elbow allowed the recording of numerous long latency (between 60 and 100 ms) late responses in the extensor digitorum communis muscle. These responses were indirect (shorter latency with proximal stimulations), constant and with an abrupt shortening of their latencies with higher stimulation intensity. These responses corresponded to motor axon reflexes [6]. The study underscores the similarities in the unusual clinical presentation and in the prolonged proximal bi-brachial weakness with respiratory failure seen in the 2 patients with meningencephalomyelitis. Our electrodiagnostic studies provide new information regarding the pathophysiological and temporal profile of severity in this bi-brachial amyotrophy, until now reported only as a consequence of lower motor neuron syndrome [1,2]. The aberrant reinnervation, with abnormal coactivation of the periscapular and diaphragm muscles and the demonstration of long latency motor axon reflexes are signs of proximal axonal reinnervation [6,7]. There were also electrophysiological signs indicative of complex misdirection of regenerated axon from cervical roots, not seen in anterior horn cell degeneration. Although clear pathological involvement of anterior cells of the cervical spinal cord and bulb has been reported in flaviviruses (2-3), our patients had signs suggestive of concurrent polyradicular involvement which is thought to be important for reinnervation to permit a progressive, but late, motor improvement.

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**References**


