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

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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 1, 3]. 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 clinicoepidemiological, 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 amyotrophy, fasciculations, and absence of abdominal cuta-

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Table 1. Clinical and laboratory features

Duration of Cerebrospinal fluid analyses Cervical MRI

Patients and month of infection

Nadir

day upper limbs muscle
strength (MRC grade)
intubation days

protein leukocytes
(n<0.4g/l) (n<5x10⁹/l)
(within the first 2 weeks after onset)

Patient 1 (female, 35) July (tick bite)

Proximal right: 1
left: 2
Distal right: 4
left: 4+

15

2.97

741

normal

Patient 2 (male, 57) June (insect bite)

Proximal right: 2
left: 2
Distal right: 4
left: 4+

50

0.7

178

normal

Fig. 1. EMG recording of patient 1 (upper trapezius muscle) in the resting state. Motor units fire rhythmically with respiration, indicating their origin as axons formerly innervating diaphragm. This confirms aberrant reinnervation of this muscle. Similar recordings were seen in other periscapular muscles (see text).

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 roentgenogram 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 Flaviviruses. The antibody titers were determined by ELISA using a commercially available kit (Immuno®) in a reference laboratory (Institut de Zoologie, Neuchatel, 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 31 IgM++, IgG 60 U, week 12 IgM- IgG 480 U). Over the next 18 months, the patients improved progressively, but both had initially prolonged supine 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 18 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]. Our report 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 meningoencephalomyelitis. 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 flavivirus encephalitis [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

Craven RB: Flaviviruses; in Belshe RB (ed): Textbook of Human Virology. St Louis, Mosby Year Book, 1991, pp 633–662.
 Jackson AC, Johnson RT: Aseptic meningitis and acute viral encephalitis; in McKendall RR (ed): Handbook of Clinical Neurology. New York, Elsevier, 1989, vol 12(56), chap 8, pp 125–148.
 Grinschgl G: Virus meningo-encephalitis in Austria. Bull World Health Organ 1955;12:535–564.
 World Federation of Neurology Research Group on Neuromuscular Diseases: Classification of neuromuscular disorders. J Neurol Sci 1994; 124(suppl):109–130.
 Kuntzer T, de Marval F, Ochsner F, de Torrente A, Kuhn M, Fitting JW: Meningo-encephalomyelitis due to flavivirus: paresie bi-brachiale et insuffisance respiratoire. Schweiz Med Wochenschr 1995;634–638. Roth G: Intranervous regeneration; the study of motor axon reflexes. J Neurol Sci 1979;41:139–148. Summer AJ: Aberrant reinnervation. Muscle Nerve 1990; 13:801–803.