Persisting Impairment Following Rocky Mountain Spotted Fever: A Case Report

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A patient initially presented in the emergency room with fever, confusion, and a petechial rash. Rocky Mountain Spotted Fever (RMSF) was diagnosed and appropriate treatment was initiated. He subsequently became obtunded and required mechanical ventilation and temporary cardiac pacing. Four weeks later, he presented to our rehabilitation unit with ataxia, hyperreflexia and upper motor neuron signs, dysesthesias, sensorimotor axonopathy demonstrated by electrodiagnostic studies, and a global decrement in cognitive capability. Although he significantly improved in functional mobility and self-care, he exhibited little improvement in his cognitive impairment at 6-month follow-up. An understanding of the natural history of, and long-term impairments associated with, RMSF will be helpful to physiatrists in developing rehabilitation care plans and in assisting such patients with community re-entry.

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In 1907, Howard T. Ricketts described the epidemiology and origin of “Snake River Measles,” which later became known as Rocky Mountain Spotted Fever (RMSF). It was first described in Idaho and Montana, hence the “Rocky Mountain” title; however, it is most common in the Southeastern United States, where 50% of reported cases occur. Most patients have neurologic symptoms, which in fact may comprise the presenting feature. While generalized neurologic impairment has been noted in acute cases, long-term survival of individuals with RMSF progressing to coma has been the exception rather than the rule. Improved critical care and antibiotics have improved survival for patients with a severe clinical course, but frequently they are left with long-term neurologic sequelae. This case report illustrates many of the chronic impairments associated with clinically severe RMSF. Awareness of such possible complications and their natural history will better prepare rehabilitation specialists in care planning and in assisting such patients with community re-entry.

CASE REPORT

A 68-year-old man was admitted to the hospital in late August 1995 after being involved in a motor vehicle accident. Evidence at the scene did not support physical injury to the patient; however, he was found sitting in his car in a “confused” state. In the emergency room, he was noted to be febrile and disoriented. Other vital signs were normal. Physical examination was otherwise remarkable for a petechial rash on his trunk, extremities, palms, and the soles of his feet. There were no reported focal neurologic findings. Admission laboratory results were remarkable for a total white blood cell count of 12 × 10^9/L, a lactate dehydrogenase level of 1,200 units/mL, and a platelet count of 96,000/µL. Protime was mildly elevated at 13.9 seconds.

Further serologic evaluations included blood cultures, human immunodeficiency virus assay, cryoglobulin antigen, C-3, C-4, anti-nuclear and anti-DNA antibodies, venereal disease research lab (VDRL) test, and serum alcohol, all of which were unremarkable. Cerebral spinal fluid (CSF) showed increased protein at 121 mg/dL, 2 white blood cells per high-power field, and 15 red blood cells per high-power field. CSF cultures and gram stain were negative. Fluorescent antibody testing of skin biopsy was not done because it was not readily available. The diagnosis of RMSF was made empirically, and the patient was treated with doxycycline. Serum was later shown to be positive for IgG to Rickettsia rickettsii at a titer of 1:128 dilutions, thereby confirming recent infection.

On day 3 of his hospital stay, the patient became obtunded. An electroencephalogram (EEG) showed diffuse slowing with disorganization of background rhythm. Findings on computed tomography (CT) without contrast were normal. Magnetic resonance imaging (MRI) showed small symmetrical zones of hypointensity in the periventricular white matter, but this finding was not considered significant. An EEG was repeated 2 days later, and showed diffuse anterior continuous alpha activity. This is present in the so-called “Alpha coma,” which is associated with brain stem involvement. Six days later the patient became arousable and began to show gradual improvement in cognitive function. He required mechanical ventilation for 7 days, and on the 8th day of hospitalization, he required temporary cardiac pacing secondary to a decrease in heart rate from approximately 80 beats/min to approximately 50 beats/min. This procedure was complicated by a pneumothorax that required chest tube placement. He also had a left lower lobe pneumonia, which resolved early in the hospital course.

The patient was transferred to a transitional care unit 14 days after admission. He gradually improved and was admitted to our rehabilitation unit 4 weeks after his initial hospitalization. The admission physical examination was notable for general cognitive impairment with a Folstein Mini Mental Status Exam score of 18/30. Cranial nerves were intact. The patient complained of dysesthesias in his lower extremities, but his sensory exam was normal to light touch, pin prick, and vibration. He exhibited impaired proprioception in both lower extremities. Muscle stretch reflexes were noted to be brisk and symmetric. Bilateral Babinski and Chaddock responses were noted. Muscle tone was normal, but he exhibited poor exercise tolerance and diffuse moderate weakness. Gait was wide-based with mild truncal ataxia. He required a front wheel walker and standby assistance for ambulation, which was initially limited to approximately 15 feet.

During the rehabilitation course, the patient was tested with the Wechsler Adult Intelligence Scale-Revised (WAIS-R),
Laboratory tests are unrevealing early in the infectious course has a bimodal peak annual incidence in spring and late summer.3 Tissue is required for diagnosis. Neuroimaging studies are mainly useful for retrospective diagnosis. Neuroimaging is nonspecific and frequently unrevealing. Suspicions of infection are warranted during spring and summer months, especially in children, and particularly if there is a history of animal exposure or tick bites.

Infection by Rickettsia spp. can disseminate to various sites, including the central nervous system. Rickettsia species cause a diffuse vasculitis by infecting and multiplying in the small vessel endothelium.

R. rickettsii is unique in its genus in that it invades and destroys intima and media smooth muscles as well. The local effects of the infection occur in two phases: (1) initial proliferation of the organism in capillary and small vessel endothelium with subsequent hypertrophy and thrombotic occlusion; and (2) subsequent perivascular leukocyte infiltrate which is predominantly mononuclear. This second phase occurs at 5 to 7 days and roughly corresponds to the antibody response.4,5

Several pathologic changes occur in the central nervous system. Typhus nodules in the brain occur in the acute phase of the infection via the vascular invasion noted above. This is also accompanied by tissue edema. Together, these are the likely cause of the acute mental status changes and neurologic signs seen early in the disease. The nodules most commonly occur in the nuclear and brain stem regions. Secondarily, areas of demyelination and granulomas can be found adjacent to, and distant from, these lesions.6 Microinfarcts of the white matter of brain stem and cortices have been found in tissue examination.7 These pathologic changes are believed to be associated with chronic EEG abnormalities after recovery. They may also account for the EEG and MRI changes seen in our patient.

Focal areas of demyelination, granulomas, and microinfarcts have been reported in several studies.5,7 Miller and Price5 reviewed 60 patients presenting at the University of Virginia Hospital between 1956 and 1970. There were nine fatalities among these cases, all of which subsequently had autopsies performed. Microscopic studies showed moderate to severe diffuse bilateral cerebral damage in eight patients. There was widespread evidence of encephalomyelitis from direct rickettsial invasion as well as from severe vasculitis. Miller and Price believed the lesions had an affinity for gray matter neuronal masses in the brain stem, particularly the reticular nuclei. Other areas of notable damage included the periaqueductal gray matter and subependymal areas adjacent to the fourth ventricle. They believed these pathologic changes correlated with the neurologic symptoms noted premortum. Signs and symptoms in decreasing order of incidence were headache, lethargy and irritability, delirium, disorientation, coma, memory disturbance, seizures, dysarthria, tremor, focal weakness, ataxia and hyperreflexia.6

Neurologic symptoms occur in about 80% of cases. These include general as well as focal neurologic findings. General signs include insomnia, confusion, delirium, anxiety, seizures, and coma. Nuchal rigidity with Kernig's and Brudzinski's signs are common.8 Focal neurologic findings are not as common, but can be seen particularly in more severely affected patients. These include transient deafness, increased muscle stretch reflexes, clonus, Babinski sign, ataxia, flaccid paralysis, tardive dyskinesia, hemiparesis, and motor and sensory neuropathies.5,7,9,13

It is probable that the general neurologic signs are related to acute vascular permeability and systemic inflammatory changes, while focal signs might be related to the formation of typhus nodules, microinfarcts, and demyelination, or perhaps hemorrhage secondary to coagulopathy. In more virulent strains, death can occur in 5 to 7 days, and can be due to pronounced cerebral edema and uncal herniation.9

In terms of neuroimaging, CT can show diffuse white matter hypodensities or small ventricles and sulci consistent with cerebral edema, but CT findings are often normal. MRI is usually normal with T-1 weighted images, but has been reported to show punctate areas of increased signal in cerebral white matter on T-2 weighted images, particularly in the perivascular spaces and end-artery distributions. Follow-up T-2 MRI typically shows some resolution of these lesions.10 T-2 weighted MRI is likely more sensitive than CT; however, this has not yet been definitively confirmed. The periventricular areas of hyperintensity on T-2 weighted MRI noted in our patient may be evidence of pathologic changes similar to those noted above. There have been few reports correlating the clinical course with neuroimaging. Most studies have been retrospective, and the clinical evaluation and management has varied among clinicians. Massey13

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reviewed 16 confirmed cases at Duke University Medical Center between 1979 and 1983. One of six patients with severe clinical presentation and subsequent head CT evaluation showed white matter lesions.

Electrodiagnostic studies can be helpful diagnostically. EEGs can be abnormal acutely and at long-term follow-up. Somatosensory evoked potentials might also have a role in identifying central conduction abnormalities, but no such studies have been reported to date. Even though clinical findings of polyneuropathy have been described, electrodiagnostic studies in such cases have never been reported.1-5,9,13,16 Nerve conduction studies and electromyography showed signs of an axonal type sensorimotor polyneuropathy in our patient.

Early diagnosis and treatment appear to be crucial in decreasing neurologic impairment. Rosenberg12 reviewed 37 cases from 1946 to 1952 in North Carolina, and did follow-up examinations and EEG studies varying from 1 to 8 years postdischarge. Of the 37 cases, 21 had some type of neurologic sequelae at follow-up. Fourteen had persistent intermittent general symptoms, including headache, nervousness, emotional lability, hyperactivity, depression, and seizures. Six had focal signs including decreased fine motor movement, hypotonia, plantar extensor responses, clonus, ataxia, mental retardation, and focal motor weakness. Twelve had abnormal EEGs and an additional 12 had EEG borderline studies. This series is interesting in that some of these patients did not receive antibiotic therapy. Twenty-four received only supportive care, which may have included immune serum and para-amino benzoic acid. Of these, 13 had persisting neurologic findings and 9 had abnormal EEGs. Thirteen patients received either chlortetracycline hydrochloride or chloramphenicol. Of these, 6 had persisting neurologic findings and 3 had abnormal EEGs. Incidence of EEG abnormalities generally had a positive correlation to the number of febrile days, with a marked increase in abnormalities among those patients who had more than 10 days of fever. Few EEG abnormalities were seen in those with early antibiotic intervention. Other studies29 found similar general and focal neurologic findings. Additional reported focal deficits include monoparesis, hemiparesis, hyperreflexia, hearing loss, and transverse myelitis with tetraparesis.

Early antibiotic treatment also seems to significantly reduce mortality. Vianna and Hinman40 reviewed 260 laboratory-confirmed, physician-reported cases occurring between 1941 and 1970 on Long Island, NY. Eighteen of the patients died; however, there were no fatalities among patients receiving antibiotics in the first week of the illness.

Neuropsychological information concerning survivors of RMSF is sparse. Gorman27 followed 42 confirmed cases from 1 to 10 years after their initial presentation. His study was the first to perform cognitive testing on survivors, and patients were stratified based on the severity of their acute disease. Severity of the acute illnesses were rated as mild if the patients were irritable and lethargic, moderate if stupor and hallucinations were present, and severe if coma occurred for longer than 3 hours. Patients were given a battery of psychometric tests, including Weschler Intelligence Scale for Children, Wide Range Achievement test, Finger Tapping Test, Halstead Reitan, Bender-Gestalt Visual-Motor Performance Test, and Connor’s Behavioral Rating Scale. Patients in the severe group had consistently lower verbal and performance IQ scores. They also had a higher rate of emotional and behavioral disturbances, as well as showing evidence of learning disability compared with the mild and moderate patients. Two patients in the severe group were troubled by emotional outbursts, one had severe depression, one had persistent cranial nerve III palsy and “clumsiness,” and two had aphasia and hemiparesis at discharge that resolved by the time of follow-up.

Few studies have followed patients for long-term functional impairment. Archibald and Sexton16 interviewed 9 of 25 patients with reported persisting neuromotor impairments at the time of discharge from the hospital. These were selected from 105 cases of RMSF admitted to Duke University Medical Center. Range of time to follow-up was 1 to 18 years. Persistent complaints included dysarthria, impaired reading, memory, and intellectual function, delayed speech, proximal motor weakness, spastic paraparesis, deafness, bowel and bladder dysfunction, vestibular dysfunction, numbness, and paresthesias. Functional deficits related to these impairments included difficulties with balance and in making sudden movements, frequent falls and fractures, difficulty with basic self-care activities, bowel and bladder incontinence or urinary retention, and generalized weakness. Standardized functional impairment evaluations were not documented in this series. Presumably, patients with persisting deficits had a more severe clinical course, but this was not specifically documented.

The literature indicates that if the infection involves a more virulent strain and/or takes a severe clinical course, persistent cognitive or neurologic sequelae are likely. This is especially true if neurologic symptoms, particularly coma, are present during the acute phase of the illness. In the postacute phase of recovery, patients should undergo a comprehensive rehabilitation evaluation. If altered mentation or coma occurred during the acute illness, neuropsychological testing should be performed to rule out cognitive or learning disability. Behavioral testing should also be considered because emotional disturbances have also been reported.10 These issues are particularly important in the pediatric and young adult population, because appropriate assistance and psychosocial support can then be provided for return to school and work, as well as general community re-entry.

In concurrence with the above studies, our patient exhibited general and focal neurologic findings, as well as a global decrement in cognitive function. He gradually improved with acute and continuing physical and occupational therapy, and eventually became independent in ambulation and basic self-care. However, he continued to exhibit marked cognitive impairment that showed little clinical improvement at follow-up.

Admission to an acute rehabilitation unit is appropriate for patients who have focal motor weakness, ataxia, bulbar findings, or more severe cognitive findings. As our patient demonstrated, physical therapy, occupational therapy, and speech therapy are likely to improve functional outcome. Focal weakness, tetraparesis, and balance impairments can be treated with therapeutic interventions. Patients may also need assistance with training, assistive devices, and equipment related to daily self-care tasks. Neuropsychological testing, monitoring for behavioral disturbances, and assisting the patient with work and community re-entry can be greatly facilitated in this setting as well.

As more people survive RMSF, the rehabilitation team will be involved in the treatment of long-term functional impairment, as well as the treatment of cognitive and behavioral disturbances of these patients. Psychiatrists, therapists, and primary care specialists must be aware of the possibility of chronic impairments and disability following this disease and must work together in the development of acute and long-term treatment plans.

References


