Comparison of CT and MR Features with Clinical Outcome in Patients with Rocky Mountain Spotted Fever

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PURPOSE: To compare neuroimaging findings and clinical features in patients with Rocky Mountain spotted fever and to determine the impact of imaging studies in the treatment of these patients. **MATERIALS:** We reviewed the brain CT scans (n = 44), MR images (n = 6), or both (n = 4), and one MR spinal study in 34 patients with Rocky Mountain spotted fever, proved by definitive serologic criteria. Records were reviewed with attention to clinical symptoms and therapeutic modifications based on neuroimaging; outcomes were compared with imaging findings. **RESULTS:** Abnormalities, consisting of infarctions, cerebral edema, meningeal enhancement, and prominent perivascular spaces, were found on four of 44 CT scans and on four of six MR studies. The spinal MR study showed abnormal enhancement of the lower spinal cord and cauda equina. Nonspecific clinical symptoms were present in all patients in whom neuroimaging findings were abnormal and in 80% of patients whose CT and/or MR findings were normal. After treatment, return to baseline clinical status was documented in 67% of patients with abnormal imaging findings and in 93% with normal findings. Death occurred in 17% of patients with abnormal neuroimaging results and in none of those with normal results. **CONCLUSIONS:** Abnormalities on neuroimaging studies were not common in patients with Rocky Mountain spotted fever. When present, they were subtle. Symptoms at presentation and unfavorable outcomes were more prevalent when CT or MR findings were abnormal. Abnormalities identified on neuroimaging studies did not alter clinical treatment in any patient.

Index term: Brain, infection

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Rocky Mountain spotted fever, caused by *Rickettsia rickettsii*, is the most frequently reported life-threatening tick-borne infection. Approximately 25% of cases occur in North Carolina and over 50% occur in the South Atlantic region of the United States (1, 2). Most cases occur during late spring and summer (99% of them between April 1st and September 30th) (3). The microorganisms spread hematogenously, invading endothelial cells, proliferating, and injuring the microcirculation. In the brain, Rocky Mountain spotted fever causes vasculitis and meningoencephalitis, with cerebral infarctions resulting from a destructive systemic thrombovasculitis. The severity of Rocky Mountain spotted fever is highly variable, and treatment delays are associated with a complication rate of approximately 40% to 55% (4–15). Permanent neurologic deficits are among the most prominent sequelae (8, 16); and even with adequate antibiotic therapy, mortality rates vary from 2% to 10% (1, 6, 13, 15).

The role of neuroimaging in the diagnosis and prognosis of patients with Rocky Mountain spotted fever meningoencephalitis has been addressed previously. We reviewed the neuroimaging studies in 34 patients with Rocky Mountain spotted fever and compared the results with clinical findings and outcome and assessed the impact of abnormal findings on the therapy of patients.

Materials and Methods

From 1990 to 1995, 34 patients (22 male and 12 female; 3 to 66 years old; mean age, 33 years) were treated

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in our hospital for Rocky Mountain spotted fever, which was confirmed by indirect fluorescent antibody reaction. Of these patients, 28 had computed tomography (CT) of the brain (44 studies; 34 without contrast enhancement, 10 after contrast administration), six had contrast-enhanced brain magnetic resonance (MR) imaging, and four had both CT and MR studies of the brain. All 28 patients had a CT study of the head on admission and 16 had follow-up CT examinations at some time during their hospitalization. All six MR imaging studies of the brain were obtained upon admission. CT examinations were performed using contiguous 5-mm-thick sections from the base of the skull to the vertex. Contrast-enhanced studies were obtained with the same technique before and after intravenous administration of 150 mL of 60% nonionic iodinated contrast material. MR imaging was performed with a 1.5-T unit, and 5-mm-thick T1-weighted (600/15/1 [repetition time/echo time/excitations]) sagittal and axial noncontrast images; 5-mm-thick T2-weighted (4000/19–93/1) images; and contrast-enhanced T1-weighted axial and coronal images (with the same parameters as above) were obtained. MR contrast material was administered intravenously at a dose of 0.1 mmol/kg. One patient had MR imaging of the thoracolumbar spine (with two different surface-coil placements) in which sagittal and axial precontrast and postcontrast T1-weighted images and sagittal T2-weighted images were obtained (with the same parameters as above).

Our retrospective review of the CT and MR imaging studies was performed with special attention to the presence of hydrocephalus, infarction, dilatation of perivascular spaces, edema, and meningeal enhancement. In addition, all patient records were reviewed for neurologic signs and symptoms at presentation, clinical outcome, and changes in therapy dictated by abnormalities detected on neuroimaging studies.

Results

Of the 44 CT studies obtained in 28 patients, four had abnormal findings. These abnormalities included focal arterial (basal ganglia) infarction in one patient, diffuse cerebral edema in one patient, and diffuse meningeal enhancement in two patients (Figs 1–3). Of the six patients who had MR imaging, four had intracranial abnormalities consisting of focal arterial infarctions (involving the basal ganglia and the left frontal region) in one patient, diffuse edema in one patient, diffuse meningeal enhancement in one patient, and prominent perivascular spaces in the region of the basal ganglia in one patient (Figs 4 and 5). In the patient who had MR imaging of the spine, the study showed abnormal enhancement of the ventral and dorsal surfaces of the distal spinal cord as well as enhancement of the cauda equina (Fig 6).

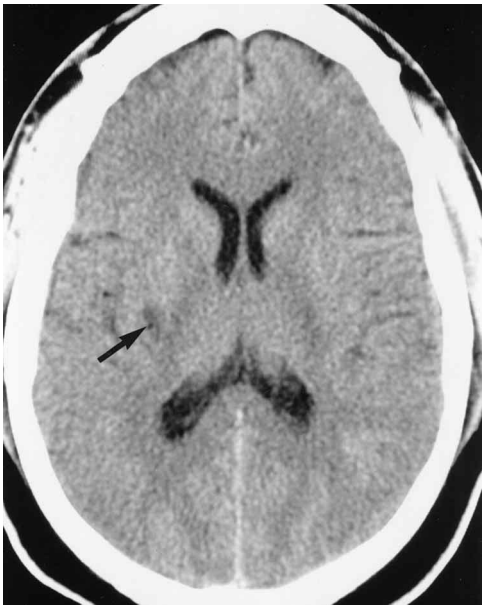

Fig 1. Focal arterial infarction on CT. Axial noncontrast CT section shows small area of low density (*arrow*) in posterior aspect of right lentiform nucleus compatible with either a lacunar infarction or edema. There was elevated pressure, pleocytosis, and increased proteins in the cerebrospinal fluid. This patient presented with motor drift on the left and returned to normal after treatment. No follow-up study was obtained.

Ninety-four percent of our patients presented between the months of April and September. Clinical findings at presentation in patients with abnormal CT (n = 4) and/or MR imaging (n = 4) studies were headache (100%), fever (100%), cutaneous rash (83%), meningismus (50%), confusion (67%), focal neurologic deficits (67%), and seizures (17%). Clinical findings at presentation in patients with normal neuroimaging studies (n = 8) were headache (81%), fever (73%), meningismus (38%), confusion (35%), focal neurologic deficits (31%), and seizures (12%). Specifically, the patients with lacunar infarctions (Figs 1 and 4) presented with left-sided motor drift and left-sided weakness, respectively. The patient with diffuse edema (Fig 2) had severe headaches and obtund reflexes. Both patients with meningeal enhancement (Figs 3 and 5) had seizures and posturing and one also had hyperreflexia and was unresponsive. The patient with abnormalities on the spine imaging study (Fig 6) presented with ataxia and left-sided paraparesis. Death occurred in 17% of the patients who had abnormal neuroimaging studies and in none of those with normal CT or MR findings.

After antibiotic treatment, a return to normal neurologic status occurred in 67% of patients

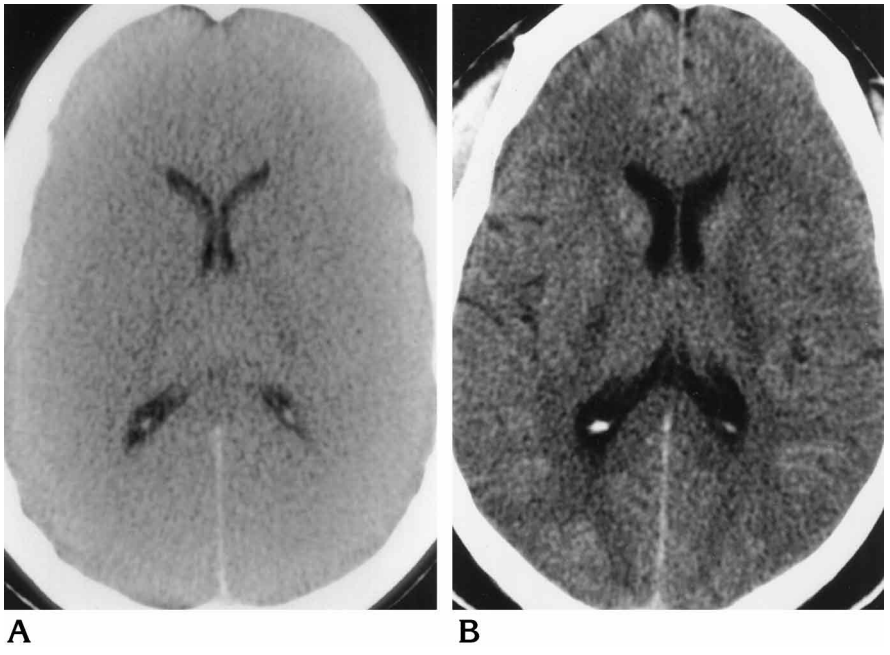

Fig 2. Cerebral edema.

A, Noncontrast CT scan shows diffuse cerebral edema with sulcal effacement and loss of density differences between gray and white matter.

B, CT scan obtained 1 week later shows resolution of edema. The patient was clinically normal and was discharged.

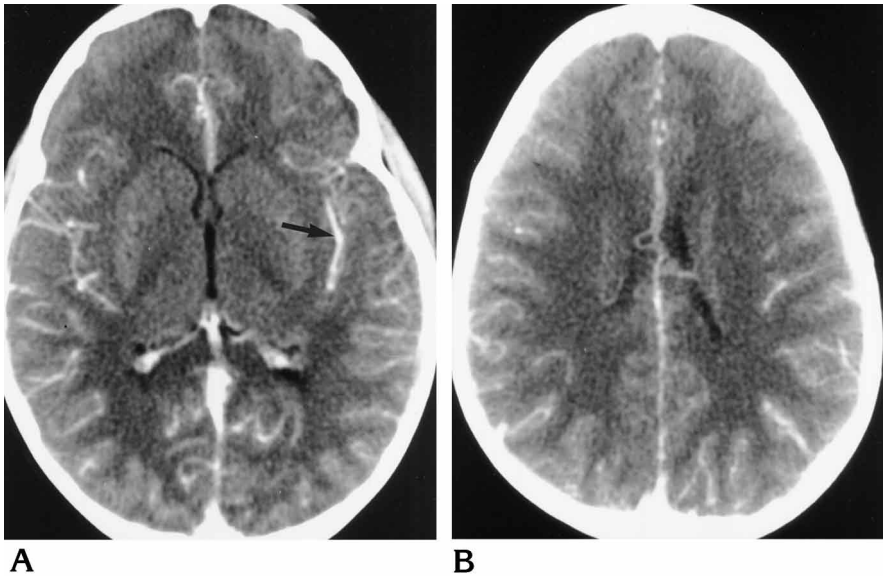

Fig 3. Meningeal enhancement on CT. Axial postcontrast CT sections show enhancement of the subarachnoid space in both cerebral hemispheres, particularly at the level of the left sylvian fissure (*arrow*). However, some of the enhancement may represent prominent vessels. At presentation, this patient was posturing and unresponsive and died during hospitalization. Autopsy showed meningitis with swollen and congested vessels in the leptomeninges and neuronal necrosis in the hippocampi.

with abnormal neuroimaging studies and in 93% of those with normal imaging findings. Mild residual neurologic deficits remained in 17% of those with abnormal neuroimaging studies and in 4% of those with normal studies. One patient with abnormal imaging findings died and one patient with normal findings remained paraplegic. Autopsy in one patient with meningeal enhancement (Fig 3) showed meningitis and neuronal necrosis in the hippocampi. Lower extremity weakness and decreased sensation were permanent sequelae in the patient with the abnormal MR study of the spine. Clinical management during the hospitalization of all patients was not altered by the presence of abnormalities on CT or MR studies, and repeat CT scans obtained in 16 patients during their hospitalization failed to reveal new findings.

Discussion

Because the initial symptoms of Rocky Mountain spotted fever are nonspecific, prompt diagnosis and initiation of appropriate antibiotic therapy are dependent on a high index of clinical suspicion. The characteristic cutaneous

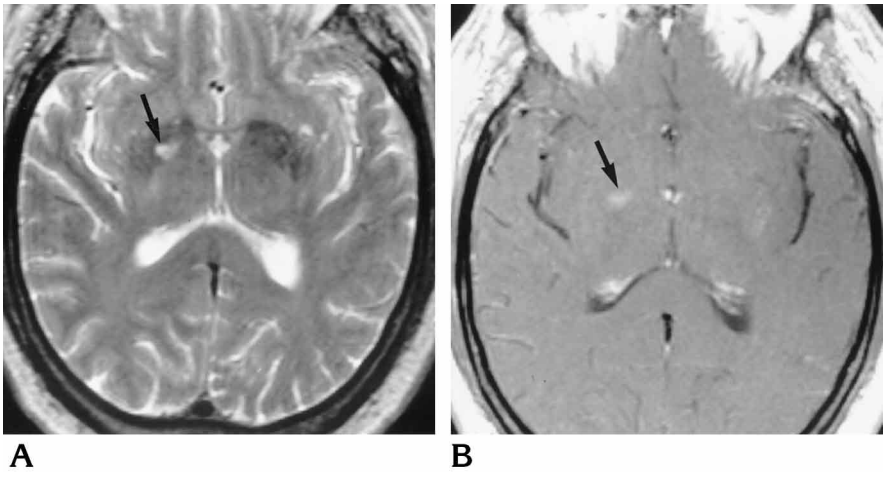

Fig 4. Focal arterial infarction on MR imaging.

A, Axial T2-weighted image shows area of high signal intensity (*arrow*) in right globus pallidus and some punctate hyperintensities elsewhere in both basal ganglia.

B, After contrast administration the abnormality (*arrow*) in the right globus pallidus enhances and is compatible with a lacunar infarction. The fact that the other punctate hyperintensities seen in *A* do not enhance suggests that they represent dilated perivascular spaces. This patient presented with mental status alteration and left-sided weakness but returned to normal state after treatment.

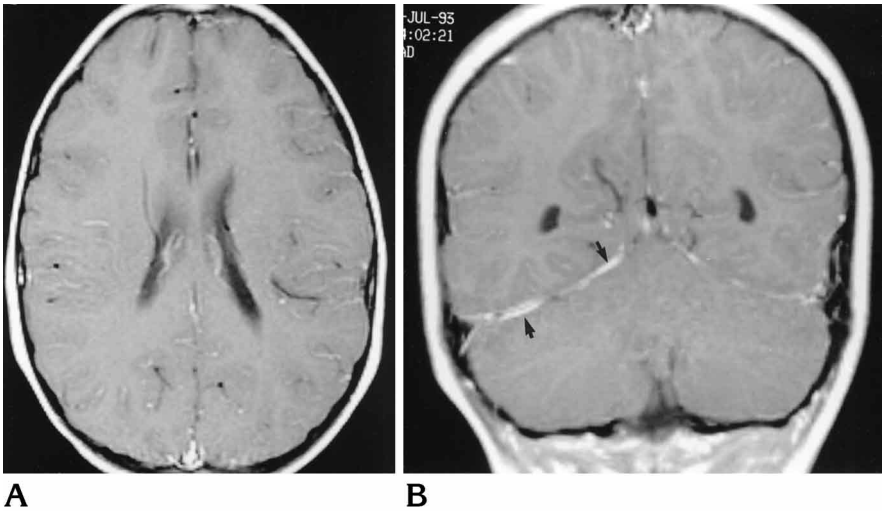

Fig 5. Meningeal enhancement on MR imaging.

A, Axial T1-weighted image after contrast administration shows enhancement of the subarachnoid space in both cerebral hemispheres. Some of this enhancement, however, could be related to vessels. Analysis of cerebrospinal fluid showed pleocytosis, increased proteins, and no organisms. This patient was unresponsive and posturing at presentation but returned to normal state after treatment.

B, Coronal contrast-enhanced T1-weighted image shows questionable increased enhancement of the right tentorium (*arrows*).

rash is often absent during the acute phase of the disease and is found in only 50% of these patients during the entire course of the disease (2). Patients older than 15 years are prone to an atypical presentation and absence of rash (3). The classic clinical triad of fever, rash, and headache is present in only a minority of patients (2). Only adequate treatment prevents permanent neurologic disabilities and death. Treatment delay of more than 5 days after the onset of the disease leads to complications in 40% to 55% of patients (6, 13). Permanent neurologic deficits occur in 23% of patients treated inadequately (4, 6). Without treatment, mortality reaches 20% (5). The severity of the neurologic symptoms and sequelae has been established. At presentation, shock, coma, and seizures closely correlate with a fatal outcome (3, 6).

Most articles describing the neuroimaging features of Rocky Mountain spotted fever are based on a small number of patients in whom many of the neuroimaging (particularly CT) findings were reported as normal (8, 9, 16). In the minority of patients, abnormal CT findings include diffuse white matter changes, sulcal effacement consistent with edema, and focal areas of low density thought to represent infarctions (8, 10). MR imaging confirms all of these findings but in addition may show dilatation of perivascular (Virchow-Robin) spaces (16). These observations are in accordance with our study in which only four of 28 patients had abnormal CT scans showing focal arterial infarctions (n = 1), diffuse edema (n = 1), and meningeal enhancement (n = 2). In four of six patients who had MR imaging, abnormal findings included focal arterial infarctions (n = 1), diffuse edema (n = 1), meningeal enhancement (n = 1), and prominent perivascular spaces. Thus, the abnormalities detected by both imaging techniques were remarkably similar and

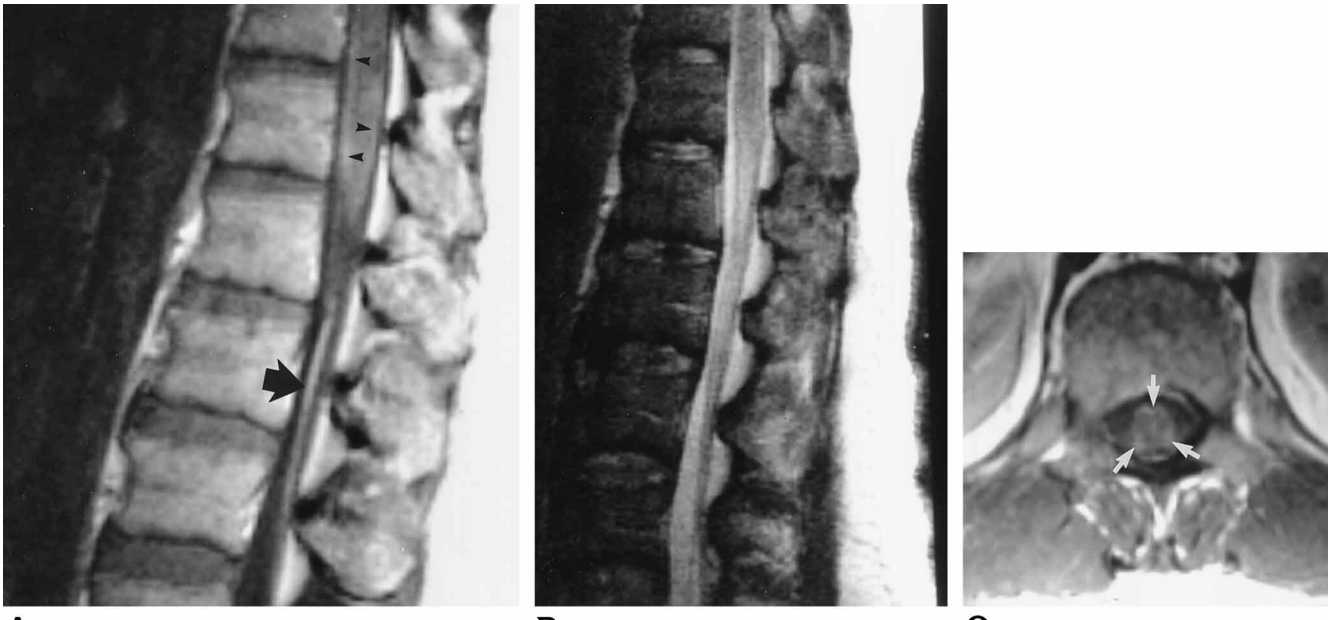

Fig 6. Abnormal enhancement of the distal spinal cord, conus medullaris, and cauda equina.

A, Midsagittal T1-weighted MR image after contrast administration shows enhancement of the ventral and dorsal surface of the conus medullaris (*arrowheads*) and of the cauda equina (*arrow*). This patient presented with mental status changes, ataxia, aphasia, and bilateral lower extremity weakness. Residual paraparesis remained after treatment.

B, Corresponding T2-weighted MR image shows a questionable area of abnormally high signal intensity in the distal conus medullaris at the level of L-1.

C, Axial postcontrast T1-weighted MR image shows abnormal enhancement (*arrows*) on the surface of the distal thoracic spinal cord. Analysis of cerebrospinal fluid showed lymphocytosis and elevated proteins. Two years after presentation, the patient has mild residual bilateral lower extremity weakness.

subtle in four of our patients. The significance of dilatation of the perivascular spaces (only seen with MR imaging in one of our patients) is questionable. The neuroimaging findings closely correlate with the pathologic findings of leptomeningeal and cerebral vasculitis, edema, petechia, infarctions, and arteriolar thrombonecrosis (8, 9, 17). At autopsy, gliosis and demyelination have been noted on histopathologic examination (4, 1). The chronic imaging features of Rocky Mountain spotted fever are not addressed in this study.

Acute neurologic manifestations of Rocky Mountain spotted fever include headache (often severe), seizures, mental status changes, coma, focal deficits, vertigo, hearing loss, neuropathy, and lethargy (2, 4, 6, 8, 9, 13, 18). In our patients with abnormal CT or MR findings, symptoms were more common and more severe than in those with normal CT and MR results. In addition, death occurred more often when imaging studies were abnormal. Prognosis also differed in both groups of patients. Those with abnormal CT or MR studies had an increased prevalence and severity of sequelae and had a higher death rate. Thus, an abnormal CT or MR study indicates a worse prognosis. Despite this, the clinical treatment of our patients was not changed by the presence of abnormalities on neuroimaging studies.

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