
A 31-year-old man with no previous pertinent medical or surgical history presented with seizures and a progressive cognitive decline. He became tremulous, and he had a variable but constant fine action tremor. There were saccadic eye movements on voluntary gaze to either side. He developed myoclonus superimposed on psychomotor slowing with periods of agitation, followed by incoordination, suggesting mild cerebellar dysfunction. There were no other abnormal neurological findings. Laboratory investigation included an elevated protein level in the cerebrospinal fluid and nonspecific slowing in an electroencephalogram. Computed tomography and magnetic resonance imaging of brain and spinal cord were normal, and brain scan showed no indication of cerebral blood flow changes; an extensive metabolic workup was negative. The dementia seemed to progress more rapidly than expected from most metabolic or other dementing diseases; 8 months into his course, a left frontal lobe biopsy was performed, revealing rare microvascular endothelial cell nuclear clusters (Fig. A).

Subsequently, his dementia continued to deepen, and he died 4 years after the onset of his illness. Autopsy revealed scattered dilated capillaries and scattered clusters of dilated small vessels in the cerebrum (Fig. B) and cerebellum, mostly in the white matter, and a few in the pons. A few capillaries and larger dilated vessels had atypical endothelial cell nuclei or endothelial cell nuclear clusters. There were numerous white matter perivascular foci of demyelination and axonal loss, mild gliosis, and scattered small calcifications.

With mycoplasmal involvement in similar cases demonstrated by Zu-Rhein et al (1) and by Ferreira (2), and with similar findings in a frontal lobe biopsy from one of our patients who continues to do well (3), we immunostained slides of the cerebrum from the autopsy using the antibody method for mycoplasmal species previously described (3). We found thickened endothelial cells (Fig. C) with positive immunostaining for mycoplasma (Figs. F, G). Uninfected control adult cerebellar samples showed consistent cross-reactivity or background staining with this unabsorbed antibody, especially in the white matter, with little background in the thin endothelial cells (Figs. D, E). Positive control lung with mycoplasmal pneumonia had a heavily immunoreactive population of type II pneumocytes in which electron microscopy showed typical mycoplasmal cells. Using the “pop-off” method for electron microscopy on a slide of the temporal lobe from our patient, we found white matter vascular lumen and intraendothelial cell bacteria with the morphology of mycoplasma species (Figs. H–J). No extravascular bacterial cells were seen. Excessive collagen fibrils were adjacent to thin-walled dilated blood vessels (Fig. K). The clinical and neuropathological findings are much the same as those of Zu-Rhein et al (1, 4) and of Ferreira (2). Direct slide comparison of our case, kindly done by Dr. James Powers, revealed that our endothelial lesions were fewer than those in the previously reported autopsy cases.

Previous cases have variable perivascular fibrosis, and in our autopsy case, we note collagen bundles along very thin-walled dilated blood vessels. Abnormal microvessels, including increased vascular density and an inability to meet metabolic demand, develop in chronic cerebral hypoxia (5), and such changes may play a role in chronic human mycoplasmal encephalopathy. Perivascular fibrosis was not a finding in our previous biopsy case (3).

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REFERENCE

Roy H. Rhodes, MD, PhD
Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School-University of Medicine and Dentistry of New Jersey, New Brunswick, New Jersey rhodesrh@umdnj.edu

Brian A. Anderson, MD, FRCPC
Department of Medicine (Neurology)
University of Manitoba, Winnipeg
Manitoba, Canada
FIGURE. (A) Frontal lobe biopsy blood vessel has clusters of atypical vascular endothelial cell nuclei and a widened lumen. (B) Temporal lobe white matter at autopsy has groups of dilated blood vessels with atypia of endothelial cell nuclei. (C) Leptomeningeal blood vessels over cerebellar folia at autopsy are stained for CD34 showing thick endothelial cell cytoplasm. (D) Noninfected control cerebellar leptomeningeal blood vessel has mild background staining in thin endothelial cells using the antmycoplasma antibody; there is moderate background staining in the molecular layer. (E) The white matter with a blood vessel in the cerebellum of an uninfected control shows mild vascular endothelial background stain and moderate parenchymal immunostain with the mycoplasma antibody. (F) Immunostaining for mycoplasma in a cerebellar leptomeningeal blood vessel of the infected patient (the largest vessel shown in [C]) stains widened endothelial cell cytoplasm but not luminal contents. (G) Dilated cerebellar white matter blood vessels with endothelial cells that are immunostained for mycoplasma. (H) Electron microscopy of autopsy temporal lobe reveals an endothelial cell with an atypical nucleus and mycoplasma in its swollen cytoplasm. (I, J) The swollen endothelial cell has mycoplasmal cells with a nucleoid (arrow), polar terminal organelles (a), a slight constriction separating different densities (b), and single terminal organelles with (c) and without dense attachment organelles (d) in spherical and flask-shaped cells. (K) A dilated blood vessel in temporal lobe white matter has collagen fibrils (cf) along its adventitial aspect. Original magnification: (A, B) H&E stain 400 ×; (C) anti-CD34, diaminobenzidine (DAB) 200 ×; (D, E) anti-Mycoplasma pneumoniae (1:200), DAB 200 ×; (F) anti-M. pneumoniae (1:200), DAB 600 ×; (G) anti-M. pneumoniae (1:200), DAB 200 ×. Scale bars = (H, K) 500 nm; (I, J) 100 nm.