Focal neurologic signs in western equine encephalitis

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Focal neurologic signs developed in a 75-year-old woman who had presented with encephalitis. A diagnosis of western equine encephalitis was made from serologic findings. Although she was improving clinically the patient died from acute dissection of an aortic aneurysm 11 days after admission to hospital. The pathological findings — perivascular infiltrates and multifocal necrosis in the deep grey matter — were consistent with the diagnosis of western equine encephalitis. Similar findings in the basal ganglia and spinal cord corresponded to the focal clinical signs.

Des signes neurologiques en foyer sont apparus chez une femme de 75 ans atteinte d'encéphalite. Un diagnostic d'encéphalite équine nord-américaine de l'Ouest a été posé à partir des résultats de tests sérologiques. En dépit d'une amélioration clinique la patiente est décédée de la dissection aiguë d'un anévrisme de l'aorte 11 jours après son admission à l'hôpital. Les résultats de l'autopsie — des infiltrats périvasculaires et une nécrose multifocale dans la matière grise profonde — étaient compatibles avec le diagnostic d'encéphalite équine nord-américaine de l'Ouest. Des observations similaires dans le noyau lenticulaire, le noyau caudé, l'avant-mur, le noyau amygdalien et la moelle épinière correspondaient aux signes cliniques en foyer.

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Western equine encephalitis, endemic in western Canada and the United States, is usually a self-limited disease.[1] The exceptions involve children and, occasionally, fulminant infections in adults.[2,3] Among 25 Manitoba patients in the summer of 1981 only one death was attributed to the disease. Few published reports describe the clinical or pathological features of this disease in self-limited cases. We present a case in which there were focal neurologic signs that were accounted for at autopsy.

Case report

Clinical course

One week before being admitted to hospital in August 1981 a 75-year-old woman noted lightheadedness, lethargy, cough, fever and progressive left-sided weakness, with unsteadiness of gait. The past history was not contributory. Her temperature was 39.5°C and blood pressure 160/90 mm Hg. No signs of cranial nerve abnormalities were apparent. There was mild left hemiparesis with brisk muscle-stretch reflexes and an equivocal left plantar response. Despite her complaint of numbness in both hands the results of a sensory examination were normal. There were no signs of cerebellar dysfunction or nuchal rigidity. The rest of the general examination yielded normal findings. The erythrocyte and leukocyte counts were normal, as were the serum biochemistry values. The serum glucose concentration was 111 mg/dL (6.2 mmol/L). A chest x-ray film showed an ill defined dense area in the middle lobe of her right lung suggestive of pneumonitis. A contrast-enhanced computerized tomographic scan of the head was normal. The cerebrospinal fluid was under normal pressure and contained 36×10^6 leukocytes (60% polymorphonuclear and 40% mononuclear cells) per litre; the protein and glucose levels were 0.66 (normally 0.15 to 0.45) g/L and 50 mg/dL (2.8 mmol/L) respectively.

A presumptive diagnosis of a central nervous system infection was made. Because penicillin G therapy had been started the day before, a bacterial cause could not be excluded; therefore, cloxacillin, chloramphenicol and tobramycin were given. Western equine encephalitis was strongly considered, as it was endemic at the time. Over the next 12 to 18 hours the patient became comatose, with flaccidity of the left side and rigidity of the right. Her right plantar response became extensor. The focal neurologic signs, an electroencephalogram showing diffuse slowing with accentuation of delta activity in the posterior region of the left temporal lobe of the brain and the patient's worsening condition led us to consider a diagnosis of herpes simplex encephalitis.

A biopsy specimen from the right temporal lobe, however, showed a few perivascular collections of lymphocytes in the cerebral cortex but no infiltration of the space and no neuronal involvement. Electron microscopy added no information. Fluorescent antibody testing for herpes simplex virus gave negative results. Neither staining nor culture of brain tissue, cerebrospinal fluid and serum for bacteria, fungi and *Mycobacterium tuberculosis* revealed any organisms. Treatment with adenine arabinoside was started because herpes simplex could not be excluded as the cause of the encephalitis. All antibiotic administration was stopped.

A chest x-ray film obtained the day after admission showed mediastinal widening. Angiography revealed an aortic aneurysm starting distal to the origin of the left subclavian artery; the cerebral vessels were

not involved. Pleural aspiration revealed a hemorrhagic effusion, but the blood pressure remained steady, which suggested that the dissection had stabilized. Over the next 6 days she improved, regained consciousness and responded to simple questions. Her left hemiparesis lessened steadily, and no other focal signs persisted.

Eleven days after admission the patient's condition deteriorated, with rapidly progressive shortness of breath and loss of consciousness. She died in cardiorespiratory arrest despite resuscitative efforts.

Fig. 1—Areas of tissue necrosis (small arrows) in right putamen. Note blood vessels surrounded by inflammatory cells (large arrow). (Periodic acid–Schiff [PAS]; original magnification ×32.)

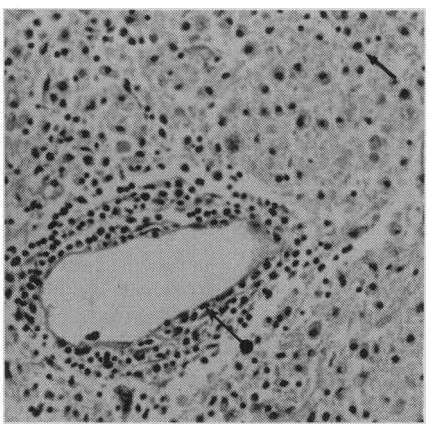

Fig. 2—Area of tissue necrosis in right putamen. Note infiltrated venule (large arrow), macrophages (small arrow) and mononuclear inflammatory cells. (PAS; original magnification ×125.)

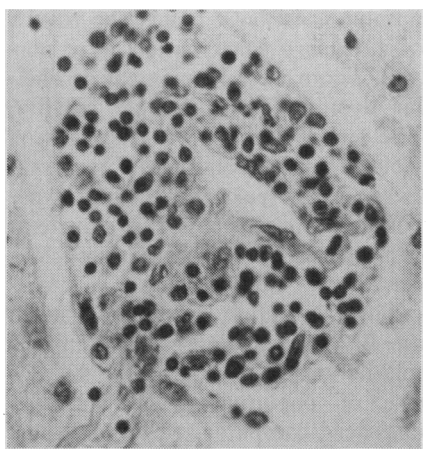

Fig. 3—Arteriole in basal ganglion, showing invasion of wall by mononuclear cells. (Hematoxylin–eosin; original magnification ×500.)

Serologic findings

The titres of hemagglutination-inhibiting antibody to the virus causing western equine encephalitis were 1:64 in blood obtained at the time of admission and 10 days later. Antibody separated from the last serum specimen by sucrose density-gradient centrifugation proved to be IgM directed against this virus, which suggested recent infection. There was no serologic evidence of recent infection with other viruses.

Autopsy findings

The cause of death was determined to be massive left hemothorax due to an aortic aneurysm starting distal to the origin of the left subclavian artery and extending to the iliac arteries. No occlusion of extracranial or intracranial vessels was noted. There was minimal atherosclerosis. The brain and spinal cord appeared normal on gross examination. No other important abnormalities were present.

Microscopic examination of tissue from the brain and spinal cord showed abnormalities consistent with western equine encephalitis. Tissue fixed with formalin was em-

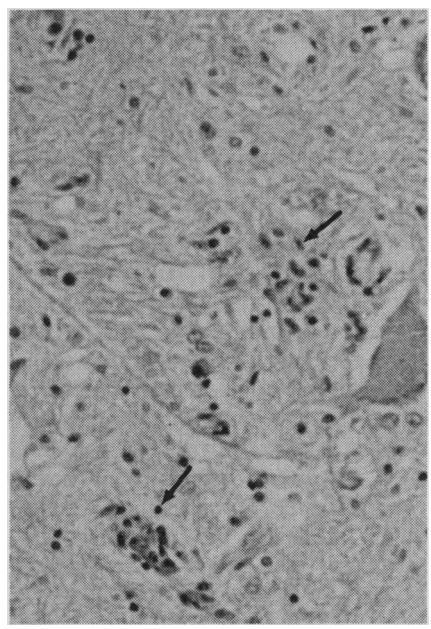

Fig. 4—Anterior horn of lumbar spinal cord. Note collections of microglial mononuclear cells (arrows) within otherwise normal area, typical of minor changes seen in cerebral cortex, brain stem and some levels of spinal cord. (PAS; original magnification ×125.)

bedded in paraffin and examined by light microscopy after staining with hematoxylin–eosin, luxol-fast blue, the periodic acid–Schiff method and silver methenamine. In the cerebral cortex there were a few microglial nodules and occasional infiltrates of lymphocytes together with a few plasma cells and polymorphonuclear leukocytes surrounding arterioles. Many foci of necrosis were evident in the corpus striatum (Fig. 1), especially on the right side. While some of the zones of necrosis contained small blood vessels that had a prominent endothelium with mononuclear infiltrates (Fig. 2), the abnormal blood vessels were frequently unrelated to areas of necrosis. The walls of a few blood vessels had been invaded by lymphocytes and occasional polymorphonuclear cells (Fig. 3). The periodic acid–Schiff method of staining and silver methenamine showed no evidence of fungal infection.

The brain stem was less affected, although the findings were similar to those in the cerebral cortex. No abnormalities were seen in the cerebellum. At all levels the spinal cord showed vascular changes like those seen in the putamen, and there were many collections of microglial cells within the anterior horns (Fig. 4). There were no specific changes in the neurons.

No microorganisms were cultured from tissue specimens.

Discussion

The basic pathological findings in western equine encephalitis are perivascular infiltration and multifocal necrosis, which occur preferentially in the deep grey matter.[4,5] Lesser involvement occurs in the grey matter of the brain stem, spinal cord and cerebral cortex, as well as in the white matter at all levels.[6,7] Variable glial abnormalities are seen in the areas of necrosis. The pathological findings in our patient closely resembled this pattern. The lack of involvement of the cerebral cortex, white matter and vascular endothelium may reflect the relatively benign form the illness took.

Clinically, western equine encephalitis usually presents as nonspecific encephalomyelitis.[1,4,5] Our patient had prominent focal neurologic signs that, although they had largely receded by the time of death, could be accounted for by the pathological findings in the basal ganglia and spinal cord.

When focal neurologic signs occur in patients with encephalomyelitis two specific diagnoses need to be considered: herpes simplex encephalitis, which may respond to treatment with adenine arabinoside,[8] and western equine encephalitis. In this case, the focal signs were consistent with the underlying pathological abnormalities, and herpes simplex virus was absent.

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