A presumptive case of fatal Murray Valley Encephalitis acquired in Alice Springs

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Abstract

A presumptive case of Murray Valley Encephalitis (MVE) acquired in Alice Springs in March 1997 is reported. The patient subsequently died in Mackay. The diagnosis of Murray Valley Encephalitis was supported by the detection of flavivirus IgM in cerebrospinal fluid. Low titres of IgM specific to Murray Valley Encephalitis and Alfuy were detected in a single serum sample. The patient's travel movements indicate that his infection was acquired in the Alice Springs vicinity. This conclusion was further supported by the detection of Murray Valley Encephalitis activity in sentinel animals in the area and by the presence of large numbers of the principal mosquito vector of Murray Valley Encephalitis in the Northern Territory. *Comm Dis Intell* 1998;22:103-104

Introduction

Murray Valley Encephalitis (MVE) is an arboviral disease endemic to northern areas of the Northern Territory and Western Australia. The last Australia-wide epidemic in 1974 resulted in 58 cases.[1] Since then notifications have only occurred in northern Australia with two confirmed cases in Western Australia in early 1997 and a further case in early 1998.

Case Report

A 60 year old male was admitted to the Mackay Base Hospital on 3 April 1997 with severe headache, fever and confusion. He described a two week history of myalgia and arthralgia that had begun while he was in Alice Springs. He had then flown to Mackay with an overnight stop in Cairns. Soon after admission he had a generalised fit and was transferred to the Intensive Care Unit. The initial results included a normal CT brain scan and a marked monocyte response (white blood cells, WBC, 540/mm^3) in his cerebrospinal fluid (CSF). CSF was also submitted for Gram stain, bacterial culture, and antigen studies for *N. meningitidis*, *H. influenzae*, and *S. pneumoniae*, all of which were negative. A presumptive diagnosis of herpes encephalitis was supported by the detection of herpes simplex virus (HSV1) antigen in a lesion on his lip and he was commenced on intravenous Acyclovir. However, polymerase chain reaction (PCR) testing for HSV antigen in CSF was subsequently negative. Serological studies for IgG and IgM to Ross River virus, Barmah Forest virus, MVE, Kunjin, Alfuy, Kokobera, Stratford and Edge Hill were all negative in blood collected on 3 April. An EEG on 7 April detected changes suggestive of a diffuse encephalopathy.

The patient's condition initially improved, but deteriorated on 10 April when he developed a dense right hemiplegia, increased confusion and a productive cough. He was intubated and managed for aspiration pneumonia. A repeat lumbar puncture demonstrated a persistent monocytosis (WBC 30/mm^3). CSF was submitted for Ziehl-Neelsen stain, cryptococcal antigen studies, and complement fixation for measles, HSV and varicella zoster virus; all CSF tests were again negative.

A CT brain scan on 11 April detected a focal low density region in the left internal capsule consistent with a left middle cerebral artery infarct. When the scan was repeated on 16 April this area was considerably larger and was consistent with a massive infarct involving the left middle and anterior cerebral arteries. He continued to deteriorate and died on 25 April. A post-mortem examination was not performed.

Subsequent investigations

Flavivirus IgM was subsequently detected by enzyme immunoassay (EIA) in serum collected on 9 April, and haemagglutination inhibition assays of serum fractions demonstrated low titres of MVE specific and Alfuy specific IgM (1:40 for both). Specific IgM to Kunjin virus was not detected.

Arboviral serology was then performed on the CSF sample from 3 April. Flavivirus IgM was detected, however there was insufficient sample for virus specific assays. Virus isolation was unsuccessful from both the CSF and the serum samples.

The patient was a resident of Alice Springs and had not travelled elsewhere in the Northern Territory for many months prior to his illness. He worked at a site 8 km south of Alice Springs in the vicinity of known mosquito breeding grounds, and fellow workers at this site had recently complained of mosquito problems (O. Harris, personal communication). He also reported receiving numerous mosquito bites while watching a football match in Alice Springs in the days prior to his illness but there were no other complaints about mosquitoes at this match or at any other locations within the town area.

As the incubation period of mosquito-borne arboviral encephalitides, including MVE, is 5-15 days,[2] it is likely

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that his infection was acquired in the vicinity of Alice Springs. MVE is endemic in the 'Top End' of Northern Territory but had not been detected south of Tennant Creek since 1974.[3] A sentinel chicken flock was established on the southern outskirts of Alice Springs in November 1996, and although no evidence of MVE activity was detected when the flock was bled on 17 March, seven of nine chickens had seroconverted to MVE virus when bled on 22 April.[4] Subsequent investigations on sera from sentinel cattle provided further evidence of flavivirus activity in the Alice Springs region during this period. No cattle were positive when tested in January and February, one had positive flavivirus serology by ELISA on 17 March and five had seroconverted to MVE virus by 15 May.

The suspected principal vector of MVE in the Northern Territory is the mosquito *Culex annulirostris*.[3] Following heavy rains across much of the Northern Territory in early 1997, mosquito surveillance detected high numbers of *Cx. annulirostris* in Alice Springs. Numbers began to rise in early February and reached a peak of up to 1,100 per CO_2 baited trap per night by late February. Numbers remained high until mid-March then steadily declined to below 100 per trap by May.

The Territory Health Services issued a MVE virus alert for the entire Northern Territory, including Alice Springs, in early May immediately following the detection of MVE activity in sentinel chickens in Tennant Creek. Positive serum samples from the Alice Springs sentinel flock had not been confirmed at that time.

Discussion

Infection with MVE virus is the most likely explanation of this patient's illness and death, however this diagnosis could not be confirmed and there were a number of atypical features. The detection of specific IgM in CSF is one of the laboratory diagnostic criteria published by the Centers for Disease Control and Prevention, Atlanta, for arboviral encephalitis.[5] In this case flavivirus IgM was detected in CSF but there was insufficient sample for virus specific assays. The only flaviviral antibodies detected in serum were low titres of IgM to MVE and Alfuy in a single sample. Taken in conjunction with the CSF result, this supports the likelihood of MVE infection, as Alfuy is not a recognised cause of human encephalitis. MVE antibodies were not detected in serum taken on the day of admission at which time the patient had been unwell for two weeks. IgM antibodies would often be present in serum by this stage, but their appearance may occasionally be delayed.

The patient presented with an acute encephalitic illness consistent with MVE. However, the extensive cerebral infarct that subsequently developed was unusual and we are not aware of other case reports of cerebral infarcts in adults with MVE.

The patient's movements suggest that the infection was acquired in the Alice Springs vicinity and this is supported by the detection of MVE activity in sentinel chickens and cattle, and the presence of high numbers of the vector *Cx. annulirostris* in the region.

In this instance, the detection of seroconversions in sentinel animals was such that human transmission appears to have occurred before a MVE virus alert could be issued. This emphasises the need for resources to allow more frequent bleeding and testing of sentinel animals so that warnings can be issued as early as possible.

This presumptive case of MVE is the first recognised as acquired in Alice Springs since 1974[3] and it is a reminder that MVE may be present in central Australia following favourable environmental conditions. This patient's subsequent travel also reinforces the importance of interstate coordination of arboviral surveillance.

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