A case of Kunjin virus encephalitis in a traveller returning from the Northern Territory

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Case History

On 6 May 2001, a 67-year-old Australian born, Caucasian male presented to the Emergency Department of the Austin and Repatriation Medical Centre (A&RMC) with a 3 day history of fever, lethargy and confusion. This occurred one week after returning from a trip to the Northern Territory.

His previous medical problems included ischaemic heart disease, a repaired abdominal aortic aneurysm, hypertension, hyperlipidaemia and congestive cardiac failure. He smoked 20 cigarettes per day and had a history of heavy alcohol consumption. He had no history of diabetes.

His medications were aspirin, frusemide, lisinopril, simvastatin, and a nitroglycerol patch. Fifty years ago, he had an adverse reaction to penicillin with angioedema and an urticarial rash.

Four weeks before admission he went on a fishing trip in the Northern Territory. He travelled by road, through outback regions of Victoria, New South Wales, Queensland, the Northern Territory and South Australia, spending time in Daly River, Coolum, Darwin, Dunmarra, Avon Downs, Innaminka and Mataranka. He was away for 3 weeks and camped in tents or outside in a swag throughout the trip. He recalls numerous times where he was exposed to mosquitoes with large numbers of bites at Dunmarra. During the time away, he remained well as did his 5 travelling companions. There was no contact with any farm or non-domesticated animals.

Four days after his return to Melbourne, he developed 'flu-like symptoms. He had fever and rigours plus a mild headache. He became increasingly lethargic and was intermittently confused. He had no other features of meningism, no respiratory symptoms and no rash. Over the following 24 hours, his symptoms progressed and he was brought in to the Emergency Department of the A&RMC.

On arrival, he was febrile at 39^{O}C and his conscious state fluctuated from being fully alert and orientated to being difficult to rouse. Initial laboratory studies revealed a haemoglobin of 145 g/L (range 130-180), a white cell count of 10.8 x 10^9/L (4.0-11.0) with neutrophils making up 8.10 x 10^9/L (2.0-7.5) and lymphocytes 1.51 x 10^9/L (1.0-4.0), and a platelet count of 168 x 10^9/L (150-400). Erythrocyte sedimentation rate was 11 mm/hr (<20). There were occasional reactive lymphocytes seen on the blood film. His sodium was 128 mmol/L (135-145), his creatinine 0.120 mmol/L (0.030-0.110), a random blood glucose was 10.2 mmol/L (3.3-8.0) and the C-reactive protein (CRP) level was 1.5 mg/L (1.6-8.7). The remainder of his biochemical screen was unremarkable as were his arterial blood gases. These results were consistent with an acute infective process of a viral type. The low sodium would fit with inappropriate secretion of anti-diuretic hormone, which is known to occur in infections of the central nervous system. His renal impairment was most likely secondary to volume depletion and the elevated glucose has revealed a new diagnosis of diabetes mellitus.

Computerised tomography of his brain was performed with and without contrast and was normal. His cerebrospinal fluid (CSF) had 196 polymorphs/ l, 36 lymphocytes/ l and 5 erythrocytes/ l. Protein was 0.55 g/L (<0.45) and glucose 6.3 mmol/L (2.2-5.5). Gram stain showed no bacteria. These results fit with an acute infection of the central nervous system, such as an encephalitis or a meningitis. Three sets of blood cultures were taken.

The picture was felt to be consistent with a viral encephalitis although bacterial meningitis including *Listeria*, staphylococcal sepsis or melioidosis were considered possible. Intravenous acyclovir was commenced, as were intravenous co-trimoxazole and vancomycin, because of the penicillin allergy. Serum was sent for arboviral serology and CSF was sent for polymerase chain reaction (PCR) testing for herpes simplex virus (HSV), enteroviruses and Murray Valley encephalitis virus (MVE). Magnetic resonance imaging of his brain with gadolinium contrast and FLAIR sequence showed some age related ischaemic change but no features suggesting HSV encephalitis.

Over the following days, his conscious continued to fluctuate. A multiplex PCR for HSV, cytomegalovirus and Varicella-zoster virus was negative so the acyclovir was ceased. Enteroviral and MVE PCRs were also negative. There was no growth from any cultures of CSF or blood so the vancomycin was discontinued after 5 days. After a week his condition had improved and he stopped having episodes of confusion. He received the co-trimoxazole for a total of 10 days. He was discharged on day 17 and at follow-up has made a complete recovery.

Investigations subsequently revealed the likely diagnosis of Kunjin (KUN) encephalitis. Results of serological testing are presented in Table 1. Clear four-fold rises were seen over several bleeds in flavivirus group-specific antibody and in KUN specific antibody. A smaller rise was seen in Japanese encephalitis (JE) antibody, while MVE antibody was not

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Table 1. Results of immunofluorescence (IF) serological investigations

Test	7 May 2001	11 May 2001	18 May 2001	19 June 2001
Flavivirus Total IF	<10	40	320	320
Flavivirus IgM IF	Negative	Indeterminate	Indeterminate	Negative
KUN Total IF	<10	10	40	40
KUN IgM IF	Negative	Negative	Negative	Negative
MVE Total IF	<10	<10	<10	<10
MVE IgM IF	Negative	Negative	Negative	Negative
JE Total IF	<10	<10	20	20
JE IgM IF	Negative	Negative	Negative	Negative

detected. Serological cross-reactions between flaviviruses are common. These serological results were supported by the referral of sera to the Queensland Health Pathology and Scientific Services, who also obtained results consistent with KUN virus infection using haemagglutination inhibition assay (not shown). Serology for melioidosis, rickettsia, leptospirosis, Q fever, Ross River, Barmah Forest and Dengue fever were also negative.

Comment

KUN is a member of the flavivirus family along with MVE, JE and dengue virus. Its name is taken from one of the Aboriginal clans living near the Mitchell River in north Queensland, from where the virus was first isolated. It can occur throughout much of Australia, being most common in the Northern Territory and northern Western Australia. However, it is more prevalent than MVE in temperate southeastern areas.[1] It has been recently found to be a variant of West Nile virus, which occurs in Africa, Asia and Europe, and which recently caused an outbreak of encephalitis in New York.[2]

Approximately 15 cases of KUN encephalitis have been recorded around Australia.[1] KUN causes a clinically similar illness to MVE but is generally less severe. It can also cause a non-encephalitic illness with fever, malaise and possibly joint involvement. Its natural host appears to be wading birds but other birds and mammalian vertebrates have shown serological evidence of infection. The major vector is the freshwater mosquito *Culex annulirostris* but other mosquitoes can become involved seasonally. There is no specific treatment or vaccine available.

Flavivirus activity in Australia is monitored through mosquito monitoring programs, sentinel chicken surveillance and human disease surveillance. Detection of KUN in humans and sentinel chicken flocks in the southern States of Australia is rare. In the first half of 2001, sentinel chicken flocks seroconverted to KUN virus in northern Victoria, western New South Wales, the central and 'Top End' regions of the Northern Territory and northern Western Australia.

Diagnosis is generally made serologically with paired sera. The time between onset of symptoms and seroconversion is generally between 2 and 5 weeks.[3] Differentiating the various flaviviruses is not always possible but neutralisation or epitope blocking enzyme immunoassay can be used to separate MVE from KUN. It may also be possible to isolate the virus from an acute serum sample.[3] As diagnosis is not always straight forward, clinicians in southern States need to remember the possibility of flaviviruses in cases of encephalitis, particularly in those with an appropriate travel history. This case also serves as a reminder of the importance of mosquito born Diseases that particularly occur during the summer and autumn months and are most likely to be acquired in the northern areas of Australia.

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References

1. Russell RC, Dwyer DE. Arboviruses associated with human disease in Australia. Microbes and Infection 2000;2:1693-1704.
2. Briese T, Jia XY, Huang C, Grady LJ, Lipkin WI. Identification of a Kunjin/West Nile-like flavivirus in brains of patients with New York encephalitis. *Lancet* 1999;354:1261-1262.
3. Phillips DA, Aaskov JG, Atkin C, Wiemers MA. Isolation of Kunjin virus from a patient with a naturally acquired infection. *Med J Aust* 1992;157:190-191.